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2010 年 ASCO 肺癌部分论文摘要解读

7000 A randomized trial comparing endosonography followed by surgical staging versus surgical mediastinal staging alone in non-small cell lung cancer: The ASTER study

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Abstract:

Background: Invasive mediastinal staging in patients with resectable non-small cell lung cancer (NSCLC) can be performed with endosonography (ES) followed by surgical staging (SS; for negative findings) or SS alone. We conducted a prospective randomized multicenter trial to compare both strategies. Primary endpoint was detection of nodal metastasis (N2/3), secondary endpoints were the rate of futile thoracotomy and complications. **Methods:** Consecutive patients with (suspected) resectable NSCLC in whom invasive mediastinal staging was indicated based on computed or positron emission tomography were randomly assigned between ES [combined transoesophageal and endobronchial ultrasound (EUS-FNA and EBUS-TBNA)] followed by SS (in case of negative findings) or SS (mediastinoscopy, mediastinotomy or video-assisted thoracoscopic surgery) alone. Thoracotomy with systematic mediastinal lymph node dissection was performed in the absence of mediastinal metastases after SS in both arms. **Results:** 241 patients were randomized as planned: 123 to ES+SS and

118 to SS alone. Nodal metastases were found in 62 patients (50%) (56 by EUS/EBUS + 6 by subsequent SS) vs. 41 (35%) by SS alone (p = 0.019). The sensitivity for mediastinal metastases for ES+SS was 94% (95% CI, 85- 98) versus 80 % (95 CI, 68-89) for SS alone (p = 0.042). Thoracotomy was futile in 8 patients (7%) staged by ES+SS vs. 21 (18%) in those staged by SS alone (p = 0.009). The rate of complications during staging was similar in both arms (6 vs. 7 patients, p = 0.8), however 12/13 were due to SS. **Conclusions:** Starting mediastinal staging with endosonography in resectable NSCLC 1) improves the detection of nodal metastasis 2) reduces futile thoracotomies 3) and has a similar complication rate, as compared to surgical staging alone.

7000 译文 比较非小细胞肺癌超声内镜分期后加做手术分期和单独手术分期的随机临床试验：ASTER 研究

摘要

背景：对于不可切除的非小细胞肺癌患者，可以由超声内镜分期未发现纵膈转移的患者再行手术分期（ES＋SS），或者直接进行手术分期（SS）。我们建立了一个前瞻性随机多中心临床试验来对比这两个方法。主要研究目的是发现 N2/N3 淋巴结转移，次要研究目的是降低无益的开胸术和由此引起的并发症的比率。**方法**：入组患者为：基于 CT 和 PET 提示为可疑不可切除非小细胞肺癌患者，随机分成 2 组，1.经联合经食道和支气管内镜超声(EUS-FNA and EBUS-TBNA),为阴性发现患者再进行手术分期；2.单独手术分期，包括纵膈镜检查，纵膈切开术和胸腔镜手术。在两组的分期方法都没有发现纵膈转移的情况下，再行开胸手术，并进行系统的淋巴结清除术。**结果**：把 241 例患者随机分组：123 例入 ES＋SS 组，118 例入 SS 组。在 ES＋SS 组中，62 例患者（50%）最终发现淋巴结转移，其中 56 例通过 EUS/EBUS 发现，6 例 EUS/EBUS 未发现，后经 SS 发现；在 SS 组中，41 例患者（35%）发现有淋巴结转移（p=0.019）。ES+SS 组纵膈转移的敏感性为 94%（95%CI，85-98），而 SS 组的敏感性为 80%（95CI，68-89）。开胸手术在 ES+SS 组的仅 8 例患者（7%）是无益的，而在 SS 组的 21 例患者（18%）中是无益的（p=0.009）。在分期过程中发生并发症的比率在这两组中类似（6 例患者比 7 例患者，p=0.8），并且，13 例中有 12 例是因为 SS 引起的。**结论**：在不可切除的非小细胞肺癌中应用超声内镜成像首先进行纵膈分期的益处有三：1）提高了淋巴结转移的检测率；2）

降低了不必要的开胸手术；3）SS 还会出现手术相关的并发症。

7004 A phase III, intergroup, randomized, double-blind, chemoprevention trial of selenium (Se) supplementation in resected stage I non-small cell lung cancer (NSCLC)

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Abstract:

Background: Selenium was reported to have possible lung cancer chemopreventive benefits based on a large skin cancer trial secondary observation. (JAMA 1996; 276: 1957-1963). Since that time, research continued to suggest that Se could decrease risk of second primary tumor (SPT) in persons with resected NSCLC. In 2007, a publication from another group suggested an increased association of Se with type 2 diabetes (Annals Int Med 147:217-223).

Methods: From Oct 2000-Nov 2009, 6 groups, led by ECOG, carried out a double blind, placebo controlled trial using selenized yeast 200 micrograms daily in a 2:1 randomization vs. placebo for 48 mo in completely resected stage I NSCLC. Participation was 6-36 mo post-op and required a negative mediastinal node biopsy, no excessive vitamin intake, normal liver function, a negative chest x-ray, and no other evidence of recurrence. Planned size of 1,960 participants had been designed to detect a 40% decrease in SPTs with 80% power.

Methylation studies of sputum and blood (S. Belinsky) add important biologic correlates to this project. **Results:** Interim analysis occurred in Oct 2009 after 1,561/1,772 pts reached step 2 (completion of the 4 week (step 1) run-in period requiring at least 75% of the study drug to be taken). Endpoints included SPTs, recurrence, and toxicity. A total of 216 SPTs developed of which 84 (38.9%) were lung cancer. SPT (lung/overall) incidence was 1.36/3.66 per 100 person yrs for placebo vs. 1.91/4.11 for Se (p=.150). 5 yr progression free survival was 78% for placebo vs. 72% for Se. Study was stopped according to futility analysis. Grade 1 or 2 toxicity occurred in 38% of placebo and 39% Se. Grade 3 toxicity was 3% placebo vs. <1% Se. Compliance was excellent (>95% at 2 yrs). **Conclusions:** No increase in diabetes mellitus or skin cancer was detected. Se was safe but conferred no benefit over placebo. Methylation studies are continuing.

7004 译文 已经切除的 I 期非小细胞肺癌的 III 期，intergroup，随机，双盲，硒（Se）补充化学预防临床试验

摘要

背景：基于对大规模皮肤癌的后续观察，硒可能对肺癌的化学预防有益。（JAMA 1996; 276: 1957-1963）从那时起，不断的有研究提示硒可能降低已切除非小细胞肺癌的第二原发肿瘤的风险。在 2007 年，另一团队的出版物提示硒可能与 2 型糖尿病的增加有关。（Annals Int Med 147:217-223）**方法**：从 2000 年 10 月到 2009 年 11 月，6 个团队，在 ECOG 领导下，进行了一个双盲、安慰剂对照的临床试验，入组患者为完全切除的 I 期非小细胞肺癌，随访时间为 48 月，采取硒强化组：安慰剂组 2:1 随机取样，试验组使用硒强化的酵母 200mg 每日对照安慰剂。入组条件还应满足：术后 6 个月到 36 个月内，纵膈淋巴结活检阴性，没有过度的维生素摄入，肝功能正常，胸部 X 光片阴性，且没有复发的证据。计划的 1960 位参与者已经被设计为在 80%的权重下发现在继发的原发肿瘤中有 40%的下降。S. Belinsky 关于痰和血的甲基化研究发现与该试验设计有高度的生物相关性。**结果**：2009 年 10 月的中期结果分析显示，1561/1772 例患者达到第 2 阶段（要求第 1 阶段完成在 4 周以上，并且需要至少摄入 75%以上的研究用药）。研究目的为观察第二原发肿瘤，肿瘤复发和毒性作用。共有 216 例发生了第二原发肿瘤，其中 84 例（38.9%）为肺癌。安慰剂组第二原发肿瘤（肺/全身）发生率为 1.36/3.66 每 100 人年，

而硒强化组为 1.91/4.11（p=0.150）。安慰剂组的 5 年无进展生存率为 78%，而硒强化组为 72%。该试验在中期结果分析后，因试验药物无意义而终止。依从性非常好(>95% at 2 yrs)。**结论：**没有发现增加糖尿病和皮肤癌，硒是安全的，但是与对照组相比没有益处。甲基化研究正在继续。

7007 A randomized, open-label, phase III trial of NOV-002 in combination with paclitaxel (P) and carboplatin (C) versus paclitaxel and carboplatin alone for the treatment of advanced non-small cell lung cancer (NSCLC)

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Abstract:

Background: NOV-002 is a formulation of disodium glutathione disulfide (GSSG). GSSG is a naturally occurring substance that functions as a component of the glutathione (GSH) pathway, vital to the regulation of the intracellular redox state. A key function of the GSH/GSSG redox couple is to dynamically regulate protein functions, including cell signaling pathways, through the reversible formation of mixed disulfides between protein cysteines and GSH (S-glutathionylation). Based on positive results from a randomized, phase I/II study of carboplatin and paclitaxel (CP) with or without NOV-002, as well as positive results from 2 ex-U.S. phase II studies with cisplatin-based chemotherapy, an international

phase III randomized trial was launched. **Methods:** Patients with advanced NSCLC (stages wet IIIB and IV, inclusive of all histological subtypes) were eligible if they had a PS of 0-1 and adequate end-organ function. Patients with CNS metastases were excluded. Eligible patients were randomized to C (AUC 6), P (200 mg/m2), and NOV-002 (Group A) or C and P alone (Group B). NOV-002 was administered as two-60 mg IV boluses on day -1 of cycle 1 and as one IV bolus on day 1 of each cycle, followed by daily 60-mg subcutaneous injections. A total of 725 events were required to detect a difference in overall survival (OS) from 10.0 to 12.5 months with 85% power and a two-sided significance level of 0.05. No interim analysis was performed. **Results:** From 11/06 until 9/09, 903 patients were randomized, with target enrollment reached in March 2008. Patient characteristics for Groups A and B were as follows: stage IV (91.5/90.8%), PS 1 (76.6/72.6%), male (69.9/72.4%), never smoker (22.3/19.1%) median age (59.6/59.5), and histology (adenocarcinoma [40.0/36.8%] squamous [41.2/40.8%]). The median overall survival for Groups A and B was 10.2/10.8 months (p = 0.375), median progression-free survival was 5.3/5.6 months, objective response rate was 26.6/26.0% and 54/53% of patients completed at least six cycles of chemotherapy. Major toxicities for Groups A and B included grade 3/4 neutropenia (29.7/26.3%), febrile neutropenia (2.2/1.8%), grade 3/4 thrombocytopenia (3.8/2.9%), and grade 3/4 neuropathy (2.9/2.4%). Adverse events resulting in death in Groups A and B were reported in 5.6 and 3.1%, respectively. **Conclusions:** The addition of NOV-002 to CP does not improve overall survival in patients with advanced NSCLC. NOV002 does not appear to add to the overall toxicity of chemotherapy.

7007 译文 NOV-002 联合紫杉醇（P）/卡铂（C）vs 紫杉醇和卡铂治疗 NSCLC 的随机、开放的 III 期临床试验

摘要

背景：NOV-002 是头孢替坦谷胱甘肽二硫化物（GSSG）的一个部分。GSSG 是一个天然物质，是谷胱甘肽途径（GSH）中的一个环节。谷胱甘肽途径对于调节细胞内的氧化还原状态十分重要。通过在半胱氨酸和 GSH 之间可逆性的形成混合性二硫化物，GSH/GSSG 氧化还原偶联可以动态的调节蛋白功能，包括调节细胞信号通路。关于卡铂

和紫杉醇联用或不联用 NOV-002 的 I/II 期试验已取得了阳性结果，而两个美国以外的顺铂为基础的化疗联用或不联用 NOV-002 II 期试验也取得了阳性结果，基于以上结果一个国际性的III期随机临床试验也已经开始。**方法：**入组标准为 PS 0-1 分，足够好的终末脏器功能，进展期的 NSCLC 的病人（III期或Ⅳ期，包括所有组织类型。有中枢神经系统转移的病人被排除。随机分配到 A 组和 B 组，其中 A 组为卡铂（AUC 6），紫杉醇（200 mg/m2）和 NOV-002，B 组为单独使用卡铂和紫杉醇。在第 1 周期的第 1 天给予 NOV-002 60mg 静脉推注，2 次。以后每个周期的第 1 天给予 1 次静脉推注，之后每天给予 60mg 皮下注射。在 85%的权重及双边有效等级为 0.05 时，为了得出在 10-12.5 个月的总生存率上的区别，需要 725 个事件。没有进行间断分析。**结果：**从 2006 年 11 月至 2009 年 9 月，903 例病人被随机分组，2008 年 3 月达到入组目标。A 组和 B 组病人特征如下：IV 期（91.5/90.8%），PS1（76.6/72.6%），男性（69.9/72.4%）,从未吸烟者（22.3/19.1%），中位年龄（59.6/59.5）及组织学（腺癌【40.0/36.8%】,鳞癌【41.2/40.8%】）.A 组和 B 组的总体中位生存率分别为 10.2/10.8 月（p=0.375）,中位无进展生存期分别为 5.3/5.6 月,客观有效率分别为 26.6/26.0%，完成 6 个周期化疗的病例数分别为 54/53%。A 组和 B 组的主要毒性包括：3/4 度中性粒细胞减少（29.7/26.3%）,中性粒细胞减少性发热（2.2/1.8%），3/4 度血小板减少（3.8/2.9%）和 3/4 度神经毒性（2.9/2.4%）。A 组及 B 组报道的不良事件导致的死亡分别为 5.6%及 3.1%。**结论：**晚期 NSCLC 病人在卡铂和紫杉醇中加入 NOV-002 并不能提高整体生存率。NOV002 似乎不会增加化疗的总体毒性。

7008 Impact of KRAS mutations on adjuvant carboplatin/paclitaxel in surgically resected stage IB NSCLC: CALGB 9633

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Abstract:

Background: CALGB 9633 randomized surgically resected stage IB NSCLC patients to carboplatin/paclitaxel (CP) or observation (OBS). A retrospective assessment suggested a survival benefit in patietns with tumors > 4.0 cm in size (G. Strauss JCO 2008). KRAS mutations were associated with lack of benefit from adjuvant chemotherapy in the JBR.10 trial. The impact of KRAS mutations on outcome in CALGB 9633 was evaluated. **Methods:** Pretreatment tumor specimens from CALGB 9633 were evaluated for presence of KRAS (codons 12, 13, 61) mutations using mass spectrometry. Outcomes based on presence/absence of KRAS mutations were evaluated. **Results:** Tumor specimens were available for KRAS genotyping from 267/344 (78%) patients (CP: 139; OBS: 128). KRAS mutations were detected in 71 (27%) of all KRAS evaluable patients: CP: 35 pts (25%); OBS 36 pts (28%). KRAS mutations were more common in adenocarcinomas vs. non-adeno (41% vs. 11%; $p < 0.0001$) and in $\geqslant$ 4.0 cm vs. < 4 cm (32% vs. 18%; $p = 0.0144$). 5 yr OS (90% CI) for all pts receiving CP: KRAS WT: 62% (53-69) Mut: 55% (35-63); HR 1.2 ($p = 0.581$). 5 yr OS for pts with $\geqslant$ 4.0 cm tumors receiving chemo. KRAS WT: 73% (62-82); Mut: 38% (23-54); HR = 2.3 ($p = 0.011$). 5 yr OS (90% CI) for all pts on OBS: KRAS WT: 59% (50-67) Mut: 67% (52-78); HR 1.1 ($p = 0.747$). 5 yr OS for pts with $\geqslant$ 4.0 cm tumors on OBS. KRAS WT: 66% (54-76); Mut: 61% (42-75); HR = 1.4 ($p = 0.366$). Interaction for KRAS mutations and tumor size ($\geqslant$ 4.0 cm vs. < 4 cm) is significant ($p=0.0036$) in a multivariate analysis including all patients and adjusting for treatment, KRAS, tumor size and their interactions. Adjuvant CP in KRAS WT pts with > 4.0 cm tumors was suggestively associated with a benefit (HR = 0.69; $p = 0.18$) while in KRAS mut pts there was no benefit (HR = 1.2; $p = 0.5457$) However a three-way interaction between KRAS mutation, treatment and tumor size was not significant. **Conclusions:** KRAS mutations may identify a subset of stage IB NSCLC

pts, especially those with ≥ 4.0 cm tumors, that have a worse prognosis and derive less benefit from adjuvant CP.

7008 译文 KRAS 突变对于手术切除的 IB 期 NSCLC 患者行铂+紫杉醇方案化疗敏感性的影响：CALGB 9633

摘要

背景：CALGB 9633 研究将手术切除的 IB 期 NSCLC 患者随机分配为卡铂/紫杉醇（CP）组和观察组（OBS）。在既往的回顾性研究中发现肿瘤直径>4cm 的患者可从辅助化疗中获益（G. Strauss JCO 2008）。在 JBR.10 试验中又发现 KRAS 突变和辅助化疗疗效相关。本文主要研究 KRAS 突变对于 CALGB 9633 试验的结果的影响。**方法**：用质谱法测定肿瘤标本中 KRAS（12,13,61 密码子）突变的情况。根据 KRAS 突变存在与否来分析本实验的结果。**结果**：267/344（78%）例患者的肿瘤标本可以测定 KRAS 的基因型（CP 组 139 例，OBS 组 128 例）。所有测定 KRAS 的患者中有 71 例（27%）患者存在 KRAS 突变：CP 组 35 例（25%），OBS 组 36 例（28%）。腺癌中 KRAS 突变较非腺癌常见(41% vs 11%，P<0.0001)；直径≥4cm 的肿瘤中 KRAS 突变多于直径<4cm 的肿瘤（32% vs 18%，P=0.0144）。接受 CP 方案化疗的患者中 5 年 OS（95%可信区间）分别为：KRAS 野生型 62%（53-69），突变型 55%（35-63）；HR1.2（P=0.581）。肿瘤直径≥4cm 的患者化疗后 5 年 OS 情况为：KRAS 野生型 73%（62-82），突变型 38%（23-54）；HR 2.3（P=0.011）。OBS 组患者的 5 年 OS 分别为：KRAS 野生型 59%（50-67），突变型 67%（52-78）；HR1.1（P=0.747）。在 OBS 组中肿瘤直径≥4cm 的患者 5 年 OS 分别为：KRAS 野生型 66%（54-76），突变型 61%（42-75）；HR 1.4（P=0.366）。在所有患中进行对应的治疗、KRAS 情况、肿瘤大小和生存的关系的多因素分析提示，KRAS 突变和肿瘤大小（≥4cm vs <4cm）之间的相互影响很明显（P=0.0036）。KRAS 野生型、直径>4cm 的患者接受 CP 方案的辅助化疗更能获益（HR=0.69，P=0.18），而 KRAS 突变的患者不能获益（HR=1.2，P=0.5457）。但 KRAS 突变、治疗方法及肿瘤大小三者之间的相互作用并不明显。**结论**：可以将 KRAS 突变者，尤其是肿瘤直径≥4cm 的 IB 期 NSCLC 患者看作其中的一个亚型，该亚型预后较差，对于辅助的 CP 化疗获益少。

7009 Initial results of LC-MAP: An institutional program to routinely profile tumor specimens for the presence of mutations in targetable pathways in all patients with lung adenocarcinoma

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Abstract:

Background: Mutated oncogenes underlie the behavior of lung adenocarcinomas and can serve as targets for therapy. Determining the presence of these molecular abnormalities can direct the care of individual patients, qualify them for clinical trials, and aid research. To acquire this information on as many patients as feasible, in JAN 2009 our multidisciplinary Disease Management Team began a program (the Lung Cancer Mutation Analysis Project - LC-MAP), to prospectively detect all recurrent mutations in EGFR, KRAS, BRAF, HER2, PIK3CA, MEK1 and AKT1 and the EML4-ALK fusion gene in all patients diagnosed with lung adenocarcinoma with sufficient tissue. **Methods:** Patients sign an institutional consent to permit the use of previously obtained ("leftover") tissue for mutation profiling after standard morphologic and molecular diagnostic studies are complete. After PCR-based testing for EGFR exon 19 deletions and L858R, KRAS mutations are determined by direct sequencing, then remaining DNA is studied in a multiplexed mass-spectrometry-based system (Sequenom) to study 40 additional mutations in 7 genes. The EML4-ALK translocation is assayed by ALK FISH. **Results:** In the first six months, 301 patients entered the program. We completed all proposed testing in 92%. Mutations detected include 72 KRAS, 63 EGFR, 22 EML4-ALK, 1 BRAF, 4 PIK3CA, 0 HER2, 0 AKT1, and 0 MEK1. Based on this information, 27 patients

with EGFR mutations received an EGFR tyrosine kinase inhibitor. No patient with wild type EGFR or a KRAS mutation received an EGFR TKI. 24 patients were entered on clinical trials testing agents targeting the specific molecular abnormality detected. **Conclusions:** (1) The presence of relevant mutations can be routinely determined in patients with adenocarcinoma of the lung. (2) The mutational data obtained can be used to select erlotinib or gefitinib for individuals with EGFR mutations and to identify patients appropriate for clinical trials of targeted therapies. (3) This effort supports making upfront genotyping of lung adenocarcinomas part of routine care. Support: P01 CA129243, Chandler Fund.

7009 译文 一项对所有肺腺癌患者的肿瘤标本中存在的所有靶向途径中的突变进行常规描述的多中心研究项目——LC-MAP 的初步结果

摘要

背景：肺肿瘤组织的基因突变与肺腺癌的肿瘤特性相关，也可以成为肿瘤靶向治疗的目标。发现这些分子学异常有助于肿瘤患者个体化治疗、筛选出适合的患者进入临床试验，并进行有目的的研究。为了在尽可能多的患者中获得这些突变的信息，2009 年 1 月我们的多学科疾病治疗小组启动了一个项目（肺癌突变分析计划：LC-MAP），对所有确诊肺腺癌并有标本量足够，就检测肿瘤组织经常出现突变的基因，包括 EGFR、KRAS、BRAF、HER2、PIK3CA、MEK1 及 AKT1 和 EML4-ALK 融合基因。**方法**：所有患者均签署了知情同意书，允许以前取得的组织学标本在用于标准的形态学及分子诊断学研究之后，剩余部分的病理标本可以用于基因突变的检测。先用 PCR 法测定 EGFR 的 19 外显子缺失和 L858R，用直接基因测序检测 KRAS 突变，然后剩余的 DNA 用以质谱法为基础的多线路系统（Sequenom）在 7 个基因中检测另外 40 种突变。通过 ALKFISH 技术来检测 EML4-ALK 易位。**结果**：前 6 个月有 301 名患者入选该项目。92%的患者完成了预定的检测。检测到的突变包括 72 例 KRAS、63 例 EGFR、22 例 EML4-ALK、1 例 BRAF、4 例 PIK3CA、0 例 HER2、0 例 MEK1 及 0 例 AKT1。据此结果，27 例存在 EGFR 突变的患者接受了 EGFR-TKI 的治疗。所有 EGFR 野生型或有 KRAS 突变的患者都没有接受 EGFR-TKI 治疗。24 例患者参加了临床试验以接受针对特殊分子靶向治疗药物。**结论**：1）肺腺癌患者中可以常规检测到相关的基因突变。2）获得的突变数据有助于存在 EGFR 突变的患者选择厄罗替尼或吉非替尼治疗，也可作为患者适合加入靶向治疗临床试验的

证据。3）本项目的结果使得基因型的测定成为肺腺癌患者常规检测的项目之一。

7010 Association of genetic variations in DNA-methyltransferases, histone-methyltransferases, and methylated DNA-binding proteins with recurrence and survival in early-stage non-small cell lung cancer treated with surgery alone or surgery and chemotherapy

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Abstract:

Background: Genetic polymorphic variants (SNPs) of DNA- and histone-modifying genes, in particular O6- methylguanine DNA-methyltransferase (MGMT), have been implicated in increased risk for development of lung cancer. **Methods:** 165 SNPs in these genes were genotyped in 461 stage 1 and 2 non-small cell lung cancer (NSCLC) patients treated with surgery (N=337) or surgery and chemotherapy (n=124) and analyzed for association with recurrence and survival. Median survival times and recurrence rates were 89.1 months and 27.5 % (93/337) for surgery and >133.6 months and 29% (36/124) for surgery and chemotherapy, respectively. **Results:** We identified three classes of SNPs that were differentially prognostic or predictive of recurrence and survival in early stage NSCLC. Class 1 contained two SNPs (in MGMT) which were prognostic biomarkers for clinical outcome independent of treatment modality. Six SNPs in class 2 (MBD2, SUV39H2, MBD4, EZH1(2x), EZH2) correlated with treatment outcome for surgery alone, but not with surgery and chemotherapy, hence their effect could be reversed by chemotherapy. The last class 3

contained SNPs, which were associated with surgery and chemotherapy, but not surgery alone. For example, we observed hazard ratios for rs4751104 for recurrence of surgery and chemotherapy of 4.94 (95% CI, 1.92-12.71) and 0.89 (95% CI, 0.47- 1.67) for surgery alone. The association of most SNPs remained significant after adjusting for multiple comparisons using a q-value at 10%. By using a combination of SNPs in class 2 or 3, we were able to build genetic predictors for outcome of surgery or surgery and chemotherapy, with p < 10-6 and < 10-4, respectively. **Conclusions:** These results suggest that specific genetic variations in the genes mentioned above modulate clinical outcomes in patients who undergo surgery or surgery and chemotherapy for early stage NSCLC. These results may be used to build predictive models for identifying surgical patients at increased risk of adverse outcome, who may benefit from addition of chemotherapy independent of clinical stage.

7010 译文 在接受手术和手术加化疗两种不同方法治疗的早期非小细胞肺癌患者中，DNA 甲基转移酶，组蛋白甲基转移酶及甲基化的 DNA 连接蛋白的基因变异（SNPs）情况与肺癌复发和生存的相关性

摘要

背景：在 DNA 和组蛋白的修饰基因的多态性变异中，认为特别是 O6－甲基鸟嘌呤－DNA—甲基转移酶（MGMT）增加了肺癌发生的风险。**方法：**在 461 例Ⅰ期及Ⅱ期的非小细胞肺癌患者中ＤＮＡ甲基转移酶，组蛋白甲基转移酶及甲基化的ＤＮＡ连接蛋白的基因变异（SNPs）情况的检测，检测到了 165 个 SNPs。这些患者中有 337 例接受过手术，124 例接受过手术和化疗。并且进一步分析检测结果与复发和生存期之间的关系。手术治疗组中位生存时间为 89.1 个月，复发率为 27.5%（93/337），手术和化疗组中位生存时间＞133.6 个月，复发率为 29%（36/124）。**结果：**确定了早期非小细胞肺癌中有 3 类 SNPs 可以用于区分不同预后或预测复发和生存。第 1 类包括 2 个 SNPs（在 MGMT）是决定预后的生物学标志，与治疗无关。第 2 类包括 6 个 SNPs（MBD2, SUV39H2, MBD4, EZH1(2x), EZH2)与手术治疗的预后有关，但与手术加化疗的预后无关，因此可能化疗可以逆转它们产生的效应。第 3 类的 SNPs 与手术加化疗的预后有关，但与手术治疗的预后无关。例如，我们观察到的 rs4751104 对于手术加化疗及单纯手术后复发的危险比分别为 4.94 (95% CI, 1.92-12.71)和 0.89 (95% CI, 0.47- 1.67)。在调整 q 值为 10%的多重

比较后，大多数 SNPs 的联系继续保持。通过联合使用第 2 类和第 3 类的 SNPs，我们构建出了手术及手术加化疗的预后的基因预测者，P 值分别为＜10－6 和＜10－4。**结论：**这些结果意味着在早期 NSCLC 并接受过手术或手术加化疗的病人中，上述提到的特定的基因变异影响着临床结局。这些结果可用于构建一些手术患者的预测模型，确定它们是否存在不良的预后的因素。这些患者可能可以从不依赖于临床分期的化疗中获益。

7011 Impact of EGFR and KRAS mutations on survival in 1,000 patients with resected lung adenocarcinoma

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Abstract:

Background: Previous studies have reported trends toward improved overall survival in patients with resected adenocarcinoma of the lung and EGFR mutation compared to patients without detectable mutation (Marks, et al, 2008). Some studies demonstrated no difference in survival, but did not classify patients by KRAS mutation status. Reports on the prognostic significance of KRAS mutations have been inconsistent. In this study, we evaluated the prognostic significance of EGFR and KRAS mutations in 1,000 patients. **Methods:** Clinical information was prospectively collected on patients with completely-resected stage I-III lung adenocarcinoma at Memorial Sloan-Kettering Cancer Center who had surgery between Jan 2002-Oct 2009. EGFR mutation (exon 19 deletion or L858R) was determined by PCR, KRAS mutation was determined by sequencing. Overall survival from the date of surgery was

analyzed using Kaplan-Meier and Cox regression analyses. Patients who received an EGFR tyrosine kinase inhibitor (TKI) during their treatment were excluded (n=131). **Results:** 1,000 patients (618 women) with stage I (732), stage II (121), and stage III (147) were evaluated. Median follow-up was 16 months. After adjustment for stage, there was a trend towards better survival in EGFR mutation-positive patients (n=145) compared to wildtype (n=588), HR 0.76 95% CI 0.45 to 1.30, p=0.3. There was a trend towards worse survival in patients with KRAS mutation (n=267) compared to wildtype, HR 1.20 95% CI 0.83 to 1.70, p=0.4. Three year survival proportions for each group were: EGFR mutation 80% (95% CI 0.67 to 0.89), KRAS mutation 73% (95% CI 0.63 to 0.81), wildtype 73% (95% CI 0.69 to 0.78). **Conclusions:** This is the largest cohort of patients with resected lung adenocarcinoma reported for these mutations (n=1,000). Despite excluding patients who received perioperative EGFR TKI, the trend for patients with EGFR mutation is towards better survival compared to wildtype. A trend for survival decrement in patients with KRAS mutations was less apparent. Longer follow-up is required to determine whether these trends are statistically significant. Future analyses will include assessments of the impact of perioperative EGFR TKI and EGFR TKI at recurrence.

7011 译文 EGFR 和 KRAS 突变对 1000 名手术后肺腺癌患者生存率的影响

摘要

背景：以前的研究提示，对于手术切除后肺腺癌患者，EGFR 突变者相对于无突变者提示相对较好的总体存活率（Marks 等，2008）。有些研究提示在生存率上没有区别，但是这些患者没有按照 KRAS 突变状态进行分类。对于 KRAS 突变对于预后的预测作用目前报道并不一致。本研究在 1000 例患者进行 EGFR 突变和 KRAS 突变检测，分析突变情况对预后的影响。**方法**：Memorial Sloan-Kettering cancer center 前瞻性收集了 2002 年 1 月至 2009 年 10 月期间接受手术并完全切除的 I-III 期肺腺癌患者的临床资料。EGFR 突变（外显子 19 缺失或 L858R）通过 PCR 监测，KRAS 突变通过基因测序检测。用 Kaplan-Meier 和 Cox 回归分析分析了手术日起的总体生存率数据。所有接受过 EGFR TKI 治疗的患者都被排除在外（n=131）。**结果**：1000 例患者入选试验（女性 618 例），分期包括 I 期（732 例）、II 期（121 例）及 III 期（147 例）。中位随访时间为 16 月。在修正

分期后，EGFR 突变阳性的患者（n=145）比野生型（n=588）的生存情况好。HR 0.76，95%CI 0.45-1.30，p=0.3。KRAS 突变的患者（n=267）比野生型生存率差，HR 1.20 95%CI 0.83 到 1.70，p=0.4。各组的 3 年生存比例分别为：EGFR 突变组 80%（95%CI 0.67 到 0.89），KRAS 突变组 73%（95%CI 0.63 到 0.81），野生型组 73%（95%CI 0.69 到 0.78）。**结论**：这是在肺腺癌中针对两个突变的最大宗队列研究（n=1000）。除了那些在围手术期接受过 EGFR TKI 治疗的患者外，EGFR 突变的患者相对于野生型生存情况更好。KRAS 突变患者生存率下降，但该差别相对不明显。尚需更长期的随访以确定这些差别是否具有统计学意义。进一步的分析将会包括围手术期的 EGFR TKI 的作用分析及 EGFR TKI 对于肿瘤复发的作用。

7012 Clinical relevance of insulin regulatory pathways in non-small cell lung cancer (NSCLC) progression

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Abstract:

Background: Insulin and insulin-like growth factors are key regulators of normal metabolism and growth. Independently, and via interactions with the epidermal growth factor receptor (EGFR), the insulin receptor (IR) and insulin-like growth factor 1 receptor (IGF-1R) are implicated in the development and progression of NSCLC. Though novel agents targeting the IR/IGF-1R pathway are under investigation, no molecular markers exist to guide therapy. **Methods:** After confirming IR and IGF-1R pathway activation, RNA from control, insulin

and IGF treated cells was submitted for gene expression profiling. Using binary regression, an in vitro gene signature for IR and IGF-1R pathway activation was generated and validated in two independent early stage (I-IIIA) NSCLC data sets (cohort 1, n= 442, cohort 2, n=170) and in 63 NSCLC cell lines. Matrigel invasion, EGFR tyrosine-kinase inhibition (TKI) resistance, and miRNA expression were assayed and correlated to predicted pathway activation. **Results:** Hierarchical clustering of predicted IR/IGF-1R pathway activation ranging from high to low revealed four prognostic clusters. NSCLC tumors with concomitant high activation of IR and IGF-1R pathway had a significantly worse survival compared to those with low-intermediate activation (cohort 1, p=0.008; cohort 2, p=0.02). Invasiveness was increased in NSCLC cell lines predicted to have high pathway activation (p=0.003), as were miRNAs associated with invasiveness and metastasis (miR-155, miR-373). Conversely, miRNAs associated with tumor suppression (let-7 family) were enriched in the low- intermediate cluster. Moreover, cell lines resistant to EGFR-TKIs were more likely to have high IR/IGF-1R pathway activation (p=0.04). Work is ongoing to evaluate the differential susceptibility to EGFR-TKIs, and identify IR/IGF-1R related miRNA targets mediating EGFR-TKI resistance. **Conclusions:** A transcriptomic-based strategy delineates patterns of the IR/IGF-1R pathways that are prognostic in NSCLC, and identifies cohorts of patients who may be candidates for adjuvant therapy with IGF-1R inhibitors. Such a directed approach could improve therapeutic efficacy and subvert EGFR resistance mechanisms in NSCLC.

7012 译文 胰岛素调节途径在非小细胞肺癌进展中的临床作用

摘要

背景：胰岛素和类胰岛素生长因子是正常细胞代谢和生长的关键调节因子。胰岛素受体（IR）和类胰岛素生长因子 1 受体（IGF-1R）单独或与 EGFR 相互作用影响 NSCLC 的发生和进展。虽然目前已经有新的针对 IR/IGF-1R 途径的靶向药物在研究当中，但尚未发现有指导治疗的分子标记物。**方法：**在确认存在 IR 和 IGF-1R 途径激活以后，将对照组及胰岛素和 IGF 处理后的细胞进行 RNA 基因表达谱的测定。使用双复性的方法，一个体外的 IR 和 IGF-IR 通路活化的基因标记就产生了，被两个独立的 NSCLC 早期（I-IIIA）数据库所确认（队列 1，N=442，队列 2，N=170）,并出现在 63 个 NSCLC 细

胞系中。基质侵入，EGFR 酪氨酸激酶抑制剂抵抗及 miRNA 表达被定量分析，并与预测旁路活化相关。**结果：**对预测的 IR/IGF-1R 活化路径的从高到低分层显示四个预后群。伴有 IR 和 IGF-1R 高度活化的 NSCLC 肿瘤与其他低中活化的相比生存期显著缩短。(cohort 1, p=0.008; cohort 2, p=0.02)。在 NSCLC 细胞系中侵袭性的增加就预示着高的 IR 和 IGF-1R 的活化路径（p=0.003），同样高的 miRNA(miR-155, miR-373)与高侵袭和转移有关。相反，与肿瘤抑制相关的 miRNAs（let-7 家族）的表达集中在低中 IR 和 IGF-1R 的活化通路中。并且，在 EGFR-TKIs 抵抗的细胞系中，更容易发现有高的 IR/IGF-1R 通路活化（p=0.04）。目前正在进一步评估 IR/IGF-1R 通路活化水平对于 EGFR-TKIs 的敏感性的影响，并确立与 IR/IGF-1R 通路活化水平相关的 miRNA，这种 miRNA 可以介导 EGFR-TKIs 抵抗。**结论：**以转录组学为基础的策略来描述 IR/IGF-1R 通路活性，这一活性能预测 NSCLC 的预后。还可以用于确立应用 IGF-1R 抑制剂作为辅助治疗的受益人群。这种有针对性的方法可以提高 NSCLC 的治疗效果，和避开 EGFR 抵抗机制。

7013 KRAS and EGFR mutations in the molecular epidemiology of NSCLC: Interim analysis of S0424

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Abstract:

Background: The Intergroup molecular epidemiology study S0424 was designed to investigate relationships between tumor biology with tobacco carcinogen exposure and gender

in a cohort of early stage NSCLC patients enriched for never-smokers. Each patient completed a questionnaire on smoking history and submitted tumor and blood specimens. Here we report associations between KRAS and EGFR mutational status with histology, gender, and smoking status. **Methods:** KRAS mutations were assessed in 549 path-confirmed tumor tissue using a cold-PCR single-strand conformational polymorphism (SSCP) approach established to distinguish at least 10 different base substitutions in codons 12 and 13. DNA sequencing was used for confirmation. Preliminary EGFR mutation analysis was conducted on 195 patients using similar methodology. Researchers are blinded to patient-level data. **Results:** KRAS mutations were identified in 106/549 specimens (19.3%), and were more frequent in smokers (101/495, 20%) compared to never-smokers (5/54, 9%)(p=0.047). Among female smokers, 22% (60 of 274) had KRAS mutations, nonsignificantly higher than the 16.7% rate observed in male smokers (46/275, p=0.13). KRAS mutations were more frequent in adenocarcinomas compared to other histologies (p<0.0001). Logistic regression showed that histology and smoking status, but not gender, were independent variables for KRAS mutations. 47% of KRAS mutations were codon 12 GGT→TGT (Gly→Cys), and 72% were tobacco carcinogenesis-associated G→T transversions. G→T transversions were more frequent in smokers compared to never-smokers (p=0.03). EGFR mutations were observed in 12.8% (25/195; E19del: 9; L858R: 16) and were significantly more common in never-smokers (45%) than in smokers (9%)(p<0.0001) and in patients with adenocarcinoma (p=0.04). EGFR and KRAS mutations were exclusive with the exception of 1 patient. **Conclusions:** S0424 is the largest prospectively designed study of gender and smoking in NSCLC to date. Smoking history and adenocarcinoma histology, but not gender, were independent variables for KRAS and EGFR mutations. Additional studies exploring tobacco-associated DNA adducts and estrogen receptor expression are ongoing.

