Optimal dose of cetuximab given every 2 weeks (q2w): a phase I pharmacokinetic (PK) and pharmacodynamic (PD) study of weekly (q1w) and q2w schedules in patients (pts) with metastatic colorectal cancer (mCRC).

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Abstract

Background: The anti-EGFR-MAb cetuximab is active in mCRC. Since cetuximab has a long biological half-life, a q2w schedule was chosen to minimize dosage-related toxicity, to reduce costs, and to improve compliance. Methods: In this phase I study, cetuximab was given q2w (500 mg/m²) and q1w (400 mg/m²) at an inpatient-free market dose. PK parameters were measured in serum and skin biopsies (at pre and post-treatment) as a measure of EGFR binding, and baseline and end-of-treatment (EoT) biopsies were obtained for pharmacodynamic analysis.

Results: 29 pts have been included so far: 9 in the q1w group and 20 in the q2w group. The median age was 69 years (range 22-87) and the majority of pts were male (55/68). The majority of pts had an ECOG PS of 1 (39/68) and were previously treated (49/68). The recommended dose of cetuximab given every two weeks has not yet been determined. DLTs were defined as grade 3-4 toxicities (except for hypersensitivity reactions and grade 3 skin toxicity). To date there have been no DLTs. PK data are obtained prior to therapy and on day 28 (steady state) and have been analyzed by IHC for pMAPK and pEGFR.

Conclusions: The data presented in this poster are for Part 1 of the study only, that is, the first six weeks of treatment. The MTD of cetuximab given every two weeks has not yet been determined. Further evaluation will be available after the combination therapy Part 2 of the study is complete.

References


Study Design

- A phase 1, open-label, multicenter, pharmacokinetic, pharmacodynamic and pharmacogenomic study of weekly and q2w cetuximab dosing every 7 days and on every 2 weeks to the first of six cycles.
- AUC: area under the curve.
- Cmin: minimum serum concentration.
- PK/PD: pharmacokinetic/pharmacodynamic.
- Trough concentration: concentration at the end of the dosing interval.

Results

- The data presented in this poster are for Part 1 of the study only, that is, the first six weeks of treatment.
- The MTD of cetuximab given every two weeks has not yet been determined.