

Afatinib monotherapy in *EGFR*-mutant lung adenocarcinoma

In a prospective randomised phase 3 clinical trial, investigators compared afatinib with the combination of pemetrexed and cisplatin as initial therapy for patients with advanced lung adenocarcinoma harbouring activating *EGFR* mutations. They reported that progression-free survival was significantly longer with afatinib than with pemetrexed–cisplatin (median 11.1 months vs 6.9 months; hazard ratio 0.58, 95% CI 0.43–0.78; $p=0.001$), and response rates were substantially higher (56% vs 23%). Worsening of lung cancer-related symptoms was significantly delayed with afatinib compared with pemetrexed–cisplatin.

Pemetrexed plus cisplatin has become a standard first-line chemotherapy for advanced lung adenocarcinoma. Conversely, afatinib is a selective inhibitor that irreversibly binds to members of the ErbB family, and has shown preclinical and clinical activity

against lung cancers harbouring the *EGFR* Thr790Met resistance mutation.

Study participants were randomly assigned to receive oral afatinib (40 mg) once daily or intravenous pemetrexed (500 mg/m²) and cisplatin (75 mg/m²) every 21 days for a maximum of six cycles. The global trial included 345 treatment-naive patients with stage IIIB or IV disease.

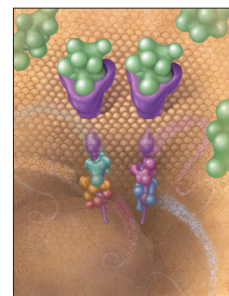
First author Lecia Sequist (Massachusetts General Hospital, Boston, MA, USA) said, "There are two things that are new about this study. This is the first study comparing afatinib with combination chemotherapy for the treatment of *EGFR*-mutation-positive lung adenocarcinoma, as well as the first study comparing an *EGFR* inhibitor to the combination of pemetrexed and cisplatin." She continued: "This study confirms that mutation-directed treatment is the best way to go, even compared with the

pemetrexed–cisplatin combination". Furthermore, "patients on afatinib had improved quality of life compared with patients on pemetrexed–cisplatin".

"The future direction of treatment for advanced lung adenocarcinomas is to individualise care based on the understanding of the oncogenic driver of the tumour", Nasser Hanna (Indiana University School of Medicine, Indianapolis, IN, USA) told *The Lancet Oncology*. "A limitation on this targeted approach is that adenocarcinomas are often complex tumours in which finding single drivers will be more challenging."

Hanna added that the next step for establishing which *EGFR* inhibitor has a therapeutic advantage in treating *EGFR*-mutant adenocarcinomas would be to compare them directly in the same trial for efficacy, cost, and side-effects.

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