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新聞發布

阿法替尼（Afatinib）是 EGFRR-突變肺癌一線治療的更佳選擇

LUX-Lung 7 trial 臨床試驗顯示，與吉非替尼（gefitinib）相比，第二代 EGFR 酪氨酸激酶抑制劑更能顯著延長晚期突變肺癌初治患者的存活期（PFS）

新加坡／盧加諾 – 在歐洲腫瘤醫學會（ESMO）於新加坡舉行的首屆 2015 亞洲會議中，研究人員報告指出，在一線療程中， 阿法替尼比吉非替尼更有效治療由 EGFR 激發突變的晚期肺癌患者。

在全球開放性隨機 IIb 期試驗 LUX-Lung 7 (LL7) trial [(1)]中，ErbB 家族的不可逆受體阻滯藥物阿法替尼，在一系列臨床相關終點中，比吉非替尼的療效更為顯著，例如存活期、時間相對治療失效和客觀有效率。首席作者、韓國首爾成均館大學醫藥學院三星醫學中心血液學/腫瘤學學系主任 Keunchil Park 教授表示：「根據這些結果，我認為對於 EGFR 突變非小細胞肺癌（NSCLC）患者的一線療程而言，阿法替尼是作為 EGFR 酪氨酸激酶抑制劑的理想選擇。」

NSCLC 是最常見的肺癌類型：表皮生長因子受體（EGFR）的基因突變，更常見於非吸煙人士和女性，發生於 50%的亞洲人及僅 10%的非亞洲人身上。標靶治療藥物阿法替尼和吉非替尼，會阻滯腫瘤生長及擴散的的主要途徑。第 III 期臨床試驗的結果，確認了兩者的療效勝於化療， 並獲認可用以治療初治患者。與第一代 EGFR 抑制劑吉非替尼不同的是，ErbB 家族的不可逆受體阻滯藥物阿法替尼相信能有效延長腫瘤反應及滯後疾病進展。

第一個面對面 LUX-Lung 7 trial 的臨床試驗，顯示對於未曾接受任何治療的 EGFR 突變 NSCLC 初治患者而言，阿法替尼是較佳的治療藥物。「相對於吉非替尼，一線阿法替尼療程能顯著降低 27%肺癌進展的風險。」Park 表示，「有趣的是，存活率的改善會隨時間而變得更顯著，存活患者的比例大幅增加，存活率為 18 個月（27% vs 15%; p=0.018）和 24 個月（18% vs 8%; p=0.018），顯示採用 ErbB 家族的不可逆受體阻滯藥物，長遠來說有更大優勢 。」

在 319 名隨機採用阿法替尼或吉非替尼的患者中，對前者出現反應的比例遠高於後者（70.0% vs 56.0%; p=0.008），反應持續時間中位值分別為 10.1 個月（95% CI, 7.82-11.10）和 8.4 個月（95% CI, 7.36-10.94）。在耐受性方面，Park 表示：「整體而言，兩者出現嚴重副作用的頻率相約，而毒性則有輕微不同。兩種療法的副作用均可以預計及易於控制， 使兩者的中止治療比率均偏低（6.3%）。

並沒參與是次研究的 ESMO 發言人、德國 Hospital Grosshansdorf 胸腔腫瘤科首席腫瘤內科醫生 Martin Reck 教授提醒，個體患者及其合併症仍然是選擇 EGFR 抑制劑的指標。他指出：「根據這些臨床研究結果，阿法替尼會成為其中一種最適合的 EGFR 酪氨酸激酶抑制劑。不過，在選擇及配給酪氨酸激酶抑制劑時，耐受性仍然是決定性因素。吉非替尼和阿法替尼的耐受性並不相同，因此療程的選擇依然取決於個別臨床決策。」

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整體存活數據的初步研究將於 2016 年舉行，屆時將提供進一步的研究結果。

對於非小細胞肺癌初治患者的未來研究方向，Reck 認為：「我們在一線 NSCLC 療程中取得的最重要成果，是實施分子病理診斷。若能夠診斷類似 EGFR 突變或 ALK 易位的可治療分子改造病變，採用標靶治療藥物，例如 EGFR-TKI 或 ALK-TKI，將成為最有效的療法。而在所有其餘患者中，鉑基礎化療仍然是標準療法。 目前的臨床試驗，正評估對於有 PDL-1 表現腫瘤的患者而言，免疫點抑制劑是否優勝於化療。試驗同時評估單一療法或混合療法，在將來能否於特定患者中取代化療。」

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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)
https://cslide.ctimeetingtech.com/library/esmo/browse/itinerary/5225

編輯備註

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- 宣傳及諮詢，以促進良好科研環境

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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)

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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

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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.