7013 译文 NSCLC 分子流行病学中的 KRAS 和 EGFR 突变：S0424 的 interim 分析

摘要

背景：S0424 是一组病例的分子流行病学研究，在早期 NSCLC 患者中进行的用以观察肿瘤生物学特性和烟草致癌物及性别之间关系的队列研究。每位患者进行关于吸烟史的

问卷调查，并留取肿瘤和血液标本。本文主要报道 KRAS 及 EGFR 突变状态与组织学、性别及吸烟史的关系。**方法：**通过 cold -PCR 单链构象方法，分析 549 份组织学确诊的肿瘤组织进行 KRAS12 和 13 基因至少 10 种取代基突变多态性。随后用基因测序证实这些突变。用类似的方法对 195 例患者的 EGFR 突变进行了初步分析。研究结果患者并不知情。**结果：**在 106/549（19.3%）例患者检测到 KRAS 突变；在吸烟者中（101/495,20%）比非吸烟者（5/54，9%）常见（p=0.047）。女性吸烟者中 22%（60/274）有 KRAS 突变，与男性吸烟者中 16.7%的突变率无显著差别（46/275，p=0.13）。腺癌中 KRAS 突变率较其他组织类型中多见（P<0.0001）。对数回归分析提示组织学和吸烟状态是 KRAS 突变的独立变数，但性别不是。47%的 KRAS 突变为密码子 12GGT→TGT（Gly→Cys），72%为烟草致癌物相关的 G→T 易位。G→T 易位在吸烟者中明显多于非吸烟者（P=0.03）。12.8%的患者存在 EGFR 突变（25/195,E19del:9；L858R:16），非吸烟者中突变率（45%）显著高于吸烟者（9%）（P<0.0001），在腺癌患者中更常见（p=0.04）。除 1 例患者外，EGFR 突变和 KRAS 突变不同时出现。**结论：**S0424 是研究 NSCLC 患者关于性别和吸烟史的最大的前瞻性研究。吸烟史和组织学为腺癌者是 EGFR 和 KRAS 突变的独立变量，但性别不是突变的影响因子。进一步研究烟草相关的 DNA 内转和雌激素受体表达的研究正在进行中。

7014 Treatment of the elderly when cure is the goal: The influence of age on treatment selection and efficacy for stage III non-small cell lung cancer (NSCLC)

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General Hospital, University Health Network, Toronto, ON, Canada; Toronto General Hospital, Toronto, ON, Canada; Radiation Medicine Program, Princess Margaret Hospital, Toronto, ON, Canada

Abstract:

Background: Treatment of elderly patients with stage III NSCLC is controversial. Limited data exist since the elderly are under-represented in clinical trials. **Methods:** Following ethics approval, we performed a retrospective review of 1,302 stage III NSCLC patients, treated at our institution 1997-2007. Patients with "wet IIIB" and N2 discovered only postoperatively were excluded, leaving 637 who were classified by treatment plan: palliative (palliative chemotherapy or radiation [≤40 Gy]); nonsurgical (>40 Gy radiation ± chemotherapy); trimodality (chemotherapy, radiation, surgery). Demographics, treatment, toxicity, and survival were analysed by age: 0-65 (n=339), 66-75 (n=223), 76+ years (n=75) and compared using log-rank and univariate statistical tests. **Results:** Patients >65 were more likely to have poor performance status (PS, p<0.0001), multiple comorbidities (p<0.0001), and to receive palliative therapy only (p<0.0001). Older and younger patients treated with nonsurgical or surgical therapy with curative intent had similar rates of Gr3/4 toxicity (39%, (0-65) 43%, (66-75) 5%, (>75) p=0.18), and toxic death (4%, 4%, 0, p=0.49). Survival was worse with increasing age, p<0.0001, likely due to greater use of palliative treatment in the elderly. When survival of patients treated with curative intent was analyzed by age there was no difference between age groups for nonsurgical (p=0.11), or surgical (p= 0.57) therapy. **Conclusions:** In well-selected fit elderly patients combined modality therapy is tolerable and is associated with survival similar to that of younger patients.

Variable	Category	0-65 %	66-75 %	76+ %	p value
Sex	F	41	38	41	0.70
	M	59	62	59	
ECOG PS	0	22	20	17	<0.0001
	1	66	52	43	
	2+	12	38	40	
Histology	Adeno	46	42	43	0.02
	Squam	31	36	40	
	Other	13	22	17	
Stage	IIIA	51	51	53	0.82

Variable	Category	0-65 %	66-75 %	76+ %	p value
	IIIB	49	49	47	
Comorbidity*	0	63	41	33	<0.0001
	1-2	31	43	40	
	3+	6	16	27	
Treatment	Palliative	14	37	69	
	Nonsurgical	46	39	21	<0.0001
	Trimodality	40	24	10	
	Palliative	7.8	7.0	11	0.64
Survival (mo)	Nonsurgical	17.4	12.6	20.0	0.11
	Trimodality	33.4	28.6	27.7	0.57

*Charlson comorbidity index (CCI), adjusted for lung cancer.

7014 译文 老年肺癌患者的治疗选择：年龄对于 III 期非小细胞肺癌（NSCLC）的治疗选择及疗效的影响

摘要

背景：对于老年的 III 期 NSCLC 患者的治疗一直有争议。因老年患者在临床试验中没有代表性，因此关于老年患者治疗选择，其可参考的数据很有限。**方法**：在伦理学允许的前提下，我们回顾性分析 1997 年到 2007 年间在我机构治疗的 1302 位 III 期 NSCLC 患者。“湿性 IIIB”期患者及术后证实仅有 N2 淋巴结受累的患者排除外在，最后共有 637 名患者进入研究，按照治疗计划分为三组：姑息治疗（姑息化疗或放疗≤40Gcy）、非手术治疗（>40Gcy 放疗±化疗）、三种类型的治疗（化疗、放疗、手术）。按年龄分为 0-65 岁（n=339），66-75 岁（n=223），76 岁以上（n=75）三个年龄组分析人口统计学、治疗、毒性及生存率等数据，并通过 Log-rank 和单变量统计学试验进行比较。**结果**：65 岁以上的患者更容易 PS 评分差（P<0.0001）,有多种合并症（P<0.0001），只接受姑息治疗（P<0.0001）。年老患者及年轻患者接受手术治疗或非手术治疗出现 3 或 4 级毒性反应的几率（39%（0-65），43%（66-75），5%（>75）；p=0.18）及因毒性反应产生的死亡率类似（4%，4%，0；p=0.49）。随着年龄增加生存率下降，P<0.0001，可能和年老患者更多选择姑息治疗有关。分析行根治治疗的不同年龄组患者之间的生存率发现，手术治疗（p=0.11）或非手术治疗（p=0.57）的生存率在各年龄组之间无显著差异。**结论**：老

年患者选择合适的综合治疗模式耐受良好，且其生存率和年轻患者类似。

Variable	Category	0-65 %	66-75 %	76+ %	p value
Sex	F	41	38	41	0.70
	M	59	62	59	
ECOG PS	0	22	20	17	<0.0001
	1	66	52	43	
	2+	12	38	40	
Histology	Adeno	46	42	43	0.02
	Squam	31	36	40	
	Other	13	22	17	
Stage	IIIA	51	51	53	0.82
	IIIB	49	49	47	
Comorbidity*	0	63	41	33	<0.0001
	1-2	31	43	40	
	3+	6	16	27	
Treatment	Palliative	14	37	69	<0.0001
	Nonsurgical	46	39	21	
	Trimodality	40	24	10	
Survival (mo)	Palliative	7.8	7.0	11	0.64
	Nonsurgical	17.4	12.6	20.0	0.11
	Trimodality	33.4	28.6	27.7	0.57

*Charlson comorbidity index (CCI), adjusted for lung cancer.

7015 A multinational pooled analysis of 434 cases of stage I non-small cell lung cancer (NSCLC) treated with volumetrically image-guided (VIGRT) stereotactic lung radiotherapy (SBRT): Results from the Elekta Collaborative Lung Research Group

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Abstract:

Background: Published lung SBRT outcomes/dose response data for inoperable NSCLC come from small phase I-II studies or larger datasets not requiring image-guided radiotherapy (IGRT) or volumetric prescriptions. This entire cohort of SBRT patients had daily online cone-beamCT. **Methods:** 434 cases of stage I (T1-2N0M0) NSCLC were treated with SBRT via VIGRT at 1 of 5 institutions from 1998-2009. Median age was 74y(42-92); 53% male, 47% female. Median FEV1 was 1.4L(65% predicted); median DLCO was 9.8 ml/min/mmHg(54% predicted). 62% of tumors were biopsy-proven; 84% of cases were staged with CT and PET. Clinical stage was IA in 76%, IB in 22%, locally recurrent in 1%. Median max tumor dimension was 2.4 cm (0.9-8.5cm). Histologies were: 41% adenocarcinoma, 34% squamous, 12% large cell, 13% NSCLC NOS. 8%, 51%, and 42% were grades 1, 2, 3. Median volumetric prescription dose (PD) was 54Gy (20-64Gy) delivered in median of 3 fractions(fx) (1-15fx) over 8d (1-27d). Median biological equivalent PD (BED_{10}) was 132Gy (60-180Gy), equal to 2-Gy fx equivalent (FE) of 110Gy (50-150Gy). Corresponding GTV and PTV mean doses (2-GyFE) were 157Gy and 137Gy. Mean follow-up = 1.3y (0.1-7.3y). **Results:** 2-y KM rates of local recurrence (LR), regional recurrence (RR) and distant metastasis (DM) were 8%, 13%, and 26%. 2y overall survival (OS) and cause-specific survival (CSS) were 58% and 84%. No statistically significant differences in LR, RR, DM, OS or CSS were identified for biopsied vs. non-biopsied tumors. On univariate analysis, stage (IA 5% v IB 16%, p=0.002), GTV max dimension (<2.7cm 4% v ≥2.7cm 12%, p=0.006), and 2GyFE PD (<88Gy 17% v ≥88Gy 5%, p<0.001) predicted LR. GTV (<115Gy 32% v ≥115Gy 4%, p<0.001) and PTV (<105Gy 24% v ≥105Gy 4%, p<0.001) 2GyFE mean doses also predicted LR. Cox multiple regression confirmed the relationship

between PD and LR, independent of GTV size (p=0.01). **Conclusions:** This is the first Lung SBRT dataset of patients treated uniformly with daily online VIGRT and resulted in excellent local control for stage I NSCLC. A 2-GyFE dose of 88 Gy (BED_{10} 105 Gy) predicted superior local control.

7015 译文 用容积调强（VIGRT）立体定位肺放疗（SBRT）技术对 434 例 I 期 NSCLC 患者进行治疗的多国合作研究分析：来自 Elekta collaborative Lung Research Group 的结果

摘要

背景：已有报道关于不能手术的 NSCLC 患者立体定位肺放疗的获益和剂量强度之间的关系的数据。但是这些数据来自于小样本的Ⅰ-Ⅱ期临床试验或是来自于无影像引导和容积描述技术的数据。这个关于 SBRT 病人的整体的队列研究每日都有在线 CBCT 技术进行验证。**方法：**从 1998 年到 2009 年在 5 家机构中 1 家中，434 名 I 期（T1-2NOMO ）NSCLC 患者接受了通过容积调强技术进行的ＳＢＲＴ治疗。中位年龄为 74 岁（42－92），53%为男性，47%为女性。中位 FEV1 为 1.4L（65%预测值），中位 DLCO 为 9.8 ml/min/mmHg(54% 预测值)。62%肿瘤经过病理证实，84%通过 CT 和 PET 分期。临床ⅠA 期为 76%，ⅠB 期为 22%，局部复发为 1%。中位最大肿瘤直径为 2.4cm(0.9-8.5cm)。组织学为 41%腺癌，34%鳞癌，12%大细胞癌，13%NSCLC。肿瘤分化程度 1,2,3 级分别为 8%，51%和 42%。中位剂量（PD）为 54Gy(20-64Gy),分 3 次（均值，1-15 次）在 8 天（均值，1-27 天）内给予。中位等效生物剂量(BED10) 为 132Gy (60-180Gy)，相当于每次 2Gy 治疗累积剂量 110 Gy. 肿瘤区和治疗计划靶区的平均剂量相当于每天 2Gy 治疗累积剂量 157Gy 和 137 Gy。中位随访年份为 1.3 年（0.1-7.3 年）**结果：**2-y KM 的局部复发率，区域复发率及远处转移率分别为 8%,13%和 26%两年总生存及病因特异性生存率（CSS）为 58%和 84%。没有在活检及未活检的肿瘤中均未发现 LR, RR, DM, OS 或 CSS 有显著区别。在单变量分析中，分期(IA 5% v IB 16%, p=0.002), 肿瘤区最大直径(<2.7cm 4% v ≥2.7cm 12%, p=0.006), 相当于每次 2Gy 的等效生物剂量(<88Gy 17% v ≥88Gy 5%, p<0.001)预测 LR.肿瘤区剂量(<115Gy 32% v ≥115Gy 4%, p<0.001)，治疗计划靶区剂量(<105Gy 24% v ≥105Gy 4%, p<0.001)。每次 2Gy 等效剂量平均剂量也可预测局部复发。Cox 多变量回归也确定了等效生物剂量和局部复发的关系，与肿瘤区大小无关

(p=0.01)。**结论：**这是第一份关于肺 SBRT 的数据组，病人每天统一用在线容积调强技术治疗，结果提示对于 I 期 NSCLC 有很不错的控制率。等效生物剂量达到 105 Gy 以上预示着可以很好的控制肿瘤。

7016 Thoracic radiation therapy in locally advanced NSCLC patients (pts) with EGFR mutations

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Abstract:

Background: NSCLC pts with EGFR mutations have improved outcomes with EGFR-targeted therapy and with chemotherapy, compared to wild-type (wt) pts. There is in vitro and clinical evidence to suggest that EGFR mutations may also confer radiation sensitivity. We examined pts with locally advanced NSCLC and known EGFR mutation status to assess for differences in locoregional recurrence rates (LRR) after thoracic radiation therapy (TRT). **Methods:** We retrospectively reviewed 1445 pts who underwent EGFR testing at our centers from 2004-09 and identified 109 with locally advanced NSCLC who were treated with TRT. We compared LRR, distant metastases (DM), relapse-free survival (RFS) and overall survival (OS) between EGFR mutant and wt pts. **Results:** Among 109 pts, 27 (25%) were EGFR mutant and 82 (75%) were wt. Demographics included mean age 61.7 years, 69% female, 92% white, and 84% never/former smokers. Most had stage III disease (IIIA 64%, IIIB 28%), and EGFR mutants had relatively more IIIA than wt (82% vs. 59%;

p=0.08). TRT was given as definitive (45%), adjuvant (25%), and neoadjuvant (30%) therapy; more wt than mutant pts received definitive RT (48% vs. 19%). Intensity-modulated RT was given in 48%, and the median TRT dose was 59.4 Gy (range, 28.8 - 74 Gy), with no difference by mutation status. Most patients received concurrent (81%) and/or adjuvant chemotherapy (58%). The median follow-up was 25.4 months. There was a significantly lower rate of LRR at 2 years in the EGFR mutant versus wt pts (19% vs. 46%; p=0.005), which remained significant after adjusting for stage, TRT dose, and TRT timing (HR 0.35, 95% CI 0.15-0.84; p=0.018). Mutant versus wt status was not associated with 2-year RFS (40% vs. 34%; p=0.16) and DM (62% vs. 63%; p=0.15), and the observed difference in 2-year OS (90% vs. 68%; p=0.12) did not reach significance. **Conclusions:** In NSCLC, mutant EGFR was associated with a decreased risk of LRR compared to EGFR wt tumors, suggesting that EGFR mutations may confer radiation sensitivity. EGFR mutation status was not associated with RFS and DM, and observed differences in OS did not reach significance.

7016 译文 具有 EGFR 突变的局部进展的 NSCLC 患者的胸腔放射治疗

摘要

背景：具有 EGFR 突变的 NSCLC 患者行 EGFR 靶向治疗及化疗的效果比 EGFR 野生型者要好。体外实验及临床证据也提示 EGFR 突变也可能提高放疗的敏感性。我们对局部进展的 NSCLC 患者行 EGFR 突变检测，结合其突变情况来分析胸腔局部放疗（TRT）后的放疗区域局部复发率（LRR）。**方法**：我们回顾性分析了 2004-2009 年间在我中心行 EGFR 检测的 1445 例患者，证实其中 109 例局部进展的 NSCLC 患者接受过 TRT 治疗。我们比较了 EGFR 突变组和野生型组两组之间的 LRR、远处转移（DM），无复发生存期（RFS）及总生存期（OS）。**结果**：109 名患者中有 27 名（25%）为 EGFR 突变型，82 名（75%）为 EGFR 野生型。统计学数据包括平均年龄 61.7 岁，69%为女性，92%为白种人，84%无吸烟史。绝大部分处于 III 期（IIIA 64%，IIIB28%）。IIIA 期患者中 EGFR 突变率更高（82% vs 59%；p=0.08）。45%以 TRT 为最终治疗，25%作为辅助治疗，30%作为新辅助治疗；接受最终治疗的患者中 EGFR 野生型者较突变型多见（48% vs 19%）。48%患者的照射剂量是经过剂量调整的，中位 TRT 剂量为 59.4Gy（28.8-74Gy），和突变状态无关。大部分患者接受了同步化疗（81%）和/或辅助化疗（58%）。中位随访期为

25.4 月。在 EGFR 突变组 2 年的 LRR 率明显低于野生型患者（19% vs 46%；p=0.005），在调整了分期、TRT 剂量及 TRT 时间（HR 0.35, 95% CI 0.15-0.84；p=0.018）后该差别仍很明显。突变型和野生型状态和 2 年 RFS（40% vs 34%；p=0.16）及 DM（62% vs 63%；p=0.15）无关，2 年的 OS（90% vs 68%，p=0.12）也无显著性差异。**结论**：NSCLC 患者中，EGFR 突变型者比野生型者 LRR 的风险要低，提示 EGFR 突变可能会提高放疗敏感性。EGFR 突变状态和 RFS 及 DM 无关，两组的 OS 也没有达到统计学显著差异。

7017 Utilization of adjuvant therapy among completely resected non-small cell lung cancer (NSCLC) patients in the National Comprehensive Cancer Network (NCCN) Outcomes Database Project

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Abstract:

Background: In recent years, adjuvant chemotherapy has become the standard of care for completely resected (R0) stage II and IIIA NSCLC patients, while the use of adjuvant therapy in stage IB remains controversial. We evaluated the use of adjuvant therapy among R0 stage IA-IIIA NSCLC patients in the NCCN Outcomes Database Project. **Methods:** Completely resected stage I-IIIA NSCLC patients who did not receive preoperative therapy were selected

for analysis. Eligible patients received adjuvant treatment at 8 participating NCCN institutions between 01/2007 and 06/2009 and were at least 90 days postsurgery. Adjuvant therapy was defined as therapy initiated within 3 months of surgery. Analyses were done on 12/11/09. **Results:** A total of 498 patients met the inclusion criteria. Patient characteristics were: male 42%; median age 67 yrs; stage IA 39%, IB 35%, II 16%, IIIA 10%; lobectomy (uni or bi) 84% (N=416); adenocarcinoma 58% (N=289); performance status (PS) 0-1 54% (N=271), PS ≥2 3% (N=16), and undocumented PS 42% (N=211). Adjuvant treatment category is presented by stage in the Table. Of patients receiving adjuvant therapy, 5 (4%) did so on a clinical trial. The most common reason for not receiving adjuvant systemic therapy in stage II-IIIA was patient refusal (26%). **Conclusions:** Adjuvant therapy was commonly administered to stage II and IIIA patients. Radiation was most common among stage IIIA patients. While the majority of R0 NSCLC patients received treatment that follows NCCN guidelines, relatively few patients at these NCCN centers are participating in clinical trials.

Adjuvant treatment category by stage

	Stage			
Treatment category	IA (N=193)	IB (N=174)	II (N=79)	IIIA (N=52)
No treatment	190 (98%)	126 (72%)	25 (32%)	14 (27%)
Chemotherapy	2 (1%)	43 (25%)	43 (54%)	20 (38%)
Cisplatin-based	2 (100%)	25 (58%)	25 (58%)	10 (50%)
Carboplatin-based	0 (0%)	14 (33%)	17 (40%)	8 (40%)
Other	0 (0%)	4 (9%)	1 (2%)	2 (10%)
Chemotherapy + targeted therapy	0 (0%)	2 (1%)	0 (0%)	0 (0%)
Targeted therapy alone	0 (0%)	2 (1%)	2 (3%)	1 (2%)
Sequential chemo/RT	1 (<1%)	0 (0%)	6 (8%)	13 (25%)
Concurrent chemo/RT	0 (0%)	0 (0%)	1 (1%)	3 (6%)
RT alone	0 (0%)	1 (<1%)	2 (3%)	1 (2%)

7017 译文 NCCN 数据库中完全手术切除后的 NSCLC 患者中辅助治疗的应用

摘要

背景：近几年，辅助化疗已经成为 II 期及 IIIA 期 NSCLC 患者根治性手术（R0）后的标准治疗，但是在 IB 期患者中仍有争议。我们评估了 NCCN 数据库中 IA-IIIA 期患者 R0 后辅助化疗的使用情况。**方法：**选择术前没有接受过化疗的 I-IIIA 期根治性手术后的患者作为研究对象，在 2007 年 1 月至 2009 年 6 月之间于 NCCN 所属的 8 个医疗机构对符合条件的患者行辅助化疗，至少持续至术后 90 天。辅助化疗的定义是在术后 3 个月内开始的化疗。2009 年 11 月 12 日对资料进行分析。**结果：**共 498 名患者符合入选条件。患者特征：男性占 42%，中位年龄 67 岁；IA 期占 39%，IB 期 35%，II 期 16%，IIIA 期 10%；肺叶切除者（单侧或双侧）84%（N=416）；腺癌占 58%（N=289）；PS 0-1 占 54%（N=271）；PS≥2 占 3%（N=16），无 PS 评分者占 42%（N=211）。辅助化疗的情况见下表。在所有接受辅助化疗的患者中，5（4%）是通过参加临床试验完成的辅助化疗。II-IIIA 期患者未行辅助化疗最常见的理由为患者拒绝（26%）。**结论：**II 到 IIIA 患者已经普遍行辅助化疗。放疗在 IIIA 期患者中使用最普遍。虽然绝大部分 R0 后的 NSCLC 都按照 NCCN 指南接受治疗，但在这些 NCCN 结构中参加临床试验的相对很少。

Adjuvant treatment category by stage

	Stage			
Treatment category	IA (N=193)	IB (N=174)	II (N=79)	IIIA (N=52)
No treatment	190 (98%)	126 (72%)	25 (32%)	14 (27%)
Chemotherapy	2 (1%)	43 (25%)	43 (54%)	20 (38%)
Cisplatin-based	2 (100%)	25 (58%)	25 (58%)	10 (50%)
Carboplatin-based	0 (0%)	14 (33%)	17 (40%)	8 (40%)
Other	0 (0%)	4 (9%)	1 (2%)	2 (10%)
Chemotherapy + targeted therapy	0 (0%)	2 (1%)	0 (0%)	0 (0%)
Targeted therapy alone	0 (0%)	2 (1%)	2 (3%)	1 (2%)
Sequential chemo/RT	1 (<1%)	0 (0%)	6 (8%)	13 (25%)
Concurrent chemo/RT	0 (0%)	0 (0%)	1 (1%)	3 (6%)
RT alone	0 (0%)	1 (<1%)	2 (3%)	1 (2%)

7018 Adoption of adjuvant chemotherapy for non-small cell lung cancer: A population-based outcomes study

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Abstract:

Background: Since 2004 several clinical trials have demonstrated that adjuvant chemotherapy (ACT) improves survival in patients with non-small cell lung cancer (NSCLC). Here we evaluate the uptake of ACT and its impact on outcomes in the general population of Ontario, Canada. **Methods:** All cases of NSCLC diagnosed in Ontario 2001-2006 who underwent surgical resection (n=6,311) were identified using the population-based Ontario Cancer Registry (OCR). The OCR captures diagnostic and demographic information on ~ 98% of all incident cancer cases in Ontario. We linked electronic records of treatment to the registry. We described time trends in the uptake of ACT and compared hospitalizations and survival of all surgical patients diagnosed 2001-2003 with those diagnosed 2004-2006. **Results:** Demographic, disease, and treatment-related characteristics did not differ between the 2001-2003 and 2004-2006 cohorts. Over the study period the proportion of cases receiving ACT increased from 7% (192/2,953) to 31% (1,034/3,358, $p<0.0001$). In 2004-2006, ACT was used in 60% of cases with resected stage II/III disease. Among cases for which drug details were available, 82% of patients received cisplatin and 16% received carboplatin-based therapy. The proportion of cases admitted to hospital remained stable between 2001-2003 and 2004-2006: 36 and 37% within 6 months of surgery. However, within 2 years of surgery there

was a 34% reduction in cases admitted to hospital with metastatic disease (p<0.0001). During the study period there was a substantial improvement in 4-year survival among all surgical cases from 52.5 to 56.1%, p=0.007. Younger age, less co-morbidity, shorter length of surgical hospital stay, more extensive surgery, stage II/III disease, and region where surgery was performed were independently associated with administration of ACT. **Conclusions:** There has been rapid uptake of ACT for NSCLC which is not associated with an increased rate of hospitalization. The adoption of ACT is associated with a substantial improvement in overall survival suggesting benefits seen in the relevant clinical trials are generalizable to the general population. Efforts to reduce underutilization of ACT in clinical practice are needed.

7018 译文 NSCLC 中辅助化疗的使用：一项人口基础结果研究

摘要

背景：2004 年以后有些研究已经证实了在非小细胞肺癌患者中行辅助化疗（ACT）可提高生存率。本研究在 Canada Ontario 的人群中评估了 ACT 的采用情况及对于患者结局的影响。**方法**：对于 2001-2006 年间在 Ontario Cancer Registry（OCR）登记的所有接受手术切除并确诊的 NSCLC 患者都进行鉴定（n=6311）。OCR 获得了 Ontario 确诊的所有肿瘤患者中的 98%病例的诊断学和统计学信息。我们描述了随时间变化采用 ACT 的趋势，并比较了 2001-2003 年间诊断的与 2004-2006 年间诊断的手术后患者的生存率的区别。**结果**：2001-2003 年间的病例和 2004-2006 年间的病例在人口统计学、疾病及治疗相关的特征之间没有明显区别。在整个研究期间接受 ACT 的病例的比例由 7%（192/2953,）上升至 31%（1034/3358，p<0.0001）。2004-2006 年间，在 II-III 期的术后患者中 60%使用了辅助化疗。在化疗的具体用药细节详细的病例中，82%的患者使用了顺铂治疗，16%患者使用了含卡铂的方案。2001-2003 年和 2004-2006 年前住院治疗的病例比例保持稳定：术后 6 个月内住院率 36-37%。但在术后 2 年因肿瘤转移住院的病例了减少 34%（p<0.0001）。所有术后病例的 4 年生存率由 52.5%上升至 56.1%，p=0.007。影响 ACT 使用较多的独立因素包括：年轻患者、合并症少、因外科手术住院时间短、手术范围充分、分期为 II/III 期，以及执行手术的区域。**结论**：NSCLC 患者采用 ACT 的比例在迅速增加，行 ACT 并不增加住院率。在相关的临床试验中发现的 ACT 可以提高 NSCLC 患者生存率的结果也适用于普遍的人群。在临床实践中应该减少 ACT 未充分

应用的情况。

7019 A phase III adjuvant vinorelbine plus cisplatin (NP) versus NP plus endostar (NPE) in patients (pts) with completely resected stage IB-IIIA non-small cell lung cancer (NSCLC): An interim preliminary result

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Abstract:

Background: Adjuvant chemotherapy demonstrated a 5-15% benefit in 5-yr survival in early-stage NSCLC and the results are far from perfect. Endostar is a recombinant human Endostatin, could inhibit tumor angiogenesis. In a phase III trial, the addition of Endostar to NP regimen resulted in higher clinical benefit rate compared with NP alone in advanced NSCLC pts. Because of these promising results, we investigated adjuvant NP regimen with or without Endostar in early-stage NSCLC, and the preliminary results of the first enrolled 545 pts were reported. **Methods:** Completely resected pts (stage IB to IIIA) were randomized to receive adjuvant NP plus Endostar (arm A, N 25mg/m2 on d1 and d8 plus P 80 mg/m2 split 3 days, and iv plus Endostar 7.5mg/m2 per day iv for consecutive 14 days. Every 21 days as one cycle for 4 cycles) or NP regimen alone (arm B). Study design: open, multicenter, randomized (1:1), stratified by gender, stage and histology. Main endpoint: overall survival.

Results: 545 pts (arm A 274; B 271) from 39 centers in China were included between 9/2007 and 04/2009. Two arms were well-balanced with regard to age, gender, histology, staging, and resection type. The follow-up time is 22 months. The cumulative death in arm A was 18 cases and in arm B 19 cases. Median survival was 19.4 months in arm A and 20.5 months in arm B (p=0.8965). The cumulative relapse disease in arm A was 73 cases and in arm B 64 cases. The median relapse-free survival time was 21.9 months in arm A and 18 months in arm B (p=0.3257). 78.6% of pts in arm A finished 4 cycles of treatment and 76.3% of pts in arm B received 4 cycles of chemotherapy. There was no significant difference in cardiac toxicities in two arms. **Conclusions:** This preliminary result showed no significant OS advantage for adding Endostar to adjuvant NP currently. Pts in arm A experienced a longer median relapse-free survival time (21.9 months vs. 18 months) than in arm B, although there was no statistical difference now. Over two third of pts have finished 4 cycles of chemotherapy in each arm. The toxicity profiles for both treatment arms were tolerable in this study. The pts enrollment and follow up are ongoing.

7019 译文 IB-IIIA 期完全切除的 NSCLC 患者中应用长春瑞滨+顺铂（NP）vs NP+恩度（NPE）辅助化疗比较的 III 期研究：试验中期的初步结果

摘要

背景：早期 NSCLC 行辅助化疗对于 5 年生存率可提高 5-10%，这个结果远远不够理想。恩度是重组的人内皮他丁，可以抑制肿瘤血管生长。在一个 III 期临床试验中，NP+恩度的方案对于进展期 NSCLC 患者的临床获益明显高于单纯的 NP 方案。基于这些结果，我们观察了早期 NSCLC 中辅助性 NP 方案加或不加恩度的区别，这里报告先入组的 545 名患者的初步结果。**方法：**IB 到 IIIA 期完全手术切除后的患者被随机分配到两组：NP+恩度组（Arm A：N 25mg/m2 d1，d8，+ P 80mg/m2，分成三天使用，并静脉推恩度 7.5mg/m2/d，连续使用 14 天，每 21 天为 1 个周期，共 4 个周期）和 NP 组(Arm B)。研究设计：开放、多中心、随机（1:1）,根据性别、分期、组织学分类。主要终点：整体生存率。**结果：**2007-9 至 2009-4 间来自中国 39 个中心的 545 名患者（A 组 274，B 组 271）入组试验。2 组在年龄、性别、组织学、分期和手术类型上都得到很少的平衡。随访时间为 22 个月。A 组累计死亡 18 例，B 组 19 例。A 组中位生存期 19.4 月，B 组 20.5

月（P=0.8965）。A 组复发病例 73 例，B 组 64 例。A 组中位无复发生存时间 21.9 月，B 组 18 月（P=0.3257）。A 组 78.6%患者完成了 4 周期化疗，B 组有 76.3%患者完成化疗。两组的心脏毒性无显著差异。**结论：**本初步结果的报道显示在常用的辅助性 NP 化疗基础上增加恩度并不能显著的改善 OS。A 组患者的无进展生存时间比 B 组长，但并没有达到统计学差异。两组都有 2/3 以上的患者完成了 4 周期的化疗。本研究显示两种方案的毒性反应都是可以耐受的。目前患者还在继续入组和随访当中。

7021 Validation of the lung cancer staging system revisions using a large prospective clinical trial database (ACOSOG Z0030)

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Abstract:

Background: A new revision of the international lung cancer staging system has been recently introduced. The revisions are largely focused on the T descriptor. We sought to test the validity of this new system on a separate prospectively collected cohort of patients from a recent multicenter trial of early-stage lung cancer. **Methods:** We reviewed the prospectively collected data from 1,087 patients undergoing pulmonary resection for lung cancer in the ACOSOG Z0030 trial. TNM descriptors and overall staging were assessed using both the 6th and 7th editions of the AJCC/UICC lung cancer staging system. Survival results were

analyzed according to both staging allocations. **Results:** The number of patients by stage in the 6th and 7th edition allocations respectively were as follows: IA (454, 453); IB (417, 314); IIA (42, 180); IIB (107, 75); IIIA (44, 64); IIIB (23,1); there were no stage IV patients by either version. Overall survival comparisons are provided in the Table. **Conclusions:** This study provides the first external validation of the recently revised lung cancer staging system using a large multicenter database. Inasmuch as its revisions concentrate predominantly on the T descriptor, the 7th edition does produce prognostic results that demonstrate monotonic progression, distinction between groups, and homogeneity within groups. The 7th edition of the AJCC/UICC lung cancer staging system appears to be an improvement over the preceding system.

6th edition T/N stage	Median survival (yrs)	5-year survival (%)	p value*
T1	NA	73.5	-
T2	6.9	59.1	<0.0001
T3	2.6	24.3	0.0002
T4	2.4	44.4	0.5232
N0	8.7	68.2	-
N1	4.0	43.3	<0.0001
N2	2.7	36.1	0.6881
IA	NA	76.0	-
IB	7.9	62.9	<0.0001
IIA	3.9	46.1	0.0181
IIB	3.9	41.2	0.7026
IIIA	1.8	28.0	0.2678
IIIB	2.4	44.4	0.4806
7th edition T/N stage			
T1	NA	74.4	-
T1a	NA	75.4	-
T1b	9.1	73.1	0.3896
T2	6.9	59.2	-
T2a	6.9	61.2	0.0058
T2b	5.1	51.1	0.0631

6th edition T/N stage	Median survival (yrs)	5-year survival (%)	p value*
T3	3.0	39.6	0.2088
T4	1.4	-	0.0041
N0	8.7	68.2	-
N1	4.0	43.3	<0.0001
N2	2.7	36.1	0.6881
IA	NA	77.0	-
IB	8.5	64.9	0.0002
IIA	4.4	48.5	0.0003
IIB	3.6	42.9	0.4668
IIIA	1.8	30.6	0.1203

T1 vs. T2, p value < 0.0001; T2 vs. T3, p value = 0.0021; T3 vs. T4, p value = 0.0041.

* Stage groups were consecutively compared (i.e., IA vs. IB, IB vs. IIA, etc.).

7021 译文 通过一个大型前瞻性临床试验数据来验证肺癌分期系统修订本

摘要

背景：最近公布了一个新的国际性肺癌分期系统修订本。该版本很多是针对 T 的描述的修订。我们通过一个独立的前瞻性按队列收集近期的一个关于早期肺癌的多中心临床试验的患者的研究来验证这个新的系统。**方法：**我们分析了前瞻性收集的 ACOSOG Z0030 试验中 1087 名行肺切除手术的肺癌患者的数据。分别根据 AJCC/UICC 第 6 版和第 7 版肺癌分期系统来进行 TNM 描述和总体分期的评估。分别根据 2 个分期结果来分析其生存率结果。**结果：**根据第 6 版和第 7 版分期系统分期的患者结果分别如下：IA（454,453），IB（417,314），IIA（42,180），IIB（107,75）；IIIA（44,64），IIIB（23,1）。根据两种版本都没有分出 IV 期的患者。总体生存率比较见表。**结论：**本研究通过一个大型多中心数据首次从外部验证了最近修订的肺癌分期系统。由于修订本主要聚焦于 T 的描述，该版本的确起到了预言预后的作用，是对以前的分类系统的一个补充。

6th edition T/N stage	Median survival (yrs)	5-year survival (%)	p value*
T1	NA	73.5	-
T2	6.9	59.1	<0.0001
T3	2.6	24.3	0.0002
T4	2.4	44.4	0.5232
N0	8.7	68.2	-
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IIIB	2.4	44.4	0.4806
7th edition T/N stage			
T1	NA	74.4	-
T1a	NA	75.4	-
T1b	9.1	73.1	0.3896
T2	6.9	59.2	-
T2a	6.9	61.2	0.0058
T2b	5.1	51.1	0.0631
T3	3.0	39.6	0.2088
T4	1.4	-	0.0041
N0	8.7	68.2	-
N1	4.0	43.3	<0.0001
N2	2.7	36.1	0.6881
IA	NA	77.0	-
IB	8.5	64.9	0.0002
IIA	4.4	48.5	0.0003
IIB	3.6	42.9	0.4668
IIIA	1.8	30.6	0.1203

T1 vs. T2, p value < 0.0001; T2 vs. T3, p value = 0.0021; T3 vs. T4, p value = 0.0041.

* Stage groups were consecutively compared (i.e., IA vs. IB, IB vs. IIA, etc.).

7022 The impact of stage migration on survival after resection in the UICC 7 TNM classification of lung cancer

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Abstract:

Background: A change of staging classification has been associated with improvements in stage-specific survival without improvement of overall survival (Feinstein, 1985). We aim to estimate in patients with resected non-small cell lung cancer (NSCLC), included in the IASLC staging database (Goldstraw, 2006) 1) the magnitude and direction of stage migration between the 6th and 7th editions of the UICC-TNM classification, and 2) its impact on stage-specific outcome. **Methods:** Resected NSCLC cases were extracted from the IASLC database and classified according to the 6th and 7th editions of UICC-pTNM. Cases having received preoperative chemotherapy and/or radiotherapy were excluded from the set; postoperative deaths were included, as were substages A and B for stage III only. Migration was estimated by calculating the rate of patients classified in any higher or lower UICC-7 p-stage over the corresponding UICC 6 p-stage. Outcome was estimated by the Kaplan-Meier method and expressed as 5-year survival rate (5y SR) with lower and upper 95% confidence intervals (95%CI). **Results:** Stage distribution of 15,952 cases with full pathological data, classified according to UICC 6 and 7, with corresponding overall and stage specific 5-y SR are in the Table. Overall, 2,480 cases (16%) migrate, of whom 1,747 (11%) to a higher and 733 (5%) to a lower stage. Substantial changes in 5y SR occur for pI (+3%) and pIIIB (-10%). **Conclusions:** The change of TNM staging classification of resected NSCLC from UICC6 to

7 results in the net migration of 1 out of 6 cases, to a higher stage in 70% of them, with substantial changes in 5y SR for p-stages I and IIIB. This stage migration should be accounted for when comparing outcome across series using different TNM classifications.

