MEET CONNIE:*
A PATIENT WITH THIRD-LINE mCRC

*A hypothetical case study of a patient eligible for third-line mCRC therapy.

mCRC = metastatic colorectal cancer.

PATIENT Connie*
GENDER Female
AGE 68
OCCUPATION Salesperson

*This case study is a hypothetical example and does not represent an actual patient.

WHAT CLINICAL CHARACTERISTICS AFFECT YOUR THIRD-LINE TREATMENT DECISION?

Medical history
- Osteoarthritis

Presentation
- Initial presentation of mild abdominal discomfort and mild anemia
- Colonoscopy revealed a nonobstructing mass in the left colon
- CT scan revealed liver and lung metastases that were unresectable

Prior therapy
- First-line treatment: FOLFOX + bevacizumab
  - Progressed on therapy after 9 months
- Second-line treatment: FOLFIRI + bevacizumab
  - Progressed on therapy after 7 months with liver and lung metastases

Performance status
- ECOG PS = 1

Laboratory results
- ALT: 135 U/L; AST: 250 U/L
- CBC
  - WBC: 4.0 x 10^3 mL/µL
  - Neutrophil: 1.6 x 10^3 mL/µL
  - Hb: 9.0 g/dL
  - PLT: 125 x 10^3 mL/µL
- Bilirubin: 1.8 mg/dL

Mutational status
- WT *RAS* (wild type in both *KRAS* and *NRAS*)

Imaging results
- CT scan indicated diffuse metastatic involvement of lung and liver

Surgery consult on metastatic disease
- Unresectable due to number of metastatic sites

ALT = alanine aminotransferase; AST = aspartate aminotransferase; CBC = complete blood count; CT = computed tomography; ECOG PS = Eastern Cooperative Oncology Group Performance Status; Hb = hemoglobin; PLT = platelet; WBC = white blood cell count; WT = wild type.

Indication

Vectibix® is indicated for the treatment of patients with wild-type *RAS* (defined as wild-type in both *KRAS* and *NRAS* as determined by an FDA-approved test for this use) metastatic colorectal cancer (mCRC):

- As first-line therapy in combination with FOLFOX.
- As monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy.

Limitation of Use

Vectibix® is not indicated for the treatment of patients with *RAS*-mutant mCRC or for whom *RAS* mutation status is unknown.

Important Safety Information

BOXED WARNING: DERMATOLOGIC TOXICITY

Dermatologic Toxicity: Dermatologic toxicities occurred in 90% of patients and were severe (NCI-CTC grade 3 and higher) in 15% of patients receiving Vectibix monotherapy.

- In Study 20020408, dermatologic toxicities occurred in 90% of patients and were severe (NCI-CTC grade 3 and higher) in 15% of patients with mCRC receiving Vectibix®. The clinical manifestations included, but were not limited to, acneiform dermatitis, pruritus, erythema, rash, skin exfoliation, paronychia, dry skin, and skin fissures.

44.9% INCREASE (3.1-MONTH ABSOLUTE DIFFERENCE) IN MEDIAN OS WITH VECTIBIX® + BSC VS BSC ALONE[1]

SIGNIFICANT IMPROVEMENT IN OS IN PATIENTS WITH WT *RAS** mCRC (*P* = 0.0135)[1]

The third-line 20100007 study: a phase 3, open-label, multicenter, randomized (1:1) study of 377 patients with chemorefractory WT *KRAS*† mCRC treated with Vectibix® Q2W + BSC or BSC alone[1,2]

- Prespecified key secondary endpoints: OS, PFS, and ORR‡ in patients with WT *RAS* mCRC[1]
- The primary endpoint conducted in WT *KRAS* (exon 2 in codons 12 and 13) was OS. In a prespecified secondary endpoint analysis in the WT *RAS* subgroup, *RAS* tumor mutation status was available for 86% of patients: 270 (72%) patients had WT *RAS* tumors, 54 (14%) had mutant *RAS* tumors, and 54 (14%) had unknown *RAS* tumor status[1]

