Patients with EGFR expressing NSCLC benefit most from necitumumab added to chemotherapy

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Patients with epidermal growth factor receptor (EGFR) expressing advanced squamous non-small-cell lung cancer benefit most from necitumumab added to gemcitabine and cisplatin chemotherapy, according to a subgroup analysis from the SQUIRE trial presented today at the European Lung Cancer Conference (ELCC) 2016 in Geneva, Switzerland.

The randomised phase III SQUIRE trial demonstrated that the addition of necitumumab to gemcitabine and cisplatin chemotherapy improved overall survival in patients with stage IV squamous non-small-cell lung cancer by 1.6 months compared to chemotherapy alone. The current study analysed outcomes in the subgroup of patients with EGFR expressing tumours compared to those with no EGFRs.

Out of 982 patients in the SQUIRE trial, 95% had EGFR expressing tumours and 5% had tumours with no EGFR protein. The addition of necitumumab to gemcitabine and cisplatin chemotherapy improved overall survival and progression free survival by 21% and 16%, respectively, as compared to chemotherapy alone in patients whose tumours expressed the EGFR protein. There was no benefit in patients with no EGFR in their tumours.

Dr Luis Paz-Ares, Chief of medical oncology at the University Hospital 12 De Octubre in Madrid, Spain, lead author, said: "Necitumumab is targeted at EGFR so it makes sense that the drug is active in patients with the receptor. Our analysis showed that the drug had no effect when the receptor was absent, presumably because there was no target to bind to. We cannot make robust conclusions because the subgroup of patients with negative EGFR was very small, but the hypothesis generated here is that those tumours do not respond well to necitumumab."

"Based on this analysis, the European Medicines Agency has decided that necitumumab is approved only for patients with EGFR expressing tumours," continued Paz-Ares. "On the other hand the US Food and Drug Administration has taken the more conservative approach which recognises that SQUIRE was designed for all-comers without prior selection, and this subgroup analysis is insufficient evidence to conclude that patients with EGFR negative tumours are not candidates."

He concluded: "Our results need to be interpreted with caution. A confirmatory study in patients with EGFR negative tumours is needed to assess whether they are good candidates for necitumumab or not."

Commenting on the findings, Prof Robert Pirker, programme director for lung cancer at the Vienna General Hospital in Vienna, Austria, not involved in the study, said: "This subgroup analysis shows that the effect of necitumumab was slightly greater in patients with EGFR expressing tumours than it was in the entire SQUIRE population. It indicates that immunohistochemical detection of the EGFR receptor improves clinical activity of necitumumab. The findings are consistent with previous studies suggesting that monoclonal antibodies in combination with chemotherapy work better in patients with EGFR expressing cells."

Pirker added that a more thorough analysis is needed. He said: "Information on outcome of patients with cut-off levels higher than in the current analysis would be of interest. We also need to know the effect of necitumumab according to both percentages of positive cells and their staining intensity. This could be combined with fluorescence in situ hybridisation (FISH) analysis to detect gene amplification. This could give us a clearer picture of which patients benefit most from necitumumab."

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