	UICC 6	UICC 7	Net migration
Total	15,952 (100%)		2,480 (16%)
5y SR	47% (46-48)		0%
pI	8,092 (51%)	6,766 (42%)	-
5y SR	63% (62-64)	66% (65-67)	+3%
pII	3,544 (22%)	4,831 (30%)	1,476 (9%)
5y SR	39% (37-41)	41% (40-43)	+2%
pIIIA	3,091 (19%)	3,792 (24%)	701 (4%)
5y SR	25% (23-26)	24% (23-26)	-1%
pIIIB	1,042 (7%)	297 (2%)	71 (<1%)
5y SR	19% (17-22)	9% (6-13)	-10%
pIV	183 (1%)	266 (2%)	232 (2%)
5y SR	21% (15-27)	13% (9-17)	-8%

7022 译文 肺癌的第 7 版 UICC -TNM 分期对于手术后 NSCLC 患者的分期偏移及对生存期的影响

摘要

背景：分期分类的变化和分期相关的生存率提高相关，但是总体生存率并没有变化。我们的目的是评价 IASLC 分期数据库中的手术后 NSCLC 患者的：1）第 6 版和第 7 版 UICC-TNM 分期系统之间分期移行的强度和方向；2）对于各期生存率的影响。**方法：**从 IASLC 中提取出术后的 NSCLC 病例，根据 UICC-pTNM 的第 6 和第 7 版进行分期。术前接受过化疗或放疗者被排除在外。术后的死亡病例包括在统计范围内，仅作为 IIIA 或 IIIB 期。通过计算那些和 UICC 6 比较根据 UICC 7 的病理结果偏高或偏低的患者比例来评估分期偏移。用 Kaplan-Meier 方法评估结果，以 5 年生存率及 95% CI 表达（5y SR）。**结果：**15952 名患者的病理学数据，根据 UICC6 及 UICC 7 的分期结果，以及相

应的总体 5y SR 及各期的 5ySR 见下表。共有 2480 名患者发生分期偏移（16%），其中 1747（11%）名偏移到高一级分期，733（5%）偏移到低一级分期。5y SR 的改变发生在 P I 期（+3%）和 P IIIB 期（-10%）。**结论：**手术后 NSCLC 患者分别根据 UICC 6 和 UICC 7 分期其 TNM 分期每 6 例中有 1 例发生偏移，其中 70%偏移到高一级分期，并伴有 PI 期和 P IIIB 期的 5y SR 改变。当使用不同的 TNM 分类系统来作比较时应该考虑到此偏移。

	UICC 6	**UICC 7**	**Net migration**
Total	15,952 (100%)		2,480 (16%)
5y SR	47% (46-48)		0%
pI	8,092 (51%)	6,766 (42%)	-
5y SR	63% (62-64)	66% (65-67)	+3%
pII	3,544 (22%)	4,831 (30%)	1,476 (9%)
5y SR	39% (37-41)	41% (40-43)	+2%
pIIIA	3,091 (19%)	3,792 (24%)	701 (4%)
5y SR	25% (23-26)	24% (23-26)	-1%
pIIIB	1,042 (7%)	297 (2%)	71 (<1%)
5y SR	19% (17-22)	9% (6-13)	-10%
pIV	183 (1%)	266 (2%)	232 (2%)
5y SR	21% (15-27)	13% (9-17)	-8%

7023 Prognostic significance of the number of tumor (+) N2 nodes in N2 stage IIIA non-small cell lung cancer after curative resection

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Abstract:

Background: N2 stage IIIA non-small cell lung cancer (NSCLC) has heterogeneous prognosis. Further prognostic stratification may help to improve the management of patients in this category. We investigated the prognostic value of the number of positive N2 lymph nodes in patients who were registered as pathologic N2-stage IIIA NSCLC in our institution. **Methods:** From January 1997 to December 2004, 250 patients were classified as pathologic N2 stage IIIA after curative resection with mediastinal lymph node dissection. With exclusion of 44 patients with previous induction chemotherapy, incomplete resection, and post-surgical mortality, 206 patients were included. Patients were grouped by the number of positive N2 lymph nodes (1 vs 2-5 vs ≥6) and analyzed for survival outcomes. Results: The median age was 59 years old and 145 (70.4%) patients were male. Pneumonectomy was undergone in 43 (21%) patients, and lobectomy or bilobectomy was in 163 (79%) patients. Of 178 (86%) patients who were given adjuvant therapy, 59 (33%) patients received only radiotherapy and 119 (67%) patients had both chemotherapy and radiotherapy. With a median follow-up of 41.3 months, 5-year disease-free survival (DFS) was 27.2% (95% CI, 21.6-33.7) and 5-year overall survival (OS) was 37.7% (31.5-44.7). Seventy-nine (38%) patients had 1 (N2a) positive N2 lymph node, and 95 (46%) and 32 (16%) had 2-5 (N2b) and 6 or more (N2c), respectively. The number of positive N2 lymph nodes was associated with DFS (p=0.005) and OS (p=0.024). The 5-year DFS were 37%, 22%, and 9% and 5-year OS were 47%, 35%, and 25% in N2a, N2b, and N2c, respectively. A multivariate analysis including age, sex, weight loss, pathologic T stage, and adjuvant therapy identified the number of positive N2 lymph nodes was an independent prognostic factor. Hazard ratios (95% CI) of N2b and N2c with respect to N2a were 1.52 (1.07-2.17) and 2.32 (1.44-3.74) for DFS, and 1.77 (1.22-2.58) and 1.91 (1.17-3.14) for OS, respectively. Conclusions: The number of positive N2 lymph nodes

was an independent prognostic factor in patients with completely resected N2-stage IIIA NSCLC. It might be considered in the future staging system.

7023 译文 根治术后 IIIA 期 NSCLC 患者的 N2 淋巴结数量的预后意义

摘要

背景：IIIA 期 NSCLC 患者的不同 N2 情况可导致不同的预后结果。进一步提高分期对于预后的预示作用有助于不同分期的患者采用不一样的治疗方法。我们对本机构内所有根据手术分期为 IIIA 期 N2 的患者的 N2 淋巴结数量进行了预后提示意义的评估。**方法：1**997 年 1 月至 2004 年 11 月间，共有 250 名患者通过根治性手术及纵膈淋巴结清除术分期为 IIIA-N2 期。其中有 44 名患者分别因曾接受诱导化疗、手术切除不完全或术后死亡排除在外。206 例入选本研究。患者根据 N2 淋巴结数进行分组（1、2-5 及大于等于 6 个），分别分析其生存率情况。**结果：**中位年龄 59 岁，145 名（70.4%）为男性患者。43（21%）名行全肺切除术，163（79%）名患者行肺叶切除术或双肺叶切除术。178 名（86%）患者接受了辅助治疗，其中 59 名（33%）名患者只接受了放疗，119 名（67%）名患者同时接受了放疗和化疗。中位随访期为 41.3 月。5 年无疾病生存率（DFS）为 27.2%（95%CI 21.6-33.7），五年总生存率（OS）为 37.7%（31.5-44.7）。79（38%）名患者有 1 个阳性的 N2 淋巴结（N2a），95（46%）名有 2-5 个 N2 淋巴结（N2b），32 名（16%）有 6 个或以上的 N2 淋巴结（N2c）。N2 阳性的淋巴结数量和 DFS 及 OS 相关。三组中 5 年 DFS 分别为 37%、22%、及 9%。5 年 OS 为 47%、35%及 25%。多变量分析包括年龄、性别、体重减轻、病理 T 分期及辅助治疗等，显示阳性的 N2 淋巴结数量为独立预后因素。N2b 及 N2c 相对于 N2a 的危害比（95% CI）分别为：DFS 1.52（1.07-2.17）及 2.32（1.44-3.74），OS 1.77（1.22-2.58）及 1.91（1.17-3.14）。**结论：**N2 阳性的淋巴结数量对于完全手术切除的 IIIA 期 N2 NSCLC 患者是独立的预后因素，在以后的分期系统中可以考虑到这点。

7024 RTOG 0229: A phase II trial of neoadjuvant therapy with concurrent chemotherapy and high-dose radiotherapy (XRT) followed by resection and consolidative therapy for LA-NSCLC

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Abstract:

Background: Multimodality therapy has curative potential in stage III NSCLC. Mediastinal clearance after chemoXRT is associated with superior outcome and may serve as an intermediate marker for efficacy. RTOG 0229 evaluated induction concurrent chemo and full-dose XRT(61.2Gy) in stage III NSCLC. **Methods:** Pts with stage III NSCLC (pathologically proven N2 or N3) were eligible. Surgeons were required to demonstrate expertise in surgery after chemoXRT. Induction chemo and full dose XRT (CBDCA AUC =2.0, paclitaxel 50 mg/m^2 q week x 6, 50.4 Gy to the mediastinum and primary tumor and boost of 10.8 Gy to gross dz). The mediastinum was reassessed prior to or at the time of resection. Pts who had not progressed received CBDCA AUC =6, paclitaxel 200 mg/m^2 q 21d x 2. The primary endpoint was mediastinal nodal sterilization (MNS). **Results:** 60 pts were accrued, 57 were eligible. Median age: 59 , 61% M, PS =0: 77%, N2: 98% N3: 2%. Histology: 51% adeno, 19% SCC, 28% NSCLC-NOS. 95% received RT per protocol; 91% received induction chemoXRT as per protocol, 49% with dose modifications. Grade 3/4 toxicities:

heme 35%, GI 14%, pulmonary 23%. 43 pts (75%) were evaluable for the primary endpoint; 36 pts underwent resection. 7 pts had residual mediastinal dz. 27/43 (63%) achieved mediastinal clearance. The primary endpoint of the study was met (improving MNS from 50 to 70% with power of 80% and significance level of 0.05). There was a 14% (5/37) incidence of grade 3 postoperative pulmonary complications. There was only one postop grade 5 toxicity (3%). Median follow-up is 20 months. **Conclusions:** This multi-institutional trial confirms the ability of neoadjuvant concurrent chemo and full dose XRT to sterilize known mediastinal nodal disease. The acceptable postoperative complication profile supports the contention that trimodality therapy remains a viable option for carefully selected NSCLC pts presenting with stage III disease.This project was supported by RTOG grant U10 CA21661 and CCOP grant U10 CA37422.

	Overall survival	**Progression-free survival**
Median (mos) (95% CI)	26.6 (18.1, not reached)	13.1 (8.0, 18.9)
1-year rate (95% CI)	77% (64, 86)	52% (38, 64)

7024 译文 RTOG 0229：LA-NSCLC 手术及根治性治疗后用化疗合并大剂量放疗（XRT）作为新辅助治疗的 II 期临床试验

摘要

背景：综合治疗对于III期患者具有潜在的治愈作用。放化疗后行纵膈淋巴结清除术预后良好，同时可作为治疗有效的中间标志。RTOG 0229 评估了III期NSCLC患者行诱导性化疗+足量放疗的意义。**方法**：选择III期（病理证实N2 或N3）NSCLC患者为研究对象，化疗+XRT后由外科医生行评估以决定是否手术。诱导性化疗及足量XRT（CBDCA AUC=2.0，紫杉醇 50mg/m^2 每周 1 次×6 次，50.4Gy剂量照射纵膈、肺部原发灶及 10.8Gy的追加剂量行整体dz照射）。在手术前或术中对于纵膈进行重新评估。无进展的患者接受CBDCA AUC=6，紫杉醇 200mg/m2 每 21d一次×2 次治疗。第一终点为纵膈淋巴结消失（MNS）。**结果**：共有 60 名患者，57 名符合入选条件。中位年龄 59 岁，61%男性，PS=0 者占 77%，N2：98%，N3：2%。组织学：腺癌 51%，SCC 19%，28% NSCLC-NOS。95%根据进程行RT，91%按照进程行诱导化放疗，49%经过剂量调整。3/4 级毒性反应包

括：血液学 35%，GI 14%，肺部 23%。43 名（75%）患者评估了第一终点；36 名患者接受了手术切除。7 名患者有残余的纵膈DZ。27/43（63%）名患者实现了纵膈清除，实现了第一终点（增加MNS到 50%-70%，强度大 80%，显著性水平为 0.05）。有 14%（5/37）患者出现了术后肺部并发症。只有一例患者出现了 5 级毒性反应（3%）。中午随访期为 20 月。**结论：**这个多中心试验证实了新辅助同步化疗+XRT对于清除已知的纵膈淋巴结的能力。术后并发症情况可，也支持三种治疗方法联合对于某些III期NSCLC患者是个很好的选择。

	Overall survival	**Progression-free survival**
Median (mos) (95% CI)	26.6 (18.1, not reached)	13.1 (8.0, 18.9)
1-year rate (95% CI)	77% (64, 86)	52% (38, 64)

7025 Seven-year follow-up of preoperative chemoradiotherapy in superior sulcus tumor: Report of a Japan Clinical Oncology Group Trial (JCOG9806)

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Abstract:

Background: We previously reported (J Clin Oncol 2008) the safety and efficacy of preoperative chemoradiotherapy followed by surgical resection in superior sulcus tumor (SST). Seven-year follow-up data are presented. **Methods:** Pathologically documented non-small cell lung cancer (NSCLC) patients (pts) with invasion to the first rib or more superior chest wall were eligible. Those with distant metastasis, pleural dissemination or mediastinal node involvements were excluded. Pts received 2 cycles of MVP chemotherapy q 4weeks; mitomycin C 8mg/m^2 on day 1, vindesine 3mg/m^2 on days 1 and 8, and cisplatin 80mg/m^2 on day 1. Radiotherapy, 45Gy/27fr. with 1 week split, to the tumor and ipsilateral supraclavicular nodes was started on day 2. Patients went on to thoracotomy 2-4 weeks after completion of the chemoradiotherapy, or received boost radiotherapy. **Results:** From May/99 to Nov/02, 76 patients were entered. Seventy five were fully assessable. As of Nov/09, all patients were followed-up for 7 years. Forty-one patients died: 31 (76%) due to NSCLC, 3 (7%) to treatment-related adverse events, 5 (12%) to other causes, and 2 (5%) to unknown causes. The median overall survival (OS) was 7.61 years, with 5- and 7-year OS rate of 56 and 52%, respectively. OS according to background characteristics is summarized in the table. Five- and 7-year OS rates of pts with (n=51) or without (n=24) pathologic complete resection (R0) were 71% and 67%, and 25% and 21%, respectively. Seven-year OS rate of the pts with pathologic complete response (n=12) was 92%. The median progression-free survival (PFS) was 2.31 years, with 5- and 7-year PFS rate of 45% and 44%, respectively. **Conclusions:** The efficacy of this trimodality approach in patients with SST were confirmed by 7-year follow-up data.

OS according to baseline factors

Clinical factor	MST (year)	OS at 5-year	OS at 7-year	p value
c-T3 (n=55)	Not reached	62	60	0.0048
c-T4 (n=20)	2.26	40	30	
c-N0 (n=58)	6.34	53	50	0.3831
c-N1-3 (n=17)	9.18	65	59	
Sq (n=27)	8.42	59	59	0.4394
Non-sq (n=48)	5.65	54	48	

Two-sided log-rank test, unadjusted for multiplicity

7025 译文 肺上沟瘤术前放化疗的 7 年随访——来自日本临床肿瘤组试验的报道

摘要

背景：我们之前报告了肺上沟瘤（SST）术前化疗继之以手术切除的安全性和有效性。现在报告 7 年随访的数据。**方法：**病理证实为NSCLC累及第一肋及以上胸壁的肿瘤入选其中。有远处转移、胸膜播散或纵膈淋巴结受累的病例排除在外。患者接受 4 周 1 次的MVP化疗共 2 次：丝裂霉素C 8mg/m^2 d1，长春地辛 3mg/m^2 d1、d8，顺铂 80mg/m^2 d1。放疗从d2 开始，剂量为 45Gy/27fr，1 周完成，照射肿瘤及肿瘤侧锁骨上淋巴结。在放化疗结束后 2-4 周行开胸手术，或继续追加放疗。**结果：**从 99 年 5 月到 02 年 12 月，76 名患者入组。75 名患者进行了充分评估。到 09 年 12 月所有患者都随访了 7 年。41 明患者死亡：31 名（76%）因NSCLC死亡，3 名（7％）因治疗相关的副反应死亡；5(12%)因其他原因；2(5%)原因未知。中位总生存期（OS）为 7.61 年，5 年及 7 年OS分别为 56％和 52%。**结论：**7 年随访数据显示，三种方法联合的治疗方法对于SST是有效的。

OS according to baseline factors

Clinical factor	MST (year)	OS at 5-year	OS at 7-year	p value
c-T3 (n=55)	Not reached	62	60	0.0048
c-T4 (n=20)	2.26	40	30	
c-N0 (n=58)	6.34	53	50	0.3831
c-N1-3 (n=17)	9.18	65	59	
Sq (n=27)	8.42	59	59	0.4394
Non-sq (n=48)	5.65	54	48	

7026 Treatment for superior sulcus tumors (SST): Effect of surgery first followed by adjunct concurrent chemoradiotherapy on survival of patients with marginally resectable SST

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Abstract:

Background: The role of preoperative treatment for locally advanced SST (LA-SST) has not been well defined. We compared two IRB-prospective phase II trials of patients (pts) with LA-SST (T3-4 N0-3 M0) treated at The University of Texas M.D. Anderson Cancer Center. **Methods:** Trial A (16 pts, 1988 to 1997) was induction chemotherapy consisting of cyclophosphamide (500 mg/m2 i.v.), VP-16 (100 mg /m2 i.v.) and cisplatin (80 mg/m2 i.v.)×2-3 cycles followed by en bloc resection, then post operative radiotherapy (RT) with 60-66Gy/30-33 Fx depending on the surgical margin. Trial B (32 pts, 1992 to 2007) was immediate en bloc resection followed by concurrent chemoradiotherapy (CCRT). The RT was 1.2 Gy/Fx, bid, with 60 Gy/50 Fx or 64.8 Gy/54 Fx depending the surgical margin status. Concurrent chemotherapy consisted of cisplatin (50 mg/m2 i.v.) and VP-16 50 mg, p.o. given on the day 1 and 8 RT, repeated every 29 days ×4 cycles. **Results:** Median follow-up was 41 months (range, 2-155 months). Median age was 55 (range, 34-69 years). The AJCC 6th clinical stage was 27 stage IIB, 5 stage IIIA and 16 IIIB pts. Six percent (1/16) of pts had KPS less than 90 in trial A compared to 50% in trial B (16/32; p=0.003). All other patient factors including ethnicity, gender, tumor histology, baseline weight loss, clinical stage, and total RT treatment dose were evenly distributed between the two trials. Median overall survival (OS)

was 18.6 months and 112.2 months for trial A and B respectively (p=0.0005). The 5-year OS fractions for trial A and B was 18.8% and 53.1% (p=0.0005); 5-year local-regional control was 60.0% and 88.8% (p=0.02); distant metastasis-free survival was 36.7% and 58.1% (p=0.06); and disease-free survival was 26.7% and 54.9, respectively (p=0.02). **Conclusions:** This study suggests that immediate surgery followed by CCRT significantly improved survival and recurrence rate compared to pre-operative induction chemotherapy followed by surgery and RT in pts with marginally resectable LA-SST.

7026 译文 肺上沟瘤（SST）的治疗：先手术（切缘阴性）后辅助性同步放化疗对于生存率的影响

摘要

背景：局部进展的SST（LA-SST）术前的治疗作用还没得到很好描述。我们比较了两个IRB——前瞻性II期临床试验的LA-SST（T3-4，N0-3，M0）患者的治疗及预后。**方法：**试验A（1988 到 1997 年之间 16 名患者行诱导化疗：环磷酰胺 500mg/m^2 iv，VP-16 100mg/m^2 iv，顺铂 80mg/m^2 iv 共 2-3 周期，随后行瘤灶的整体切除术，术后根据切缘情况给予 60-66Gy/30-33 Fx的放疗（RT）。试验B（1992-2007 年间的 32 名患者）诊断后立即行瘤灶的整体切除术，术后予以同步放化疗（CCRT），RT剂量为 1.2Gy/Fx bid，根据切缘情况决定为 60Gy/50Fx或 64.8Gy/54Fx。同步化疗方案为顺铂（50mg/m^2 iv）和 VP-16 50mg po RT的d1 和d8，每 29 天重复 1 次共 4 次。**结果：**中位随访期 41 月（2-155 月），中位年龄 55 岁（34-69 岁），根据AJCC 6th分期：IIB 27 名，IIIA 5 名，IIIB 16 名。试验A有 6%（1/16）患者KPS<90%，试验B有 50%患者KPS<90%（16/32,P<0.003）。所有其他患者因素包括种族、性别、肿瘤组织学、基础体重下降、临床分期及总的RT剂量是平均的分布到 2 组试验中的。中位总生存期（OS）两组分别为：A组 18.6 月，B组 112.2 月（p=0.0005）。5 年的OS分级分别为A-18.8%，B-53.1%（p=0.0005）。5 年的局部控制率分别为 60.0%和 88.8%（p=0.02）；无远处转移生存率为 36.7%和 58.1%（p=0.06）；无疾病生存率为 26.7%和 54.9%（p=0.02）。**结论：**本研究提示对于手术可切除的LA-SST，立即手术继之以CCRT相对于术前诱导化疗术后RT可明显提高患者生存率，降低复发率。

7028 Prognostic value of three microRNA expression profiles in early-stage squamous cell lung cancer (SqCLC)

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Abstract:

Background: About 50% of NSCLC patients (pts) will develop distant metastases following pulmonary resection. Currently, apart from clinical stage at diagnosis, there are no reliable clinical factors to select high risk pts for adjuvant chemotherapy. We previously demonstrated high prognostic value of selected microRNAs in frozen tissues of early stage SqCLC (Skrzypski et al, J Clin Oncol 27; 15s: 2009). In the present study we evaluated the feasibility and prognostic relevance of this assay in formalin fixed paraffin embedded (FFPE) samples. **Methods:** FFPE tumor tissue was obtained from 72 stage I-II SqCLC pts. Of those, 30 pts developed distant metastases and 42 had no relapse after a median follow-up of 5.6 years (range, 3.8-7.1 years). MicroRNA was isolated from paraffin blocks after macrodissection of tumor tissue, and extracted with RecoverAll kit (Ambion). Expression of 5 microRNAs was analyzed by RT-PCR assays (Appliedbiosystems). Raw expression data were normalized vs. the expression of U6 RNA and calibrated by ΔΔCt method. After z-score transformation, the risk score was constructed based on the expression of 3 MiRs. **Results:** MicroRNA yield from tumor tissue was successful in 92% of cases. Expression of MiR 192* and MiR 10b was significantly related to the time to distant metastases (log-rank; p=0.001 and p=0.003, respectively), whereas MiR 532-3p was of borderline significance (p=0.08). The risk score based on the expression of MiRs 192*, 10b and 532-3p was significantly related to the time to

distant metastases (log-rank; p=0.00006). With the risk score median as a cut-off value, the test sensitivity for distant relapse prediction was 80% at the specificity level of 72%. **Conclusions:** Prognostic test based on microRNA assessment in FFPE is feasible and robust. Three-miRNA expression profile: 192*, 10b and 532-3p is strongly related to the risk of distant metastases in operable SqCLC. The results are being validated.

7028 译文 早期鳞状细胞肺癌（SqCLC）患者的三种 MicroRNA 表达情况对于预后的提示价值

摘要

背景：约 50%NSCLC 患者在手术切除后会发生远处转移。目前，除了诊断时的临床分期标准外，尚没有可用来选择高风险患者行辅助化疗的指标或标准。我们之前已经报道过早期 SqCLC 患者的冰冻组织中选择性的 MicroRNA 表达有很好的提示预后的价值(Skrzypski et al, J Clin Oncol 27; 15s: 2009)。本研究是在福尔马林固定、石蜡包埋的样本中评估 MicroRNA 的表达情况及提示预后的意义。**方法：**我们获得了 72 名 I-II 期 SqCLC 患者的石蜡包埋肿瘤组织样本，患者平均随访 5.6 年（3.8-7.1 年）后 30 名出现了远处转移，42 名无复发表现。切片后从石蜡块中分离出肿瘤组织，然后用 RecoverALL 试剂盒（Ambion）提取 MicroRNA。通过 RT-PCR 测定 5 种 microRNA 的表达。初步的表达数据通过 U6 RNA 的表达标准化，并用 ΔΔCt 方法校正。通过 Z-score 转换后，用 3MiRs 的表达和危险度评分相结合。**结果：**92%的患者中有 microRNA 的表达。其中 MiR 192 和 MiR10b 的表达和远处转移的时间明显相关（Log-rank；分别为 p=0.001 和 p=0.003），但 MiR532-3p 的显著性意义正处于临床状态（p=0.08）。MiRs192、10b 及 532-3p 的表达相关的危险度评分和远处转移时间显著相关（log-rank：p=0.00006）。以危险度评分的中位值作为 Cut-off 值，在 72%的特殊表达水平及对于远处转移的预测敏感性为 80%。**结论：**测定 FFPE 中 MicroRNA 的表达来预言肿瘤的远处转移是简单易行且有意义的。三种 MicroRNA 的表达谱：192,10b 及 532-3p 和可手术的 SqCLC 患者的远处转移风险明显相关。该结果有待进一步确证。

7029 VDAC1 and prognosis in surgically resected non-small cell lung cancer

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Abstract:

Background: The likelihood of relapse following surgery for non-small cell lung cancer (NSCLC) is determined by clinical and genetic factors. Metabolic status of tumors may influence outcome. The voltage dependent anion channel type 1 (VDAC1), regulates mitochondrial ATP/ADP exchange and was explored in relation to survival following surgical resection. **Methods:** A NSCLC gene expression library curated from publically available data (NCBI GEO), comprised ten independent datasets (n=618 samples). The VDAC1 expression distribution was stratified into tertiles, prior to logrank univariate and Cox multivariate survival analyses. Analysis was performed using R and TMev. Across all the datasets, p values were corrected for multiple comparisons by calculating q values based on the method of false discovery rates. Genes that were determined as significant in at least 50% of the datasets were retained to generate a meta-signature comprising consistently differentially expressed genes correlated with VDAC1. **Results:** In a combined univariate analysis, VDAC1 overexpression conferred worse overall survival (OS) 52 vs. 101.6 months (m), p=0.0323. Cox regression analysis showed VDAC1 expression to be an independent prognostic factor ($p<0.0001$), as was stage ($p<0.0001$) but not age nor gender. Stage I patients had much better survival with low VDAC1, H R 0.52 (C.I. 0.31 - 0.82). A subset of 41 genes were

significantly and consistently differentially regulated in VDAC1 overexpressing samples in >20% of the datasets; 6 genes > 50%. CSNK1A1, G3BP1, HNRNPC, HSPA4, HSPA9 and UBE2D2, all of which are upregulated. HNRNPC, HSPA4, HSPA9 and UBE2D2 are involved in protein ubiquitination pathways and CSNK1A1 regulates EIF2 function. HSPA9 is also involved in anti-apoptosis pathways while G3BP1 is linked to Ras protein signal transduction. **Conclusions:** VDAC1 overexpression is associated with shorter survival following surgical resection of NSCLC, especially for stage I patients. Further, the association between VDAC1 and genes regulating protein ubiquitination, apoptosis and EIF2 function protein suggests a role for these processes in more aggressive NSCLCs and may reflect potential molecular pathways for therapeutic development.

7029 译文 VDAC1 和手术切除的非小细胞肺癌的预后

摘要

背景：NSCLC 患者术后复发的可能性和临床及遗传因素有关。肿瘤的代谢状态也可能影响预后。1 型电压依赖的阴离子通道（VDAC1）调节线粒体的 ATP/ADP 转换，进来发现 VDAC1 的表达分布与手术切除后患者的生存期相关。**方法：**从公共的数据库（NCBI GEO）中获得 NSCLC 基因表达信息库，包括 10 个独立的数据组（n=618 样本）。VDAC1 表达分布被分配到 tertiles，然后进行单变量的 Logrank 及多变量的 Cox 生存情况分析。用 R 和 TMev 进行分析。所有数据的 p 值都根据方法的假阳性比例计算 q 值以进行复杂比较的校正。在数据库中至少认为 50%以上病例出现基因是有显著意义的，这些基因确定下来后产生一个 meta 标记，组成持续、有差别表达的和 VDAC1 相关的基因。**结果：**在一个组合的单变量分析中，VDAC1 过度表达提示更差的整体生存率（OS）52 月 vs101.6 months (m)，p=0.0323.Cox 回归分析提示 VDAC1 表达是一个非独立危险因素(p<0.0001), 和分期相关(p<0.0001)，但是和年龄或性别无关。I 期患者 VDAC1 低表达者生存情况要好的多，H R 0.52 (C.I. 0.31 - 0.82).数据库中 20%以上样本中 VDAC1 的过度表达都受一个 41 个基因组成的亚型明显及始终差异性的调节控制。其中有 6 个基因>50%：CSNK1A1, G3BP1, HNRNPC, HSPA4, HSPA9 及 UBE2D2,都是上调基因。HNRNPC, HSPA4, HSPA9 和 UBE2D2 包含在蛋白质遍在蛋白化途径中，CSNK1A1 调节 EIF2 的功能. HSPA9 也包含在抗凋亡途径中，而 G3BP1 和 Ras 蛋白质信号传到途径相连接。**结论：**1 型电压

依赖的阴离子通道（VDAC1）的过度表达与手术切除后 NSCLC 生存期短相关，尤其在 I 期患者中。而且，VDAC1 和那些调节蛋白质遍在蛋白化、细胞凋亡及 EIF2 功能蛋白质的基因之间的关系提示在侵袭性更大的 NSCLC 中这些过程可能起到一定作用，可能会反映一些潜在的分子治疗途径。

7032 Use of serum autoantibodies to identify early-stage lung cancer

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Abstract:

Background: EarlyCDT-Lung measures autoantibodies to a panel of six cancer-associated antigens (p53, NY-ESO1, CAGE, GBU4-5, Annexin1, and SOX2) with a specificity of 90% and a sensitivity of 45% for small cell lung cancer (SCLC) and 34% for non-small cell lung cancer (NSCLC). We report confirmatory data for clinical sensitivity and specificity determined in an independent, prospective, post-validation dataset. **Methods:** Four hundred and fifty three (453) patients with newly diagnosed, untreated lung cancer were matched for age, sex, and smoking history to high-risk individuals. Patient and control samples were collected from multiple locations in the USA, Canada, and Europe and measured on EarlyCDT-Lung. 258/359 (72%) of NSCLC were known early-stage disease (ie stage 1 or 2), 10/28 (36%) of SCLC were limited disease, and 66 were unknown stage. A larger series of 211 SCLC patients with matched high-risk controls obtained from a single European center

was measured for autoantibodies to the same six cancer-associated antigens (Oncimmune Ltd, Nottingham, UK). **Results:** In the multicentre group (n=453), for early-stage disease the positivity rate was 35% (89/258) for NSCLC and 40% (4/10) for SCLC. In the single center SCLC dataset (n=211) the positivity rate for limited disease was 47% (41/87). Combining both groups (n=664 lung cancers) gave an overall positivity of 40% of lung cancers. For early-stage disease, the positivity rate was 35% (89/258) of NSCLC and 46% (45/97) for SCLC. Overall specificity for all high-risk individuals (n=1,029) was 88%. **Conclusions:** This large dataset further confirms that up to 40% of lung cancer, including early-stage disease, can be identified through a blood test. EarlyCDT-Lung and CT scanning have the potential for early detection of a large subset of lung-cancers.

7032 译文 利用血清自身抗体诊断早期肺癌

摘要

背景：早期 CDT-Lung 通过 1 个含六个癌症相关的抗原（p53，NY-ES01、CAGE、GBU4-5、Annexin1 及 SOX2）的试剂盒来测定自身抗体，发现在小细胞肺癌（SCLC）中特异性为 90%，敏感性为 45%，NSCLC 中位 34%。本文报告来自一个独立、前瞻性、经验证有效的数据组的关于其临床敏感性及特异性的确实数据。**方法：**453 例新诊断、未治疗的肺癌患者行年龄、性别、高危患者的吸烟史等的匹配。患者及对照组样本来自 USA、加拿大、欧洲等不同地区，测定其早期 CDT-Lung。258/359（72%）名 NSCLC 患者处于早期（1 或 2 期），10/28（36%）名 SCLC 为局限性疾病，66 名患者分期未知。一个欧洲中心有 1 组 211 名 SCLC 患者及相匹配的 211 名高风险对照也都进行了这 6 个癌症相关抗原的自身抗体检测（Oncimmune Ltd, Nottingham, UK)。**结果：**在这个多中心的人群中（n=453），早期的 NSCLC 患者中阳性率为 35%（89/258），SCLC 为 40%（4/10）。在单中心的 SCLC 数据（n=211），局限期疾病的阳性率为 47%（41/87）。两组综合起来（n=664 肺癌），肺癌患者中总的阳性率为 40%；早期疾病中，NSCLC 的阳性率为 35%（89/258），SCLC 为 46%（45/97）。对于所有高风险个体（n=1029）其总体特异性为 88%。**结论：**这个巨大的数据结果进一步证实在高至 40%的肺癌患者，包括早期患者，可以通过血液检查来证实。早期 CDT-Lung 和 CT 扫描也许可以作为很大一部分肺癌的早期诊断手段。

7033 Demographics of populations at high risk of lung cancer and results of the Early CDT-Lung test

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Abstract:

Background: EarlyCDT-Lung measures autoantibodies (AABs) to six cancer-associated antigens (p53, NY- ESO-1, CAGE, GBU4-5, Annexin1, and SOX2) and has been reported to identify up to 40% of lung cancers, both early- and late-stage disease. **Methods:** Prospective blood collections (with individual questionnaires) were carried out in three different community-based locations in two countries (US, two sites; UK, one site) in order to assess demographic features of high-risk populations. Some demographic features were not recorded at all sites. For the statistical comparisons, analysis of variance was generally used, taking into account imbalance in subgroup numbers, unevaluable data and multiplicity of testing, where necessary, and with sample-matching, where appropriate. **Results:** Unmatched Datasets: from separate analyses of the US (Florida n=320, Midwest n=940) and UK (n=2046) datasets there was no difference for any of the AAB assays between (i) males and females, (ii) the main ethnic groups (US only) for participants in samples collected in Florida and the Midwest, and (iii) the presence or absence of benign autoimmune diseases (UK data only). There was evidence for an effect of age for some antigens, with mean AAB levels rising with age (especially >70yrs). This may be confounded by the fact that the incidence of cancer also

increases with age. Further investigation is required. Matched Datasets: for sets of samples matched for age, sex, and smoking, there was no significant difference for any autoantibody assay between (i) US (n=353) and UK (n=353) high-risk individuals and (ii) within US (Florida, n=275 and Midwest, n=275) samples. **Conclusions:** Within a high risk population the demographic features described above should not be used to exclude individuals from AAB testing as an aid to early detection of lung cancer.

7033 译文 肺癌高危人群的人口统计学研究和早期 CDT 肺测试的结果

摘要

背景：早期 CDT-Lung 测定 6 种癌相关抗原(p53, NY- ESO-1, CAGE, GBU4-5, Annexin1, and SOX2)的自身抗体（AABs），有报道称其可鉴定 40%的肺癌，不管是早期的还是晚期的。**方法：**在两个国家的三个不同地区（US 两个地点，UK 一个地点）前瞻性收集高风险人群的血液标本（同时行个人问卷调查），评估其高风险人群的人口统计学特点。有些人口统计学特点的数据缺失。统计学比较方面，广泛利用方差分析，并将亚群之间的不平衡、不可评估的数据及多样化的测试都考虑在内，在必要且合适的地方行样本匹配。**结果：**不匹配的数据集：从 US（Florida n=320，Midwest n=940）及 UK（n=2046）各自分离的分析结果看，AAB 测定并不随以下因素而变化：i）男性和女性，ii）在 Florida 和 Midwest 收集的标本之间的主要种族差别（来自 US 的数据）；iii）是否存在良性自身免疫病（仅来自 UK 数据）。证据提示有些抗原受年龄影响，平均 AAB 水平随着年龄增加而升高（尤其是>70 岁者）。这个结果可能会引起人们困惑，因为肿瘤的发生本身也是随着年龄增加而增加的。尚需要进一步的观察。匹配的数据：对于年龄、性别、吸烟史等均匹配过的样本集，在 US（n=353）和 UK（n=353）的高风险人群之间以及 US 内不同地区（Florida，n=275，Midwest，n=275）之间并没有在自身抗体的测定中发现显著差异。**结论：**在高风险人群中前面描述的人口统计学特点不应用于将某些个体排除在以 AAB 测定预测早期肺癌的人群之外。

7034 Postoperative survivin expression in stage III non-small cell lung cancer (NSCLC) patients treated with neoadjuvant chemoradiation

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Abstract:

Background: In a previous report, high pretreatment survivin was associated with poor prognosis and low pretreatment survivin was associated with pathological complete response (pCR) in stage III NSCLC patients treated with neoadjuvant chemoradiation (Fidler et al ASCO 2009). The objective of this study was to compare survivin expression in pretreatment tissue with expression in post-treatment in patients with residual tumor after neoadjuvant chemoradiation. **Methods:** Stage III patients who underwent neoadjuvant platinum based chemoradiation (40Gy) with sufficient pretreatment tissue available were identified. Patients with less than a pathological CR were selected for analysis. Tumors were stained for nuclear and cytoplasmic expression of suvivin (frequency 0-4 and intensity 0-4) by Immunohistochemistry (IHC) (Novus Biologicals). Data was analyzed using the McNemar's test. **Results:** 33 patients who underwent neoadjuvant chemoradiation had pretreatment tissue with adequate tumor specimens for analysis. 19 patients had available tumor remaining in pathological specimens after definitive resection. Patient characteristics: 10 females, median age 61.4; 11 adenocarcinoma, 6 squamous. For these 19 patients, median OS: 20.0 months, median time to recurrence: 11.7 months. Residual tumors had increased cytoplasmic survivin intensity compared with the same patients' pretreatment specimens (p=0.013). **Conclusions:** In this small sample size, residual tumor had increased cytoplasmic survivin expression compared with pretreatment tissue specimens suggesting that survivin may be a mechanism for resistance to chemoradiation. Adding agents that target survivin to chemoradiation is a

reasonable strategy to improve outcomes in locally advanced NSCLC. These results require validation in a larger number of patients.

