新薬により肺がん生存期間が改善する（Abstract # CRA8007）

GALAXY-1:新たな画期的標的治療薬は進行肺腺がん患者の生存期間を改善する

GALAXY-1: First in class targeted drug improves survival for patients with advanced lung adenocarcinoma

第49回American Society of Clinical Oncology年次集会で発表された大規模第II相試験GALAXY-1の結果、初回治療後に進行した進行肺腺がん患者のセカンドライン治療において、新たな熱ショック蛋白質90（Hsp90）阻害薬ganetespibとドセタキセルの併用は、標準的なセカンドラインドセタキセル単独療法と比較し、全生存期間が延長することが示された。EGFRやALKなどの肺がんの増殖を促進する多くの蛋白質の形成にはHsp90を必要とする。今年のASCOで報告された252人の患者は、ドセタキセルとganetespib併用またはドセタキセル単独療法を行う群に無作為に割り付けられた。Ganetespib併用群ではドセタキセル単独群と比較し、全生存期間が長かった（9.8か月対7.4か月）。この併用療法は特に進行肺がんの初回診断から6か月以上経過した患者において興味深く、これらの患者群ではganetespibとドセタキセル併用で全生存期間が67%改善した（全生存期間中央値10.7か月対6.4か月）。最近開始された第III相試験GALAXY-2においてこれらの患者群のスタディが現在施行されている。これらの結果が確認されればganetespibはこの条件の患者の予後を改善するここ10年間で初めての治療法となるであろう。

Full Text

Findings from GALAXY-1, a large phase II study presented at ASCO's 2013 annual meeting, finds that a novel heat shock protein 90 inhibitor (Hsp90), ganetespib, when combined with docetaxel in second-line therapy, leads to longer overall survival compared to standard second-line docetaxel alone in patients with advanced lung adenocarcinoma that progresses after initial therapy. If confirmed in an ongoing phase III trial, this would be the first treatment to improve patient outcomes in this setting in a decade.

Hsp90 belongs to a class of proteins known as molecular "chaperones." Chaperones help newly formed proteins assume the proper shape needed to perform their specific biologic function. Formation of many proteins that drive lung cancer growth, such as EGFR and ALK, requires Hsp90. Blocking such chaperones is a completely new strategy in cancer therapy, and is promising because it can disable many different cancer-fueling proteins at the same time. In addition, this strategy may still work in patients who develop mutations that make them resistant to traditional targeted drugs, because blocking the chaperone will inhibit the function of the mutated proteins, too.

"This is the first randomized study to demonstrate therapeutic benefit with a heat shock protein inhibitor in patients with cancer," said lead study author Suresh S. Ramalingam, M.D., a professor of medical oncology at the Winship Cancer Institute of Emory University in Atlanta, Georgia, USA. "We hope that the ongoing phase III study will confirm our findings, as patients with this common form and stage of lung cancer urgently need more effective treatments."

All patients in this clinical trial had disease that progressed despite standard treatment with platinum-based chemotherapy. The current study reports on the primary enrollment stage of the trial, which completed in November 2012. The 252 patients were randomly assigned to treatment with docetaxel plus ganetespib or docetaxel alone. Those in the ganetespib arm had longer overall survival (9.8 vs. 7.4 months) compared to docetaxel alone.

The combination was particularly interesting in patients who were at least six months from initial diagnosis of advanced lung cancer as that group of patients experienced a 67 percent improvement in overall survival with the combination of ganetespib and docetaxel (median overall survival 10.7 months vs. 6.4 months). This group of patients is being studied in a recently launched phase III trial, GALAXY-2, that is comparing docetaxel plus ganetespib to docetaxel alone.

"Ganetespib, in combination with docetaxel, shows promising early results in lung adenocarcinoma. We're hopeful about the outcome of an ongoing phase III study, which could help more patients with this form of advanced lung cancer access this promising drug," said Marjorie Zauderer, M.D., ASCO spokesperson and lung cancer expert.

Early Hsp90 drugs did not succeed in clinical trials due to liver toxicity and insufficient efficacy. This is the first randomized clinical trial of a second-generation Hsp90 inhibitor and the first time an agent in this class has been shown to be both safe and effective. This study was limited to patients with stage IV lung adenocarcinoma. Adenocarcinoma is the most common type of lung cancer overall. Progress in second-line therapy for NSCLC has plateaued in the past decade, so the survival improvement seen with the addition of ganetespib is significant.

Researchers are planning to separately assess outcomes in subsets of patients defined by genetic markers in the tumor or markers in blood. In the present study to date, the observed improvements in progression-free survival and overall survival did not appear to be associated with EGFR mutations status, KRAS mutations status, or baseline level of LDH in blood.

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