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LETTER TO THE EDITOR

Re-treatment with cetuximab in patients with severe hypersensitivity reactions to cetuximab. Two case reports

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To the Editor

A 68-year-old Caucasian woman was offered 3rd line therapy with cetuximab (weekly) and irinotecan (each 3 weeks) for oxaliplatin and irinotecan resistant metastatic colorectal cancer. Routine pre-medication to prevent hypersensitivity reaction to cetuximab consisted of clemastine 2 mg intravenously (i.v.) 30 minutes before the infusion of cetuximab. Thirty minutes after initiation of loading dose of cetuximab, she developed severe hypotension (61/50) and generalised urticaria. The infusion was discontinued immediately and she recovered quickly after treatment with clemastine 2 mg i.v.

She had extensive progressive disease (PD) without other effective therapeutic options [1] and therefore we discussed re-treatment with her. She was informed about the risk of fatal hypersensitivity reactions and informed consent was obtained. One week later she was re-challenged to cetuximab. Oxygen, epinephrine, and resuscitation equipment were available for prompt treatment of possibly anaphylaxis. She was pre-medicated with prednisolone 50 mg orally 24, 12, and 3 hours and clemastine 2 mg i.v. 30 minutes before cetuximab infusion. The infusion rate of cetuximab was gradually increased according to Table I. She had no evidence of an acute reaction during or after the infusion. Treatment was continued using the same pre-medication and infusion rate. Nine weeks later a CT-scan revealed PD and therapy was discontinued.

A 57-year-old Caucasian man was offered 3rd line therapy with cetuximab (weekly) and irinotecan (each 3 weeks) for oxaliplatin and irinotecan resis-

tant metastatic colorectal cancer. He received routine pre-medication with clemastine. Thirty-five minutes after initiation of loading dose cetuximab, he developed severe hypotension (74/39), bradycardia (pulse rate 46), dyspnoea, a slightly blurred consciousness and pruritus. The infusion was discontinued immediately and an i.v. injection of adrenaline (0.2 ml) and clemastine 2 mg was promptly administered. He reacted with tremor, tachycardia and breast pain, a rise in the blood-pressure and normalization of breathing. One hour later he developed a generalised bright-red, blazing, urticaria especially localised in the face and breast and back lasting for the next eight hours.

In view of the experience with the previous patient, it was considered reasonable to re-challenge with cetuximab. The patient was informed about the risk and informed consent was obtained. One week later he was re-treated with cetuximab under close monitoring. The pre-medication and infusion rate of cetuximab was as in the previous patient and as stated in Table I. He showed no evidence of an acute reaction during or after the cetuximab infusion and treatment was continued using the same treatment protocol. After nine series of cetuximab CT-scan showed a partial response, the patient is still on treatment and in excellent performance.

Discussion

We are not aware of other case reports of re-treatment with cetuximab after severe hypersensitivity reactions. The efficacy of cetuximab and irinotecan in

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Table I. Re-challenge with cetuximab after hypersensitivity reactions. Premedication and infusion rate of cetuximab.

Premedication	
Time	Medication
24 hours before treatment	Prednisolone 50 mg orally
12 hours before treatment	Prednisolone 50 mg orally
3 hours before treatment	Prednisolone 50 mg orally
30 minutes before treatment	Clemastine 2 mg intravenously
Cetuximab	
Time	Infusion rate
0–2 hours	10% of original infusion rate
2–2.5 hours	25% of original infusion rate
2.5–3 hours	50% of original infusion rate
3 hours–	Initial planed infusion rate

patients with irinotecan resistant metastatic colorectal cancer was confirmed in the BOND study [1] and therefore cetuximab was approved for patients with irinotecan resistant metastatic colorectal cancer in US and EU in 2004.

In clinical studies using cetuximab, grade 3 and 4 hypersensitivity reactions led to cessation of therapy in 1.2% to 3.5% of patients [1,2]. The manufacturer does not recommend re-treatment of cetuximab in patients with grade 3 or 4 hypersensitivity and there are no guidelines as yet regarding the procedure for re-challenge. The two patients described were re-treated under controlled conditions. Using pre-medication with steroid and decreased infusion rate, none of the patients had evidence of an acute reaction during or after the cetuximab infusion. Treatment could be continued according to the

planned schedule as pre-medication and infusion rate were kept unchanged. As suggested by the one patient with a long lasting partial response pre-treatment with steroid and decreased the infusion rate of cetuximab did not seem to affect the efficacy of cetuximab.

Based on our experience with especially the last of the two presented cases we would recommend the first therapeutic re-challenge to be performed with the patient hospitalized in an intensive care unit.

Conclusion

Re-challenge with cetuximab after hypersensitivity reactions may be considered in selected patients with refractory, progressive colorectal cancer without other therapeutic options.

Conflict of interest and funding

No conflict of interest or financial support.

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