7034 译文 接受新辅助放化疗治疗的 III 期 NSCLC 患者术后生存素的表达

摘要

背景：以前曾有报道发现，在接受过新辅助放化疗治疗的 III 期 NSCLC 患者中，治疗前的高生存素和预后差相关，低生存素和病理学完全缓解（pCR）相关 (Fidler et al ASCO 2009)。本研究的目的是比较治疗前组织的生存素表达及新辅助放化疗后仍有残存肿瘤的患者治疗后的生存素表达情况。**方法：**测定那些接受过以铂为基础的新辅助放化疗(40Gy)且治疗前组织样本充足的III期患者。选择那些病理学未达到CR的患者进行分析。通过免疫组化（IHC）测定肿瘤组织细胞核及胞浆内生存素的表达（频率 0-4，强度 0-4）。使用 McNemar’s 测试进行数据分析。**结果：**33 名接受了新辅助放化疗且治疗前组织标本足够的患者参加了分析。其中 19 名患者在手术切除后发现仍有肿瘤组织残余。患者特点：10 名女性，平均年龄 61.4；11 名为腺癌，6 名鳞癌。这 19 名患者中位 OS 为 20 月，复发中位时间为 11.7 月。和同一患者的治疗前标本相比，残余的肿瘤组织细胞浆内生存素的强度增加（p=0.013）。**结论：**在这个小样本的试验中，残存的肿瘤组织细胞浆生存素的表达比治疗前组织样本增强，提示生存素可能和对放化疗抵抗的的机制相关。在局部进展的 NSCLC 行放化疗是增加针对生存素的药物是一个合理的治疗策略，有助于提高疗效。这些结果需要在大样本的患者群中进行验证。

7044 Phase II trial of consolidation chest radiotherapy for extensive-stage small cell lung cancer

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Abstract

Background: A recent randomized trial demonstrated the local control and overall survival benefits of radiotherapy (RT) given to a common recurrence region (brain) for extensive stage small cell lung cancer (ES-SCLC) patients who respond to chemotherapy. The chest is another common post-chemotherapy recurrence area in ES-SCLC, with historical post-chemotherapy chest failure rates exceeding 50%, many of which cause distressing symptoms which negatively impact patients' quality of life and/or hasten death. The purpose of this trial is to define the effect of post- chemotherapy chest RT for ES-SCLC on rate of development of symptomatic chest failures. **Methods:** Eligible patients had biopsy-proven ES- SCLC, attained an objective radiologic disease response after receiving at least one chemotherapy cycle and signed study consent. Target accrual was 33 patients. Study patients were also offered prophylactic cranial irradiation (PCI). PCI and chest RT were given simultaneously 4-6 weeks after chemotherapy completion. Three dimensional conformal techniques were used to plan thoracic RT and the target volume was the post-chemotherapy residual chest disease plus margin. PCI dose was 25 Gy/10 daily fractions. Chest RT dose was 40 Gy/ 15 daily fractions. Patients were followed during and after RT for toxicity, local control, disease-free and overall survival. **Results:** 32 of 33 accrued patients were evaluable. All but three patients completed RT with no delays. One patient received 1 chemotherapy

cycle, three received 3 cycles and 28 received 4 cycles. There were 4 complete responses and 28 partial responses to chemotherapy. Maximal acute RT toxicity was grade 2 esophagitis (18 patients). There were no treatment-related deaths. With a median follow-up of 7.8 months, the median time to disease progression was 8.1 months. Median survival has not been reached. There have been 11 chest recurrences, 6 in the irradiated region and 4 being symptomatic. There have been 13 distant-only failures and 6 combined distant/chest failures. **Conclusions:** Our data suggests post-chemotherapy consolidation chest RT for ES-SCLC patients who respond to chemotherapy is well- tolerated and decreases chest failure rates compared to historical data.

7044 译文 广泛期小细胞肺癌胸部巩固放疗的 II 期临床试验

摘要

背景：最近有一个随机试验证实化疗有效的广泛期小细胞肺癌患者接受最常见的转移部位颅脑的预防性放疗放疗可以使局部控制和总生存受益。胸部是化疗后另一个常见复发部位，回顾性资料证实化疗后胸部复发率超过 50%，引起了患者生活质量的降低和死亡的加速等。这个试验的目的是为了确认广泛期小细胞肺癌化疗后的给予胸部放疗对于胸部复发后症状发展速度的影响。**方法：**入选的患者是经过活检证实为广泛期的小细胞肺癌，在接受至少一个周期化疗后影像学证实有效的患者，并签署了知情同意。准备入组 33 例患者。研究也为患者提供了预防性头颅照射（PCI）。PCI 和胸部放疗在化疗完成后同步进行。试验使用三维适形成像技术设计胸部放疗，目标体积是化疗后残余的胸部病灶及周边。PCI 剂量是 25Gy/10，每日 1 次。胸部放疗的剂量是 40Gy/15，每日 1 次。对患者在接受放疗期间和放疗后的毒性反应，局部控制情况，疾病进展和总生存进行随访。**结果：**33 例患者中 32 例可以评估。除了 3 例患者外，所有患者都按时完成了放疗。1 例患者接受了 1 个周期化疗，3 例接受了 3 个周期化疗，28 例接受了 4 个周期化疗。其中 4 例患者获得了完全缓解，28 例患者获得部分缓解。最常见的急性放疗毒性反应是 2 度的放射性食管炎（18 例）。没有发生治疗相关的死亡。中位随访时间为 7.8 个月，中位疾病进展时间(TTP)为 8.1 个月。中位生存尚未随访到。有 11 例患者出现胸部复发，其中 6 例出现在受照射区域其中 4 例有症状。13 例出现只有远处的转移，6 例出现了远

处/胸部的联合复发。**结论：**我们的数据提示对化疗有效的广泛期小细胞肺癌患者化疗后胸部巩固放疗耐受性良好，与历史数据相比有更低的胸部复发率。

7045 Pretreatment positron emission tomography (PET) scan standardized uptake value (SUV) as a prognostic variable for overall survival in limited-stage small cell lung cancer (L-SCLC)

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Abstract

Background: PET imaging has been increasingly utilized in L-SCLC. However, the prognostic value of the staging SUV has not been well elucidated. **Methods:** From 1/2004-12/2008, 59 patients with L-SCLC were treated with definitive chemoradiation at M. D. Anderson Cancer Center and received a pretreatment staging PET scan. The median radiation therapy (RT) dose was 45 Gy in 30 fractions delivered twice daily (range 40.5-61.8 Gy). Thirty two percent of patients (n = 19) underwent induction chemotherapy, though all initial PET scans were taken prior to any treatment. The median value for the maximum SUV of the primary lesion (pSUVmax) was 12.0 (range 1.3-34.6), and for the nodal disease (nSUVmax) it was 11.5 (range 3.1-35.5). Twenty eight percent of patients had assessable follow-up PET imaging within one year of completing treatment. Overall survival (OS) was measured from the end of RT to the date of death or, if not documented, the last follow-up at our institution. Kaplan-Meier analysis was utilized to determine 1, 2, and 3-year estimates of OS. Univariate analysis was then performed to evaluate the effect of pSUVmax and

nSUVmax on OS. **Results:** The median change in pSUVmax after treatment was -63% (range +21 to -90%). At a median follow-up of 16.4 months (range 2.9-68.5 months), 1-, 2-, and 3-year rates of OS were 74%, 60%, and 46%, respectively. On univariate analysis, a pSUVmax of > 13 was of borderline significance (p = 0.05), and a pSUVmax of >14 was statistically significant as a prognostic factor for OS (p < 0.05). A higher pSUVmax was correlated with an improved survival up to a level of 18. At pSUVmax>18, small patient numbers limited analysis. Initial nSUVmax did not correlate with OS. **Conclusions:** Most patients who receive definitive chemotherapy and RT for L-SCLC experience marked PET scan responses. Unexpectedly, a higher initial pSUVmax was associated with better OS. This finding could be due to improved outcomes with accelerated RT in high-SUV patients, such that there is a more beneficial fractionation for patients with low SUVmax levels in L-SCLC. Individualized treatment may be indicated based on pretreatment SUV.

7045 译文 治疗前 PET 扫描的标准摄取值（SUV）作为局限期小细胞肺癌总生存（OS）的预后变量

摘要

背景：PET 成像在小细胞肺癌中的应用越来越广泛。然而，SUV 分期的预后价值并没有被很好的阐明。**方法：**从 2004 年 1 月到 2008 年 12 月，59 例局限性小细胞肺癌患者在 M.D. Anderson 癌症中心接受了计划的放化疗，并且都接受了治疗前的 PET 扫描分期。中位放疗剂量为 45Gy/30，每日 2 次（从 40.5-61.8Gy）。虽然所有最初的 PET 扫描在任何治疗前就已经完成，但是仍有 32%的患者（n=19）接受了诱导化疗。原发病灶的最大 SUV 值（pSUVmax）的中位数为 12.0（1.3—34.6），结节病灶的最大 SUV 值（nSUVmax）的中位数为 11.5（3.1—35.5）。28%的患者在完成 1 年的治疗期间接受了可评估的 PET 成像的随访。总生存（OS）从结束放疗到死亡日期，如果没有记录，就从我们机构的最后一次随访来判断。Kaplan-Meier 分析用来确定 1,2,3 年 OS 的评估。单变量分析用来评估 pSUVmax 和 nSUVmax 对 OS 的影响。**结果：**pSUVmax 在治疗后的中位变化为-63%（+21%到-90%）。在 16.4 个月的中位随访期中（2.9-68.5 个月），1,2,3 年的总生存率分别为 74%，60%，46%。在单变量分析中，pSUVmax>13 是有意义的界限（p=0.05），pSUVmax>14 时 pSUVmax 作为影响 OS 的预后因素具有统计学意义。到 18 为止，更高

的 pSUVmax 与生存的改善相关。pSUVmax>18 时，由于患者数太小因此无法分析。最初的 nSUVmax 与 OS 不相关。**结论**：大多数局限性小细胞肺癌接受计划的放化疗的患者经过了 PET 扫描的标记。意外的是，更高的初始 pSUVmax 与更好的 OS 相关。这个发现可能会加速放疗在高 SUV 患者中的进行，区分出低 SUVmax 水平的局限期小细胞肺癌患者。个体化治疗可能会基于治疗前的 SUV 值进行。

7046 A phase IIa study of ABT-263 in patients with relapsed small-cell lung cancer (SCLC)

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Abstract:

Background: ABT-263, a novel BH3 mimetic, binds with high affinity (Ki ≤ 1 nM) and inhibits multiple antiapoptotic Bcl-2 proteins. SCLC is an aggressive cancer, which constitutes nearly 15% of all lung neoplasms in the United States and has few effective treatment options after first-line therapy. SCLC tumors frequently overexpress Bcl-2. Results from a phase I trial showed that single-agent ABT-263 was well tolerated and had activity in previously treated patients (pts) with SCLC and other neuroendocrine carcinomas. **Methods:** This is an open-label, multicenter phase IIa trial assessing safety and preliminary efficacy of ABT-263 in pts with extensive-stage SCLC. ABT-263 was dosed orally at 325 mg once daily,

following a 7-day lead-in dose of 150 mg, on a 21-day cycle until progressive disease (PD) or intolerable toxicity. Key eligibility criteria included measurable SCLC and ECOG status ≤ 1. Endpoints include tumor response by RECIST, progression-free survival, time to progression, overall survival, and ECOG performance status. Tumor assessments were performed at the end of every 2 cycles. Adverse events (AE) were graded by NCI CTCAE V3. **Results:** 39 pts were enrolled from 06/09 to 12/09; 21 discontinued due to PD and 4 withdrew consent. 14 remain on study (4 with stable disease). Median time on study was 49 days (35, NA). 6 pts had dose reductions due to AEs and 11 had serious AE (SAE, Table). The most common AEs were diarrhea (43%), back pain (43%), and thrombocytopenia (TCP; 29%). The most common grade 3/4 AE was TCP (29%). 4 pts had dose interruptions due to AEs. **Conclusions:** Preliminary results from this phase II study show that ABT-263 has an acceptable safety profile. SCLC antitumor activity was noted in the phase I portion of the study and the evaluation of tumor response is ongoing in the phase II portion. Updated results of this ongoing study will be presented.

Patients	**SAE**
401	Obstruction right mainstem bronchus
	Metastatic SCLC
402	Neutropenic fever
	Dehydration
	Hypotension
406	Shortness of breath
407	Bone metastasis
	PD
410	Death
411	Neutropenic fever
413	Volume depletion
	Vomiting-dehydration
414	Pneumonia

Patients	SAE
417	Hyponatremia
	Constipation
428	PD
429	Pleural effusion
	Anemia

7046 译文 ABT-263 治疗复发性小细胞肺癌患者的 IIa 期研究

摘要

背景：ABT-263，是一种新的 BH3 的类似物，与多种抗凋亡 Bcl-2 蛋白具有很高的亲和性（Ki≤1nM）并具有抑制多种抗凋亡 Bcl-2 蛋白的作用。小细胞肺癌是一种侵袭性的癌症，在美国占肺部肿瘤的 15%，在一线治疗后缺乏有效的治疗手段。小细胞肺癌的肿瘤细胞通常过度表达 Bcl-2。I 期试验结果显示单臂 ABT-263 耐受性良好，对以前接受过治疗的小细胞肺癌和其他神经内分泌癌的患者具有一定的作用。**方法：**这是一个开放的、多中心的，主要评估 ABT-263 治疗广泛期小细胞肺癌患者的安全性和初步疗效的 IIa 期试验。ABT-263 的剂量定为经过 150mg 口服每天一次，一周的引导后，继续 325mg 口服，每天一次，直到疾病进展或出现不能耐受的毒性反应为止，21 天为一周期。主要的入选标准包括可确定的小细胞肺癌和 ECOG 状态≤1 分。终点包括 RECIST 标准可评价的肿瘤疗效，PFS，TTP，OS 和 ECOG 状态。每两个周期进行一次肿瘤评估。不良事件（AE）用 NCI CTCAE V3 进行分度。**结果：**在 09 年 6 月至 09 年 12 月间收集了 39 例患者，21 例因为疾病进展没有继续接受试验，4 例退出试验。14 例继续了研究（4 例疾病稳定）。中位研究时间为 49 天（35，NA）。6 例患者因为不良事件药物减量，11 例发生了严重的不良事件（SAE，见表）。最常见的不良事件是腹泻（43%），背痛（43%），和血小板减少（TCP，29%）。最常见的 3/4 度的不良事件是血小板减少（29%）。4 例患者因为不良事件停药。**结论：**II 期研究的初步结果显示 ABT-263 有可接受的安全性。在 I 期试验中已注意到了对小细胞肺癌的抗癌活性，关于抗肿瘤疗效情况正在 II 期试验中进行。最新的研究结果将会在不久后公布。

患者	严重不良事件
401	右主支气管阻塞
	小细胞肺癌转移
402	中性粒白细胞减少引起发热
	脱水
	低血压
406	呼吸急促
407	骨转移
	病灶进展
410	死亡
411	中性粒白细胞减少引起发热
413	血容量不足
	呕吐引起脱水
414	肺炎
417	低钠血症
	便秘
428	病灶进展
429	胸腔积液
	贫血

7047 Should large cell neuroendocrine carcinoma of the lung (LNEC) be classified and treated as a small cell lung cancer (SCLC) or with other large cell carcinomas (OLC)?

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Abstract:

Background: To compare the presenting and prognostic characteristics, cause-specific survival (CSS) rates, and overall survival (OS) rates of patients with LNEC to those with SCLC or OLC, particularly those undergoing definitive resection without radiotherapy (S-NoRT). **Methods:** The Surveillance Epidemiology and End Results Database (SEER-17) from 2000-2006 was used. Differences between population characteristics were compared using chi-square and Kruskal-Wallis tests. The logrank test was used to compare differences in OS and CSS. **Results:** There were 1001 pts with LNEC (281 in the S-NoRT group), 9,417 patients with OLC (1212 S-noRT), and 35,047 SCLC patients (414 S-noRT). Patients with SCLC were more likely to be female, white non-Hispanic, and present with stage IV disease than patients with LNEC or OLC. Among S-no RT, those with SCLC were more likely to have nodal and mainstem bronchus involvement and to undergo a sublobar resection than patients with LNEC or OLC. Median follow-up in the S-noRT patients was 14 months (range, 3-83 months). OS and CSS of SCLC patients were significantly worse than that for patients with either LNEC or OLC. Multivariate analysis showed that OS was significantly affected by age, sex, stage, number of nodes resected or positive, and tumor size. When restricted to patients with stages T1A-BN0, CSS and OS remained worse in the SCLC group than the other groups. **Conclusions:** Presenting characteristics and survival of patients with LNEC are more similar to that of OLC than SCLC. Our results confirm patients with LNEC should be classified and treated as OLC.

7047 译文 肺部大细胞神经内分泌癌（LNEC）应该像小细胞肺癌（SCLC）还是其他大细胞肺癌（OLC）那样分类和治疗？

摘要

背景：为了对比肺部大细胞神经内分泌癌（LNEC）患者和小细胞肺癌（SCLC）及其他大细胞肺癌（OLC）患者当前和预后特点，病因特异性生存（CSS）率和总生存率（OS）之间的区别，特别是那些没有经过放疗就进行手术切除的患者（S-NoRT）。**方法：**使用监测流行病学和最终结果数据库(SEER-17)。人群特点之间的区别通过卡方(chi-square)和克鲁斯卡尔-瓦利斯二氏检验（Kruskal-Wallis tests）进行对比。OS 和 CSS 之间的区别通过对数秩和检验（logrank test）来区分。**结果：**研究收集了 1001 例 LNEC 患者（其中 281 例是 S-NoRT 类型），9417 例 OLC 患者（1212S-NoRT），35047 例小细胞肺癌患者（414S-NoRT）。小细胞肺癌患者比 LNEC 患者和 OLC 患者更可能在女性，非西班牙裔的白色人种中发生，更容易发展到疾病Ⅳ期。在 S-NoRT 类型中，小细胞肺癌患者比 LNEC 和 OLC 患者更可能有结节性病灶和主支气管受累，更可能要进行亚叶段切除。S-NoRT 患者的中位随访时间为 14 个月（3-83 个月）。小细胞肺癌的患者的 OS 和 CSS 明显比 LNEC 患者和 OLC 患者差。多因素分析显示 OS 受到年龄、性别、肿瘤分期、淋巴结切除或是阳性的数量、肿瘤大小的显著影响。把患者限制在 T1a-b，N0 范围内，小细胞肺癌患者的 CSS 和 OS 依旧比其他两种肺癌的患者更差。**结论：**LNEC 患者的表现特点和生存相比小细胞肺癌与 OLC 更像。我们的结果证实 LNEC 患者应该类似 OLC 这样来分类和治疗。

7048 Sabarubicin (SABA) in combination with cisplatin (DDP): Maximum tolerated dose (MTD) evaluation (phase I step) followed by a phase II step in patients (pts) with small cell lung cancer-extensive disease (SCLC-ED)

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Abstract:

Background: SABA, a 3rd generation anthracycline with promising activity as single agent in solid tumors was evaluated to establish the MTD in combination with DDP (phase I), followed by a phase II evaluating SABA + DDP as first line therapy in SCLC-ED pts. **Methods:** In phase I, MTD was evaluated with ascending SABA doses of 40, 60, 80 and then 10 mg/m2 increments (day 1) together with a fixed dose of DDP 80 mg/m2 (day 2) in pts with solid tumors. In phase II, SABA 80 mg/m2 and DDP 80 mg/m2 iv q21 days for 6 cycles were primarily assessed for complete or partial response (CR/PR); secondarily for overall survival (OS), duration of tumor response (DTR), time to progression (TTP), and safety in chemotherapy-naive SCLC-ED pts. **Results:** Phase I recruited 17 pts. Best response was PR in 3 (23.1%) pts. Dose-limiting toxicity occurred in 2 of 5 pts at SABA 90 mg/m2, i.e. grade (G) 4 thrombocytopenia and G 4 neutropenia associated with G 3 pyrexia. MTD for phase II was 80 mg/m2. In phase II 17 males, 8 females with SCLC-ED (mean age 63 years) were enrolled. One (4%) pt was excluded from the efficacy population for a delay of study therapy for non-medical reasons. Nineteen (79.2%) pts achieved CR (1; 4.2%) or PR (18; 75%), 4 (16.7%) SD, and 1 (4.2%) progressed. Median OS, DTR and TTP were 11.6, 3.8 and 6.5 months, respectively. In phase II treatment-related AEs referred mainly to the gastrointestinal (69 AEs in 21 (84%) pts) or hematological system (84 AEs in 19 (76%) pts). Premature study discontinuation occurred in 7 (28%) pts due to 8 AEs. In 13 (52%) pts 20 G 4 related AEs were reported, 18 of 20 were blood/lymphatic system. In total, 2 cardiac SAEs occurred: 1/42

(2.4%) G 2 heart failure and 1 G 2 (2.4%) tachycardia. No clinically significant signals were detected in laboratory and physical evaluation, ECG and echocardiography. Fatal AEs with a suspected relationship to SABA + DDP occurred at the lowest SABA dose (40 mg/m²) in phase I and in phase II (80 mg/m2) in one pt each. **Conclusions:** SABA in combination with 80 mg/m2 DDP reached MTD at 80 mg/m2. SABA + DDP were effective and safe as first line treatment in SCLC-ED, which appears comparable to standard regimens.

7048 译文 沙柔比星(SABA)联合顺铂：最大耐受剂量（MTD）评估（I 期试验）后治疗广泛期小细胞肺癌的 II 期试验

摘要

背景：沙柔比星(SABA),是第 3 代蒽环类抗生素在和顺铂联合治疗实体肿瘤中的最大耐受剂量作为一个单一因素已经经过评估（I期），接着对SABA联合顺铂一线治疗广泛期小细胞肺癌患者的评估进行了II期的试验。**方法：**在I期试验中，通过使用逐渐增加的SABA剂量 40,60,80 然后 10mg/m^{2}增量（第 1 天）联合顺铂 80mg/m2（第 2 天）治疗实体肿瘤的患者来评估SABA的最大耐受剂量。在II期试验中，每个周期SABA 80mg/m^2，顺铂 80mg/m^{2}静脉注射，每 21 天为 1 周期，总共 6 个周期，主要是对完全或部分缓解（CR/PR）进行评估；其次是总生存（OS）、肿瘤起效时间（DTR）、进展时间(TTP)和已经接受过化疗的广泛期小细胞肺癌患者的安全性进行评估。**结果：**I期收集了 17 例患者。最好疗效是部分缓解（PR），一共有 3 例患者（23.1%）。5 例接受SABA 90mg/m^{2}中有 2 例发生剂量限制毒性，即 4 度的血小板减少，4 度的中性粒细胞减少伴 3 度发热。II期试验的MTD确立为 80mg/m^2。在II期试验的 17 例男性中，8 例广泛期小细胞肺癌（平均年龄 63 岁）入组。1 例患者（4%）因为非医疗原因延迟治疗而出组。19 例患者（79.2%）达到了CR（1,4.2%）或PR（18,75%），4 例（16.7%）SD，1 例（4.2%）PD。中位OS、DTR、TTP分别为 11.6，3.8 和 6.5 个月。II期治疗相关性不良事件主要涉及胃肠道（在 21 例患者(84%)中共有 69 次不良事件)和血液系统(19 例患者(76%)共有 84 次不良事件)。不完善研究的中断导致了 7 例（28%）患者的 8 次不良事件。在 13 例患者（52%）中 20 次 4 度的相关不良事件被报道，20 次中 18 次都发生于血液或淋巴系统。整体研究人群中，2 例发生心脏严重不良事件：1/42（2.4%）2 度心衰和 1 例（2.4%）2 度心动过速。没有发现临床上有意义的实验室和体格检查、ECG和超声心动异常。致死性的不良事件

与SABA+顺铂治疗可疑有关，分别发生于 1 例I期试验SABA最低剂量（40mg/m2）组和 1 例II期试验（80mg/m2）组。**结论：**SABA联合 80mg/m^2顺铂的最大耐受剂量可以到 80mg/m^2。SABA+DDP作为一线治疗与标准方案相比在广泛期小细胞肺癌的治疗中是安全有效的。

7049 Phase II study of irinotecan and carboplatin followed by maintenance sunitinib in the first-line treatment of extensive-stage small cell lung cancer

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Abstract:

Background: Angiogenesis contributes to tumor growth in small-cell lung cancer (SCLC). Inhibiting angiogenesis may be one strategy to delay disease progression in patients who have received initial platinum-doublet chemotherapy. This phase II study investigated the use of maintenance sunitinib following first-line irinotecan and carboplatin in patients with extensive stage SCLC. **Methods:** Eligible patients were aged > 18 years, had previously untreated extensive-stage SCLC, ECOG PS 0 or 1; adequate organ function; and no active brain metastasis. Patients received up to 6 cycles of irinotecan 60 mg/m2 on days 1, 8, and 15, and carboplatin AUC=4 on day 1; cycles were repeated every 28 days. Patients were reevaluated for response every 8 weeks. All patients without progression or intolerable toxicity continued on single- agent sunitinib 25 mg orally daily until progression. The primary endpoint was 1-year overall survival. **Results:** 34 patients were enrolled between 2/09 and 10/09. Baseline

characteristics included: median age 65 years (range, 41-80); male, 53%; and ECOG 0, 44%. A median of 3 cycles of irinotecan/carboplatin were given; 4 patients (12%) received maintenance sunitinib for a median of 4 weeks (range: 4-8+). After a median follow-up of 25 weeks (range: 9-42), 31 patients remain alive, and 4 are continuing sunitinib. The objective response rate with chemotherapy was 47% (95% CI 30-65), and an additional 38% had stable disease. The median time-to- progression (TTP) was 7.6 months. The 6-month overall survival was 91% (additional time is required before 1 year OS can be assessed). No grade 3/4 toxicities have been observed in the 4 patients who have received sunitinib. **Conclusions:** In this phase II trial, maintenance sunitinib was well-tolerated following platinum doublet chemotherapy as first-line treatment for extensive-stage SCLC. Early assessment of activity is encouraging, however additional follow-up is required

7049 译文 广泛期小细胞肺癌一线伊立替康和卡铂治疗后舒尼替尼维持治疗的 II 期试验

摘要

背景：新生血管在小细胞肺癌的生长中有重要作用。在接受初级铂类二联化疗的患者中，抑制血管生成可能是一个延迟疾病发展的策略。这个II期试验是研究广泛期小细胞肺癌一线使用伊立替康和卡铂治疗后舒尼替尼维持治疗。**方法：**入选患者的年龄>18 岁，患有未经治疗的广泛期小细胞肺癌，ECOG PS 0 或 1；器官功能良好；没有症状的脑部转移。患者 6 个周期的治疗，每个周期的 1,8,15 天使用 60mg/m^2的伊立替康，每个周期的第 1 天使用卡铂AUC=4；28 天为一周期。每 8 周对患者的疗效进行重新评估。所有没有进展和可以耐受毒性的患者以舒尼替尼单药继续每天口服直到肿瘤进展。主要的终点是 1 年总生存。**结果：**从 09 年 2 月到 09 年 10 月总共入组了 34 例患者。基本特征包括：中位年龄 65 岁（41—80 岁）；男性，53%，ECOG 0：44%。中位治疗为 3 个周期的伊立替康和卡铂联合治疗；4 例患者（12%）接受舒尼替尼的维持治疗，中位时间为 4 周（4—8 周余）。在中位 25 周的随访期（9-42 周）内，31 例患者仍存活，4 例持续服用舒尼替尼。化疗的客观有效率为 47%（95% CI，30-65），另外有 38%患者疾病稳定。中位进展时间（TTP）为 7.6 个月。6 个月总生存率为 91%（1 年生存评估之前必须附加的时间）。在观察的 4 例接受舒尼替尼的患者中，没有发现 3/4 级的毒性反应。**结论：**在II期试验中，在经过铂类二联一线治疗的广泛期小细胞肺癌患者中，舒尼替尼维持治疗的

耐受性良好。早期的活性评价是鼓舞人心的，然而需要进一步的随访。

7050 Phase I open-label study of cediranib plus etoposide (E) and cisplatin (P) as first-line therapy for patients (pts) with small cell lung cancer (SCLC) or lung neuroendocrine cancer (NEC)

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Abstract:

Background: Cediranib is an oral, highly potent inhibitor of VEGF signaling with additional activity versus c- Kit. This study assessed cediranib plus EP as first-line therapy for extensive stage/metastatic lung cancer. **Methods**: Pts received up to six 21-day cycles of EP (E 100 mg/m2, days 1-3; P 80 mg/m2, day 1) with once-daily cediranib from day 4 of cycle 1 until disease progression or toxicity and were eligible for safety review if they completed the first 21 days of cediranib or had a dose limiting toxicity (DLT). The primary objective was assessment of safety and tolerability. If < 33% pts in a cohort experienced a DLT the dose was deemed tolerable and 12 additional pts recruited to an expanded cohort. **Results:** At data cut-off (Aug 09), 22 pts (50% male; mean age 60 years; SCLC/NEC histology 82%/18%; WHO PS 0/1/2 14%/77%/9%) had received treatment. Recruitment to the 30 mg cohort was stopped at 4 pts (all SCLC) when 20 mg became the recommended dose with chemotherapy. The following results relate to cediranib 20 mg + EP (n = 18, 14/4 SCLC/NEC). As only 1/6

pts in the initial 20 mg cohort experienced a DLT (hemoptysis), this combination was considered suitable for cohort expansion. Adverse events (AEs) reported in ≥ 50% pts receiving cediranib 20 mg + EP were nausea, vomiting, neutropenia and diarrhea. The incidences of hypertension (all G1 or 2) and fatigue (n = 1 G3) were both 39%. Five pts discontinued treatment due to an AE: anemia, duodenal ulcer bleeding, increased creatinine (all n = 1, G3) and hemoptysis (n = 2, G3). There were no cediranib dose reductions (mean daily dose 18.5 mg) and all pts received the planned dose of EP. In a preliminary efficacy assessment (RECIST), 10/14 (71%) SCLC pts achieved a partial response (PR) (12/18 [67%] including 30 mg cohort). In the 20 mg cohort, the mean best change from baseline in tumor size was -53.3%. Median PFS was 8 months and 5/8 ongoing pts had a PR. **Conclusions:** Cediranib 20 mg + EP is well tolerated and has shown evidence of activity in SCLC and lung NEC. Preliminary median PFS is favorable compared with EP historical data. The AE profile is consistent with previous cediranib studies. Further investigation is warranted.

7050 译文 西地尼布+依托泊甙/顺铂一线治疗 SCLC 或神经内分泌癌的 I 期开放研究

摘要

背景：西地尼布是一个口服的、高效的、抑制 VEGF 信号通路中 c- Kit 的抑制剂 。研究主要是评估西地尼布+EP 一线治疗广泛期/转移的肺癌。**方法**：患者接受 21 天为 1 周期的 EP 方案(E 100 mg/m2, days 1-3; P 80 mg/m2, day 1)，共 6 周期，从第一周期的第 4 天开始每天一次的西地尼布直到疾病进展或毒性反应停药 。可进行安全性评价的患者应该是完成 21 天的西地尼布治疗或出现了剂量限制毒性。主要的评估目标是安全性和耐受性。如果有<33%患者出现 DLT，这个剂量认为是可耐受的，再扩大入组 12 例患者。**结果：**资料截止到 2009 年 8 月，22 患者(50%男性;平均年龄 60 岁;SCLC/NEC 组织学 82%/18%;WHO PS 0/1/2 14%/77%/9%)接受治疗。当 20mg 成为化疗的推荐剂量后，30mg 组在入组 4 例（SCLC）患者后终止。以下是关于西地尼布 20 mg + EP (n = 18, 14/4 SCLC/NEC)的结果：只有 1/6 患者出现 DLT (咯血),认为这种组合适合扩大样本。≥50%的不良事件(AEs)是在接受西地尼布 20 mg+EP 组出现恶心，呕吐，嗜中性白细胞减少症和腹泻。高血压和(所有 G1 或 2)疲劳(所有 n=1，G3)两者都为 39%.5 例患者由于 AE：贫血，十二指肠溃疡出血，肌酐升高(所有 n=1，G3)和咯血(n=2,G3)中断治疗。所有患者

没有出现西地尼布减量(每日平均剂量 18.5 mg)，均接受规定的 EP 方案剂量。初步疗效评估(RECIST),10/14(71%)SCLC 患者达到部分缓解 (PR) (12/18[67%]包括 30mg 组)。在 20mg 组，肿瘤大小从基线到最大改变为-53.3%.中位 PFS 为 8 个月，5/8 正在治疗的患者疗效为 PR。**结论**：西地尼布 20mg+EP 治疗的耐受性良好，在 SCLC 和肺 NEC 中显现出疗效。初步中位 PFS 优于 EP 方案的历史数据。AE 与西地尼布以前的研究一致。进一步调查研究是有必要的。

7051 Long-acting somatostatin analogues survival differences in limited- and extensive-disease SCLC patients.

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Abstract:

Background: Long acting somatostatin analogues combined with platinum analogues have demonstrated an antiproliferative effect on growth of human SCLC xenografs. **Methods:** 114 (52 with limited disease) previously untreated SCLC patients with positive somatostatin receptors were included in the study. All patients performed 111In-Octreotide scanning before CHT, every 3 months and up to 4 times. All patients were treated with paclitaxel 190mg/m2 + carboplatin AUC=5.5 for up to 8 cycles. 48 hours after each CHT 30/114 patients (Group A) also received 30mg lanreotide (somatuline) in order to block somatostatine receptors for 2 weeks. 40/114 patients (Group B) received 60mg lanreotide to block somatostatine receptors

for 4 weeks. 44/114 patients (Group C, control) received only CHT. No differences were observed between the 3 Groups regarding LD and ED patient ratios, age and PS. Patients in Groups A and B after the completion of the CHT continued maintenance therapy with lanreotide. Both non and hematological toxicity had no statistical significant differences between the Groups and generally toxicity was well managed. **Results:** Group A (median: 375.days, 95%CI: 206.3-543.7) had a survival benefit (p<0.001) in comparison to Group B (median: 347 days, 95%CI: 319.1-374.9 days). In limited disease patients group A had a statistical significant benefit compared to control group and to group B. 537 95% CI 449.8-624.2, 300 95%CI 244.2-355.8, 347 95%CI 187.9-506 respectively (p=0.04 Tarone-Ware test). **Conclusions:** Long acting somatostatin analogues could be used as an additive therapy in combination to antineoplastic agents in patients positive for somatostatine receptors. 30 mg dose improve survival only in limited disease SCLC patients

7051 译文 长效生长抑素类似物治疗局限期和广泛期 SCLC 患者的生存差异

摘要

背景：已经证明长效生长抑素类似物联合铂类对人类SCLC xenografs的生长有抗增殖作用。**方法：**入组 114 例未接受治疗的生长抑素受体阳性的患者（52 例为局限期）。所有患者在诱导化疗（CHT）前进行 111In-奥曲肽筛查，每 3 个月一次，共 4 次。所有患者均接受紫杉醇 190mg/m^2+卡铂 AUC=5.5，治疗达 8 周期。A组为 30/114 每个CHT患者 48h 后也接受 30mg兰瑞肽（lanreotide）（促生长素抑制素）2 周以阻止生长抑素受体。B组为 40/114 患者接受 60mg兰瑞肽 4 周以阻止生长抑素受体。44/114 患者(GroupC,对照组)只接受CHT.三组局限期（LD）和广泛期（ED）患者的比值，年龄，PS没有差别；A和B两组患者在完成CHT后重新开始兰瑞肽维持治疗。血液和非血液毒性组间没有统计学差异，一般毒性较好处理。**结果：**A组（中位：375 天, 95%CI:206.3-543.7)与B组(中位:347 天,95%CI:319.1-374.9)比较生存受益(p<0.001)。在局限期A组生存与对照组和B组比较明显受益，分别为 537 天（95% CI，：449.8-624.2),300 天(95%CI：244.2-355.8),347 天（95%CI，187.9-506），(p=0.04 Tarone-Ware test)。**结论：**在生长抑素受体阳性患者长效生长抑素类似物能作为辅助方法与抗肿瘤药物联合。30mg剂量只在局限期SCLC患者中改善生存。

7052 Randomized phase II study (EORTC 08062) of amrubicin as single agent or in combination with cisplatin versus etoposide-cisplatin as first-line treatment in patients (pts) with extensive disease small cell lung cancer (ED SCLC)

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Abstract:

Background: Outcome for pts with ED SCLC remains poor, despite standard treatment with platinum and etoposide (E). Amrubicin (A) is a synthetic anthracycline and a potent topoisomerase II inhibitor, with less cardiotoxicity than doxorubicin, approved in Japan for the treatment of NSCLC and SCLC. **Methods:** Eligible pts had previously untreated, histologically confirmed ED SCLC, WHO performance status (PS) 0-2 and measurable disease according to RECIST. Pts were randomized to 3 weekly cycles of either (1) A alone 45 mg/m2 d1-3, (2) cisplatin (C) 60 mg/m2 d1 and A 40 mg/m2 d1-3 or (3) E 100 mg/ m2 d1, d2-3 i.v/po and C 75 mg/m2 d1. The primary endpoint was overall response rate (ORR) aiming at ORR = 80% and powered to rule out an ORR < 55% in any experimental arm. Patients were stratified by center, gender and PS. To declare success, 19 responses out of 27 eligible pts who started treatment (ORR of at least 70%) were needed in each arm using a Fleming design. **Results:** The number of randomized/eligible pts who started treatment was

33/28 in Arm 1, 33/30 in arm 2 and 33/30 in arm 3, respectively. Major patient characteristics including age, sex and PS were well balanced between the arms. The median number of chemotherapy cycles received was 5, 6 and 6. Primary prophylaxis with pegfilgrastim was added in the later part of the trial in arms 1-3 (57%, 43%, 37%); grade (G) 3-4 hematological toxicity in arms 1-3 was neutropenia (73%, 73%, 69%); thrombocytopenia (17%, 15%, 9.4%), anemia (10%, 15%, 3.1%) and febrile neutropenia (17%,15%,14%). Early deaths including treatment related were 1, 3 and 3 pts respectively. Cardiac toxicity did not differ among the 3 arms. Out of 88 eligible pts who started treatment, the response rate assessed by investigators was 17 (61%), 23 (77%) and 19 (63%) for arm 1, 2 and 3, respectively. **Conclusions:** A + C was associated with the highest response rate and further evaluation of this combination is warranted. Independent central review is still on-going.

