Media contact
ESMO Press Office
E-mail media@esmo.org

新闻稿

阿法替尼——EGFR 突变型肺癌一线治疗的更佳选择

LUX-肺癌 7 试验表明，相较于吉非替尼，第二代 EGFR 酪氨酸激酶抑制剂能显著改善晚期突变型肺癌患者的 PFS

新加坡/卢加诺——研究人员在新加坡举办的首届欧洲肿瘤医学会（ESMO）亚洲区域大会上报告称，作为一线治疗用药，阿法替尼似乎比吉非替尼更能让 EGFR 激活突变型晚期肺癌患者获益。

在全球、随机、开放标签的 IIb 期 LUX-肺癌 7（LL7）试验中，相较于在一系列临床相关端点（例如：无进展生存期、治疗失败的时间和客观反应率）中使用的吉非替尼，不可逆的 ErbB 家族阻滞剂阿法替尼能显著提高疗效。时任韩国首尔成均馆大学医学院三星医疗中心血液/肿瘤科负责人的首席作者 Keunchil Park 教授表示：“基于这些试验结果，我认为阿法替尼是对 EGFR 突变阳性非小细胞肺癌（NSCLC）患者进行一线治疗时首选的 EGFR 酪氨酸激酶抑制剂（TKI）”。

NSCLC 是最常见的肺癌种类：在不吸烟者和女性群体中更常观察到激活表皮生长因子受体（EGFR）基因突变，亚洲人的发病率为 50%，非亚洲人的发病率仅为 10%。靶向治疗药剂阿法替尼和吉非替尼会阻滞涉及肿瘤生长和扩散的关键通路。三期试验结果证实二者相较于化疗的优越性，据此，二者都已获准用于治疗初治患者。跟第一代 EGFR 抑制剂吉非替尼不同的是，不可逆的 ErbB 家族阻滞剂阿法替尼对延长肿瘤响应和延缓疾病恶化非常有效。

在第一次 LUX-肺癌 7 对比试验中，阿法替尼对于先前未接受过任何治疗的 EGFR 突变阳性 NSCLC 初治患者来说是更好的选择。“相较于吉非替尼，一线阿法替尼治疗可以将肺癌恶化的风险显著降低 27%，” Park 表示，“有趣的是，无进展生存期间的改善情况随着时间的推移变得更加明显，18 个月（27%对 15%，p＝0.018）和 24 个月（18%对 8%，p＝0.018）时患者健在且病情未恶化的比例明显更高，表明使用这种不可逆的 ErbB 家族阻滞剂阿法替尼会带来更大的长期效益。”

在随机施用阿法替尼或吉非替尼的 319 位患者中，前者比之后者，反应比例明显更高（70.0%对 56.0%，p＝0.008），平均反应期限分别为 10.1 个月（95% CI，7.82-11.10）和 8.4 个月（95% CI，7.36-10.94）。对于耐受性情况，Park 表示：“总的说来，两个治疗组群出现严重不良反应的频率相似，毒性状况略有不同。两种治疗方案中观察到的不良反应可预测、可管理，致使两个治疗组群治疗中止的几率相当低。”

时任德国 Grosshansdorf 医院胸腔肿瘤科首席肿瘤医师的 ESMO 发言人 Martin Reck 医生（未参与这项研究）提醒，患者个人及其并存病仍将引导 EGFR 抑制剂的选择。他表示：“在这些试验结果之后，阿法替尼将成为最具吸引力的 EGFR 酪氨酸激酶抑制剂之一。不过，在酪氨酸激酶抑制剂的挑选和配量方面，耐受性仍然起着决定性的作用。吉非替尼和阿法替尼之间的耐受性情况不同，治疗方法的选择仍将基于患者的临床决策。”

The primary analysis of overall survival data is planned in 2016 and will provide further responses.
计划在 2016 年进行总体生存数据的初步分析，届时将提供进一步的反应情况。

