

letter to the editor

Six cases of treatment with panitumumab in patients with severe hypersensitivity reactions to cetuximab

Five patients were offered third-line therapy with cetuximab and irinotecan every second week for oxaliplatin- and irinotecan-resistant metastatic colorectal cancer and one patient was offered first-line therapy with cetuximab and Nordic FLOX (Halfdan) [1, 2]. All patients had KRAS wild-type colorectal cancer. To prevent hypersensitivity reaction to cetuximab, all patients received routine premedication consisting of clemastine 2 mg i.v. 30 min before the infusion of cetuximab. In addition, patients received prednisolone 50 mg orally as part of antiemetic regimen. Two and four patients developed hypersensitivity reaction grade 3 and 4, respectively, leading to cessation of cetuximab. Five patients were treated with panitumumab 6 mg/kg in combination with irinotecan 180 mg/m² every second week without premedication and one patient was treated with panitumumab 6 mg/kg in combination with FLOX (Halfdan) every second week. All patients tolerated panitumumab without any infusion reaction. Patient characteristics, response, time to progression and overall survival after treatment with panitumumab in combination with irinotecan or oxaliplatin are shown in Table 1. One patient had stable disease for 4.6 months. All

patients developed skin toxicity grade 2 or 3 and diarrhoea grade 3 was seen in one patient.

In clinical studies using cetuximab, grade 3 and 4 hypersensitivity reactions led to cessation of therapy in 1.2%–3.5% of patients [3]. The manufacturer does not recommend retreatment of cetuximab in patients with grade 3 or 4 hypersensitivity. Panitumumab is a fully human mAb targeting epidermal growth factor receptor. In a randomized phase III study, the compound almost halved the risk of disease progression/death versus a control group receiving best supportive care (hazard ratio 0.54; 95% confidence interval 0.44–0.66; $P < 0.0001$) [4]. One case report of treatment with single-agent panitumumab after severe hypersensitivity reactions to cetuximab has been published [5]. In the present report, six patients were treated with panitumumab in combination with irinotecan or oxaliplatin. None of the patients had evidence of an acute reaction during or after the panitumumab infusion. Treatment could be continued according to the planned schedule.

Treatment with panitumumab in combination with irinotecan or oxaliplatin after hypersensitivity reactions to cetuximab may be considered in patients with KRAS wild-type colorectal cancer.

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Table 1. Patient characteristics, response, time to progression and overall survival after treatment with panitumumab and irinotecan

Patient, age	PS	Disease, status	Hypersensitivity reaction, cetuximab	Panitumumab + irinotecan or oxaliplatin			
				Response	TTP (months)	OS (months)	Side-effects ^a
Male, 78	1	c. recti, lung metastases	Grade 3 (bronchospasm)	NC	4.6	4.6+	Skin (2), diarrhoea (3) neutropenia (4)
Male, 65	1	c. coli, bone metastases, retroperitoneal lymph nodes	Grade 4 anaphylaxis	PD	–	3.0	Skin (2), fatigue (2)
Male, 58	2	c. coli, liver metastases	Grade 4 anaphylaxis	PD	0.7	1.7	Skin (2), infection (2)
Male, 60	2	c. coli, lung, liver and peritoneal metastases	Grade 4 anaphylaxis	PD (NE?)	2.7	3.1	Skin (2), infection (2)
Female, 73	1	c. coli, retroperitoneal lymph nodes	Grade 3 (quincke oedema)	NE (one infusion)	–	–	–
Male, 57	0	c. coli, liver metastases	Grade 4 anaphylaxis	NE (one infusion)	–	–	Skin (3)

^aGrade of toxicity in brackets.

NC, no change; NE, non-evaluable; PD, progression; PS, performance status; OS, overall survival; TTP, time to progression.

references

1. Cunningham D, Humblet Y, Siena S et al. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. *N Engl J Med* 2004; 351: 337–345.
2. Sørbye H, Glimelius B, Berglund A et al. Multicenter phase II study of Nordic fluorouracil and folinic acid bolus schedule combined with oxaliplatin as first-line treatment of metastatic colorectal cancer. *J Clin Oncol* 2004; 22: 31–38.
3. Peeters M, Balfour J, Arnold D. Review article: panitumumab—a fully human anti-EGFR monoclonal antibody for treatment of metastatic colorectal cancer. *Alint Pharmacol Ther* 2008; 28: 269–281.
4. van Cutsem E, Peeters M, Siena S et al. Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. *J Clin Oncol* 2007; 25: 1658–1754.
5. Cartwright TH, Genther R. Successful administration of panitumumab alone after severe infusion reaction to cetuximab in a patient with metastatic colorectal cancer. *Clin Colorectal Cancer* 2008; 7: 202–203.

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