7052 译文 广泛期小细胞肺癌一线治疗：氨柔比星单药或联合顺铂与依托泊甙/顺铂比较的随机 II 期研究(EORTC 08062)

摘要

背景：尽管标准治疗方案为铂/依托泊甙，但对广泛期（ED）SCLC 治疗效果差。氨柔比星是合成的蒽环类抗生素，是拓扑异构酶 II 有效的抑制剂，比多柔比星有更小的心脏毒性，日本批准用于 NSCLC 和 SCLC 的治疗。**方法：**患者需满足以下条件：未经治疗的、组织学上确认的 ED-SCLC，WHO PS 0-2 分，有可测量的病灶（RECIST 标准）。患者随机的接受 3 周期的单药氨柔比星(A)45 mg/m2 d1-3(1)，(2)顺铂(C)60mg/m2d1，A 40 mg/m2 d1-3 或(3)依托泊甙 E 100 mg/ m2 d1, d2-3 i.v/po 和 C75mg/m2d1。主要的研究终点是 ORR，目标 ORR=80%，在任何试验组能排除 ORR<55%。根据患者的中心，性别和 PS 分层。试验成功，在 27 例入组开始治疗的患者中 19 例有效(ORR 至少达 70%)。**结果：**第一组中开始治疗的随机/合格患者 33/28，第二组 33/30，第三组 33/30。在这些组中大多数患者的特征包括年龄，性别，PS，在两组间的分布是平衡的。化疗周期的中位数分别为 5,6 和 6。在试验的 1-3 组后半部分加上了基本的培非司亭预防性治疗(57%, 43%, 37%)在 1-3 组中 3-4 度血液学毒性是嗜中性白细胞减少症(73%,73%,69%)；血小板减少症(17%,15%,9.4%)，贫血(10%,15%,3.1%)和发热性嗜中性白细胞减少症(17%,15%,14%)。早期死亡包括治疗相关死亡三组分别为 1,3 和 3。心脏毒性在三组中没有差别。88 例合

格接受治疗的患者的有效率分别为 17(61%),23(77%)和 19(63%)。**结论：**A+C 与高的有效率相关，进一步评价这些联合是有必要的。单中心回顾正在进行中。

7053 Retrospective study of irinotecan plus cisplatin induction followed by concurrent thoracic irradiation with irinotecan plus cisplatin chemotherapy for limited-disease small cell lung cancer

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Abstract:

Background: Japanses Clinical Oncology Group (JCOG) 9104 study which compared iriontecan plus cisplatin (IP) with etoposide plus cisplatin (EP) in extensive disease small cell lung cancer patients showed a superior response rate and survival in IP group. We evaluated the efficacy and toxicity of coucnrrent iriontecan plus cisplatin (IP) chemotherapy with thoracic radiotherapy in limited-disease SCLC (LD-SCLC). **Methods:** From January 2006 to October 2009, thirty chemotherapy-naíve patients with LD-SCLC planned IP induction chemotherapy followed by IP concurrent chemoradiotherapy (CCRT). Twenty-nine patients (97%) were male, and 29 (97%) had an Eastern Cooperative Oncology Group performance status of 0 or 1. The median age was 60 years. Treatment consisted of one to six cycles of 21-day cycles of irinotecan 65mg/m2 and cisplatin 30mg/m2 intravenously (IV) on days 1 and 8 followed by two 21-day cycles of iriontecan 60mg/m2 IV and cisplatin 30mg/m2, with

concurrent thoracic radiotherapy. **Results:** The objective response was observed in 30 (100%, partial response [PR], 30) of 30 patients after induction chemotherapy and also 28 (100%, complete response [CR], 5; PR, 23) of 28 patients who got concurrent chemoradiotherapy after IP CCRT. After median follow up of 24.2 months, the estimated median survival was 34.2 months (95% CI, 21.2 - 47.2) with 1- and 2-year overall survival rates of 89.1% and 60.9%, respectively. Median progression-free survival (PFS) was 11.6 months with a 1- and 2-year PFS of 46.5% and 22.6%, respectively. The most common toxicities was grade 3 or 4 neutropenia noted in 30% of patients during induction chemotherapy and 15% during CCRT. Febrile neutropenia occurred in 7 % of patients during induction chemotherapy and 7% during CCRT. There was neither grade 3 or 4 esophagitis and radiation pneumonitis nor grade 2 alopecia. **Conclusions:** IP induction chemotherapy followed by CCRT using IP in LD-SCLC showed a promising activity with favorable 1- and 2-year survival rates, and favorable toxicity in this study. Further studies is warranted for using IP during CCRT.

7053 译文 局限期小细胞肺癌伊立替康/顺铂诱导化疗后同步胸部放疗+伊立替康/顺铂化疗的回顾性研究

摘要

背景：日本临床肿瘤小组(JCOG)9104 研究比较了伊立替康/顺铂(IP)与依托泊甙/顺铂(EP)治疗广泛期 SCLC 的效果，结果显示 IP 组显现出较高的有效率和生存。本试验将评价同步伊立替康/顺铂(IP)化疗联合胸部放疗在局限期 SCLC 中的有效性和毒性。**方法：**从 2006 年 1 月至 2009 年 10 月 30 例 LD-SCLC 未化疗患者在 IP 诱导治疗后使用 IP 联合放疗(CCRT)治疗。29(97%)例患者为男性，29(97%)例 ECOG 评分为 0 或 1。中位年龄为 60 岁。治疗包括每 21 天为 1 周期的伊立替康 60mg/m2 /顺铂 30mg/m2 (IV)d1，8，1-6 周期，随后 21 天为 1 周期的伊立替康 65mg/m2 (IV)/顺铂 30mg/m2，同步胸部照射。**结果：**诱导化疗后在 30 例患者都观察到了客观疗效（100%,部分缓解率[PR],30)，28 例在 IP CCRT 治疗后接受同步放化疗的患者客观疗效(100%,完全缓解[CR],5;PR,23)中位随访时间达 24.2 个月，估计中位生存为 34.2 个月(95%CI,21.2-47.2)，1 年和 2 年总生存率分别为 89.1%和 60.9%;中位 PFS 为 11.6 个月,1 年和 2 年 PFS 分别为 46.5%和 22.6%。最常见的毒性反应是 3 或 4 度的嗜中性白细胞减少症，在 30%的诱导化疗和 15%的 CCRT

中均可见到。发热性嗜中性细胞减少症在诱导化疗和 CCRT 二者都为 7%。既没有 3 或 4 度的急性食管炎和放射性肺炎，也没有 2 度脱发。**结论：**在 LD- SCLC IP 诱导化疗后应用 IP 的 CCRT 治疗在 1 年和 2 年生存率上显现出有希望的疗效，可耐受的毒性反应。进一步的研究证明在 CCRT 同时应用 IP。

7054 A phase II trial of combination chemotherapy with topotecan and amrubicin in small cell lung cancer (SCLC)

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Abstract:

Background: We previously conducted a phase I trial of combination chemotherapy with topotecan and amrubicin for SCLC and found acceptable toxicity profiles with a favorable efficacy. The aim of this phase II trial was to further evaluate its efficacy and toxicity in this population. **Methods:** Primary endpoint was objective response. Thirty one chemo-naïve and 28 relapsed patients with SCLC were separately enrolled between 2004 and 2009. Topotecan and amrubicin were administered on days 1 to 5 and 3 to 5, every 3 weeks at doses of 0.75 and 35 mg/m2/day, respectively. Response and toxicity were assessed according to the RECIST guideline and NCI-CTCAE v3.0. **Results:** Demographics of the 59 pts were as

follows: M/F:52/7, ECOG-PS 0/1/2:14/41/4, and smoker/non-smoker:54/5. A median numbers of courses administered were 4 and 3 in chemo-naïve and pretreated pts, respectively. Objective response was obtained in 23 (74%) of the 31 chemo-naïve and 12 (43%) of the 28 relapsed pts. Myelosuppresion was the principal toxixity with grade 4 leukopenia, neutropenia, thrombocytopenia and anemia of 46%, 80%, 25% and 7%, respectively. Grade 3-4 febrile neutropenia was observed in 41% of the pts, of whom one patient further developed Grade 5 septic shock. Other grade 3 or greater non-hematological toxicities included diarrhea, pneumonitis, vomiting, fatigue and hyponatremia in 2%, 3%, 5%, 9% and 2%, and one patient each developed fatal diarrhea and pneumonitis. At the time of data analysis with a median follow-up time of 43.2 months, MST and median PFS time were 14.9 and 5.3 months in the chemo-naïve pts and 10.2 and 5.1 months in the relapsed pts, respectively. **Conclusions:** This combination seemed effective for SCLC despite the moderate toxicity profiles.

7054 译文 托泊替康和氨柔比星联合化疗治疗小细胞肺癌的 II 期临床研究

摘要

背景：先前进行的托泊替康和氨柔比星的联合化疗治疗 SCLC 的 I 期临床试验，在得到较好疗效的同时毒性反应也可以接受。II 期临床试验的目的是进一步评估这些人群的疗效和毒性反应。**方法：**主要终点为客观疗效。从 2004 年至 2009 年入组 31 例未接受过化疗和 28 例复发的 SCLC 患者。托泊替康 0.75 mg/m2/天， d1-5 和氨柔比星 35mg/m2/天，d3-5，每 3 周为 1 周期。疗效和毒性分别以 RECIST 和 NCI-CTCAEv3.0 进行评估。**结果：**59 例患者统计数据如下：M/F:52/7,ECOG-PS 0/1/2:14/41/4,吸烟/不吸烟:54/5. 在初次化疗和预先有处理的化疗患者的中位治疗数分别为 4 和 3。31 例未化疗患者中 23 例获得客观疗效(74%)，28 例复发患者中 12 例获得客观疗效(43%)。血液系统为主要的毒性，包括 4 度白细胞减少（46%），嗜中性粒细胞减少（80%），血小板减少（25%）和贫血（7%）,41%的患者中观察到 3-4 度发热性嗜中性粒细胞减少，其中 1 例患者发展为 5 度感染性休克。其他 3 度或更高级的非血液学毒性包括：2%腹泻，3%肺炎，5%呕吐，9%疲乏和 2%低血钠，1 例患者发展为严重的腹泻和肺炎。至资料分析时中位随访时间为 43.2 个月。MST 和中位 PFS 时间在未化疗患者中分别为 14.9 和 5.3 个月，在复发患者中分别为 10.2 和 5.1 个月。**结论：**尽管有中等毒性但这种联合似乎对 SCLC 有效。

7055 Phase II study of oral topotecan plus bevacizumab (topo-bev) for second-line treatment of small cell lung cancer (SCLC)

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Abstract:

Background: Topotecan has been FDA-approved for second-line treatment of relapsed SCLC. Alteration in tumor vasculature by addition of bevacizumab could increase delivery of topotecan to tumor cells and enhance its efficacy. **Methods:** This is an open-label, multicenter, single-arm phase II study of oral topotecan 2.3 mg/m2/dx5 + IV bevacizumab 15 mg/kg/d1 q21d for second-line treatment in adults with first relapse of SCLC, adequate organ function, and ECOG PS $\leq$ 2. Treatment was planned for 8 cycles or until disease progression or the development of unacceptable toxicity. The primary efficacy endpoint was PFS rate at 3 months. The study had 90% power with 5% type 1 error to detect a 40% relative improvement in 3-month PFS rate from 50% for topotecan (historical control) to 70%. Secondary endpoints included ORR, PFS, OS, and safety evaluation. **Results:** Fifty subjects were enrolled from July 2008 to April 2009. Mean age was 61 y (28-80); 52% female; 98% Caucasian. 92% of patients had ECOG PS 0 or 1 and 86% had extensive disease at baseline. 57% of subjects had sensitive disease (TTP > 90 d from end of prior chemotherapy). Six subjects were on treatment and 44 had discontinued, most commonly for progression (24) and adverse events (AEs) (10). 3-month PFS rate was 60.3% (95% CI, 44.6, 72.9). Median PFS and OS were

17.4 and 31.6 weeks, respectively. ORR was 10% (CR+PR 95% CI, 3.3, 21.8). Gr3, 4 or 5 AEs were reported in 58% of patients. Gr3/4 neutropenia and thrombocytopenia occurred in 44% and 50% of patients. No grade 3/4 proteinuria or hypertension were reported. Nonhematologic toxicity was primarily nausea, diarrhea, vomiting, asthenia, and fatigue. There were 5 non-disease-related deaths: thrombocytopenia, upper GI hemorrhage, respiratory distress/failure, pneumonia, sepsis. **Conclusions:** The primary efficacy endpoint of improvement in 3-month PFS was not met. A marginal benefit of this combination cannot be ruled out.

7055 译文 口服托泊替康+贝伐单抗(topo-bev)用于小细胞肺癌二线治疗的 II 期研究

摘要

背景：FDA 已经批准托泊替康用于复发的 SCLC 的二线治疗。通过贝伐单抗改变肿瘤的脉管系统能够增加托泊替康对肿瘤细胞传递，加强其疗效。**方法：**这是一个开放的，多中心，单臂的口服托泊替康 2.3mg/m2/dx5+贝伐单抗 15 mg/kg/d1 q21d，IV，用于成人一线复发后的二线治疗的 II 期研究。患者有良好的器官功能，ECOG PS≤2。治疗方案为 8 周期或直至疾病进展，或出现不能耐受的毒性反应为止。主要的疗效终点为 PFS 率能达到 3 个月。本研究按照 90%的把握度，5%的 1 类错误水平，能够发现托泊替康（历史对照)3 个月时的 PFS 率相对提高 40%，也即使从 50%增加到 70%。次要终点包括 ORR, PFS, OS, 和安全性的评估。**结果：**从 2008 年 7 月到 2009 年 4 月有 50 例患者入组。平均年龄 61 y (28-80)，52%为女性，98%高加索人（白种人）。92%患者的 ECOG PS 为 0 或 1，86%为疾病广泛期。57%的受试者为疾病敏感复发（从上一次化疗结束的 TTP>90 d），5 例患者继续接受治疗，44 例已经终止治疗。一般疾病进展(24)，不良反应事件(AEs)(10)。3 个月 PFS 率为 60.3%(95% CI, 44.6, 72.9)。中位 PFS 和 OS 分别为 17.4 和 31.6 周, ORR 为 10%(CR+PR 95% CI, 3.3, 21.8). 58%的患者中报告有 3, 4 或 5 度的 AEs。44%的患者中发生 3/4 度嗜中性白细胞减少症，50%患者发生血小板减少症。没有 3/4 度蛋白尿和高血压的报道。非血液学毒性主要为恶心，腹泻，呕吐，虚弱和乏力。有 5 例非疾病相关的死亡：血小板减少症，上消化道出血，呼吸障碍/衰竭，肺炎，败血症。**结论：**主要研究终点 3 个月 PFS 的改善未达到。这种联合最终获益情况不能排除。

7056 Combination chemotherapy with sunitinib (IND 74019; NSC 736511) for untreated extensive-stage small cell lung cancer (SCLC): CALGB 30504 phase IB safety results

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Abstract:

Background: CALGB conducted a phase IB trial to determine the dose of sunitinib that can be safely combined with cisplatin and etoposide in extensive SCLC. **Methods:** Patients with PS 0-1, adequate organ function and extensive SCLC were eligible. The treatment plan was cisplatin 80 mg/m2 d1 and etoposide 100 mg/m2 d1-3 every 21 d up to 6 cycles. Three cohorts of 6 patients at dose levels of 25, 37.5, or 50 mg/day days 1-14 every 21 days were planned. Every 2 week conference calls were held to assess toxicity. Toxicity during cycle 1 was evaluated for dose limiting toxicity (DLT). In cohort 1 prophylactic granulocyte growth factor support was not allowed. **Results:** In cohort 1, there were no protocol defined DLTs. However most patients had prolonged neutropenia and required delayed start of ≥ cycle 2 chemotherapy. In cohort 1, two patients requiring treatment delays for neutropenia were given granulocyte growth factor support during cycles 3-6 and were able to receive therapy as scheduled without DLT. The trial was amended to give prophylactic granulocyte growth factor support to all patients from cycle 1 onward while repeating the sunitinib 25 mg d 1-14 level 1 dose for cohort 2. Of 6 patients on cohort 2, two patients died from complications of febrile neutropenia and a third had febrile neutropenia with neutrophil count of zero cycle 3 d 10. When the second patient died on cohort 2, sunitinib concurrent with chemotherapy in this setting was deemed unsafe, and sunitinib was immediately and permanently stopped for all

remaining patients. The trial has been amended to a randomized phase II trial in which maintenance sunitinib after chemotherapy is being evaluated. **Conclusions:** The combination of sunitinib 25 mg/day days 1-14 to standard dose cisplatin and etoposide appeared to cause prolonged neutropenia and an unacceptable rate of treatment-related mortality. Granulocyte growth factor given after chemotherapy in this setting did not prevent severe neutropenia and infections. This combination of chemotherapy and sunitinib is not recommended, even with growth factor support.

7056 译文 舒尼替尼联合化疗(IND 74019; NSC 736511)在未治疗的广泛期小细胞肺癌中的应用：CALGB 30504 IB 期安全性结果

摘要

背景：CALGB 进行的 IB 期临床试验是确定舒尼替尼联合依托泊苷/顺铂治疗广泛期 SCLC 时舒尼替尼的剂量安全性试验。**方法：**入选患者 PS 评分 0-1 分，器官功能良好，广泛期 SCLC。治疗方案是顺铂 80 mg/m2 d1 和依托泊苷 100 mg/m2 d1-3，每 21 为 1 周期，共 6 周期。舒尼替尼分为 3 个不同剂量组，分别为 25,37.5,或 50 mg/天，d1-14，21 天为 1 周期。每 2 周电话评估毒性。第 1 周期评估剂量限制毒性(DLT)。在第一个剂量组不允许患者使用粒细胞集落刺激因子。**结果：**在第一组中，没有出现试验方案中规定的剂量限制毒性。然而，大多数患者有持续很长时间的嗜中性白细胞减少症，并且需要延迟第二次化疗周期的开始时间。2 例患者由于嗜中性白细胞减少症延迟治疗，在第 3-6 周期中给予粒细胞集落刺激因子支持治疗后能够继续接受预定的方案治疗，没有剂量限制毒性(DLT)。在第二组患者在重复使用第一组舒尼替尼 25mgd1-14 剂量时从第 1 周期开始给予所有患者应用粒细胞集落刺激因子支持治疗。第二组 6 例患者中 2 例由于发热性嗜中性粒细胞减少的并发症死亡，第 3 例患者在 3 周期的第 10 天患有发热性嗜中性粒细胞减少症，嗜中性白细胞计算为 0。当第二组中第 2 例患者死亡后，舒尼替尼与化疗的联合认为是不安全的，舒尼替尼立即和永久的在所有其他受试者中停止使用。这个试验随后被修改为评估化疗后舒尼替尼维持的治疗的随机、II 期临床试验。**结论：**舒尼替尼 25 mg/day d1-14 与标准剂量的顺铂/依托泊苷的联合引起持续的嗜中性白细胞减少症和不能耐受的治疗相关的死亡率。在这个试验中化疗后给予粒细胞集落刺激因子并未阻止严重嗜中性白细胞减少症和感染的发生。即使有粒细胞集落刺激因子支持治疗也

不推荐舒尼替尼与化疗的联合。

7057 Phase II study of amrubicin and carboplatin in patients with the refractory or relapsed small cell lung cancer (SCLC)

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Abstract:

Background: Amrubicin achieved the high response rate of 78.8% and median survival of 11.3 months in patients with previously untreated extensive disease SCLC. The combination of amrubicin with platinum derivative showed additive effect against a human small cell lung cancer cell line. In the phase I study of amrubicin plus carboplatin for untreated SCLC patients with 70 year or older, the recommended dose was determined to be 35 mg/m2 of amrubicin on days 1-3 and AUC of 4 mg min/mL of carboplatin on day 1. We examined the safety and efficacy of the combination of amrubicin plus carboplatin for refractory or relapsed SCLC. **Methods:** Patients with previously treated SCLC were eligible if they had a performance status of 0 to 2, were 75 years or younger, and had adequate organ function. Patients received the combination of carboplatin with AUC of 4 mg min/ml using the Calvert formula on day 1 plus amrubicin 30 mg/m2 on days 1-3 every 3 weeks. The trial was designed as a phase II study, with response rate as the primary endpoint. A planned sample size was 27. **Results:** From June 2005 through April 2009, 28 patients (22 men and 6 women; median age,65 years; range, 55 to 74 years) were enrolled. At the time of recurrence, 3 patients had limited disease and 25 patients had extensive disease. The overall response rate

was 35.7% (95% CI, 18.6% to 55.9%). In patients with sensitive disease, the response rate was 63.6% (95% CI, 30.8% to 89.1%). The median survival time was 184 days (range 24 to 1,290 days).Hematologic toxicities included grade 3 to 4 neutropenia in 86% of patients, grade 3 to 4 thrombocytopenia in 46%, and grade 3 to 4 anemia in 61%. Grade 3 infection developed in only 7% of patients. No patients had grade 3 to 4 diarrhea, nausea, or vomiting. There was no treatment death. **Conclusions:** This regimen is effective and well tolerated in patients with relapsed or refractory SCLC.

7057 译文 氨柔比星+卡铂治疗耐药性和复发性小细胞肺癌（SCLC）的 II 期试验

摘要

背景：氨柔比星在对未经治疗的广泛期小细胞肺癌患者的治疗中取得了 78.8%的高的有效率和 11.3 个月的中位生存期。氨柔比星和铂类联合对人类的小细胞肺癌细胞系显示出更强的作用。在氨柔比星+卡铂治疗 70 岁及以上的未经治疗的小细胞肺癌患者的 I 期临床中，推荐剂量为 35mg/m2 的氨柔比星 d1-3 天，第 1 天卡铂 AUC=4mg min/ml。我们验证了氨柔比星+卡铂对耐药和复发小细胞肺癌的安全性和有效性。**方法：**治疗过的 SCLC 患者满足以下条件即可入组：PS 0-2，≤75 岁，器官功能良好。第 1 天依照 Calvert 公式计算卡铂 AUC=4mg min/ml，氨柔比星 30mg/m2，d1-3，每 3 周为 1 周期。这个试验为 II 期试验，研究的主要终点是有效率。计划的样本量为 27 例。**结果：**从 2005 年 6 月到 2009 年 4 月，28 例患者（22 例男性和 6 例女性，中位年龄 65 岁：从 55 岁到 74 岁）入组。在复发的时候，3 例患者有局限性的病灶，25 例患者有广泛期的病灶。总的有效率是 35.7%（95% CI, 18.6%-55.9%）。在疾病敏感的患者中，有效率是 63.3%（95% CI,30.8%-89.1%）。中位生存期 184 天（从 24-1290 天）。血液学毒性包括在 86%的患者中出现 3-4 度的嗜中性粒细胞减少，在 46%的患者中出现 3-4 度的血小板减少，在 61%患者中出现 3-4 度的贫血。只在 7%的患者中发生 3 度感染。没有患者发生 3-4 度的腹泻，恶心和呕吐。没有治疗相关的死亡发生。**结论：**这种疗法对复发和耐药的小细胞肺癌患者是有效并且耐受性良好。

7060 Evaluation of neoadjuvant "window of opportunity" trials with targeted therapy in patients with surgically resectable non-small cell lung cancer

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Author(s):
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Abstract:

Background: "Window of opportunity" trials administer a short course of targeted therapy (TT) prior to surgical resection. The purpose of this study was to assess the perioperative safety of this approach compared to standard therapy in early stage non-small cell lung cancer (NSCLC) patients. **Methods:** Patients (cstage I/II) enrolled in two clinical trials received either preoperative EGFR tyrosine kinase inhibitor (erlotinib, n=22) or VEGFR inhibitor (pazopanib, n=18), followed by surgical resection. These patients were propensity matched (1:2) using a logistic regression model to patients undergoing surgical resection alone. Preoperative time to resection, operative data, and postoperative complications were compared. **Results:** Patients were treated with neoadjuvant TT for a median of 21 days (range 11- 28). Time from first clinic visit to resection was significantly longer in this group than in control patients (48 vs. 25 days, $p<0.0001$). Despite the time delay, there was no significant increase in pathologic upstaging in the TT group compared to control (33% vs. 24%, $p=0.38$). There was no difference in operative time, blood loss, or thoracoscopic conversion rates between the TT and control groups (Table). There was no significant difference in the percentage of patients experiencing any complication (45% in TT group vs. 34% in control group, $p=0.24$) or in the overall rates of major complications (Table). There were no 30-day mortalities in either group. **Conclusions:** "Window of opportunity" trials are a powerful tool

to assess response to TT in NSCLC patients, allowing for radiologic and pathologic assessment of treatment effects. Such trials can be safely undertaken prior to surgery in early stage NSCLC patients, with no increase in pathologic upstaging. Surgery can be performed safely in these patients with no increase in major complications.

	TT (N=40)	Control (N=80)	p value (Fisher's exact test)
Operative factors			
Operative time (min.)	144	157	0.24
Estimated blood loss (cc)	205	195	0.79
Complications			
Any	45%	34%	0.24
Cardiovascular	20%	25%	0.65
Respiratory	23%	19%	0.64
Renal failure	0%	1%	1.0
Infectious	13%	8%	0.50
Operative	5%	1%	0.26

7060 译文 对于接受外科手术切除前用靶向治疗的新辅助治疗的“机会窗口”进行评估

摘要

背景：“机会窗口”试验是在手术切除前行短暂的靶向治疗（TT）。本研究的目的是评估早期 NSCLC 患者行此治疗和常规标准治疗之间手术期间安全性的区别。**方法：**临床分期 I/II 期的患者进入临床试验的两个小组，分别为接受术前 EGFR TKI（erlotinib，n=22）或 VEGFR 抑制剂（pazopanib，n=18），随后行手术切除。这些患者通过对数回归模式和只接受手术治疗的患者之间形成 1:2 的匹配。同时比较术前治疗时间、手术相关数据及术后并发症。**结果：**患者接受新辅助 TT 的中位时间为 21d（11-28d）。本次首次门诊就诊至手术的时间明显比对照组长（48d vs. 25d，p<0.0001）.除了时间延迟，TT 组和对照组之间并没有其他病理分期增加等显著区别。（33% vs. 24%, p=0.38）。TT 组和对照组之间在手术时间，失血量、胸腔镜转换率方面没有显著区别（见表）。患者术后发生合并症的百分比（45% in TT 组 vs 34% in 对照组）或主要合并症的总发生率方面并没有

显著差异（表）。两组均没有出现 30 天内死亡的情况。**结论：**“机会窗口”试验是评估 NSCLC 行 TT 的有效性的有力工具，可以对治疗效果性影像学及病理学评估。这样的试验可以很安全的在早期 NSCLC 患者术前进行，而不增加病理分期。这些患者可以很安全的接受手术治疗，而不增加主要的并发症。

	TT (N=40)	Control (N=80)	p value (Fisher's exact test)
Operative factors			
Operative time (min.)	144	157	0.24
Estimated blood loss (cc)	205	195	0.79
Complications			
Any	45%	34%	0.24
Cardiovascular	20%	25%	0.65
Respiratory	23%	19%	0.64
Renal failure	0%	1%	1.0
Infectious	13%	8%	0.50
Operative	5%	1%	0.26

7062 Multicenter phase II study evaluating docetaxel, CDDP, and cetuximab as induction regimen prior to surgery in chemotherapy-naive patients with NSCLC stage IB-IIIA (INN06-study): Preliminary results

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Abstract:

Background: Despite several theoretical advantages, neoadjuvant/perioperative chemotherapy in patients with early stage NSCLC has not proven to be superior to the standard adjuvant approach. The aim of this study has therefore been to increase the efficacy of neoadjuvant treatment by combining a platinum doublet (cisplatin/docetaxel) with a monoclonal antibody targeting the EGFR (cetuximab). **Methods:** Between 01/2007 and 12/2009, 33 patients (planned sample size = 40) with primarily resectable NSCLC stage IB to IIIA were included. Treatment consisted of two cycles cisplatin (40 mg/m2 d1+2) and docetaxel (75 mg/m2) q3 weeks, accompanied by the administration of cetuximab (400 mg/m2 d1, then 250 mg weekly). The primary endpoint was radiological response. Secondary endpoints included toxicity, metabolic response (PET), pathological response, recurrence-free survival and overall survival. **Results:** At the time of this interim-analysis 31 patients were evaluable for radiological response, 22 for PET-response. Toxicity data were complete for 25 patients. In total, 65 cycles of the study treatment were applied. The following grade 3/4 toxicities were reported (>5% of cases): Neutropenia 48%, electrolyte disorders 28%, nausea 12%, skin toxicity 8%. A severe anaphylactic infusion reaction was seen once. 18/31 patients (58%) achieved PR (RECIST criteria). 13/31 (42%) were classified as stable disease. No patient showed disease progression. A metabolic response (PET) was documented in 63% of the patients. All patients underwent surgery after completion of study treatment. Surgical morbidity was not increased compared to historical controls. Survival data are still immature. **Conclusions:** In this study, two cycles of cisplatin/docetaxel/cetuximab showed promising efficacy in the neoadjuvant treatment of early-stage NSCLC. Toxicities were manageable and as expected. Recruitment of this trial is ongoing and an updated analysis will be presented at the meeting.

7062 译文 一个多中心的 II 期试验（INN06-study）的初步结果：使用多西他赛，CDDP 及西妥昔单抗作为诱导方案对于未行化疗的 IB-IIIA 期 NSCLC 患者行术前治疗的评估

摘要

背景：除了一些理论上的优势，早期 NSCLC 患者行新辅助/手术前化疗并没有证明优于标准的辅助化疗途径。所以本研究的目的是将一个含铂的双药化疗方案（顺铂+多西他赛）和一个针对 EGFR 的单克隆抗体（西妥昔单抗）相结合以提高新辅助治疗的有效性。**方法：**2007 年 1 月至 2009 年 12 月间（计划的样本量为 40）最初可以手术切除的 IA 到 IIIA 期 NSCLC 患者入选研究。治疗包括 2 周期的顺铂(40 mg/m2 d1+2)和多西他赛(75 mg/m2) q3 weeks，同时予西妥昔单抗(400 mg/m2 d1, 然后 250 mg 每周一次)。主要终点为影像学有改善，第二终点包括毒性反应、代谢反应（PET）、病理学反应、无复发生存期及总体生存期。**结果：**截止本次中间分析时间为止，31 名患者可行影像学评估，22 名患者可行 PET 评估。25 名患者完成了毒性反应评估。总共进行了 65 个周期的治疗。3/4 级毒性反应（>5%的病例出现）包括：中性粒细胞减少 48%，电解质紊乱 28%，恶心 12%，皮肤毒性 8%。曾观察到一例严重的过敏性渗出反应。18/31 名患者（58%）获得了 PR（RECIST 标准）。13/31(42%)被认定为 SD。没有出现疾病进展的病例。63%的患者出现了 PET 改善。所有患者在本研究的治疗完成后都接受了手术治疗。手术死亡率和既往历史上的对照相比并没有增加。生存期数据还不完善。**结论：**本研究中，早期 NSCLC 患者行 2 周期的新辅助的顺铂+多西他赛+西妥昔单抗治疗有希望能有效。毒性反应是可控制的。本研究还在继续入组患者，会议上会公布最新更新的分析。

7064 Multimodal management of locally advanced (N2) non-small cell lung cancer (NSCLC): Is there a role for surgical resection? A single institution experience

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Abstract:

Background: The treatment of locally advanced (N2) NSCLC is a controversial topic. Concurrent chemotherapy plus radiotherapy (CT-RT) is considered the standard of care for these patients (pts). Recently, no overall survival (OS) benefit was shown in pts receiving trimodality treatment (surgical resection after CT-RT). We present a single institution experience managing stage III (N2) NSCLC pts to determine if surgery (S) improves survival compared to definitive CT-RT alone. **Methods:** From 1996 to 2006, 71 stage IIIA/IIIB (N2) NSCLC pts were treated. 34 received cisplatin-based concurrent CT and hyperfractioned 3D-CRT [1.2 Gy b.i.d.; median dose: 66.5 Gy (range: 64-74)] and 37 underwent S [32 lobectomy (L) and 5 pneumonectomy (P)] preceded by neoadjuvant and/or followed by adjuvant therapy. Survival curves were estimated by Kaplan-Meier analysis. **Results:** Most pts (87%) were men. Median age was 59. A statistically significant correlation between T4c and definitive CT-RT (p=0.027), as well as between T1c and S (p=0.024) was noted. After a median 31.5 mo follow-up (range 5-140), median OS was 42 mo (IC 95: 26.7-57.3) for the S group vs. 41 mo (IC 95: 36.3-45.7) for CT-RT pts (p=0.974). The estimated survival at 5 years was 25.1% after S vs. 21.2% after CT-RT. Median PFS was 24 mo (IC 95: 6.9-41.1) after S and 49 mo (IC 95: 41.5-105.5) after CT-RT (p=0.401). Pts responding to CT-RT had a 43 mo OS (IC 95: 36.7-49.2) compared to 21 mo (IC 95: 10.9-31.0) for non-responders (p=0.007). pN0 status at thoracotomy was present in 14 (37.8%) pts after induction therapy, but no significant differences were found in OS between pN0 and pN2 pts. In the S group, subjects undergoing L showed a 33 mo PFS (IC 95: 0-77.7) vs. 18 mo (IC 95: 4.3-31.7) in P pts (p=0.21). Both arms were generally well-tolerated but 2 (5.4%) treatment-related deaths occurred in the S group. **Conclusions:** According to published data, S rendered no OS benefit compared to CT-RT in stage III N2 NSCLC. Any radiological response to CT-RT prognosticated an OS benefit. Even though pts selected for S seemed to have less locally

advanced tumors, they showed similar survival outcomes to those exclusively treated with definitive CT-RT.

7064 译文 对于 N2 局部晚期 NSCLC 的多种模式：外科手术还有作用吗？一个单中心研究

摘要

背景：局部进展（N2）的 NSCLC 治疗一直有争议。同步化疗+放疗（CT-RT）被认为是这些患者的标准治疗。近来采用 CT-RT 后再手术治疗的三种治疗联合方案还没有显示出现明显的 OS 优势。我们提供了一份来自单个机构的治疗 III 期（N2）NSCLC 的经验以判定手术相对于单纯的 CT-RT 能否改善其生存情况。**方法：**1996-2006 年间治疗了 71 名 IIIA/IIIB（N2）期 NSCLC 患者。34 名接受了以铂为基础的同步化疗+超分割 3D-CRT[1.2 Gy b.i.d；中位剂量：66.5 Gy (范围：64-74)]。37 名患者在新辅助治疗后接受了手术（S）治疗（32 名叶切除术（L），5 名全肺切除术（P）），之后有的还进行辅助治疗。通过卡普兰-迈耶曲线评估其生存率曲线。**结果：**87%患者为男性，中位年龄 59 岁。T4C 和 CT-RT（p=0.027）及 T1C 和 S（p=0.024）之间的相关性具有统计学显著性意义。在平均随访 31.5 月（95%CI 36.3-45.7）后，S 组的中位 OS 为 42 月（95%CI 26.7-57.3），CT-RT 组委 41 月（95%CI 36.3-45.7）（p=0.974）。估计的 5 年生存率手术后组为 25.1% vs. CT-RT.后组为 21.2%。S 组平均 PFS 为 24 月（95% CI 6.9-41.1），CT-RT 组为 49 月（95% CI 41.5-105.5）（p=0.401）。对 CT-RT 有效的患者 OS 为 43 月（95% CI 36.7-49.2），无效者为 21 月（95% CI 10.9-31.0）（p=0.007）。诱导化疗后开胸手术的患者中 14 名患者（37.8%）为 pN0 状态，但是 pN0 和 pN2 患者之间的 OS 并没有显著差异。S 组中，接受 L 者 PFS 为 33 月（95%CI 0-77.7），而接受 P 者为 18 月（IC 95:4.3-31.7）（p=0.21）。两组治疗的耐受性一般都很好，但是 S 组有 2 例（5.4%）出现治疗相关的死亡。**结论：**根据已经公布的数据，III-N2 期 NSCLC 中行 S 并不能比 CT-RT 获得更好的 OS。CT-RT 后影像学改善可提示 OS 改善。虽然选择 S 的患者似乎局部进展者减少，但是其总的生存结果和只选择 CT-RT 治疗者类似。

7065 The impact of PET imaging on outcomes in patients with stage III non-small cell lung cancer (NSCLC) treated with chemoradiation: A subset analysis of HOG LUN 01-24/USO-023

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Abstract:

Background: FDG-PET is part of the NCCN recommendations for the pretreatment evaluation of patients with early stage NSCLC. Others have reported improved survival in patients with stage III NSCLC staged by PET. It has been hypothesized that improved outcomes can be realized by PET imaging to reduce treating patients with unsuspected stage IV disease and may improve planning. We, therefore, evaluated the role of PET scan and outcomes treated on a phase III study of cisplatin (P), etoposide (E), and concurrent chest radiation (XRT) with our without consolidation docetaxel (CD). **Methods:** Eligible patients received standard treatment with EP and concurrent XRT. Those with nonprogression were subsequently randomized to receive CD versus observation (OO). Log-ranked tests were used to evaluate the association of pretreatment PET with overall survival. Comparisons were made of the entire patient set (n=243) with respect to PET versus no PET along with comparison of only randomized patients (n=166). **Results:** The PET versus no PET groups were well matched except that PET patients on average had a better performance status (62% vs. 52%) and lower stage IIIA (45% vs. 31%). Overall survival outcomes by PET are summarized in the Table. **Conclusions:** This retrospective, subset analysis of a phase III trial

suggests that the use of PET at baseline did not result in substantially better outcomes for patients with stage III NSCLC treated with chemoradiation.

Patient population	PET MST	NO PET MST	HR	p value
All (n=243)	22.8 mo (n=169)	20.1 mo (n=74)	0.84	0.3352
Randomized (n=166)	24.7 mo (n=113)	25.4 mo (n=53)	0.77	0.2250
CD (n=82)	21.5 mo (n=51)	35.1 mo (n=31)	0.58	0.0624
OO (n=84)	28.4 mo (n=62)	17.6 mo (n=22)	1.13	0.6934

7065 译文 PET 对放化疗治疗的 III 期 NSCLC 患者结果的影响：HOG LUN 01-24/USO-023 的一个亚组分析

摘要

背景：FDG-PET 是 NCCN 推荐的对早期 NSCLC 患者行治疗前评估的手段之一。也有人报道 III 期 NSCLC 患者使用 PET 进行分期可提高 III 期患者的生存率。我们猜测这是因为 PET 扫描可以对减少那些实际上是 IV 期患者的治疗，从而改善了 III 期患者的生存率情况，并有助于改进治疗计划。因此我们评估了 1 个 III 期临床试验中 PET 扫描的作用及通过顺铂（P）、依托泊苷（E）及同步胸部放疗（XRT）治疗后合并或不合并使用多西他赛（CD）的结果。**方法**：符合条件的患者接受标准的 EP 方案及同步 XRT 治疗。 对于那些无进展患者随后随机分配到 CD 组或观察组（OO）。使用 Log-Ranked 检验来评估治疗前 PET 和总体生存率的关系。比较所有患者（n=243）中接受 PET 和不接受 PET 组的情况，并和随机分配的患者进行比较。**结果**：行 PET 和不接受 PET 检查的两组之间进行了很好的匹配，但是 PET 组患者的平均 PS 状态更好（62% vs 52%），分期更低（IIIA 期）（45% vs 31%）。PET 组的 OS 结果见下表。**结论**：这个对于 1 个 III 期试验的回顾性亚组分析提示，在接受化疗的 III 期 NSCLC 患者中，采用 PET 进行基线评估并不能在得到一个统计学有意义的更好的生存期结果。

Patient population	PET MST	NO PET MST	HR	p value
All (n=243)	22.8 mo (n=169)	20.1 mo (n=74)	0.84	0.3352
Randomized (n=166)	24.7 mo (n=113)	25.4 mo (n=53)	0.77	0.2250
CD (n=82)	21.5 mo (n=51)	35.1 mo (n=31)	0.58	0.0624
OO (n=84)	28.4 mo (n=62)	17.6 mo (n=22)	1.13	0.6934

7066 Role of surgery in patients with stage IIIA non-small cell lung cancer (NSCLC): Lessons learned from a tertiary referral cancer center experience

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Abstract:

Background: Stage IIIA NSCLC comprises a heterogenous group of tumors due to differences in primary tumor size and the size and location of nodal disease. The optimal therapeutic approach remains to be defined. Recently published results of the Intergroup (INT) 0139 trial suggest that a trimodality approach incorporating lobectomy (L) is superior to bimodality therapy with chemoradiation (CRT) alone. Pneumonectomy (P), however, did not extend the same benefit. Herein, we report the outcomes of stage IIIA patients (pts) treated at the Fox Chase Cancer Center (FCCC). **Methods:** We analyzed the outcomes of 249 pts with stage IIIA NSCLC (T3 N1; T1-3, N2) treated at FCCC between 01/2000 and 12/2008. Of the 249 pts, 105 underwent L, 41 underwent P and 103 pts were treated with definitive CRT alone. We used Kaplan-Meier estimators to compare survival between these three treatment groups. To account for confounding demographic variables and treatment selection bias, we weighted

the estimators by propensity score based weights. Confounding characteristics were similar among the groups after weighted adjustments. **Results:** The median age of this 249 pt cohort was 65 years; 43% were male. Most pts (96.5%) had N2 disease. After propensity score based weighting, the groups were balanced for age, sex, ECOG performance status, smoking history, histology, T and N stage. Lobectomy yielded superior overall survival (OS) when compared to CRT (median OS 39 months (mos) vs. 22 mos, p=0.038 after propensity score adjustment). One, two, and five year OS was higher for L (88%, 63% and 40% respectively) compared to CRT (75%, 45% and 29% respectively). There was no significant survival benefit for P over CRT (median OS 28 mos vs. 22 mos, p=0.534). Further details of the comprehensive analyses will be provided at the meeting. **Conclusions:** Pts undergoing definitive treatment for stage IIIA NSCLC at FCCC were well balanced for demographic variables by the propensity score analysis. L was significantly superior to CRT for survival whereas P was not. Our results corroborate the findings of the INT 0139 trial and further call in to question the role of P in the management of stage IIIA NSCLC.

