Pertuzumab and Erlotinib in Patients With Relapsed Non-Small Cell Lung Cancer: A Phase II Study Using 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography Imaging

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AUTHOR SUMMARY

ABSTRACT

Background. Combination blockade of human epidermal growth factor receptor (*HER*) family signaling may confer more enhanced antitumor activity than single-agent blockade. We performed a single-arm study of pertuzumab, a monoclonal antibody that inhibits *HER2* dimerization, and erlotinib in relapsed non-small cell lung cancer (NSCLC).

Methods. Patients received pertuzumab (840-mg loading dose and 420-mg maintenance intravenously every 3 weeks) and erlotinib (150-mg or 100-mg dose orally, daily). The primary endpoint was response rate (RR) by 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) at day 56 in all patients and those with epidermal growth factor receptor (*EGFR*) wild-type tumors.

Results. Of 41 patients, 28 (68.3%) experienced treatment-related grade ≥ 3 adverse events, including pneumatoxis intestinalis (3 patients), resulting in early cessation of enrollment (Fig. 1). Tissue samples from 32 patients showed mutated *EGFR* status in 9 of 41 (22%) and wild-type *EGFR* in 23 of 41 (56%). The FDG-PET RR for patients with assessments at day 56 was 19.5% in all patients ($n = 41$) and 8.7% in patients with wild-type *EGFR* NSCLC ($n = 23$). Investigator-assessed computed tomography RR at day 56 was 12.2%.

Conclusion. FDG-PET suggests that pertuzumab plus erlotinib is an active combination, but combination therapy was poorly tolerated, which limits its clinical applicability. More research is warranted to identify drug combinations that disrupt *HER* receptor signaling but that exhibit improved tolerability profiles. *The Oncologist* 2014;19:175–176

DISCUSSION

Although a previous phase I study [1] demonstrated safety and tolerability of pertuzumab and erlotinib in NSCLC patients, this current study found that tolerability of the combination was generally poor. In addition, the occurrence of adverse events (AEs) requiring dose reductions was seen in a greater proportion of patients (34.1%) compared with single-agent erlotinib studies (12%–19%).

Recent studies of cetuximab in combination with erlotinib or afatinib in NSCLC show similar results. With the exception of pneumatoxis, the AEs observed in the present study were consistent with toxicities associated with *EGFR* inhibition. However, the severity of AEs was higher than those seen in single-agent studies of either erlotinib or pertuzumab.

We observed modest signs of activity, including prolonged progression-free survival and overall survival, among patients with FDG-PET and computed tomography (CT) responses. However, the early termination of enrollment resulted in only 41 patients receiving study treatment and only 22 (54%) being evaluable for FDG-PET response at day 56.

Comparison of the FDG-PET/CT results with our previous erlotinib single-agent study shows modestly higher FDG-PET response rates (RRs) and an increased magnitude of quantitative response (maximum standardized uptake value decline). Similar observations can also be made when comparing our results with a study of single-agent pertuzumab.

For the overall population, the centrally assessed CT RR was 19.5% compared with 7.8% in our previous erlotinib study. The higher CT RR for pertuzumab and erlotinib may be attributed to

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