评论非小细胞肺癌初治患者的未来研究方向时，Reck 表示：“我们在一线 NSCLC 治疗方面取得的最重要的一项改进是分子诊断的实施。如果能够诊断出诸如 EGFR 突变或 ALK 转移之类的可治疗类分子改变，使用 EGFR-TKI 或 ALK-TKI 之类的靶向药剂进行治疗将是最有效的治疗方案。对于其他所有患者，标准做法依然是采用铂类药物化疗。当前试验是要评估免疫检查点抑制剂是否将优于对 PDL-1 肿瘤患者的化疗，以及单一疗法或联合疗法将来是否会取代对选定患者采用的化疗。”

-完-

References

(1) Abstract LBA2_PR “Afatinib (A) vs gefitinib (G) as first-line treatment for patients (pts) with advanced non-small cell lung cancer (NSCLC) harboring activating EGFR mutations: results of the global, randomized, open-label, Phase IIb trial LUX-Lung 7 (LL7)” *K. Park1, E. Tan2, L. Zhang3, V. Hirsh4, K. O'Byrne5, M. Boyer6, J.C. Yang7, T. Mok8, M. Kim9, D. Massey10, V. Zazulina11, L. Paz-Ares12 1Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, 2Division Of Medical Oncology, National Cancer Centre, Singapore, 3Cancer Center, Sun Yat-Sen University, Guangzhou, China, 4Department Of Oncology, McGill University, Montreal, Canada, 5Translational Research Institute, Princess Alexandra Hospital and Queensland University of Technology, Brisbane, Australia, 6Department Of Medical Oncology, Chris O'Brien Lifehouse, Camperdown, Austrlia, 7Department Of Oncology, National Taiwan University Hospital and National Taiwan University, Taipei, Taiwan, 8State Key Laboratory Of South China, Hong Kong Cancer Institute, The Chinese University of Hong Kong, Hong Kong, China, 9Medicine Ta Oncology, Boehringer Ingelheim GmbH, Ingelheim, Germany, 10Biometrics/clinical, Boehringer Ingelheim Ltd UK, Bracknell, United Kingdom, 11Medical, Boehringer Ingelheim Ltd UK, Bracknell, United Kingdom, 12Department Of Medical Oncology, Instituto de Biomedicina de Sevilla, Seville, Spain*, **will be presented during the ESMO Asia 2015 Congress Presidential Symposium on Sunday 20 December, 16:30 SGT – Hall 406**

Abstract will be available online on 19th December 2015, 23:55 hours (SGT)
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ABSTRACT LBA2_PR

Afatinib (A) vs gefitinib (G) as first-line treatment for patients (pts) with advanced non-small cell lung cancer (NSCLC) harboring activating EGFR mutations: results of the global, randomized, open-label, Phase IIb trial LUX-Lung 7 (LL7)

K. Park1, E. Tan2, L. Zhang3, V. Hirsh4, K. O'Byrne5, M. Boyer6, J.C. Yang7, T. Mok8, M. Kim9, D. Massey10, V. Zazulina11, L. Paz-Ares12 1Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, 2Division Of Medical Oncology, National Cancer Centre, Singapore, 3Cancer Center, Sun Yat-Sen University, Guangzhou, China, 4Department Of Oncology, McGill University, Montreal, Canada, 5Translational Research Institute, Princess Alexandra Hospital and Queensland University of Technology, Brisbane, Australia, 6Department Of Medical Oncology, Chris O'Brien Lifehouse, Camperdown, Austrlia, 7Department Of Oncology, National Taiwan University Hospital and National Taiwan University, Taipei, Taiwan, 8State Key Laboratory Of South China, Hong Kong Cancer Institute, The Chinese University of Hong Kong, Hong Kong, China, 9Medicine Ta Oncology, Boehringer Ingelheim GmbH, Ingelheim, Germany, 10Biometrics/clinical, Boehringer Ingelheim Ltd UK, Bracknell, United Kingdom, 11Medical, Boehringer Ingelheim Ltd UK, Bracknell, United Kingdom, 12Department Of Medical Oncology, Instituto de Biomedicina de Sevilla, Seville, Spain

Aim: The irreversible ErbB family blocker A and the reversible EGFR tyrosine kinase inhibitor G are approved for firstline treatment of advanced EGFR-mutant (m+) NSCLC. We have conducted a global randomized Phase IIb trial toprospectively compare the efficacy and safety of first-line A vs G in pts with EGFRm+ NSCLC.