7066 译文 在 IIIA NSCLC 中外科手术的作用：该研究为单个肿瘤中心的三组数据

摘要

背景：IIIA 期 NSCLC 所包含的肿瘤有不同大小的原发肿瘤灶和不同大小及分布的淋巴结。其最佳治疗方法仍有待定义。最近公布的 INT 0139 试验结果提示：三种有效治疗方法联合的途径包含肺叶切除术（L），比单纯的化放疗（CRT）2 种治疗方法联合的效果好。但是全肺切除术（P）却没有这种优势。在这里我们报告了在 Fox Chase Cancer Center（FCCC）治疗的 IIIA 期患者的结局**方法：**我们分析了 2000 年 1 月至 2008 年 12 月间在 FCCC 治疗的 249 名 IIIA 期（T3N1;T1-3N2）患者的结局。249 名患者中，105 名患者接受了 L，41 名患者行 P，103 名患者只接受了 CRT。我们用 kaplan-meier 估计值来比较这三种不同治疗组之间的生存情况。为考虑到混杂的人口统计学变量及治疗选择偏倚，我们用倾向性评分对于估计值进行了加权。经过加权调整后各组之间的混杂特点达到了相似。**结果：**249 名患者中位年龄 65 岁，43%为男性。大部分患者（96.5%）为 N2。在计权倾向性评分后，各组之间的年龄、性别、ECOG PS、吸烟史、组织学、T 和 N 分期等都得到了平衡。和 CRT 相比，肺叶切除术后的整体生存情况更好（平均 OS

39 月（mos）vs22 月，倾向性得分调整后 p=0.038）。L 的 1 年、2 年及 5 年 OS（分别为 88%、63%及 40%）高于 CRT（分别为 75%、45%及 29%）。接受 P 者和 CRT 无显著生存优势（中位 OS 28 月 vs 22 月，p=0.534）。**结论：**经过倾向性得分分析后，在 FCCC 治疗的 IIIA 期 NSCLC 患者得到很好的平衡。在生存情况上，L 明显优于 CRT，而 P 没有显示此优势。我们的结果证实了 INT 0139 的结果，进一步对于 P 在 IIIA 期 NSCLC 治疗中的作用提出了质疑。

7067 Influence of surgical interventions on survival in patients with stage IIIb non-small cell lung cancer (NSCLC): The Fox Chase Cancer Center (FCCC) experience

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Abstract:

Background: NSCLC patients (Pts) with T4 and/or N3 disease are categorized as stage IIIB NSCLC. Chemoradiation (CRT) is the standard of care for pts with dry (without malignant pleural effusion) stage IIIB NSCLC. Published results of Intergroup trial, INT 0139, suggests that lobectomy improves survival over CRT in stage IIIA disease. We evaluated the role of surgery in patients with dry stage IIIB to discern whether surgery would have a similar impact in technically resectable cases. **Methods:** Outcomes of NSCLC pts with dry IIIB disease, treated at FCCC between 01/2000 and 12/2008, were analyzed. Stage IIIB patients were dichotomized in two cohorts, those who had surgery versus those treated non-surgically. The propensity score method was used to balance the two cohorts for histology, age, sex, and smoking status. Kaplan-Meier estimators were used to compare overall survival (OS) between

treatment cohorts. **Results:** The median age was 62 years (y) for the 194 pts with stage IIIb disease, of whom 51% were male. Most pts were Caucasian (85%) and smokers (87%). Sixty two pts had adenocarcinoma (32%), 68 squamous cell (35%) and 64 (33%) had NSCLC not otherwise specified. S was performed in 58 pts (29 lobectomies, 11 pneumonectomies and 18 other procedures) (30%) and 136 (70%) underwent CRT alone. After propensity score based weighting, there were no significant differences in patient characteristics, between the two cohorts. S was significantly superior to CRT (median OS 25 months (mos) vs. 16 mos, p=0.009). One, two and five y OS were 70%, 52% and 40% and 64%, 31% and 13% in the S group and CRT group, respectively. Progression-free survival and OS by T and N descriptors will be presented at the meeting. **Conclusions:** After propensity based weighting, OS of dry stage IIIB pts treated surgically was superior to pts treated with CRT. A fresh look at the role of surgery in select patients with dry stage IIIB disease may be warranted.

7067 译文 外科手术的介入对 IIIb 期 NSCLC 病人的生存影响：来自 The Fox Chase Cancer Center (FCCC)

摘要

背景：T4 和/或 N3 的 NSCLC 患者被分类为 IIIB 期 NSCLC。CRT 是无恶性胸腔积液（干性）IIIB 期 NSCLC 的标准治疗方法。团体之间（Intergroup trial）研究（INT 0139）公布的结果提示肺叶切除术可以提高 IIIA 期患者的生存期。我们在干性 IIIB 期患者中评估外科手术的作用以辨别对于那些技术上可切除的病例手术治疗是否也有类似提高生存期的作用。**方法：**2000 年 1 月至 2008 年 12 月之间在 FCCC 治疗的干性 IIIB 期患者进行结局分析。IIIB 期患者被对分到两组队列中：手术治疗的和未手术治疗的。利用倾向评分（propensity score）方法来平衡两组之间的组织学、年龄、性别、吸烟史等区别。利用 kaplan－Meier 估计值来比较两个治疗组的总体生存期（OS）。**结果：**194 名患者的中位年龄 62 岁，51% 为男性。大部分患者为高加索人（85%）和吸烟者（87%）。62 位患者为腺癌（32%），68 位为鳞癌（35%），64 位患者为未进一步分类的 NSCLC（33%）。58 位（30％）患者进行了 S（29 位叶切除术，11 位全肺切除术，18 位行其他术式），136 位患者单纯接受 CRT。经过倾向性得分加权后，两组之间在患者特点上无显著差异。S 比 CRT 明显有优势（中位 OS 25 月 vs. 16 月, p=0.009) S 组的 1 年、2 年及 5 年 OS 分

别为 70%、52%及 40%，CRT 组分别为 64%、31%及 13%。接受 P 者和 CRT 无显著生存优势（中位 OS 28 月 vs 22 月，p=0.534）。结论：经过倾向性得分分析后，接受手术治疗的干性 IIIB 期 NSCLC 患者的 OS 优于 CRT。有理由重新考虑 S 在一些选择性的干性 IIIB 期患者中的治疗作用。

7068 Surgeon-determined variability in quality of surgical resection of lung cancer

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Abstract:

Background: Surgical resection is the main curative modality for patients with non-small cell lung cancer (NSCLC). Curative intent requires attainment of certain quality measures, including R0 resection, examination of hilar/pulmonary and mediastinal lymph nodes. Pneumonectomy and wedge resections may be associated with increased morbidity or suboptimal oncologic outcomes. We have previously demonstrated disparity in attainment of good quality resection (GQR) criteria in a large community cohort. We hypothesized that individual surgeons' practice may be the major determinant of attainment of GQR and sought to examine the extent of variability in surgical practice. **Methods:** All curative-intent resections for NSCLC in the Memphis Metropolitan Area from 1/1/04 to 12/31/08 were reviewed for quality measures and attainment of GQR by NCCN and RADIANT trial criteria. Surgeons were grouped by rate of failure to attain GQR criteria and the number of patients at

risk was stratified by surgeon group. **Results:** 746 surgeries performed by 21 board-certified cardiothoracic or general thoracic surgeons were included. Performance is demonstrated (Table). Seven surgeons failed to meet NCCN criteria and 5 surgeons failed to meet RADIANT criteria in 100% of cases, affecting 168 and 134 patients. **Conclusions:** There is a wide amplitude of variability in performance of GQR by board-certified surgeons in this community-based cohort. In an era emphasizing quality of care and potential pay for performance there needs to be improvement in the characteristics of surgical resection in NSCLC.

Rate (%)	**Surgeons N = 21**	**Patients N = 746**
Resection with positive margins		
<5	<5	<5
5-10	5-10	5-10
>10	>10	>10
Resection without mediastinal lymph nodes		
<10	<10	<10
10-50	10-50	10-50
>50	>50	>50
Resection without any lymph nodes		
<10	<10	<10
10-20	10-20	10-20
>20	>20	>20
Pneumonectomy rate		
<5	<5	<5
5-15	5-15	5-15
>15	>15	>15
Wedge resection rate		
<5	<5	<5
5-15	5-15	5-15
>15	>15	>15

Rate (%)	Surgeons N = 21	Patients N = 746
Failure to meet NCCN criteria		
<80	<80	<80
80-99	80-99	80-99
100	100	100
Failure to meet RADIANT criteria		
<80	<80	<80
80-99	80-99	80-99
100	100	100

7068 译文 取决于外科医生的肺癌手术切除术的质量差异

摘要

背景：手术切除是非小细胞肺癌（NSCLC）患者的主要根治性治疗方法。要达到根治的目的必须要求手术达到一定的要求，包括 R0 切除、肺门和纵隔淋巴结检查。肺切除术和楔形切除术可能会增加复发率或不能达到最佳手术效果。我们之前已经在一个巨大的社区队列中证实了不同个体实现高质量切除术（GQR）标准的差异性。我们假设外科医生的手术实践的个体差异是决定实现 GQR 的主要决定因素，本研究的目的就是探讨怎样来检查外科手术实践的变异性的范围。**方法：**根据 NCCN 和 RADIANT 试验标准，回顾性测定所有 1/1/04 至 12/31/08 间所有在孟菲斯中心地区接受根治性手术治疗的 NSCLC 患者的手术质量和 GQR 的实现情况。根据实现 GQR 标准的失败率对外科医生进行分组，未获得 GQR 的患者数量根据外科医生的分组进行累积。**结果：**共入组了由 21 名有执照的心胸外科或普通胸外科手术医生实施的 746 例外科手术。手术实施情况见列表。有 7 名外科医生其实施的所有手术都没有达到 NCCN 标准，5 名医生的所有手术都没有达到 RADIANT 标准，分别影响了 168 名和 134 名患者。**结论：**在这个社区队列研究中，有执照的外科医生在实现 GQR 时的差异性很大。在重视医疗质量潜在的手术报酬的时代，有必要提高 NSCLC 患者的外科手术规格和质量。

Rate (%)	Surgeons N = 21	Patients N = 746
Resection with positive margins		
<5	<5	<5
5-10	5-10	5-10
>10	>10	>10
Resection without mediastinal lymph nodes		
<10	<10	<10
10-50	10-50	10-50
>50	>50	>50
Resection without any lymph nodes		
<10	<10	<10
10-20	10-20	10-20
>20	>20	>20
Pneumonectomy rate		
<5	<5	<5
5-15	5-15	5-15
>15	>15	>15
Wedge resection rate		
<5	<5	<5
5-15	5-15	5-15
>15	>15	>15
Failure to meet NCCN criteria		
<80	<80	<80
80-99	80-99	80-99
100	100	100
Failure to meet RADIANT criteria		
<80	<80	<80
80-99	80-99	80-99
100	100	100

7069 Confirmation of the role of diabetes in the local recurrence of surgically resected non-small cell lung cancer

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Abstract:

Background: We recently demonstrated that DM was an independent risk factor for LR for patients undergoing resection of NSCLC. This investigation was performed to confirm or refute this finding in a different patient cohort. **Methods:** Patients were eligible if they did not have a second primary cancer within five years of original diagnosis, had at least three month follow-up, and did not receive radiotherapy. There were 373 and 168 patients in the original (P1) and confirmatory (P2) cohorts, respectively, with 66 and 30 patients with DM. Chi-squared (categorical) and Kruskal-Wallis (continuous) tests were used to compare characteristics of patient groups as well as failure patterns. **Results:** Median follow-up was 33 months (range, 3-98 months). Patients with DM were more likely to be older and have high grade tumors, squamous cell carcinoma, and CAD than non-diabetic patients, but did not differ in rates of surgical complications, tumor size, type of resection, number of nodes resected or positive, use of chemotherapy, T, N, or overall stage, or LVI using chi-square testing. DM was an independent risk factor for LR in a Cox model in P2 (p=0.05, HR =2.15) and in P1 (p=0.008, HR=1.90), separately from BMI, glucose control, and the presence of the metabolic syndrome. The rates of LR in the combined population with DM at 2,3, and 5 years

were 23%, 33%, and 56%; respectively; these rates were 15%, 19%, and 26% in nondiabetics. There was no association of available mean pre- or post-surgical (n=25 and 27, respectively) HbA1c values on the risk of LR for patients with DM or between patients receiving insulin (n=13), those receiving oral medications (n=39), or those diagnosed with the metabolic syndrome (n=48). DM did not significantly affect patterns of LR. **Conclusions:** DM was confirmed to be an independent predictor of the risk of LR following resection of NSCLC.

7069 译文 证实糖尿病在手术切除 NSCLC 后局部复发中的作用

摘要

背景：我们最近证实了 DM 是行手术切除的 NSCLV 患者 LR 的独立危险因素。本研究是为了在另一个不同的患者队列中确认或驳斥该发现。**方法**：患者必须符合以下入选条件：诊断的最近 5 年内没有发现第二肿瘤，随访至少 3 月以上，没有接受过放疗。在最初的队列（p1）和确认的队列（p2）中分别有 373 名和 168 名患者，分别有 66 名和 30 名患有 DM。使用差方分析（绝对的）和 Kruskal－Wallis 分析来比较两组患者的特征及不足模式。**结果**；中位随访 33 月（3－98 月）。DM 患者更多是老年患者，肿瘤分期高，鳞癌多见，CAD 多见，但是通过差方分析发现，在术后并发症的发生率、肿瘤大小、手术类型、切除的或阳性的淋巴结数量、化疗的使用、T、N 或总体分期、以及 LVI 方面和非糖尿病者相比并没有显著差异。在 Cox 模型中，DM 是 p2（p＝0,05，HR＝2.15）及 p1（P＝0.008，HR＝1.90） LR 的独立危险因素，和 BMI、血糖控制及代谢综合征等分开。人群中 DM 患者的 2 年、3 年及 5 年的 LR 率分别为 23%，33%及 56%。非糖尿病患者中为 15%，19%及 26%。DM 患者 LR 的风险和术前或术后平均 HbA1C 值无关，和病人是否接受胰岛素或口服药物无关，也和是否诊断为代谢综合征无关。DM 不会显著影响 LR 的模式。**结论**：DM 是 NSCLC 手术后 LR 风险的独立危险因素。

7070 Review of mediastinal lymph node examination (mLNE) in a lung cancer resection (LCR) cohort

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Abstract:

Background: Optimal management after curative-intent LCR requires mLNE. mLN dissection (MLND) and systematic sampling (SS) are acceptable; random sampling (RS) and no sampling (NS) are not. Forty percent of LCR in national databases have NS. We estimated the relative role of surgical and pathology (Path) practice on poor mLNE. **Methods:** Review of operation (OP) notes and Path reports from all LCR in a metropolitan area from 1/1/04 to 12/31/08. mLNE was categorized as: MLND, defined by the ACOSOG Z0030 trial; SS, defined by either ACOSOG Z0030, OSI RADIANT or the ECOG 1505 trial; RS, LNE not meeting the preceding criteria; NS, no LN examined. We compared operating surgeons' claims to the Path report and a blinded independent surgery reviewer (ISR). **Results:** N = 732; median age = 68 years; 52% male; 76% Caucasian; 95% insured; 45% had adeno-, 36% had squamous cancer. 11% had pneumonectomy, 12% wedge resection, the others lobe/bilobectomy. All LCR were by board-certified thoracic surgeons. The Table shows mLNE reported by the 3 observers. None met Path criteria for MLND; no surgeons claimed SS. Highest concordance rate (CR) occurred with RS and NS. Of 249 (34%) LCR with all 3 observers concordant, 85% were NS, 15% RS. The surgeons were concordant in 61% of MLND claims. CR between ISR and Path report was 49% (33% with NS excluded).

Conclusions: There is poor concordance between claimed mLNE procedures after LCR, and objective review of Path reports and OP notes. Identified problems are as follows:1) High proportion of suboptimal mLNE. 2) Wide gap between CR of ISR and pathology review; suggests that pathology examination of mLN material is frequently incomplete. 3) Inaccurate terminology used by operating surgeons to describe mLN retrieval. Interventions to improve the process of mLN mapping and mLNE are urgently needed.

	mLN procedure claimed by operating surgeon N (%)			
	MLND	**SS**	**RS**	**NS**
	326 (45)	0	56 (8)	350 (48)
ISR	198 (61)	-	2 (4)	12 (3)
MLND, n = 121 (29%)	1 (0.3)	-	-	1 (0.3)
SS, n = 2 (<1%)	77 (24)	-	6 (11)	273 (78)
RS, n = 189 (26%)	50 (15)	-	6 (11)	273 (78)
NS, n = 329 (45%)	71			
CR, % Overall Excluding NS	64			
Path report	-	-	-	-
MLND, n = 0 (0%)	50 (15)	-	3 (5)	11 (3)
SS, n = 64 (9%)	221 (68)	-	43 (77)	100 (29)
RS, n = 364 (50%)	55 (17)	-	10 (18)	239 (68)
NS, n = 304 (42%)	39			
CR, % Overall Excluding NS	11			

7070 译文 在一个肺癌切除术（LCR）队列研究中回顾纵隔淋巴结检查（mLNE）情况

摘要

背景：选择根治性 LCR 后的最佳治疗有赖于 mLNE。mLN 切除（MLND）和系统取样（SS）都是有效的方法，但随机取样（RS）和未取样（NS）不能计算在内。在国家资料库中 40%的 LCR 都是 NS。我们的目的是评估在未行有效的 mLNE 的病例中外科手术和病理学检查的相关作用。**方法：**回顾分析 1/1/04 至 12/31/08 期间在一个大城市区域内

的所有 LCR 的手术记录和病理报告。mLNE 情况分为以下几类：MIND（ACOSOG Z0030 试验定义）；SS（ACOSOG Z0030 和 OSI RADIANT 或 ECOG 1505 试验定义）；RS（LNE 不符合前面的标准）；NS（未行 LN 检查）。我们比较了病理报告内容和外科手术评论家对于手术医生的手术评估的差别。**结果**：N=732；平均年龄 68 岁；52% 为男性，76% 为高加索人；95%参加医疗保险；45%为腺癌，36%为鳞癌，11%进行了肺切除术，12%行楔形切除术，其他患者行肺叶或两个肺叶切除术。所有 LCR 都是具有证实资格的胸外科医生施行的。下表展示了 3 名观察者报告的 mLNE 情况。没有一例符合 MLND 的病理学标准；没有外科医生确定按要求进行了 SS。RS 和 NS 的一致性最高。在三名观察者都有统一意见的 249（34%）例 LCR 中，85%是 NS，15%是 RS。61%的外科医生符合 MLND 要求。ISR 和病理报告之间的 CR 未 49%（其中 33%的 NS 除外）。 **结论**：在要求的 LCR 后 mLNE 和客观的病理报告及手术记录之间的一致性很差。主要的问题包括：1）未达理想标准的 mLNE 比例高。2）ISR 和病理学检查之间很大的一致性差异；3）手术的外科医生在描述 mLN 检索时使用了不准确的专业用语。目前迫切需要采取干预措施以提高 mLN 描述和 mLNE 的水平。

	mLN procedure claimed by operating surgeon N (%)			
	MLND	**SS**	**RS**	**NS**
	326 (45)	0	56 (8)	350 (48)
ISR	198 (61)	-	2 (4)	12 (3)
MLND, n = 121 (29%)	1 (0.3)	-	-	1 (0.3)
SS, n = 2 (<1%)	77 (24)	-	6 (11)	273 (78)
RS, n = 189 (26%)	50 (15)	-	6 (11)	273 (78)
NS, n = 329 (45%)	71			
CR, % Overall Excluding NS	64			
Path report	-	-	-	-
MLND, n = 0 (0%)	50 (15)	-	3 (5)	11 (3)
SS, n = 64 (9%)	221 (68)	-	43 (77)	100 (29)
RS, n = 364 (50%)	55 (17)	-	10 (18)	239 (68)
NS, n = 304 (42%)	39			
CR, % Overall Excluding NS	11			

7071 Accuracy of endobronchial ultrasound-directed transbronchial needle aspiration (EBUS-TBNA) for mediastinal staging in patients (pts) with non-small cell lung cancer (NSCLC)

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Abstract:

Background: Accurate staging is critical in defining which pts are surgical candidates in NSCLC. CT and 18FDG-PET can identify mediastinal lymphadenopathy (LAD) but lack specificity. Thoracotomy/thoracoscopy (T) or mediastinoscopy (M) are the gold standards for staging. EBUS-TBNA is a minimally invasive method for sampling mediastinal and hilar LAD and may avoid the need for T or M. **Methods:** We reviewed all pts who underwent EBUS-TBNA procedures from 2006 to 2009 at the University of Miami/Sylvester Comprehensive Cancer Center. Pts were selected for inclusion if the procedure was done for diagnosis and/or staging of NSCLC. All positive EBUS-TBNA's for NSCLC were considered true positives (TP). A false negative (FN) was defined as a negative EBUS-TBNA when T or M was positive for NSCLC. A true negative (TN) was defined as a negative EBUS-TBNA confirmed by a negative T or M for NSCLC. A TN was also recorded in pts who did not have T or M but were followed up for > 1 year and did not have NSCLC diagnosed in the location of the EBUS-TBNA. If NSCLC was diagnosed within 1 year in a location of a negative EBUS-TBNA, this was considered a FN. All other cases were labeled as non-diagnostic (ND).

The accuracy of preprocedure CT and PET for nodal staging was compared to EBUS- TBNA using McNemar's test for paired data. **Results:** 151 pts underwent EBUS-TBNA, 69 of whom had the procedure for nodal staging of NSCLC. There were 43 TP's, 4 FN's, 17 TN's and 5 ND procedures. The sensitivity, specificity, positive predictive value negative predictive value (NPV) and accuracy of EBUS-TBNA for nodal staging were 91%, 100%, 100%, 81% and 94% respectively. The accuracy of EBUS-TBNA was superior to CT (94% vs 77%, p=0.004). Among the 52 pts who had PET, the accuracy of EBUS-TBNA was superior to PET (96% vs 73%, p=0.019). Among the 23 pts who had T or M after EBUS-TBNA, the results were concordant in 21 (91%). **Conclusions:** EBUS-TBNA was more accurate than CT and PET for mediastinal staging of NSCLC. T and M can be avoided in up to 62% of cases, but the relatively low NPV of EBUS-TBNA suggests that the more invasive staging modalities should be pursued in negative or non-diagnostic cases.

7071 译文 支气管内超声引导支气管细针抽吸活检(EBUS-TBNA)用于 NSCLC 病人纵隔分期

摘要

背景：正确的分期对于确定 NSCLC 患者是否适合手术治疗很关键。CT 和 18 FDG-PET 可以辨别纵膈淋巴结病变（LAD），但是缺乏特异性。开胸术/胸腔镜检查（T）或纵膈镜检查（M）是分期的金标准。EBUS-TBNA 是一种纵膈和肺门 LAD 取样的微创方法，可以避免行 T 或 M 检查。**方法：**我们回顾了 2006 至 2009 年间在 University of Miami/Sylvester Comprehensive Cancer Center 行 EBUS-TBNA 的所有患者。那些采用此操作来进行 NSCLC 诊断和/或分期的患者被入选研究。所有阳性的 EBUS-TBNA's 被认为是真阳性（TP），假阴性（FN）被定义为 EBUS-TBNA 阴性而 T 或 M 阳性者。真阴性（TN）被定义为 EBUS-TBNA 和 T 或 M 均阴性。TN 也可代表那些没有行 T 或 M 但是随访 1 年以上 EBUS-TBNA 仍没有发现 NSCLC 者。如果在 EBUS-TBNA 阴性的局部在 1 年内被诊断为 NSCLC，则为 FN。所有其他病例被标记以 ND（无诊断）。对于配对的数据用 McNemar's 检验来验证之前的 CT 及 PET 和 EBUS-TBNA 相比对于淋巴结分期的准确性。**结果：**151 名患者进行了 EBUS-TBNA，69 名患者进行了 NSCLC 的淋巴结分期。有 43 名 TP，4 名 FN，17 名 TN，5 名 ND。敏感性、特异性、阳性预测值、

阴性预测值及 EBUS-TBNA 淋巴结分期的准确率分别为 91%、100%、100%、81%及 94%。EBUS-TBNA 的准确度优于 CT(94% vs 77%, p=0.004). 在 52 名行 PET 检查的患者中，EBUS-TBNA 的准确度也优于 PET(96% vs 73%, p=0.019)。23 名 EBUS-TBNA 后行 T 或 M 者，有 21 名结果是一致的（91%）。**结论：**EBUS-TBNA 对 NSCLC 纵膈淋巴结分期比 CT 和 PET 准确。62%的患者可以避免行 T 和 M。但是 EBUS-TBNA 的 NPV 相对低，提示对于阴性或未诊断病例应该寻找更多侵入性的分期方法。

7072 Does the revised TNM staging system for lung cancer better estimate actuarial rates of local/regional recurrence after surgery?

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Abstract:

Background: The International Association for the Study of Lung Cancer (IASLC) recently recommended changes to the TNM classification of lung cancers. For early-stage disease, increasing tumor size and nodal status are of primary prognostic relevance for overall survival. However, the ability of the old and the new staging system to predict the risk of local/regional recurrence (LRR) has not been evaluated. Therefore, we examined whether the proposed changes in AJCC 7 would refine the risk of LRR in patients who undergo surgery for early-stage NSCLC. **Methods:** The medical records and pertinent radiographs for all patients who underwent surgery for early-stage (N0-N1) NSCLC at Duke between 1995 and 2005 were reviewed. Patients undergoing suboptimal surgery (sublobar resections, positive

margins), or those who received any preoperative therapy or postoperative radiation therapy were excluded. Disease recurrence at the surgical margin, ipsilateral hilum, and/or mediastinum was considered a LRR. Stage was assigned based on both AJCC 6 and AJCC 7. Actuarial rates of LRR were estimated using the Kaplan-Meier method. **Results:** Of 975 patients who underwent surgery during the time interval, 741 were eligible for this analysis. Surgery consisted of lobectomy in 91% (n=672) and pneumonectomy in 9% (n=69) of patients. 82% (n=605) of patients were pathologic N0 (pN0) and 18% (n=136) were pN1. Adjuvant chemotherapy was administered to 7% (n=52). Median follow-up was 35 months. Conversion from AJCC 6 to AJCC 7 resulted in 25% stage migration (upstaging in 15%; downstaging in 10%). For all patients, the 5-year actuarial risk of LRR was 20% (95% CI 17%-24%). 5-year rates of LRR for stage IA, IB, IIA, and IIB disease using AJCC 6 were 12%, 26%, 40%, and 27%, respectively. Using AJCC 7, corresponding rates were 12%, 21%, 34%, and 38%, respectively. **Conclusions:** The risk of LRR increases monotonically with stage in the new AJCC 7 system, but not for the older AJCC 6 system. Thus, the newer staging system is better in predicting the risk of LRR. This information will be valuable when designing future studies of postoperative RT.

7072 译文 修订版的肺癌 TNM 分期系统能更好的估计外科手术后局部/区域性复发的发生率？

摘要

背景：The International Association for the Study of Lung Cancer (IASLC)最近推荐了肺癌的 TNM 分类变化。对于早期肿瘤，肿瘤大小的增加和淋巴结受累情况是总体生存率的主要预后相关因素。但是，旧的和新的分期系统提示局部/区域性复发（LRR）的预言能力还没有得到评估。因此，我们检测了 AJCC 7 中提出的改变是否能提示早期 NSCLC 手术后发生 LRR 的风险。**方法：**回顾了 1995 年至 2005 年间在 DUKE 行手术治疗的所有早期（N0-N1）NSCLC 的医疗记录及相关影像学资料。接受了非最佳手术的患者(小叶切除，切缘阳性)，或曾行术前治疗或术后化疗者被排除在外。疾病于手术切缘、同侧肺门和/或纵膈复发者被认为是 LRR。根据 AJCC 6 及 AJCC 7 进行分期。通过 kaplan-Meier 方法来计算准备的 LRR 率。**结果：**在此期间接受手术的 975 名患者中，741

符合分析的条件。91%（n=672）患者接受肺叶切除术，9%接受全肺切除术（n=69）。82%（n=605）患者病历为 N0(pN0)，18%（n=136）为 pN1。7%患者接受了辅助化疗（n=52），中位随访期为 35 月。AJCC 6 到 7 的转变使得 25%患者分期发生改变（15%上调，10%下调）。所有患者的 5 年 LRR 的确切风险为 20%(95% CI 17%-24%). 使用 AJCC 6 分类的 IA, IB, IIA, 及 IIB 期 NSCLC 的 5 年 LRR 比率分别为 12%, 26%, 40%, 和 27%,而使用 AJCC 7 分类相应的比率为 12%, 21%, 34%, and 38%。**结论：**利用新的 AJCC7 分期各期发生 LRR 的风险都增加。因此，新的分期系统能更好的预示 LRR 的风险。该信息对于将来设计术后 RT 的研究可能很有价值。

7075 Racial disparities on the use of invasive and noninvasive staging in patients (pts) with non-small cell lung cancer (NSCLC)

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Abstract:

Background: Racial health disparities have been reported in NSCLC staging and therapeutic outcomes (Lathan, et al JCO 2006). We investigated whether such disparities exist in the era of modern noninvasive staging modalities, including PET scan use. **Methods:** NSCLC pts in the California Cancer Registry (CCR) diagnosed between 1/94 through 12/04 (reported through 10/06) were included. Cases with unknown race/ethnicity, age, or sex were excluded from the analysis. The likelihood of obtaining invasive (thoracoscopy, bronchoscopy, and mediastinoscopy) and noninvasive staging procedures (CT, MRI, PET scans), as well as surgical resection, were analyzed using logistic regression, controlling for age, sex, residence,

stage, and socioeconomic status (SES). **Results:** Of 13,762 NSCLC pts, 12,395 with adequate staging information were included. 10,217 pts (82%) were classified as white, 2,178 pts (18%) were non-white; blacks comprised 738 pts (6%). Mean age was 66 years for non-whites, 68 years for whites. No association was seen between race and the use of either non-invasive (OR 1.02, p=0.76) or invasive staging procedures (OR=0.96, p=0.44). However, compared to white pts, black pts had a lower likelihood of undergoing surgery, regardless of non-invasive (OR=0.6; <0.001) or invasive staging use (OR=0.63, p=0.02). Higher SES predicted for PET scan use (OR=1.15, p=<0.001), but not for CT (p=0.08) or MRI (p=0.6). Except for race, all other demographic variables significantly predicted for invasive staging use. There was no survival difference for those who underwent surgery between whites and non-whites, regardless of non-invasive (hazard ratio HR=0.95, p=0.45) or invasive staging (HR=1.03, p=0.79). **Conclusions:** In contrast to prior published work, we found no difference in rates of both invasive and non-invasive staging between white and non-white pts in the CCR. However, non-white pts-particularly blacks-were less likely to receive surgery. The reason for the apparent difference in surgical rates between white and non-white pts could not be explained by the variables we evaluated. Thus, other factors such as personal preference or access to care require further investigation.

7075 译文 在 NSCLC 病人侵入性和非侵入性分期的作用存在着种族的不同

摘要

背景：种族健康差异在 NSCLC 的分期及治疗成果方面已经有报道(Lathan, et al JCO 2006)。我文史研究在现代无创分期方式时代，包括 PET 扫描等手段是否也会存在这些差异。**方法：**入选在 California 癌症登记处（CCR）登记的 1994 年 1 月至 2004 年 12 月间诊断的 NSCLC 患者。那些种族、年龄或性别不详者排除在外。通过对数回归来分析获得侵入性（胸腔镜、支气管镜、纵膈镜）及非侵入性分期过程（CT、MRI、PET 扫描）及手术切除方法的可能性，并对照年龄、性别、居住地、阶段，及社会经济状态（SES）。**结果：**在 13762 名 NSCLC 患者中，12395 名有适当分期信息的患者被入选。10217 名患者（82%）是白种人，2178 名（18%）为非白种人，738 名为黑人(6%)。非白种人平均年龄为 66 岁，白种人为 68 岁。种族和患者是否采用有创分期并没有明确关联。但是，

和白种人相比，黑人尽管在采用无创(OR=0.6; <0.001)或有创的(OR=0.63, p=0.02).分期方面无差别，但是选择手术治疗的相对少。高 SES 者采用 PET 分期多见，但使用 CT 或 MRI 者无明显增加。除种族外，其他人口统计学变量都能显著的预示有创分期的使用。在接受手术的人群中，不管其使用无创的还是有创的分期，白种人和非白种人在生存期方面都无显著差异。**结论：**和以前公布的研究相比，我们发现在 CCR 的白人或非白人患者中，采用无创性分期或有创分期的比例并没有差异。但是，非白人患者，尤其是黑人，更少接受手术治疗。白种人和非白种人之间接受手术的比例的显著差异的原因，并不能用我们评估的那些变量来解释。因此，其他因素，如患者个人的倾向或对于治疗的使用权选择方面还需要进一步观察研究。

7077 Use of PET-measured response in involved mediastinal lymph nodes to predict overall survival (OS) in non-small cell lung cancer (NSCLC) patients treated with induction therapy (IT) and surgery

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Abstract:

Background: Persistent N2 disease after IT for NSCLC identifies a group of patients with poor probability of extended survival even after a complete resection. It has been reported that the degree of FDG avidity in N2 nodes prior to treatment and PET measured response in the primary site of disease may be predictors of survival after subsequent resection. We hypothesize that in patients with stage cIIIA (N2) NSCLC, PET measured changes in N2

nodes during IT may help further define prognosis and determine appropriate management. **Methods:** An IRB approved retrospective review of a single institution surgical database was performed to identify cIIIA (histologically-proven N2) NSCLC patients who had pre- and post-IT PET scans and underwent resection. SUVmax of primary tumor and N2 nodes were recorded and percentage reduction (PR) after IT calculated. OS was defined from date of surgery to date of death or last follow-up. The association of OS with age, sex, histology, metabolic response, type of resection, tumor diameter and pN2 status after IT were assessed by uni- and multivariate logistic regression models. Results: From Jan 2000 to Dec 2006 76 eligible patients were identified. On univariate analysis PET response in the N2 nodes was associated with improved median OS at thresholds of PR ≥ 0% (31 months, range 22-48 versus 15 months, range 6-NA, p=0.048) and PR > 60% (34 months, range 22-NA versus 20 months, range 13-34, p=0.013). On multivariate analysis persistent N2 disease [HR = 2.41 (1.07-4.28), p=0.032], PR in the N2 nodes of < 60% [HR = 1.82 (1.06-3.03), p=0.028] and (excluding pN2 status from analysis) PR in the N2 nodes of < 0% (increase after IT) [HR = 2.38 (1.02-5.56), p=0.044] were associated with reduced OS. **Conclusions:** Metabolic response in N2 nodes reflected by reduction in SUVmax is associated with improved OS after resection, whereas metabolic progression predicts inferior outcomes despite complete resection. Reduction of SUVmax > 60% in the N2 nodes is associated with acceptable OS independent of complete pathological response in the mediastinum.

7077 译文 应用 PET 评定纵膈淋巴结疗效预测诱导治疗（IT）和手术治疗的 NSCLC 患者的总生存期

摘要

背景：IT 后的 NSCLC 如持续 N2，即使在完全手术切除后仍很难达到到延长生存期的目的。有报道称治疗前 N2 淋巴结对 FDG 的亲和程度及原发灶对 PET 测定的反应程度可以预示后续的手术切除后患者的生存情况。我们猜测在 cIIIA（N2）期 NSCLC 患者中，在 IT 期间 N2 在 PET 测定时的改变或许可能进一步提示预后并有助于选择合适的处理方法。**方法：**在 IRB 认可的情况下，我们回顾性分析了一个医疗结构中外科手术的数据，以鉴定在 IT 前及 IT 后行 PET 扫描并进行了手术切除的 cIIIA 期（组织学证明为

N2）NSCLC 患者。记录原发灶及 N2 淋巴结的 SUVmax 及 IT 后 SUV 值减小的百分率（PR）。通过确定手术日期至死亡日期或最后随访日期之间的时间来确定 OS。通过单因素或多因素对数回归分析来评估年龄、性别、组织学、代谢反应、手术类型、IT 后肿瘤直径及 pN2 状态等因素和 OS 的关系。**结果：**2000 年 1 月至 2006 年 12 月间有 76 名患者被确认符合试验条件。单因素分析 N2 淋巴结的 PET 反应提示其和中位 OS 的改善相关，改善的阈值为 PR ≥ 0% (31 月,范围为 22-48 vs 15 月, 范围为 6-NA, p=0.048) and PR > 60% (34 月, 范围 22-NA vs 20 月，范围 13-34, p=0.013).多因素分析持续的 N2[HR = 2.41 (1.07-4.28), p=0.032]显示，N2 淋巴结的 PR < 60% [HR = 1.82 (1.06-3.03), p=0.028]和 N2 的 PR < 0% (IT 后增加) [HR = 2.38 (1.02-5.56), p=0.044]和 OS 下降相关。**结论：**SUVmax 反映 N2 淋巴结的代谢反应，和手术后 OS 的改善相关，但是代谢值增加提示预后变差，即使在完全手术后也是如此。N2 淋巴结的 SUVmax 减小>60%提示 OS 改善，是纵隔淋巴结完全病理改善的提示因素。

7079 Health-related quality of life (HRQOL) after stereotactic body radiotherapy (SBRT) for stage I non-small cell lung cancer (NSCLC)

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Abstract:

Background: In patients (pts) with stage I NSCLC who are unfit to undergo surgery, SBRT is a curative treatment which achieves local control rates of >85% in multicenter trials. grade ≥

3 toxicity is uncommon after SBRT but HRQOL has not been well studied. However, HRQOL is often compromised in the first 6 months after surgery, and generally fails to return to baseline values, particularly in elderly pts [Schulte 2009]. We analyzed both HRQOL data and clinical outcomes after SBRT. **Methods:** HRQOL data was prospectively collected from 382 consecutive SBRT pts who were referred from 70 Dutch centers, using the EORTC QLQ-C30 and lung cancer modules. Mean age was 73 years. SBRT was delivered using 3-8 treatment fractions, depending on tumor size and location. HRQOL data were available prior to SBRT (baseline; n=382), at three (n= 282), six (n= 212) and twelve months (n= 144) after SBRT. Completeness of HRQOL data was 76%, 64% and 59% of all pts who were alive and without recurrence at 3, 6 and 12 months, respectively. Thoracic CT scans were performed during each follow-up visit. **Results:** Mean baseline global QoL and physical functioning scores were 62.9 ± 1.1 (SE of mean) and 61.7 ± 1.1, respectively. Highest baseline symptoms scores were seen for dyspnea (47.1 ± 1.7), fatigue (37.4 ± 1.3) and insomnia (21.1 ± 1.6). Median survival was 39.8 months, and correlated with baseline Charlson comorbidity score (p=0.01), lung function (p=0.03), performance status (p=0.05) and physical functioning (p=0.05). At 2 years after SBRT, local-, regional-, and distant control rates were 94.3%, 87.3% and 78.2%, respectively. Late grade 3 toxicity mainly consisted of chest wall pain (3%) and radiation pneumonitis (2%); rib fractures were observed in 1%. None of the functional or symptom scales showed a significant worsening at any of the follow-up time points. **Conclusions:** The baseline physical functioning and global QoL of pts referred for SBRT were far poorer than those reported in the surgical literature. However, HRQOL scores did not decline during the first year after SBRT. The observed local control rate of >90% is consistent with literature findings.

