

PGCR 1:1 2006 (Abstract 307)

Safety and Efficacy of Panitumumab in the Treatment of Metastatic Colorectal Cancer (mCRC) From Five Clinical Studies

Jordan Berlin

Vanderbilt University Medical Center
Nashville, Tennessee

Eric Van Cutsem

University Hospital Gasthuisberg
Leuven, Belgium

Marc Peeters

Ghent University Hospital
Ghent, Belgium

J. Randolph Hecht

UCLA School of Medicine
Los Angeles, California

Edith Mitchell

Thomas Jefferson University
Philadelphia, PA

Michael Wolf

Rafael Amado

Amgen Inc.
Thousand Oaks, California

Neal J. Meropol

Fox Chase Cancer Center
Philadelphia, Pennsylvania

Background: Epidermal growth factor receptor (EGFR) expression in CRC is associated with metastatic potential and poor prognosis. Panitumumab, a fully human monoclonal antibody against EGFR, is being developed for treatment of patients with refractory mCRC.

Methods: We summarized the results of five clinical studies investigating the safety (732 patients) and efficacy (617 patients) of panitumumab monotherapy in mCRC patients after failure of oxaliplatin and/or irinotecan chemotherapy.

Results: Most patients were men (55% to 63%) and white (80% to 99%) across the studies; median age ranged from 58 to 64 years. The rates of tumor response and disease control were consistent across the studies (Table) and similar to that of other EGFR inhibitors. Median duration of response was also consistent across the studies and ranged from 13 to 18 weeks. All patients experienced ≥ 1 adverse event (AE; Table). No antipanitumumab antibodies were detected by ELISA.

Conclusions: Panitumumab was well-tolerated and consistently showed antitumor activity in patients with mCRC regardless of EGFR expression status or prior chemotherapy. Infusion reactions are rare. The findings from these five studies support the use of panitumumab for the treatment of refractory mCRC.

Summary of Safety and Efficacy of Panitumumab in the Treatment of Refractory mCRC

Clinical Study- Author(s)	Peeters, Van Cutsem (AACR 2006)	Peeters, Van Cutsem (AACR 2006)	Berlin (ASCO 2006)	Hecht (ASCO 2006)	Malik (ASCO 2005)
Phase	3	ES ^a	2	2	2
Dosing schedule	Q2W	Q2W	Q2W	Q2W	QW
Baseline EGFR staining, (%)					
< 1%	1	1	0	41	0
1% to 9%	25	26	3	56	0
$\geq 10\%$	74	73	97	2	100
Primary analysis populations (n)					
Efficacy	231	176	39	23	148
Safety	229	176	91	88	148
Prior regimens, n (%)					
Irinotecan containing only	2 (1)	0 (0)	0 (0)	0 (0)	75 (51)
Irinotecan and oxaliplatin containing	229 (99)	175 (100)	90 (99)	88 (100)	68 (47)
Efficacy^b					

Complete response (%)	0	1	0	0	0
Partial response (%)	8	11	8	13 ^c	9
Stable disease (%)	28	33	21	30 ^d	29
Disease control rate (%)	36	44	29	43	38
Progression free survival, months					
Median (95% CI)	2 (2,2)	2 (2,3)	2 (2,2)	3 (2,5)	3 (2,4)
Safety					
AEs, All (grade 3, grade4) %					
Skin-related toxicities ^e	90 (14, 0)	91 (12,1)	96 (18,0)	91 (14,0)	95 (5,0)
Paronychia	24 (1, 0)	20 (2, 0)	22 (2, 0)	18 (0, 0)	11 (0, 0)
Diarrhea	21 (1, 0)	22 (2, 0)	15 (0, 0)	23 (2, 0)	36 (2, 0)
Fatigue	24 (4, 0)	26 (5, 1)	19 (0, 0)	32 (2, 0)	51 (9, 0)
Hypomagnesaemia	38 (3, 1)	32 (3, 1)	47 (4, 4)	45 (6, 5)	NA
Infusion reactions, %	0	0	1 ^f	2 ^g	0

^aExtension study (an extension of Peeters and Van Cutsem study, AACR 2006).

^bBy central review; by local review for Peeters and Van Cutsem extension study.

^cOut of 3 patients with partial response 2 had a baseline EGFR staining <1%.

^dOut of 7 patients with stable disease 4 had a baseline EGFR staining <1%.

^eMedDRA v 7.0 or 8.0 preferred terms; graded per NCI-CTCAE v 3.0 with modifications.

^fIt was graded as severe by the investigator and did not result in the interruption of infusion.

^gIt was graded as mild by the investigator and did not result in the interruption of infusion.

NA: not applicable.