Methods: Pts with stage IIIb/IV EGFRm+ NSCLC (defined by either local or central test) were randomized (1:1) to daily A 40 mg or G 250 mg, stratified by mutation type (Del19 or L858R) and presence of brain metastases. Treatment continued until disease progression or beyond if deemed beneficial by investigator. Co-primary endpoints were: progression free survival (PFS) by independent review, time to treatment failure (TTF), and overall survival (OS). Secondary endpoints included objective response rate (ORR), disease control rate, tumor shrinkage, and safety.
Results: 319 pts were randomized to A (n=160) or G (n=159). Except for a slight gender imbalance (female: 56.9% [A] vs 66.7% [G]), baseline characteristics were similar: race (Asian: 58.8% vs 55.3%), EGFR mutation type (Del19: 57.5% vs 58.5%). Afatinib significantly improved PFS (HR=0.73; 95% CI, 0.57–0.95; p=0.0165) and TTF (HR=0.73; 95% CI, 0.58–0.92; p=0.0073) compared to G. This effect was consistent for ORR (70% vs 56%, p=0.0083), and for subgroups by mutation type and race. OS is not yet mature. The most common grade ≥3 related adverse events (AEs) were diarrhea (12.5%) and rash/acne (9.4%) with A and alanine aminotransferase increase (8.2%) with G.
Drug-related interstitial lung disease was reported for 0 (A) vs 4 pts (G; 2.5%). Treatment discontinuation due to related AEs was the same in each arm (6.3%).

Conclusions: First-line afatinib significantly improved PFS vs gefitinib in EGFRm+ pts. Consistent benefit was seen with TTF and ORR. AEs were manageable with the same low discontinuation rates in both arms.

Clinical trial identification: EudraCT: 2011-001814-33

Keywords: afatinib, gefitinib, NSCLC, EGFR

Disclosure: K. Park: employment with Samsung Medical Center and advisory board involvement with Boehringer Ingelheim (uncompensated). E. Tan: advisory board involvement with Boehringer Ingelheim, MSD and AstraZeneca and honoraria from Boehringer Ingelheim, MSD and AstraZeneca. L. Zhang: involvement with advisory boards for Boehringer Ingelheim and AstraZeneca. V. Hirsh:
honoraria for a Boehringer Ingelheim advisory board. K. O'Byrne: involvement with an advisory board for and honoraria

from Boehringer Ingelheim. M. Boyer: corporate-sponsored research from Pfizer, Peregrine Pharmaceuticals and Genetech/Roche and corporate-sponsored research and honoraria from Boehringer Ingelheim, Bristol Myers Squibb, Merck Sharpe and Dohme, and Astra Zeneca. J.C. Yang: advisory board participation for Astrazeneca, Roche/Genentech, Boehringer Ingelheim, MSD, Merck Serono, Novartis, Clovis Oncology, Eli Lilly, Bayer, Celgene, Astellas, Innopharma, and Ono Pharmaceutical; honoraria from Astrazeneca, Roche/Genentech, Boehringer Ingelheim, MSD, Merck Serono, Novartis, Clovis Oncology, Eli Lilly, Bayer, Celgene, Astellas, Innopharma, and Ono Pharmaceutical. T. Mok: Speaker's Bureau participant with AstraZeneca, Roche/Genentech, Pfizer, Eli Lilly, Boehringer Ingelheim, MSD, Amgen, Janssen, Clovis Oncology, GSK, and Novartis; advisory board participation for AstraZeneca, Roche/Genentech, Pfizer, Eli Lilly, BI, Merck Serono, MSD, Janssen, Clovis Oncology, BioMarin, GSK, Novartis, SFJ Pharmaceutical, and ACEA Biosciences, Inc.; honoraria from AstraZeneca, Roche/Genentech, Pfizer, Eli Lilly, BI, MSD, Amgen, Janssen, Clovis Oncology, GSK, and Novartis; and major stock shareholder in Sanomics Ltd. M. Kim, D. Massey, V. Zazulina: employment with Boehringer Ingelheim. L. Paz-Ares: honoraria from Boehringer Ingelheim, Roche, Lilly, AstraZeneca, Pfizer, Clovis, and BMS.