7079 译文 I 期 NSCLC 患者行 SBRT 后的健康相关生活质量（HRQOL）

摘要

背景：一些多中心的试验发现，对于那些不能行手术切除的 I 期 NSCLC 患者，SBRT 作为根治性治疗可以达到 85%以上的局部控制率。SBRT 后出现 3 级以上的毒性反应不多见，但是 HRQOL 还没有很好的研究过。然而，手术后的患者前六个月通常会出现

RQOL 下降，且一般情况下很难恢复到基线水平，尤其是在老年患者中[Schulte 2009]。我们分析了 SBRT 后的 HRQOL 数据和临床结局。**方法：**我们用 EORTC QLQ-C30 and lung cancer modules 前瞻性收集了 Dutch 中心提供的 382 名接受连续 SBRT 的患者的 HRQOL 数据。平均年龄是 73 岁。SBRT 的剂量根据肿瘤大小及部位分为 3-8 个疗程进行。HRQOL 数据包括 SBRT 前（基线，n=382）和 SBRT 后三月（n=282）、6 月（n=212）及 12 月（n=144）的数据。3 个月、6 个月及 12 个月后仍活着且没有复发的患者其 HRQOL 数据的完整性分别为 76%、64%及 59%。每一次随访都进行了胸部 CT 扫描。**结果：**平均的基线总体 QOL 和物理功能评分分别为 62.9 ± 1.1 (SE of mean) 和 61.7 ± 1.1。基线症状评分最高者为呼吸困难(47.1 ± 1.7), 乏力(37.4 ± 1.3) 和睡眠障碍(21.1 ± 1.6)。中位生存期为 39.8 个月，和基线 Charlson comorbidity 评分(p=0.01)、肺功能(p=0.03)、体能状态 (p=0.05)及物理功能状态(p=0.05)相对应. SBRT 后 2 年，局灶、局部及远处控制率分别为 94.3%，87.3% 和 78.2%。迟发的 3 级毒性主要有胸壁疼痛（3%）和放射性肺炎(2%)；1%患者出现了肋骨骨折。在此后的任何一个随访时间点都没有发现功能或症状的明显加重。**结论：**行 SBRT 的患者其基线的物理功能及总体 QOL 比行手术者要差得多。但是，在 SBRT 后第一年的 HRQOL 评分并没有明显下降。90%以上的局部控制率和文献报道的结果是一致的。

7080 Stereotactic radiosurgery for stage I NSCLC in medically inoperable patients: A prospective multicenter study

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Abstract:

Background: Surgical resection is the standard of care for patients with stage I non-small cell lung cancer (NSCLC). However, for high-risk patients stereotactic radiosurgery (SRS), offers an alternative option. Our objective was to prospectively evaluate SRS as definitive treatment for high risk patients with stage I NSCLC in a multi-institutional setting. **Methods:** This is a prospective multicenter study (14 centers) to evaluate Cyberknife SRS for the treatment of stage I NSCLC in medically inoperable patients. Patients were accrued after evaluation by thoracic surgeons and oncologists. The tumor was stratified by location. A high biological effective dose (BED) was delivered (60 Gy) in three fractions to the 80% isodose line for peripheral lesions. We evaluated the initial response rate by the modified RECIST (Response Evaluation Criteria in Solid Tumors) criteria at 3-6 months. This modification incorporated imaging with Positron emission tomography (PET) scanning. We also evaluated time to progression and overall survival. **Results:** A total of 78 patients, 63 with stage IA, 15 with stage IB peripheral NSCLC underwent SRS. Seventy patients were evaluable for response. A complete response was observed in 11 patients (16%), partial response in 37 (53%), stable disease in 20 (28%), and progression in 2 patients (3%). The median follow-up was 11 months (range 0.1-49 months); the median overall survival was not reached. The probability of 2 year overall-survival for the entire group was 62% (95% CI 42%-77%). Overall survival did not differ by stage IA vs. IB (p=0.187). During follow-up with PET and/or CT, 18 patients had recurrence: only 1 local (5%), and 17 with regional or distant recurrence. Median recurrence-free survival (RFS) was 43 months. The probability of 2 year RFS was 54% (95% CI=33%-71%). **Conclusions:** Our preliminary results of the prospective multicenter study of SRS for high-risk patients with stage I peripheral NSCLC is promising compared to standard radiation. In particular, local control was good with a low local recurrence rate (5%), with this dose of 60 Gy in 3 fractions. Additional follow-up is needed, and is ongoing to fully evaluate the results of stereotactic radiosurgery for stage I NSCLC.

7080 译文 临床上不能进行手术的 I 期 NSCLC 患者中实行三维适行立体放疗———个多中心前瞻性研究

摘要

背景：外科手术切除是 I 期 NSCLC 患者标准的治疗方法。但是，对于那些高危患者，实行三维适行立体放疗（SRS）是一个治疗选择。本研究是一个多中心研究，目的是前瞻性评估在高风险的 I 期 NSCLC 患者中 SRS 作为根治性治疗的价值。**方法：**本研究是一个前瞻性多中心（14 个中心）研究，评估电脑控制的 SRS 治疗那些医学上不能行手术治疗的 I 期 NSCLC 患者的意义。患者经过胸外科医生和肿瘤科医师的评估。肿瘤通过位置分层后，这种类型的肿瘤的治疗策略应该按局部肿瘤来处理，一个具有较高生物学效应的剂量(BED) 为 (60 Gy)分三次给予至外周损伤的 80%等剂量线。我们在 3-6 月时通过修正的的 RECIST 标准（实体肿瘤的疗效评估标准）来评估初始反应率。这个修正的标准整合和正电子扫描（PET）成像的结果。同时还评估了进展时间和总体生存时间。**结果：**共 78 名外周型 NSCLC 患者接受了 SRS，其中 IA 期 63 名，IB 期 15 名。70 名患者进行了疗效评估。其中 11 名（16%）患者获得了 CR，37 名患者获得 PR（53%），20 名（28%）获得 SD，2 名（3%）患者疾病进展（PD）。中位随访时间为 11 个月（0.1-49 月），中位总体生存期还没有得出。整组患者的 2 年总生存率可能为 62%（95% CI 42%-77%）。分期为 IA 和 IB 两组间总的生存情况无显著差异（p=0.187）。在 PET 和/或 CT 随访期间，18 名患者出现了复发，其中只有 1 名（5%）患者是局灶复发，其他 17 名患者是局部或远处复发。中位无复发生存期（RFS）为 43 个月。2 年的 RFS 比率为 54%（95% CI=33%-71%）。**结论：**我们这项在高风险 I 期外周型 NSCLC 患者中行 SRS 的多中心前瞻性研究的初步结果提示其有希望和标准的放疗作比较。而且，在分三次使用 60Gy 的剂量下，其在局灶控制无复发方面（5%）表现良好。尚需进一步的随访，以全面评估 I 期 NSCLC 患者行 SRS 的意义。

7081 Photodynamic therapy using NPe6 for bronchogenic carcinomas in central airways more than 1.0 cm in diameter

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Abstract:

Background: Photodynamic therapy (PDT) is recommended as a treatment option for centrally located early lung cancers (CLELCs), meaning roentgenographically occult squamous cell carcinomas that are located no more distally than segmental bronchi and, histologically, are either carcinoma in situ or carcinoma associated with only limited invasion. Since CLELC patients who are heavy smokers are at fairly high risk of developing a second primary lung cancer, they require treatment that will preserve their cardiopulmonary function. Most centrally located early lung cancers (CLELCs) less than 1.0 cm in diameter do not invade beyond the bronchial cartilage, and photodynamic therapy (PDT) with Photofrin is currently recommended as a treatment option for such lesions. NPe6 is a second-generation photosensitizer, and since it has a longer absorption band (664 nm) than Photofrin (630 nm), we hypothesized that NPe6-PDT would exert a strong antitumor effect against cancer lesions greater than > 1.0 cm in diameter, which are assumed to involve extracartilaginous invasion and to be unsuitable for treatment with Photofrin-PDT. **Methods:** Between June 2004 and December 2008, 75 patients (91 lesions) with CLELC underwent NPe6-PDT after the extent of their tumors had been assessed by fluorescence bronchoscopy for photodynamic diagnosis (PDD) and tumor depth had been assessed by optical coherence tomography (OCT). **Results:** Seventy-four cancer lesions Å…1.0 cm in diameter and 21 lesions >1.0 cm in diameter were

identified, and the CR rate was 94.0% (66/70) and 90.4% (19/21), respectively. After the mass of large tumors and deeply invasive tumors, had been reduced by electrocautery, NPe6-PDT was capable of destroying the residual cancer lesions. **Conclusions:** NPe6-PDT has a strong antitumor effect against CLELCs >1.0 cm in diameter that have invaded beyond the bronchial cartilage, thereby enabling the destruction of residual cancer lesions after mass reduction of large nodular or polypoid type-lung cancers by electrocautery. The PDT guidelines for lung cancers should therefore be revised, because use of NPe6-PDT will enable expansion of the clinical indications for PDT.

7081 译文 用 NPe6 光动力治疗大气道内直径大于 1.0cm 的支气管来源的肿瘤

摘要

背景：光动力治疗（PDT）是那些中央型分布的早期肺癌（CLELCs）的推荐治疗方法，CLELCs 是指那些 X 线不能发现的、局限在段支气管以近的、组织学提示为原位癌或肿瘤只有局部侵犯的鳞状细胞癌。因为具有大量吸烟史的 CLELC 患者发生第二种原发肺癌的可能性很大，在他们的治疗中要求能保护他们的心肺功能。大部分直径小于 1.0cm 的中央型早期肺癌（CLELCs）一般不会侵犯到气管软骨外，对于这种肿瘤的治疗最近推荐用光卟啉行光动力治疗（PDT）作为治疗选择。NPe6 是第二代光敏剂，它比光卟啉具有更长的吸收光谱（664nm vs 630nm），我们猜测 NPe6-PDT 或许能产生更强的抗肿瘤效应，可用于治疗直径大于 1.0cm、可能侵犯到软骨外而不适合用光卟啉-PDT 治疗的肿瘤。**方法：**2004 年 6 月至 2008 年 12 月间共有 75 名 CLELC 的患者（91 处病灶）进行了 NPe6-PDT 治疗，在治疗前他们都通过荧光支气管镜进行了肿瘤的光动力诊断（PDD）并通过光学结合体层扫描（OCT）估测肿瘤侵犯深度。**结果：**共有 74 个直径在 1cm 以下的病灶及 21 个直径 1.0cm 以上的病灶，CR 率分别为 94.0%（66/70）和 90.4%（19/21）。在大的瘤体和深入侵犯的肿瘤通过电烙术被减小后，NPe6 能破坏残留的癌灶。**结论：**NPe6-PDT 对于直径在 1.0cm 以上侵犯到支气管软骨下的 CLELCs 有很强的抗肿瘤作用，因此在大结节或息肉状肺癌通过电烧把大的瘤体切除后，NPe6 可以消灭残存的癌灶。因此 PDT 的指南应该作相应修改，因为 NPe6-PDT 的使用使得 PDT 的临床适应症扩大了。

7082 Ongoing phase II study of pemetrexed plus carboplatin or cisplatin with concurrent radiation therapy followed by pemetrexed consolidation in patients with favorable-prognosis inoperable stage IIIA/b non-small cell lung cancer: Interim update

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Abstract:

Background: There is no consensus chemotherapy regimen with concurrent radiation therapy (CRT) for inoperable stage IIIA/B non-small cell lung cancer (NSCLC). Pemetrexed (P) is synergistic with carboplatin (Cb) and cisplatin (C) in preclinical models. These doublets have shown efficacy and favorable toxicity profiles in metastatic disease in phase II/III trials. P, Cb, and C have activity as radiosensitizers. The objective of this study is to determine the toxicity, feasibility, response rates as well as of overall all survival (OS) of these doublets in stage III NSCLC. **Methods:** Pts with inoperable stage IIIA/B NSCLC were randomized to P 500 mg/m2 every 21 days combined with Cb AUC=5 (PCb) or C 75 mg/m2 (PC) IV every 21 days for 3 cycles. All pts received CRT 64-68 Gy (2 Gy/day, 5 days/week, Days 1-45). Consolidation P 500 mg/m2 IV every 21 days for 3 cycles began 3 wks after completion of chemoradiation. Primary endpoint of this ongoing trial is 2-year overall survival; secondary endpoints include toxicity, response rate, time to progression, and median survival. **Results:**

Since June 2007, 71 pts have been evaluated, PCb: 34; PC: 38. Average dose compliance was PCb: 92.2% P, 90.2% Cb; PC: 90.4% P, 89.2% C. Average dose compliance for CRT was PCb: 91.2%, PC: 85.5%. Dose interruptions occurred with 23 pts. The PCb arm had 15 pts evaluable for response: CR, 1 (6.7%); PR, 6 (40.0%); SD, 7 (46.7%) and PD, 1 (6.7%). The PC arm had 20 evaluable pts: CR, 1 (5.0%); PR, 11 (55.0%), SD, 5 (25.0%) and PD, 3 (15.0%). **Conclusions:** Overall, P plus either Cb or C in combination with CRT appears well-tolerated in treatment of locally advanced NSCLC.

7082 译文 在不能手术的预后较好的 IIIA/B 期非小细胞肺癌中用培美曲塞+卡铂或顺铂及同步放疗、随后以培美曲塞巩固治疗的一项正在进行中的 II 期临床试验：中期更新

摘要

背景：对于不能手术的 IIIA/B 期 NSCLC 患者行同步放化疗（CRT）时的化疗方案目前还没有意见一致的推荐方案。之前的临床前模型提示培美曲塞（P）和卡铂（Cb）及顺铂（C）有协同作用。在转移性肿瘤的 II/III 期试验中这种两药联合的方案显示了较好的有效性和毒性。P、Cb 和 C 有放疗增敏剂的作用。本研究的目的是观察 III 期 NSCLC 中使用这种双药化疗方案的毒性、耐受性，并观察总体生存期（OS）以判断疗效。**方法：**不能手术切除的 IIIA/B 期 NSCLC 患者被随机分配到 P 500mg/m2 + Cb AUC=5 (PCb)每 21 天 1 次组或 P 500mg/m2+C 75 mg/m2 (PC) IV 每 21 天 1 次组，共三个周期。所有患者都同时行 CRT 64-68 Gy (2 Gy/天, 5 天/周, D1-D45). 巩固治疗为 P 500mg/m2 IV 每 21 天 1 次，共三个周期，在化放疗结束后 3 周开始。本研究的第一终点是 2 年总生存率，第二终点包括毒性、有效率、疾病进展时间及中位生存率。**结果：**2007 年 6 月起有 71 名患者入组试验，PCb 34 名，PC 38 名。平均剂量耐受率：PCb 组 92.2% P，90.2% Cb；PC 组 90.4%P，89% C。CRT 的平均剂量耐受率为：PCb 91.2%，PC 85.5%。23 名患者发生了剂量中断。PCb 臂有 15 名患者评估了疗效：CR 1（6.7%）；PR 6（40.0%）；SD 7（46.7%），PD 1（6.7%）。PC 臂有 20 名患者评估了疗效：CR 1（5.0%），PR 11（55.0%），SD 5（25.0%），PD 3（15%）。**结论：**综上所述，P+Cb 或 C 化疗和 CRT 联合的方案在局部进展的 NSCLC 的治疗中具有良好的耐受性。

7083 Randomized phase II trial of tegafur-uracil (UFT) and cisplatin versus vinorelbine and cisplatin with concurrent thoracic radiotherapy for locally advanced unresectable stage III non-small cell lung cancer: NJLCG 0601

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Abstract:

Background: A treatment (UP) with tegafur-uracil (UFT) and cisplatin in combination with concurrent thoracic radiotherapy (c-TRT) could have favorable efficacy with less toxicity for locally advanced non-small cell lung cancer (LA-NSCLC). We conducted this randomized phase II study to compare this regimen to a treatment (VC) with vinorelbine and cisplatin, which is a commonly used regimen with c-TRT for LA- NSCLC in Japan. **Methods:** Patients (pts) with LA-NSCLC were randomized to receive UP (UFT400 mg/m2 on days 1-14 and 29-42 and cisplatin 80 mg/m2 on days 8 and 36) or VC (vinorelbine 20 mg/2 on days 1, 8, 29, and 36 and cisplatin 80 mg/m2 on days 1 and 29), stratified by age, gender, histology, and stage. In both arms, c-TRT began on day 1 (total 60Gy in 30 fractions). The primary endpoint was overall response rate (ORR), and secondary endpoints were progression-free survival (PFS), overall survival, and toxicity profile. Assuming that ORR of 80% in eligible pts would indicate potential usefulness while ORR of 60% would be the lower limit of interest, the estimated accrual was 33 pts in each arm. **Results:** From February 2006 to May 2009, 70 pts were enrolled from 5 institutions. Finally 66 pts were evaluable for efficacy and safety.

Patient characteristics were: Male/Female 54/12; median age 62 (range 40-75); Performance status 0/1 31/35; IIIA/IIIB 24/42. ORRs were 80% (95%CI: 67-93) and 71% (95%CI: 55-87) for the UP arm and the VC arm, respectively. With a median follow-up of 11.8 months, median PFS in the UP arm was 7.9 months and in the VC arm was 5.9 months. grade 3/4 neutropenia occurred in 20% and 58% of pts in the arms UP and VC, respectively. There was no remakable difference in other toxicities between both arms. Two pts in the VC arm died of radiation pneumonitis. **Conclusions:** Combined with c-TRT, UP achieved more preferable efficacy and safety compared with VC, suggesting a promising candidate as a standard regimen with c-TRT for LA-NSALC. Further evaluation of UP with c-TRT is warranted in a phase III setting in comparison with cisplatin-based second generation chemotherapy with c-TRT.

7083 译文 分别用替加氟尿嘧啶+顺铂和长春瑞滨+顺铂并同步胸腔放疗治疗不能手术切除的局部进展 III 期非小细胞肺癌的 II 期随机临床试验：NJLCG 0601

摘要

背景：用替加氟尿嘧啶（UFT）+顺铂方案（UP）化疗联合同步胸腔放疗（c-TRT）的方案治疗局部进展的非小细胞肺癌（LA-NSCLC）疗效较好且毒副反应较小。VC 方案是长春瑞滨+顺铂，是一个在日本常用于 LA-NSCLC 和 c-TRT 联合应用的常用方案，本实验是把 UP 方案和 VC 方案进行随机对照比较的 II 期临床试验。**方法：**LA-NSCLC 患者被随机分配到 UP 组（UFT 400mg/m2，d1-14，d29-42，顺铂 80mg/m2d8 和 d36）或 VC 组（长春瑞滨 20 mg/2 d1, 8, 29, 36+顺铂 80 mg/m2 d1，d29)，并对年龄、性别、组织学及分期进行平衡。两组都从 D1 开始行 c-TRT（60Gy/30 次）。主要终点是总体有效率(ORR),第二终点是无进展生存期（PFS）、总体生存期及毒性反应。假定合格的患者中有 80%的 ORR 提示有效，而 ORR 在 60%为有效性的下限。预计入组的患者为每组 33 名。**结果：**2006 年 2 月至 2009 年 5 月期间，5 个研究中心共有 70 名患者入选试验。最后有 66 名患者评估了疗效和安全性。患者的特点为：男性/女性 54/12；中位年龄 62 岁(fanwei 40-75);PS 0/1 分别为 31/35；IIIA/IIIB 24/42。UP 组和 VC 组的 ORRs 分别为 80%（95% CI：67-93）和 71%（95%CI：55-87）。平均随访期为 11.8 月，UP 组中位 PFS 为 7.9 月，VC 组为 5.9 月。UP 组和 VC 组发生 3/4 级的粒细胞减少分别为 20%和 58%。2

组在其他毒性反应方面没有显著差异。VC 有 2 名患者死于放射性肺炎。**结论：**和 cTRT 联合使用时，UP 比 VC 组显示更好的疗效和安全性，提示 UP 可以作为和 c-TRT 联合治疗 LA-NSALC 的候选标准方案。对 c-TRT 和 UP 方案联合的进一步评估尚需以 III 期试验的模式和其他以顺铂为基础的第二代和 c-TRT 联合的化疗方案进行比较。

7084 Safety and efficacy trial of cisplatin (P) with vinorelbine (V) followed by gefitinib (G) and concurrent thoracic radiotherapy (TRT) for unresectable locally advanced non-small cell lung cancer (LA-NSCLC): Japan Clinical Oncology Group (JCOG) 0402

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Abstract:

Background: JCOG0402 was conducted to evaluate safety and efficacy of P with V followed by G and TRT for unresectable LA-NSCLC. **Methods:** The pts received induction chemotherapy with P (80mg/m2, d1 and 22) and V (25mg/m2, d1, 8, 22, 29) followed by G (250mg, beginning on d43) and TRT (60Gy/30fr, d57-98). G was continued for 1 year if neither unacceptable toxicity nor tumor progression were observed. The primary endpoint was feasibility, which was defined as the proportion of pts who completed the TRT treatment (60Gy) and received more than 75% of the planned dose of G, without developing grade 2 or worse pneumonitis. The sample size was determined to be 37, with a one-sided alpha of 0.1

and a beta of 0.1; the expected and threshold values for the primary endpoints were 75% and 55%. **Results:** From Oct 2004 to Sep 2008, 38 pts (14 men, 24 women) with LA-NSCLC were enrolled from 12 hospitals in Japan. Most of the pts were Japanese and were never or light smokers. The median age was 59.5 years (30-69 years); PS 0: 29, 1: 9; adenocarcinoma: 37, P/D carcinoma: 1. Two pts developed grade 2 or worse pneumonitis and G was suspended in 14 pts because of transient toxicity. Of the 38 pts, 23 pts (61%) completed treatment without experiencing grade 2 or worse pneumonitis; this percentage was slightly less than our previously defined criterion for treatment feasibility. During the concurrent phase of G and TRT, grade 3/4 transaminase elevations were observed in 31%/6% of the pts, respectively. All other toxicities were relatively mild. Efficacy was evaluated among 37 pts. The overall response rate was 73% (95%CI: 56~86%, 1CR, 26PR) and the MST was 28.1 months. The 1-, 2-, 3-year survival rates were 94%, 61%, 36%, respectively. **Conclusions:** P with V followed by G and TRT was effective among highly select pts with unresectable LA-NSCLC. Although the results did not meet our criterion for feasibility, the toxicity level was acceptable. P with V followed by G and TRT might warrant further evaluation among select pts, such as EGFR mutation positive LA-NSCLC.

7084 译文 顺铂（P）+长春瑞滨（V）化疗，随后以吉非替尼（G）及同步胸腔放疗（TRT）的联合治疗方案治疗不能手术的局部晚期非小细胞肺癌（LA-NSCLC）的安全性和有效性研究：来自日本临床肿瘤学组（JCOG）0402

摘要

背景：ICOG0402 目的是评估 P+V 化疗继之以 G 和 TRT 治疗不能手术切除的 LA-NSCLC 的安全性和疗效。**方法：**患者先接受 P(80mg/m2, d1 and 22)+V (25mg/m2, d1, 8, 22, 29)方案的诱导化疗，随后以 G(250mg, d43 开始)和 TRT (60Gy/30fr, d57-98)治疗。如果没有出现严重的毒性反应或疾病进展，则 G 的治疗持续 1 年。主要终点是可行性，定义为完成 TRT 治疗（60Gy）并接受了 75%以上的计划剂量的 G 而没有出现 2 级或以上的肺炎的患者比例。预定的样本量为 37，（with a one-sided alpha of 0.1 and a beta of 0.1）；主要终点的预期阈值为 75% 和 55%。**结果：**2004 年 10 月至 2008 年 8 月间共有来自日本 12 家医院的 38 名 LA-NSCLC 患者（14 名男性，24 名女性）入组研究。绝大部分是日本

人，无吸烟史或仅有少量吸烟史。中位年龄是 59.5 岁（30-69 岁）；PS 0：29 例，PS 1：9 例；腺癌 37 例，P/D 癌 1 例。2 例患者出现了 2 级及以上的肺炎，14 名患者因暂时的毒性反应而发生了 G 治疗的暂停。38 例患者中，有 23 例患者（61%）完成了整个治疗过程，而没有出现 2 级及以上的肺炎；该比例比我们最初设计的治疗可行性的标准稍低。在 G 和 TRT 联合治疗期间，患者中出现 3/4 级转氨酶升高的比例分别为 31%/6%。所有其他的毒性反应都相对轻微。37 例患者进行了疗效评估。总体有效率为 73%(95%CI: 56~86%, 1CR, 26PR) ，MST 为 28.1 月。1 年、2 年、3 年的生存率分别为 94%、61%和 36%。**结论：**P+V 继之以 G 和 TRT 联合治疗在高度选择的不能手术切除的 LA-NSCLC 患者中是有效的。虽然结果没有达到我们的可行性标准，但是毒性反应方面表现良好。下一步马克在进一步选择的患者中，如 EGFR 突变阳性的 LA-NSCLC 患者中评估 PV 继之以 G+TRT 治疗的联合方案的疗效。

7085 N0321: A phase I study of bortezomib, paclitaxel, carboplatin (CBDCA), and radiotherapy (RT) for locally advanced non-small cell lung cancer (NSCLC)

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Abstract:

Background: In preclinical studies, bortezomib and RT combinations result in synergistic tumor killing. Our group also demonstrated promising efficacy with the sequential combination of paclitaxel/CBDCA and bortezomib in advanced solid tumors (Ma C et al,

Cancer Chemother Pharmacol.;59;207-15, 2007). Based on these data, we undertook a phase I study of bortezomib in combination with paclitaxel/CBDCA and RT. **Methods:** Systemic therapy included bortezomib (0.5-1.2 mg/m2IV days 1,4,8,11), paclitaxel (150-175 mg/m2 IV day 2), and carboplatin (CBDCA) AUC=5-6, day 2 given every 3 weeks for 2 cycles. Thoracic radiotherapy (TRT) included 60Gy/30daily fractions starting day 1. Dose escalation followed a standard 3+3 design, where the maximum tolerated dose (MTD) was defined as the highest dose where ≤2 patients (pts)/6 pts had dose-limiting toxicity (DLT) with the next higher dose having at least 3/6 pts with DLT. DLT was defined to include grade 4 neutropenia or thrombocytopenia for ≥8days, grade≥4 febrile neutropenia, grade≥4 RT dermatitis, esophagitis grade≥3 requiring hospitalization, pneumonitis grade≥3 (requiring O2), dyspnea grade ≥4 (at rest), or other non-heme grade≥4 toxicity that was not manageable with medical interventions (IVs, narcotics). **Results:** 27 pts were enrolled: M/F=17/10; stage IIIA/IIIB=9/18; ECOG PS 0/1=15/12; and median age:63 (range 45-78). 17 pts (63%) completed therapy per protocol. Dose level (DL) 1 resulted in 1/6 pts experiencing a grade 3 pneumonitis requiring oxygen (1DLT). No DLT occurred in DL 2-5. DL 6 enrolled 6 pts, with 1 DLT (grade 4 neutropenia; one for ≥8days (1DLT)). Overall, 13/27 (48%) pts experienced grade 3/4 hematologic toxicity and 6/27 (22%) pts experienced grade4 heme toxicity. No pts experienced grade 5 toxicity, and only 3 pts experienced grade 4 non-heme toxicity. DL 6 (bortezomib:1.2 mg/m2 days 1,4,8,11; paclitaxel:175 mg/m2 day 2; CBDCA:6 AUC day 2; for 2 cycles+TRT) is the recommended dose for phase II testing. With a median follow-up of 26 months, the median OS is 25 months. **Conclusions:** This treatment appears reasonably well tolerated and the median survival promising. A phase II study with this regimen has begun accruing pts.

7085 译文 N0321：Bortezomib、紫杉醇、卡铂（CBDCA）及放射治疗局部晚期的非小细胞肺癌的 I 期研究

摘要

背景：临床前研究提示bortezomib和RT联合具有协同的抗肿瘤作用。我研究组也已经证实紫杉醇/CBDCA和bortezomib联合序贯治疗晚期实体肿瘤（Ma C等，Cancer Chemother Pharmacol. 59;207-15,2007）疗效良好。在此基础上，我们进行了一项bortezomib联合紫杉醇/CBDCA及RT治疗的I期临床试验。**方法：**系统治疗包括bortezomib（0.5-1.2mg/m^2 IV，d1,4,8,11），紫杉醇（150-175mg/m^2 IV d2）和卡铂（CBDCA）AUC＝5-6，d2，每三周为一个疗程，行两个周期。胸腔放疗（TRT）包括 60Gy/30 次，从d1 开始。剂量递增按照标准的 3+3 计划进行。最大耐受剂量（MTD）被定义为≤2 名/6 名患者出现剂量限制毒性（DLT）且下一个更高的剂量组至少有 3/6 名患者出现DLT的最大剂量。DLT定义为持续 8 天及以上的 4 级中性粒细胞减少或血小板减少，≥4 级的中性粒细胞减少伴发热，≥4 级的放射性皮炎，需要住院治疗≥3 级的食道炎，≥3 级的肺炎（需要吸氧），≥4 级的呼吸困难（休息状态下），或其它≥4 级的非血液学毒性（不能通过医疗手段治疗）（IVs，narcotics）。**结果：**共入选 27 名患者：M/F=17/10；分期IIIA/IIIB＝9/18；ECOG PS 0/1＝15/12；平均年龄 63 岁（45-78 岁）。17 名患者（63%）按照试验方案完成了治疗。剂量组（DL）1 有 1/6 名患者出现了 3 级肺炎需要吸氧（1DLT）。DL2-5 中没有出现DLT。DL6 入组了 6 名患者，出现了 1 个DLT（4 级中性粒细胞减少症，持续≥8 天）。总共有 13/27（48%）名患者经历了 3/4 级血液系统毒性，6/27（22%）名患者经历了 4 级血液学毒性。没有患者出现 5 级毒该性反应。只有 3 名患者出现了 4 级非血液学毒性。DL6（bortezomib：1.2mg/m2，d1,4,8,11；紫杉醇 1.75mg/m2 d2；CBDCA：6 AUC d1 共两个周期，＋TRT）是II期试验的推荐剂量。在平均 26 个月的随访期中，中位OS是 25 个月。**结论：**该治疗方案显示的良好耐受性和中位生存情况提示该方案可能是合理的。该方案的II期临床试验目前已经开始入组病人。

7086 A phase I dose-escalation study using three-dimensional conformal radiotherapy with concurrent cisplatin and S-1 in patients with stage III non-small cell lung cancer

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Abstract:

Background: Concurrent chemoradiotherapy with the total radiation dose of 60 Gy is standard treatment for inoperable stage III non-small cell lung cancer (NSCLC). In our previous phase II trial, 60 Gy of thoracic radiotherapy concurrent with cisplatin and S-1 was a promising regimen with good survival rates (MST 33 months) and mild toxicities (Br J Cancer 2009;101,225), but the local failure rate was not preferable. According to this result, a dose-escalation study using 3-dimensional conformal radiotherapy (3D-CRT) up to 74 Gy was performed with the same chemotherapy regimen. Here, we report the feasibility and the late toxicities at 74 Gy dose level of this concurrent chemoradiotherapy. **Methods:** The eligibility criteria were: histologically or cytologically proven NSCLC, 20-75 years old, and performance status 0-1. Cisplatin (60 mg/m2 on day 1) and S-1 (orally at 40 mg/m2/dose b.i.d., on days 1-14) were administered every 4 weeks for 4 cycles and radiotherapy was started on day 1. Radiation dose was escalated from 66 Gy/33fxs (Level I) to 70Gy/35fxs (Level II), and then to 74 Gy/37 fxs (Level III). The target volume included the primary tumor and involved lymph nodes. Elective nodal irradiation was not performed. Dose constraints were as follows: the lung, V20 < 30%; the esophagus, mean dose ≤ 34 Gy and V55 ≤

30%; the spinal cord, max dose ≤ 50 Gy. Each escalation process was validated when dose limiting toxicities (DLTs) were observed in only 2 or less patients among 6 patients in each dose level. After evaluation of acute toxicities at all levels, additional 6 patients were enrolled in level III to confirm the feasibility and the late toxicities of 74 Gy. Results: Among 24 patients at level I, II, and III, 2 DLTs were observed at level I (grade 3 febrile neutropenia, mucositis, and diarrhea) and 1 DLT (grade 3 vasospastic angina pectoris) in 1 of the newly registered 6 patients at level III. At the median follow-up time of 9 months, no severe late toxicities were observed in 12 patients at level III. **Conclusions:** By using 3D-CRT, the radiation dose could be escalated to 74 Gy without increase of severe late toxicities when concurrently combined with cisplatin and S-1.

7086 译文 III 期非小细胞肺癌患者用三维适形放疗和同步的顺铂＋S-1 方案化疗治疗的 I 期剂量递增研究

摘要

背景：化疗和同步的总剂量为 60Gy 的放疗是不能手术的 III 期非小细胞肺癌（NSCLC）的标准治疗。在我们之前的 II 期试验中，60Gy 的胸腔放疗和同步的顺铂＋S-1 是一个有前途的方案，但是局部复发率方面不令人满意。在这个结果基础上，我们设计了这个三维正形放疗（3D-CRT）剂量达 74Gy 而同步的化疗方案不变的剂量递增研究。这里我们报道的主要是这个同步化放疗方案中剂量水平达 74Gy 时的可行性和迟发毒性。**方法：**入选标准包括组织学或细胞学证实的 NSCLC 患者，年龄在 20-75 岁之间，PS 0-1。化疗方案为顺铂（60mg/m2，d1）和 S-1（口服，40mg/m2, bid,d1-14），每 4 周一个疗程，共 4 个疗程；放疗是从 d1 开始。放射剂量自 66Gy/33fxs（I 级）递增到 70Gy/35fxs（II 级），然后到 74Gy/37fxs（III 级）。目标体积包括原发肿瘤及受累及的淋巴结。不进行选择性淋巴结照射。剂量约束如下所示：肺，V20<30%；食道，平均剂量≤34Gy,V55≤30%；脊髓，最大剂量≤50Gy。当剂量限制毒性（DLTs）在相应一个剂量等级中每 6 个患者只有 2 个或者更少出现时，相应一个按比例上升的过程都是确证无误的。在评估了所有等级的急性毒性后，另外的 6 个患者被登记在等级 III 以确证 74Gy 的可行性和晚期毒性。**结果：**在等级 I，II，III 包含的 24 个患者中，发现等级 I 有 2 例 DLTs（3 级中性粒细胞减少性发热，粘膜炎和腹泻），等级 III 在新近注册的 6 个患者中的 1 个有 1 例 DLTs（3

级血管痉挛性心绞痛）。在 9 个月的中位随访时间中，没有发现在 12 个 III 级的患者中有严重的晚期毒性。**结论：**通过使用三维正形放疗，同时联合顺铂+S-1 治疗，放射剂量能升高到 74Gy 而不增加严重的晚期毒性。

7087 A phase II study of concurrent pemetrexed/cisplatin/radiation (RT) for unresectable stage IIIA/b non-small cell lung cancer (NSCLC)

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Abstract:

Background: Concurrent chemoRT is standard of care for most patients with unresectable stage III A/B NSCLC but no standard chemotherapy regimen/schedule has been established. In a previous phase I study (Brade et. al, ASCO 2008), we reported that pemetrexed was the first 3rd generation deliverable at full dose concurrently with full dose RT and cisplatin. This combination was further in this study. **Methods:** Starting April/07 to Aug/09, patients with unresectable stage IIIA/B NSCLC were entered on a single arm phase II trial at 5 Canadian centers. Eligibility: < 5% weight loss; ECOG PS 0/1; no malignant effusions; FEV1 >1.3 l; adequate organ function. Staging PET scans were not routinely available. Patients received pemetrexed 500 mg/m2 day 1, cisplatin 20 mg/m2 days 1-5 q21 days x 2 concurrent with RT (61-66 Gy in 6-6.5 weeks) followed by pemetrexed/cisplatin alone x 2 q21 days (pemetrexed 500 mg/m2 day 1, cisplatin 75 mg/m2 day 1). **Results:** 39 patients were accrued.

Demographics: median age: 63 years [range 37-80]; stage IIIA/B: 15/24; Histology: adenocarcinoma (21), squamous (10), mixed (1), large cell (1), NSCLC (6); median radiation dose: 65 Gy [range 14.4-66]. Four cycles of chemotherapy were delivered in 29/39 pts (3, 2 and 1 cycle in 3, 6 and 1 patient, respectively). Twenty of 39 patients experienced grade 3/4 toxicity deemed probably/definitely related to study therapy; 10 had grade 3/4 hematologic toxicity, primarily neutropenia; grade 3/4: 8/2 patients. Grade 3 non-hematologic toxicity was observed in 14 patients: nausea/vomiting 4; esophagitis 2; electrolyte alterations 5; fatigue/syncope 4. Grade 4 hypotension/syncope was seen in 1 patient. Grade 3 pneumonitis was observed in 1 patient, grade 2 pneumonitis in 4 patients. Median overall/progression-free survivals were 19.7/11.8 months, respectively. One year overall/progression-free survivals were 80%/47%, respectively. **Conclusions:** Full dose pemetrexed/cisplatin with full dose concurrent RT is relatively well tolerated and active in stage III/B NSCLC. These data provide support for an ongoing phase III registration trial (PROCLAIM) evaluating a similar regimen.

