Multicenter Phase II Study of Panitumumab in Platinum Pretreated, Advanced Head and Neck Squamous Cell Cancer

Marco Siano, Francesca Molinari, Vittoria Martin, Nicolas Mach, Martin Früh, Stefania Freguia, Irene Corradino, Michele Ghielmini, Milo Frattini & Vittoria Espeli

LESSONS LEARNED
Panitumumab shows activity in terms of disease control rate and preventing disease progression but not for tumor shrinkage in head and neck squamous cell cancer for second-line treatment. Epidermal growth factor receptor (EGFR) copy number gain, a property of tumor cells that theoretically could identify patients more likely to experience disease response, was common among patients having disease control. Our trial, given the lower toxicity with an every-2-week schedule, provides guidance for future trials, for example, in combinations of immune therapies and anti-EGFR-antibodies.

BACKGROUND
The objective of this study was to investigate the efficacy and safety of panitumumab (anti-epidermal growth factor receptor [EGFR] antibody) given as a single agent in platinum-pretreated head and neck squamous cell cancer (HNSCC).

METHODS
Patients with advanced HNSCC previously treated with platinum-containing therapy were included. Panitumumab was administered intravenously every 2 weeks at a dose of 6 mg/kg. Primary endpoint was overall response rate (ORR) according to Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1; secondary endpoints were progression-free survival (PFS) and safety. A Simon's two-step design was chosen; 4 partial remissions (PR) in the first 32 patients were required for continuing to step two. An exploratory biomarker analysis was performed.

RESULTS
Thirty-three patients were enrolled. Two patients obtained a PR for an ORR of 6%, and 15 (45%) showed stable disease (SD) for at least 2 months, resulting in a 51% disease control rate. Median PFS was 2.6 months (95% confidence interval [CI]: 1.7-3.7), while median OS was 9.7 months (95% CI: 6.3-17.2). The most frequent adverse drug reactions were cutaneous rash (64%) and hypomagnesemia (55%). Overall, 30% of patients experienced grade 3/4
adverse events. No infusion-related reactions occurred. EGFR copy number gain (CNG) was more frequent in patients who benefitted from panitumumab. Two uncommon KRAS mutations (G48E, T50I) and 3 canonical PIK3CA mutations (all E545K) were detected. High-risk HPV16 was found in 10 patients and EGFR CNG in 13 treated patients. EGFR CNG seems to be more frequent in individuals with at least SD compared with patients with progressive disease (59% vs. 30%). PFS for patients with EGFR CNG was 4.6 months (95% CI: 1.0-9.2 months) and 1.9 months (95% CI: 1.0-3.2 months) for patients without CNG (p = .02).

CONCLUSION
Panitumumab monotherapy in pretreated HNSCC patients was well tolerated but moderately active. We observed a considerable disease control rate. Future strategies with this agent comprise right patient selection through the identification of reliable biomarkers and gene signatures predicting response and, considering good tolerability and convenience, combination strategies with novel agents and immune therapeutic agents. The Oncologist 2017;22:1-8.