

letter to the editor

Infusion reactions to the chimeric EGFR inhibitor cetuximab—change to the fully human anti-EGFR monoclonal antibody panitumumab is safe

In recent years, clinical investigators have focused upon monoclonal antibodies (mAbs) that inhibit cancer progression such as mAbs against epidermal growth factor receptor (EGFR) and vascular endothelial growth factor. Targeted therapies have rapidly gained attraction in the treatment of advanced colorectal cancer and are under active investigation. But infusion reactions (IRs) are serious complications in this modern antibody therapy of otherwise well-tolerated mAbs. In order to reduce the incidence and severity of such reactions, the newer generations of mAbs are fully human. However, there is limited clinical experience of administering a fully human mAb, such as panitumumab, to patients (pts) who have experienced IRs to a chimeric anti-EGFR mAb, such as cetuximab [1, 2]). We now report about the Austrian Compassionate Use programme, in which pts received panitumumab monotherapy after IRs to cetuximab.

Eligible chemotherapy refractory pts ($n = 20$) with metastatic colorectal cancer (mCRC) who experienced an IR after treatment with cetuximab received panitumumab monotherapy (6 mg/kg every 2 weeks) were recruited in 10 Austrian institutions. At the time of initiation, the predictive value of *KRAS* status on response to anti-EGFR therapy was not known and thus, was not an inclusion criterion for this programme. Patients included in this programme were heavily pretreated, with the majority having received at least 4 prior lines of chemotherapy (range 1–7). Median number of panitumumab cycles received was 6 (range 1–32). During the whole application period no panitumumab-related IRs were reported. Response data [3] were similar to previously published data.

The first generation of mAbs was murine-derived and highly immunogenic in humans. To overcome this issue, chimeric mAbs, such as cetuximab, were constructed by combining the antigen-binding regions of the mouse antibody with human immunoglobulin G-constant domains. Chimeric mAbs still consist of approximately 34% of mouse protein—which results in various immunogenic responses, including infusion-related reactions. Cetuximab has been associated with IRs of any grade in 15%–21% of pts, grade 3 to 4 IRs occurred to 2%–5% of pts (e.g. bronchospasm, stridor, urticaria, hypotension and cardiac

arrest) [4–6]. The clinical and economic impacts of these IRs are substantial, as they often require inpatient treatment and cause disruption of infusion or discontinuation of therapy [7].

Panitumumab is the first fully human mAb to EGFR and is approved as monotherapy for EGFR-expressing mCRC with nonmutated *KRAS* after failure of standard chemotherapy [8]. Clinical trials have reported <2% of infusion-related reactions of which approximately 1% were severe, which is most likely due to the drug's nonchimeric structure [9, 10]. No fatal reactions to panitumumab have been reported. Our data indicate that the fully human mAb panitumumab can be safely administered to pts after IRs to cetuximab.

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disclosure

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