進行肺がんの進行抑制（Abstract＃LBA7500）

LUX-lung 3トライアル:Afatinibは進行肺腺がん、特に一部の遺伝子サブセットの腫瘍において進行を遅らせる

LUX-lung 3 trial: Afatinib delays progression of advanced lung adenocarcinomas, particularly in genetic subset of tumors

第48回American Society of Clinical Oncology学会で発表された第3相国際トライアルの結果、分子標的薬afatinibを用いた初回単剤経口療法は、上皮細胞増殖因子受容体(EGFR、ErbB1としても知られる)変異を有する進行肺腺がん患者の無増悪生存期間(PFS)を延長させることが示された。このスタディにおいて研究者らは345人の患者をafatinibまたは経静脈投与による標準的な併用化学療法に無作為に割り付けた。LUX-lung 3トライアルの患者全員が中央検査でEGFR変異を有することが同定され、画像検査は個々に読影され治療の結果を評価された。追跡期間中央値8か月後に、afatinibは疾患の増悪を標準治療よりも4か月延長した（PFS:11.1対6.9か月）。19またはL858Rの欠失を有する患者308人においては、PFSはさらに長かった（13.6対6.9か月）。Afatinibによる治療を受けた患者はまた、標準的な化学療法を受けた患者と比較し、咳や呼吸困難などの肺がんに伴う一般的な症状の悪化が遅く、QOLが良好であった。Afatinibによる副作用はEGFR標的治療と同等であった。全生存期間に関するデータは2年以内に得られる予定である。

Full Text

Results from a Phase III international trial presented at ASCO's 48th Annual Meeting show that initial single-agent oral therapy with the targeted drug afatinib prolongs progression-free survival (PFS) in patients with advanced lung adenocarcinomas that harbor epidermal growth factor receptor (EGFR, also known as ErbB1) mutations, compared with standard chemotherapy. Researchers found that afatinib was particularly beneficial – leading to a doubling of PFS – in the majority of patients who had one of two common types of EGFR mutations, deletion 19 or L858R. These two mutations together account for approximately 90 percent of all EGFR mutations.

This is the first time findings from this trial – LUX-lung 3 – have been presented, and they are of particular interest because researchers compared afatinib with a relatively new first-line regimen for advanced, previously untreated lung adenocarcinoma: combined pemetrexed and cisplatin chemotherapy. This form of disease is a subtype of non-small cell lung cancer. EGFR mutated, or driven, lung adenocarcinoma is often clinically associated with patients who have never smoked and patients of Asian descent.

The EGFR pathway facilitates cancer cell growth, survival and spread. Laboratory studies have shown that afatinib chemically blocks this pathway more thoroughly and permanently than current EGFR-targeted treatments, such as gefitinib and erlotinib. Additionally, afatinib blocks the broader ErbB family of receptors that are associated with the EGFR pathway, including HER2 (ErbB2) and HER4 (ErbB4), and can inactivate further cancer cell pathways.

"By more broadly and effectively blocking the molecular pathways that facilitate the growth of these cancers, afatinib appears to be more potent than other therapies," said James Chih-Hsin Yang, M.D., Ph.D., a Professor at the National Taiwan University and the principle investigator of this multi-national study. "This new treatment could not only help patients live a longer period of time without further cancer progression, but because it's given orally, it may also require fewer visits to the doctors' office than standard chemotherapy – another important quality of life advantage."

In this study, researchers randomized 345 patients to afatinib or standard combination chemotherapy treatment, given intravenously. All participants had EGFR mutations that were identified through central testing, and the imaging scans were independently reviewed to evaluate treatment outcomes. After a median follow-up of 8 months, they found that afatinib delayed disease progression by more than 4 months over standard therapy (PFS: 11.1 vs. 6.9 months). Among the 308 patients with either deletion 19 or L858R, PFS was prolonged even further (13.6 vs. 6.9 months). Researchers noted that patients treated with afatinib were also slower to experience worsening of common lung cancer-related symptoms, including cough and dyspnea and showed a better quality of life when compared with patients receiving chemotherapy.

Side effects with afatinib were comparable to those of other EGFR-targeting therapies. Overall survival data are expected in about two years, according to Dr. Yang.

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