SUPPLEMENTAL ONLINE-ONLY CONTENT

Methods- Pre-Specified Dose Modification

Cetuximab was to be reduced by one dose level (to 200, 100, 75, or 50 mg/m^2) for grade 3/4 fatigue, paronychia, mucositis/stomatitis, headache during the cetuximab infusion, or any other grade 3 nonhematologic toxicity, grade 2 thrombocytopenia, and grade 4 neutropenia (or grade 3 neutropenia lasting >1 week), whereas erlotinib was to be reduced by one dose level (to 100 or 75 mg/day) for grade 3/4 diarrhea, nausea/vomiting, mucositis/stomatitis, or other grade 3 nonhematologic toxicities. In the event of grade 3/4 rash, treatment was omitted for 1-2 weeks and reinitiated at the same dose level following improvement. Each subsequent recurrence of grade 3/4 rash required cetuximab dose reduction, both cetuximab and erlotinib dose reduction, and finally cetuximab discontinuation. Both drugs were discontinued if grade 3/4 rash did not improve, or in the event of grade 3/4 infusion reactions, other grade 4 nonhematologic toxicity, grade 4 thrombocytopenia, or confirmation of interstitial lung disease.

Patient Disposition and Demographics

Of the 3 untreated patients, 2 did not have bi-dimensionally measurable disease and the other had a concurrent malignancy.

Treatment Exposure

The majority of therapy discontinuations were for reason of disease progression (n=9; 40.9%), death due to tumor-related disease progression (n=2; 9.1%), or study drug-related toxicity (n=8; 36.4%).

One patient with stable disease that remained on therapy at the time of trial closure continued to receive treatment post study.

Safety

Three patients—all in the third dose level cohort—died of their disease (tumor-related disease progression) within 30 days after receiving the last dose of study treatment, and 2 additional patients died for the same reason at 33 and 67 days after their last dose, respectively.