7087 译文 培美曲赛联合顺铂与放疗同步治疗不能手术切除的 IIIA/b NSCLC 的 II 期研究

摘要

背景：同步化放疗是大多数不能手术切除的 IIIA/b NSCLC 的标准治疗，但是没有标准的化疗方案。在之前的 1 个 I 期研究(Brade et. al, ASCO 2008),我们已经报告了培美曲赛是第一个三代可与的足量放疗和足量顺铂的化疗药。这里将进一部研究这个联合方案。**方法：**2007 年 4 月至 2009 年 9 月，加拿大 5 个癌症中心中不能手术切除的 IIIA/b NSCLC 进入 1 个单臂 II 期临床试验。入组标准：体重下降<5%；ECOG PS 0/1；没有恶性胸腔积液；FEV1>1.3l；充分的脏器功能。PET 扫描不作为常规使用。病人接受培美曲赛 500mg/m2 第一天，顺铂 20mg/m2 第 1-5 天，21 天一周期，2 周期化疗与放疗(61-66 Gy in 6-6.5 weeks)同步，之后用单纯培美曲赛/顺铂化疗 2 周期，仍为 21 天一周期（培美曲赛 500mg/m2 第一天，顺铂 75 mg/m2 第 1 天）。**结果：**入组 39 例。人口特征：中位年龄 63 岁[范围 37-80]；分期：IIIA/B: 15/24;组织学类型：腺癌（21）；鳞癌（10）；混合（1）；大细胞癌（1）；NSCLC (6);中位放疗 65 Gy [范围 14.4-66]。29/39 例病人完成了

4 个周期的化疗(3, 2 and 1 cycle in 3, 6 and 1 patient, respectively)。20/39 出现 3/4 级毒性与研究治疗有关。10 例出现 3/4 级血液学毒性，主要是中性粒细胞减少；3/4 级毒性分别 8/2 例。14 例出现 3 级非血液学毒性：恶心/呕吐 4 例；电解质紊乱 5 例；乏力/昏厥 4 例。4 级低血压/昏厥 1 例。1 例 3 级肺炎。4 例 2 级肺炎。中位 OS/PFS19.7/11.8 月。1 年 OS/PFS 为 80%/47%。

结论：足量培美曲赛/顺铂化疗与足量同步放疗具有相对好的耐受性和 IIIA/b NSCLC 的有效性。这些数据提供了继续 III 期研究的支持。

7088 Vinorelbine and cisplatin concurrently combined with thoracic radiotherapy in patients with unresectable stage III non-small cell lung cancer: A long-term safety and efficacy report

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Abstract:

Background: Concurrent chemoradiotherapy is the standard treatment for unresectable stage III non-small cell lung cancer (NSCLC). Few researchers, however, have reported on follow-up data of longer than three years. We investigated the long-term feasibility and efficacy of vinorelbine and cisplatin chemotherapy with concurrent thoracic radiotherapy. **Methods:** Eighteen patients received cisplatin (80 mg/m2) on day 1 and vinorelbine (20

mg/m2 in level 1, and 25 mg/m2 in level 2) on days 1 and 8 every 4 weeks for 4 cycles in phase I trial (Cancer Sci 95: 691-695, 2004). Ninety-three patients received the same chemotherapy regimen except for the fixed vinorelbine (20 mg/m2) dosage and consolidation therapy with docetaxel (J Thorac Oncol 1: 810-815, 2006). The thoracic radiotherapy consisted of a single dose of 2 Gy once daily to a total dose of 60 Gy. **Results:** A total of 111 patients were analyzed in the present study; male/female: 91/20, median age: 60, stage IIIA/IIIB: 50/61 and squamous/non-squamous histology: 26/85. The objective response rate was 82.0% (95% confidence interval [CI], 74.5-89.1). The 3-, 5- and 7-year progression-free survival and overall survival rates (95% CI) were; 20.2% (13.3-28.2), 15.2% (9.1- 22.7), 13.9% (8.1-21.3) and 43.4% (33.9-52.2), 25.2% (17.6-33.6), 22.2% (15.0-30.4), respectively. The median progression free survival and median survival time (95% CI) were 13.4 (9.8-16.4) months and 30 (24.5-38.8) months, respectively. Four patients (3.6%) experienced grade V pulmonary toxicities between 4.4-9.4 months after the start of the treatment. Cox and logistic regression analyses showed no significant prognostic factors except for age using age, gender, histology, stage, and body weight loss as independent variables. **Conclusions:** The present long-term analysis showed that approximately 15% of patients who had unresectable stage III NSCLC could be cured with vinorelbine, cisplatin, and concurrent thoracic radiotherapy. Less than 4% of patients developed fatal lung toxicity within 10 months from the start of the treatment

7088 译文 长春瑞滨加顺铂联合胸部放疗治疗不可切除的 III 期非小细胞肺癌：一个长期安全性和有效性报告

摘要

背景：联合放化疗是针对不可切除的III期非小细胞肺癌的标准治疗。然而，极少有研究者报告随访数据能超过 3 年。为此，我们针对长春瑞滨加顺铂联合胸部放疗的长期可行性和有效性进行了研究。**方法**：18 例患者在I期临床试验中接受了 4 个周期治疗，4 周为 1 周期，每 4 周的第 1 天使用顺铂（80mg/m^2），第 1 天和第 8 天使用长春瑞滨（1 级,20mg/m^2和 2 级，25mg/m^2）（Cancer Sci 95: 691-695, 2004）。93 例患者接受了同样的化疗方案，但在长春瑞滨（20mg/m^2）治疗时加用了多西他赛的巩固化疗（J Thorac Oncol

1: 810-815, 2006）。胸部放疗由每天 1 次，每次 2Gy，总剂量 60Gy组成。**结果**：当前的研究总共分析了 111 例患者；男性/女性 91/20，中位年龄 60 岁，分期IIIA/IIIB50/61，鳞状组织/非鳞状组织 26/85。客观有效率是 82.0%（95%置信区间（CI），74.5-89.1）。3-，5-和 7 年无进展生存率为 20.2% (13.3-28.2), 15.2% (9.1- 22.7), 13.9% (8.1-21.3) ；3-，5-和 7 年总生存率（95%CI）为 43.4% (33.9-52.2), 25.2% (17.6-33.6), 22.2% (15.0-30.4)。中位无进展生存期和中位生存期（95%CI）分别为：13.4 (9.8-16.4)个月和 30（24.5-38.8）个月。4 例患者（3.6%）在开始治疗后的 4.4-9.4 月间经历了 5 级的肺毒性。卡方和对数回归分析显示除了年龄，性别，组织学类型，分期，体重损失作为独立的变量外，没有显著影响预后的其他因素。**结论**：现有的长期分析显示，大约 15%患有不可切除的III期非小细胞肺癌的患者可以通过长春瑞滨加顺铂联合胸部放疗的治疗方案治愈。少于4%的患者在开始治疗后的 10 个月内会出现致命的肺毒性。

7089 Can we predict 2-year survival for radical radiation dosing schedules in advanced non-small cell lung cancer through a meta-analysis based predictive model?

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Abstract:

Background: Total dose, dose per fraction, number of fractions, and treatment time are important determinants of the biological effect of a radiation dosing schedule. Biological effective dose (BED) based on the linear quadratic model is used to design new schedules prior to testing in randomized clinical trials (RCTs). Several RCTs have tested a variety of dosing schedules in advanced unresected non-small cell lung cancer (NSCLC); however,

survival remains poor. Nevertheless, data from these RCTs could be used to optimize the dosing schedule for radical treatment of unresected NSCLC through a predictive model. **Methods:** 13 RCTs that compared various radiation schedules without chemotherapy were used to define the dose response relationship between radiation schedules and 2-year survival. Based on this relationship predictive models were developed. Predictions were compared with observations from radiation alone arms of 26 RCTs that compared various radiation schedules to the same schedules plus chemotherapy; scatter plots and pearson's correlation coefficient (r) were used for comparison. Uncertainty was quantified by computing 95% intervals around the estimates. Finally, based on predicted survival optimized schedule was searched. **Results:** Lower mortality was associated with the total dose (Odds ratio (OR)/5 Gy 0.68; 95% interval 0.56, 0.82), dose per fraction (OR/Gy 0.90; 0.79, 1.04), and number of fractions (OR/fraction 0.98; 0.93, 1.04); higher mortality was associated with total dose-squared (OR/5 Gy2 1.0; 1.0, 1.05), and treatment time (OR/week 1.25; 0.99, 1.54). The observed and predicted rates were similar (r = 0.75; 0.72, 0.77). Schedules that delivered higher total dose over a shorter time had higher survival rates compared to the standard (60 Gy, 30 fractions, 6 weeks). **Conclusions:** The developed model can better inform medical decision making through prediction of survival rates, compared to the BED model. This would help in designing new schedules for RCTs and would help in preventing futile research. This methodology can be applied to optimize chemotherapy regimens, and for other cancers such as head and neck, breast and prostate.

7089 译文 通过基于预测模型的荟萃分析，是否可以预测接受不同放疗增量方案的进展期非小细胞肺癌患者的 2 年生存率？

摘要

背景：放疗的总剂量，每次的剂量，放疗的次数和治疗时间是决定放射治疗增量方案的生物效应的重要决定因素。过去经常使用基于线性二次方模型的生物效应剂量（BED）来设计新的方案，并在随机临床试验中来测试这些新方案的可行性。一些随机临床试验已经测试了不可切除的进展期非小细胞肺癌的一系列增量方案；然而，测试结果往往显示生存率低下。尽管如此，在使用预测模型来设计不可切除的非小细胞肺癌放疗增量方

案的过程中，这些随机临床试验的数据可以用来优化这些设计方案。**方法**：13 个随机临床试验对比了不加用化疗的不同放疗方案，这些实验用来确定放疗方案和 2 年生存率之间的剂量依赖关系。基于这种关系得出了预测模型。该预测结果是从对比观察中得出，总共对比观察了单用放疗的不同方案和同样放疗方案加上化疗的 26 个随机临床试验；并用散布图和皮尔逊相关系数（r）来进行对比。不确定的通过计算估计的 95%的区间来定量。最终，得出了预测生存率的优化方案。**结果**：更低的死亡率与总剂量（优势比（OR）/5Gy 0.68；95%区间 0.56,0.82），每次的剂量（优势比/Gy 0.90；0.79,1.04），和放疗的次数（优势比/次数 0.98；0.93, 1.04）负相关；更高的死亡率与总剂量的平方（优势比/5 Gy^2 1.0；1.0,1.05），和治疗时间（优势比/周数 1.25；0.99,1.54）正相关。观察到的和预测到的比率是相似的（r=0.75；0.72,0.77）。在更短时间内总剂量更大的方案比标准方案（60 Gy,30 次，6 周）有更高的生存率。**结论**：通过预测生存率而发展出来的模型比生物效应剂量模型对医疗决策更有用。这能帮助设计用于随机临床试验的新方案，也能防止没有价值的研究的产生。这种方法论也能应用于优化化疗疗法，或改善其他肿瘤如头部、颈部、乳房和前列腺肿瘤的治疗。

7090 Docetaxel (D) and cisplatin (C) induction chemotherapy followed by concurrent thoracic radiotherapy (TRT) and biweekly D and C for stage III non-small cell lung cancer (NSCLC): A Galician Lung Cancer Group study

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Spain; Complexo Hospitalario Universitario, Vigo, Spain; Centro Oncologico de Galicia, A Coruña, Spain; Complexo Hospitalario Universitario, Santiago de Compostela, Spain.

Abstract:

Background: Concurrent chemoradiation is recommended as the evidence-based approach for the management of patients (p) with locally advanced NSCLC and a good performance status. The aim of our study was to evaluate the feasibility of induction chemotherapy with D-C followed by concurrent TRT and biweekly D-C. **Methods:** 85 p with locally advanced NSCLC, stage IIIAN2/IIIB (no pleural T4), were included in a phase II study consisting with three cycles of D 75 mg/m2 on day 1 and C 40 mg/m2 days 1-2 every 3 weeks and, if no surgery, then underwent concurrent TRT (60-66Gys, 180 cGys/d) with D 30 mg/m2 and C 30 mg/m2 every 2 weeks for four courses. Median follow-up: 12.6 months. **Results:** The p characteristics were: mean age 61 years (44-75); male/female 77/8; ECOG PS 0/1 in 25/60 p; squamous/adeno/large cell carcinoma: 51.8%/28.2%/20%; stage IIIAN2 20 p (23.5%) and stage IIIB 49 p (76.5%). 79 p were evaluable for response and 82 p for toxicity. Induction D-C response: 2 CR, 47 PR (RR 62%; CI95%:51-73), 21 SD (26.6%) and 9 PD (11.4%). 9 p underwent surgery: 1 pCR, 5 pPR, 1 pEE and 2 p unresectable. 55 p completed concurrent TRT with 8 CR, 37 PR (RR 81.8%; CI95%:71-92), 3 SD and 7 PD. The median progression-free survival (PFS) was 9 months (CI95%:8-14) and median overall survival (OS) was 18 months (CI95%:13-23). The PFS and OS at 1/2 years were 45%/20% and 64%/42% respectively. A total of 235 cycles of D-C were given (2.8 per p); main toxicities (NCI-CTC 3.0) per p grade (g) 1-2/3-4 (%) were as follows: neutropenia 10.9/25.6; anemia 30.4/3.5; nausea/vomiting 30.4/7.3; fatigue 28/0; diarrhea 17/9.7; there were ten episodes of febrile neutropenia and there was one treatment-related death. Main toxicities per p in concurrent TRT (D-C doses: 211, 3.6 per p) were: g1-2 neutropenia/anemia 12/34.4%; g1-2/3 esophagitis in 51.7/1.7% and g1-2 pneumonitis in 24.5%; there was one treatment-related death. **Conclusions: I**nduction chemotherapy with D-C followed of concurrent TRT and biweekly D-C is a feasible treatment option for locally advanced NSCLC, showing good clinical activity and tolerability with acceptable long-term survival.

7090 译文 III 期非小细胞肺癌患者在多西他赛加顺铂诱导化疗后，继续接受胸部放疗（TRT）并且同步接受每两周一次的多西他赛加顺铂化疗：一个加西利亚的肺癌群体研究

摘要

背景：循证医学推荐一般情况较好的局部进展期非小细胞肺癌患者接受同步放化疗。我们研究的目的是评估一种治疗方案的可行性，这种治疗方案为：多西他赛加顺铂诱导化疗后，继续接受两周一次的胸部放疗（TRT）并且同步接受多西他赛加顺铂化疗。**方法**：共有 85 例局部进展期肺癌患者入组了这个 II 期研究，入组患者的分期在 IIIAN2/IIIB（没有胸膜转移的 T4），这个研究的具体治疗方案为：开始进行 3 个周期的诱导化疗，每 1 周期持续 3 周，每 3 周的第 1 天使用多西他赛 75mg/m2，第 1,2 天使用顺铂 40mg/m2，3 个周期诱导化疗结束后，如果没有经过手术治疗，再接受四个周期的治疗，每个周期包括胸部放疗（60-66Gys，180cGys/d）加上同步的每两周一次的多西他赛 30mg/m2 和顺铂 30mg/m2。中位随访期为 12.6 个月。**结果**：入组患者的特征是：平均年龄 61 岁（44-75），男性/女性 77/8；ECOG PS 0/1 25/60；鳞癌/腺癌/大细胞癌 51.8%/28.2%/20%；IIIAN2 期有 20 例患者（23.5%），IIIB 期有 49 例患者（76.5%）。评估发现 79 例患者对治疗有反应，82 例患者有毒性反应。多西他赛加顺铂诱导化疗的相关治疗数据为：2 CR，47 PR（RR 62%；CI 95%：51-73），21 SD(26.6%) 和 9 PD (11.4%)。9 例患者经诱导化疗后接受手术治疗：1 例患者 CR，5 例患者 PR，1 例患者 **EE** 和 2 例患者不可切除。55 例患者完成了同步的胸部放疗及多西他赛加顺铂化疗，其中 8 例 CR, 37 例 PR (RR 81.8%; CI95%: 71-92), 3 例 SD 和 7 例 PD。中位无进展生存期（PFS）为 9 个月（CI95%：8-14），中位总生存期（OS）为 18 个月（CI95%：13-23）。中位无进展生存期和中位总生存期在 1 年/2 年的分别为 45%/20%和 64%/42%。总共进行了 235 周期多西他赛加顺铂诱导化疗（平均每例患者 2.8 周期）；1-2 度/3-4 度的主要毒性（NCI-CTC 3.0）如下：贫血 30.4/3.5；恶心、呕吐 30.4/7.3；疲劳 28/0；腹泻 17/9.7；共有 10 例偶发的粒细胞减少性发热，没有治疗相关死亡的发生。同步进行胸部放疗及多西他赛加顺铂化疗（多西他赛加顺铂接受剂量：211 周期，每例患者 3.6 周期）的患者的主要毒性为：1-2 度的粒细胞减少/贫血：12/34.4%；1-2/3 度的食管炎：51.7/1.7%；1-2 度的肺炎：24.5%；没有治疗相关死亡的出现。**结论**：局部进展期非小细胞肺癌患者可以接受这样一种治疗方案：多西他赛加顺铂诱导化疗后，继续接受胸部放疗（TRT）并且同步接受两周一次的

多西他赛加顺铂化疗。这种疗法显示出较好长期生存率、临床活性和可耐受性。

7091 A Galician Lung Cancer Group phase II study: Erlotinib as maintenance therapy after concurrent chemoradiotherapy in patients (p) with stage III non-small cell lung cancer (NSCLC)

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Abstract:

Background: Combination of platinum-based chemotherapy and radiotherapy is the standard treatment for p with unresectable stage III NSCLC, but considering the high rates of recurrence, it is necessary to improve these results. Erlotinib is an EGFR TKI that prolongs survival in p with metastatic NSCLC. In this study, we aim to evaluate the role of erlotinib as maintenance therapy after a standard concurrent chemo- radiotherapy regimen in p with stage III NSCLC. **Methods:** P with unresectable stage IIIA/IIIB without malignant effusions NSCLC who had received a standard concurrent chemoradiotherapy regimen and had no evidence of tumor progression were enrolled in this single arm, open-label phase II study and received erlotinib 150 mg/day po for 6 months. Main elegibility criteria were: PS 0-2, adequate bone marrow, hepatic and renal function and measurable disease by RECIST criteria.

Primary endpoint was the percentage of p without evidence of disease progression after 6 months of erlotinib therapy and secondary endpoints were: PFS, OS, ORR and safety profile. **Results:** A total of 66 p have been included in the study and data from 51 p are presented in this analysis. Baseline characteristics: median age 62 years (range 41-76); male 92.2%; caucasian 100%; smokers/never smokers (%) 94.1/3.9; ECOG PS 0/1/2 (%) 27.4/66.7/2.0; adenocarcinoma/squamous cell carcinoma/large cell carcinoma (%) 25.5/62.7/9.8; stage IIIA/IIIB (%) 25.5/72.5. Most common previous chemoradiotherapy regimen is cisplatin/docetaxel/RT (80.4%). 39 p were evaluable for tumor response: CR 17.9%; PR 20.5%; SD 56.4%; PD 5.1%. Median TTP was 9.9 months (95% CI 6.4-NR) and median OS was not reached yet. Most common adverse events related to erlotinib were rash 41,2% (2 p gr. 3) and diarrhea 27.4% (1 p gr. 3). **Conclusions:** Erlotinib as maintenance therapy is an active and well tolerated treatment after concurrent chemoradiotherapy in p with stage III NSCLC. In spite of the majority of patients are caucasian, males, smokers with squamous cell carcinoma, maintenance with single agent erlotinib reached a promising median TTP of 9.9 months. Data on survival will be updated.

7091 译文 一个加西利亚肺癌群体 II 期研究：III 期非小细胞肺癌患者经过同步放化治疗后继续厄罗替尼维持治疗

摘要

背景：当前不可切除的 III 期非小细胞肺癌患者的标准治疗为铂类化疗加放疗的联合治疗，但是这种联合治疗存在高复发率的缺陷，有必要加以改善。厄罗替尼是一个表皮生长因子受体的酪氨酸激酶抑制剂（EGFR TKI），能延长已经转移的非小细胞肺癌患者的生存期。在这个研究中，我们的目的是评估 III 期非小细胞肺癌患者经过同步放化治疗后，再继续厄罗替尼维持治疗中，厄罗替尼所发挥的作用。**方法**：这是一个单臂，开放的 II 期研究。患者的入组标准为：患有不可切除的 IIIA/IIIB 期非小细胞肺癌，没有恶性胸腔积液的发生，已经接受了标准的同步放化疗，并且没有肿瘤进展的证据。入组的患者接受口服厄罗替尼 150mg/天持续 6 个月的治疗。附加的入组标准为：PS 0-2，足够的骨髓造血功能、肝功能和肾功能，以及经过 RECIST 标准评估后合适的病人。主要研究目的是经过 6 个月的厄罗替尼治疗后，没有疾病进展证据的患者的百分率，次要研究

目的是：PFS，OS，ORR 和厄罗替尼治疗的安全性评估。**结果**：总共有 66 例患者入组这个研究，其中 51 例患者的数据经过分析。入组患者的基本特性是：中位年龄 62 岁（从 41-76）；男性 92.2%；高加索人 100%；吸烟者/非吸烟者（%）94.1/3.9；ECOG PS 0/1/2（%） 27.4/66.7/2.0；腺癌/鳞癌/大细胞癌（%）25.5/62.7/9.8；IIIA/IIIB 期（%）25.5/72.5。先前接受的最常见的放化疗方案是顺铂/多西他赛/放疗（80.4%）。39 例患者经过评估后，证实肿瘤对厄罗替尼的治疗客观有效病例中 CR 17.9%; PR 20.5%; SD 56.4%; PD 5.1%。中位的 TTP 为 9.9 个月（95%CI 6.4-NR），中位 OS 还没有得出。最常见的厄罗替尼相关的不良事件是皮疹 41.2%(其中 2 例患者达到 3 度)和腹泻 27.4%（其中 1 例患者达到 3 度）。**结论**：对于已经接受了常规的同步放化疗的 III 期非小细胞肺癌患者，厄罗替尼作为维持治疗是一种有效且可充分耐受的治疗方式。尽管大多数患者为高加索人，男性，吸烟，并且罹患鳞癌，但经过单纯的厄罗替尼的维持治疗，中位 TTP 还是达到了非常有希望的 9.9 个月。生存率的数据将会被更新。

7092 Concomitant pemetrexed/carboplatin chemotherapy and 3D conformal radiotherapy followed by pemetrexed/carboplatin consolidation chemotherapy for locally advanced non-small cell lung cancer: Preliminary results of a phase II study

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Abstract:

Background: Concomitant chemoradiotherapy is the standard treatment of locally advanced, non-resectable, non-small cell lung cancer (NSCLC). However, the optimal chemotherapy regimen is still controversial. The objective of this study was to evaluate the efficacy and

toxicity of a concomitant treatment using pemetrexed/carboplatin and radiotherapy followed by pemetrexed/carboplatin consolidation chemotherapy. This report presents preliminary results of 21 patients who have completed treatment in the first stage. **Methods:** Single-arm design was designed according to the Simon's two-stage version for lung cancer phase II studies. Patients received concomitant pemetrexed 500 mg/m2, carboplatin AUC 5 chemotherapy on day 1 repeated every 3 weeks for 2 cycles and 3-D conformal radiotherapy (Median dose 62 Gy (range: 60-66 Gy) with 2 Gy daily fractions.), followed by pemetrexed (500 mg/m2) and carboplatin (AUC=5) every 3 weeks for 3 cycles as consolidation therapy. The association between histopathology and tumor responses was analyzed using the Chi-square and Fisher's exact test. **Results:** 21 patients were enrolled between 01/08 and 10/09. Median age was 61 years (range 43-70), M/F 16/5, all proven NSCLC (7 squamous cell carcinoma, 14 adenocarcinoma), stage IIIA/stage IIIB 14/7. The overall response rate (85.7%,95% (CI): 61%-97%) exceeded the goal per study design. Histopathology was predictive factor for the responses found in univariate analysis. Main toxicity (grade 3 or greater, %): neutropenia 6(28.5%); febrile neutropenia 0, thrombocytopenia 2 (9.5%); anaemia 5 (23.8%); esophagitis 1 (4.8%), radiation pneumonitis 1 (4.8%) and fatigue 2 (9.5%). **Conclusions:** This first-stage data suggests that concomitant treatment with pemetrexed/carboplatin and radiotherapy was well tolerated, with promising activity in locally advanced NSCLC. Better outcomes were observed in patients with adenocarcinoma. Although the data presented herwithin appears promising, second-stage study is needed to further validate this regimen.

7092 译文 对于局部晚期非小细胞肺癌使用 3D 适形放疗和同步培美曲赛/卡铂化疗之后进行培美曲赛/卡铂巩固化疗：Ⅱ期临床试验的初步结果

摘要

背景：同步放化疗是不可切除的局部晚期非小细胞肺癌（NSCLC）的标准治疗方法。然而，对于什么是最佳的化疗方案仍有争议。这项研究的目的在于评估使用 3D适形放疗和同步培美曲赛/卡铂化疗之后进行培美曲赛/卡铂巩固化疗的疗效和毒性。报道了 21 例化放同步治疗阶段的初步结果。**方法：**本试验根据Simon的关于两阶段设计建立了单臂

Ⅱ期试验。病人在化疗第一天接受了同步培美曲赛 500mg/m^2,卡铂(AUC=5)化疗（每 3 周一次，共 2 次）以及 3D适形放疗，中位剂量 62Gy(范围 60-66Gy) ，每日剂量 2Gy, 之后给予培美曲赛（500mg/m2）,及卡铂(AUC=5)，每 3 周一次，共 3 次巩固化疗。使用Chi-square和Fisher的精确测试来分析组织病理学与肿瘤反应之间的关系。**结果：**2008 年 1 月至 2009 年 10 月间共有 21 位病人参与试验。年龄中位数为 61 岁（范围为 43-70），所有都是确诊的NSCLC（7 例鳞癌，14 例腺癌），ⅢA期 14 人，ⅢB期 7 人。总体反应率为 85.7%（95%（ＣＩ）（61%-97%），超过本次设计目标。单变量分析发现组织学是一个预测因素。主要毒性（3 度及以上，%）：中性粒细胞减少 6(28.5%)、中性粒细胞减少性发热 0、血小板减少 2（9.5%）、贫血 5（23.8%），食管炎 1（4.8%），放射性肺炎 1（4.8%）及乏力 2（9.5%）。**结论：**同步化放阶段的数据显示培美曲赛/卡铂化疗和放疗同步进行有很好的耐受性，在局部晚期NSCLC中有很好的客观有效率。腺癌患者效果更好。尽管现有数据显示这个方案可能很有希望，但是还需要巩固化疗后的结果进一步证实。

7093 Cisplatin (CDDP) and oral vinorelbine (NVBO) concomitantly with radiotherapy (RT) after induction chemotherapy (CT) in locally advanced (LA) non-small cell lung cancer (NSCLC) treatment: Clinical experience in five institutions in Spain

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Abstract:

Background: CDDP+NVBO as induction and concomitant regimen with RT has shown good efficacy outcomes and safety profile (Krzakowski, J Thor Oncol. 2008). Five Spanish institutions have collected the data of patients with LA NSCLC treated with the previously reported regimen in order to confirm the results in the clinical daily activity. **Methods:** Between February 2007 and April 2009, 19 chemo-naïve patients (p) with histologically confirmed stage IIIA/IIIB unresectable LA NSCLC were treated. Treatment consisted of NVBO D1,8 60 mg/m2 cycle (cy) 1 and 80 mg/m2 cy 2 (if no haematological/non-haematological grade 3-4 toxicity) and CDDP 80 mg/m2 every 3 weeks for 2 cy as induction. OR/NC pts received NVBO D1,8 40 mg/m2 and CDDP 80 mg/m2 every 3 weeks for 2 more cy and RT 60-66 Gy in 6.5 weeks. **Results:** Patient's characteristics were: Median age, 61 years (range 50-76); all males; smokers, 79%; adenocarcinoma, 42% / squamous, 26%; stage IIIA, 5% / IIIB, 95%. 17 p completed the 4 cy treatment; Treatment was cancelled in 1 p after cy 1 due to neutropenia, and 1 p died after cy 3 (due to disease). We analyzed 72 cy. Hematological toxicities (% cy): grade (g) 3/4 neutropenia, 9.7%; g3 anemia, 1.4%. Non-hematological toxicities (% cy): oesophagitis g 3/4, 1.4%; constipation g4, 1.4%; fever g3, 1.4%; infection g3, 4.2%. No nausea or vomiting g 3/4 were reported. 17 p were evaluable for response. 13 PR (76.5%) and 2 SD (11.8%) were reported. Survival analysis has not been performed due to short follow-up. **Conclusions:** The findings of this retrospective analysis confirm the previously reported outcomes of efficacy and safety with NVBO plus CDDP when administered as induction and concurrently with RT in stage IIIA/IIIB p. The excellent tolerance profile allowed to complete the CT/RT treatment in 90% of pts.

7093 译文 局部晚期（LA）非小细胞肺癌（NSCLC）诱导化疗后使用顺铂（CDDP）、口服长春瑞滨（NVBO）及放疗的临床研究：西班牙 5 家机构的临床经验

摘要

背景：将CDDP+NVBO作为诱导化疗和CDDP+NVBO与放疗同步进行巩固治疗显示出了很好的效果及安全性（Krzakowski,J Thor Oncol.2008）。5 家西班牙机构已经收集了用该方案治疗的局部晚期NSCLC病人的数据，目的是用来确定其在临床工作中的作用。**方法：**从 2007 年 2 月至 2009 年 4 月， 1 9 例组织学确诊为IIIA/IIIB期不可切除的未接受过化

疗的局部晚期NSCLC患者。治疗包括：NVBO 60mg/m^2,d1,d8。一周期后，如果没有出现血液性及非血液性 3-4 级毒性，则剂量提高到 80mg/m^2，进行第二周期化疗。同时每三周一次CDDP80mg/m^{2}共两周期。对于获得OR/NC病人再接受 2 个以上周期的NVBO 40mg/m^2,d1,d8，和每三周一次的CDDP80mg/m^{2}的治疗，同时进行 6-5 周放疗，总剂量达到 60-66Gy。**结果：**患者的基线特征：中位年龄 61 岁（范围 50-76）；都为男性；吸烟者占 79%；腺癌 42%，鳞癌 26%；ⅢA期 5%，ⅢB期 95%。17 例完成了 4 周期的治疗。1 例在 1 周期后出现中性粒细胞减少出组，1 例在 3 周期后死亡（由于疾病）。分析了 72 个周期的结果发现，血液毒性（％周期），3/4 度白细胞减少 9.7%，3 度贫血 1.4%；非血液性毒性（%周期），3/4 度食管炎 1.4%，4 度便秘 1.4%，3 度发热 1.4%，3 度感染 4.2%。没有报道 3/4 度恶心及呕吐。17 例可以进行疗效评估，PR13 例（76.5%），SD2 例（11.8%）。由于缺乏随访，没有进行生存分析。**结论：**这项回顾性分析的结果确认了之前报道的在ⅢA/ⅢB期使用NVBO和CDDP进行诱导化疗之后再与放疗同步治疗方案的疗效和安全性。尤其是它的良好耐受性，可以使得 90%的病人能够完成化放治疗。

7094 Outcomes of patients with stage III (clinical N2) NSCLC: A VACCR analysis

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Abstract:

Background: Management of locally advanced non-small cell lung cancer (NSCLC) lacks consensus. Also, it is unclear if outcome disparities exist according to race. We conducted a retrospective analysis of patients included in the Veterans Affairs Central Cancer Registry

(VACCR) to evaluate if these disparities exist. **Methods:** Patients with clinical N2 disease and stage 3 NSCLC diagnosed between 1995 and 2003 were included. Data abstracted included age at diagnosis, gender, race, smoking history, disease stage, tumor grade, treatment received and overall survival. Outcomes were compared using multivariate Cox proportional hazards regression analysis. **Results:** Of the 7,469 patients who met the inclusion criteria, analyses were limited to 7,238 Caucasians and African-American (AA) patients. Median age of the patients was 68 years (range: 27-93 years). Of these, 7,218 (98.5%) were male, 6,061 (82.7%) were Caucasian and 321 (4.4%) were never smokers. Median follow-up of survivors was 9 months (range: <1 - 154 months). Treatment received included: none-1,746 (23.8%), chemotherapy-1,045 (14.3%), radiation-1,689 (23%); chemotherapy and radiation (sequential or concurrent)-2,300 (31.4%), while 548 patients (7.5%) had a surgical resection (either alone or as part of multimodality therapy). Median survival (months) of the different treatments were: surgery-19.3; chemotherapy and radiation-13; chemotherapy alone-9.2; radiation alone-7.3; no treatment-4 ($p<0.0001$). On multivariate analysis, AA had a significantly decreased risk of mortality compared to Caucasians (HR 0.92; 95% CI, 0.87-0.98, $p=0.01$) while adjusting for age, disease stage and treatment type. When this was further analyzed according to type of treatment, AA had decreased mortality compared to Caucasians when chemotherapy alone was given (HR 0.81; 95% CI, 0.69- 0.96, $p=0.02$) and a trend towards decreased mortality when no treatment was given (HR 0.88; 95% CI 0.78-1.01, $p=0.06$). **Conclusions:** AA had a significantly better outcome when compared to Caucasians, especially when treated with chemotherapy, suggesting possibly a better tumor biology or pharmacogenomics. Surgery should be considered in conjunction with other modalities in patients with clinical N2 NSCLC.

7094 译文 N2 期的Ⅲ期 NSCLC 病人的结局：VACCR（退伍军人服务部中央型肺癌登记处）分析

摘要

背景：目前对于局部晚期非小细胞肺癌的处理缺乏共识。同样，种族不同是否会导致结局不同也不清楚。我们对 VACCR 的病人进行了回顾性分析来评估是否存在这种差异。**方法：**包括了 1995 年至 2003 年之间确诊为Ｎ 2 期的Ⅲ期 NSCLC 病人。干扰因素包括：确诊年龄、性别、种族、吸烟史、疾病分期、肿瘤分化程度、既往治疗和总生存。结果使用多变量的 COX 相关危险回归法分析。**结果：**在 7469 例达到入选标准的病人中，分析仅限于 7238 名高加索人及非裔美国黑人（ＡＡ）。中位年龄为 68 岁（范围 27-93 岁）。其中，7218 例（98.5%）为男性，6061 例（82.7%）为高加索人，321 例（4.4%）从不吸烟。中位生存期为 9 个月（范围：<1-154 个月）接受的治疗包括:未治疗 1746 例（23.8%），化疗 1045 例（14.3%），放疗 1689 例（23%）；放化疗（序贯或同时）2300 例（31.4%），548 例（7.5%）病人接受手术切除（单独或作为多方式治疗的一部分）。不同治疗的中位生存期为：外科手术 19.3 月；放化疗 13 月；单独化疗 9.2 月；单独放疗 7.3 月；不治疗 4 月（p<0.0001）。在多变量分析中，当调整了年龄、疾病分期和治疗类型后，与高加索人相比非裔美国黑人的死亡风险明显降低（HR0.92;95%CI,0.87-0.98,p=0.01）。当根据治疗种类进一步分析时，单独给予化疗时非裔美国黑人比高加索人死亡率低（HR0.81；95%CI,0.69-0.96,p=0.02 ），没有治疗的死亡率仍有较低的趋势（HR0.88;95%CI,0.78-1.01,p=0.06）。**结论：**与高加索人相比，非裔美国黑人有更好的结局，尤其是在接受化疗的患者中优势更加明显。这可能意味着他们有更好的肿瘤生物学及药物基因组学的特征。N2 期的 NSCLC 病人应以手术联合其他治疗方式为首选治疗。

7097 Clinical features of bronchioloalveolar carcinoma with new histologic and staging definitions

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Abstract:

Background: The description of disease consistent with bronchioloalveolar carcinoma (BAC) dates back to the 1800's. Lack of precision in prevalence and survival estimates of BAC relates to wide variations in criteria distinguishing BAC from adenocarcinoma. Our goal was to assess clinical features of BAC based on the 1999 WHO Classification ("pure BAC"), compare pure BAC patients with patients previously diagnosed as BAC not meeting the 1999 definition, and compare survival changes of pure BAC based on the old and new (2009) staging systems. **Methods:** A pulmonary pathologist reviewed each BAC tumor diagnosed from 1997 to 2007 identifying cases meeting the new criteria. Cases were restaged according to the 7th edition of the TNM classification. Pure BAC patients were analyzed under both staging systems for changes in overall survival. **Results:** Of 338 total patients who were diagnosed with BAC, 117 were classified as pure and 221 were non pure BAC. Of the 117 and 221, 78 and 178, respectively had no other primary lung cancer. One- and five-year survival for the 78 pure BAC patients were 94.8% and 83.5%, and for the 178 patients were 92.6% and 46.4%, respectively. Restaging for pure BAC cases resulted in a change in 9 of the 78 cases (12%). Compared to the old staging, patients with advanced stage under the new stage had a worse 5-year survival (53% vs. 45%); whereas, no change was observed for stage

IA. **Conclusions:** For patients with pure BAC, the new pathologic system favorably affects survival and the new staging system may more accurately reflect prognosis in advanced stage cancer. Our results have important implications for researchers, clinicians, and patients.

7097 译文 新组织学和分期定义的细支气管肺泡癌的临床特征

摘要

背景：对细支气管肺泡癌（BAC）的疾病描述可以追述到 1800。由于各个区分细支气管肺泡癌和腺癌的标准差别太大，现在缺乏精确的细支气管肺泡癌的患病率和生存率的评估。我们的目的是基于 1999 年 WHO 分类（“纯细支气管肺泡癌”）对细支气管肺泡癌的临床特征进行评估，区分纯细支气管肺泡癌和先前被诊断但没有经过 1999 年定义确证的细支气管肺泡癌，对比基于旧的和新的分期系统（2009）分期的纯细支气管肺泡癌的生存率差异。**方法**：一个肺脏病理学家综述了从 1997 年到 2007 年诊断的每一例细支气管肺泡癌，并用新的标准对这些病例进行鉴别。这些病例依照第 7 版 TNM 分期进行重新分期。纯细支气管肺泡癌患者同时使用 2 个分期系统来分析它们之间的总生存率的差异。**结果**：对于总的 338 例诊断为细支气管肺泡癌的患者，其中 117 例分类为纯细支气管肺泡癌，221 例为非纯细支气管肺泡癌。对于这 117 例和 221 例患者，其中的 78 例和 178 例分别没有患其他的初级肺癌。对其中的 78 例纯细支气管肺泡癌患者，一年和五年生存率分别为 94.8%和 83.5%，对其中的 178 例非纯细支气管肺泡癌患者分别为：92.6%和 46.4%。对纯细支气管肺泡癌患者的重新分期，78 例中有 9 例（12%）有生存率的差异。与旧的分期系统相比，在新的分期系统下分期为进展期的患者有更差的 5 年生存率（53%比 45%）；然而，没有发现两个分期系统在 IA 期的生存率差异。**结论**：对于患纯细支气管肺泡癌患者，新的病理系统对于生存率的影响是有利的，而新的分期系统可能更精确地反应了进展期癌症的预后。我们的结果对研究者、临床工作者和和患者都有重要意义。

声明：本书仅供读者参考，由于水平和时间所限，一定会有不足之处，希望读者批评、指正，以此共勉。