	WT *RAS* mCRC (n = 270)	
	Vectibix® + BSC (n = 142)	**BSC alone** (n = 128)
OS median months (95% CI)	**10.0 (8.7–11.6)**	**6.9 (5.2–7.9)**
HR (95% CI), *P* value	0.70 (0.53–0.93), *P* = 0.0135	
PFS median months (95% CI)	5.2 (3.5–5.3)	1.7 (1.6–2.2)
HR (95% CI), *P* value	0.46 (0.35–0.59), *P* < 0.0001	
ORR % (95% CI)	31% (23.5%–39.3%)	2.3% (0.5%–6.7%)

30% reduction in the risk of death[1]

*Defined as wild type in both *KRAS* and *NRAS*.[1]
†Exon 2 in codons 12 and 13.[1]
‡Response was evaluated by investigators per RECIST version 1.1.[2]
BSC = best supportive care; CI = confidence interval; HR = hazard ratio; mCRC = metastatic colorectal cancer; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; Q2W = every 2 weeks; RECIST = Response Evaluation Criteria in Solid Tumors; WT = wild type.

Vectibix® (panitumumab)
100mg/5ml | 20mg/ml for injection
First and only FDA-approved option for WT *RAS* mCRC

Please see full Important Safety Information, including **Boxed WARNING**, on pages 4 and 5.

IMPORTANT SAFETY INFORMATION

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Dermatologic Toxicity: Dermatologic toxicities occurred in 90% of patients and were severe (NCI-CTC grade 3 and higher) in 15% of patients receiving Vectibix monotherapy *[see Dosage and Administration (2.3), Warnings and Precautions (5.1), and Adverse Reactions (6.1)]*.

- In Study 20020408, dermatologic toxicities occurred in 90% of patients and were severe (NCI-CTC grade 3 and higher) in 15% of patients with mCRC receiving Vectibix®. The clinical manifestations included, but were not limited to, acneiform dermatitis, pruritus, erythema, rash, skin exfoliation, paronychia, dry skin, and skin fissures.
- Monitor patients who develop dermatologic or soft tissue toxicities while receiving Vectibix® for the development of inflammatory or infectious sequelae. Life-threatening and fatal infectious complications including necrotizing fasciitis, abscesses, and sepsis have been observed in patients treated with Vectibix®. Life-threatening and fatal bullous mucocutaneous disease with blisters, erosions, and skin sloughing has also been observed in patients treated with Vectibix®. It could not be determined whether these mucocutaneous adverse reactions were directly related to EGFR inhibition or to idiosyncratic immune-related effects (eg, Stevens Johnson syndrome or toxic epidermal necrolysis). Withhold or discontinue Vectibix® for dermatologic or soft tissue toxicity associated with severe or life-threatening inflammatory or infectious complications. Dose modifications for Vectibix® concerning dermatologic toxicity are provided in the product labeling.
- Vectibix® is not indicated for the treatment of patients with colorectal cancer that harbor somatic *RAS* mutations in exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146) of either *KRAS* or *NRAS* and hereafter is referred to as "*RAS*."
- Retrospective subset analyses across several randomized clinical trials were conducted to investigate the role of *RAS* mutations on the clinical effects of anti-EGFR-directed monoclonal antibodies (panitumumab or cetuximab). Anti-EGFR antibodies in patients with tumors containing *RAS* mutations resulted in exposing those patients to anti-EGFR related adverse reactions without clinical benefit from these agents. Additionally, in Study 20050203, 272 patients with *RAS*-mutant mCRC tumors received Vectibix® in combination with FOLFOX and 276 patients received FOLFOX alone. In an exploratory subgroup analysis, OS was shorter (HR = 1.21, 95% CI: 1.01-1.45) in patients with *RAS*-mutant mCRC who received Vectibix® and FOLFOX versus FOLFOX alone.
- Progressively decreasing serum magnesium levels leading to severe (grade 3-4) hypomagnesemia occurred in up to 7% (in Study 20080763) of patients across clinical trials. Monitor patients for hypomagnesemia and hypocalcemia prior to initiating Vectibix® treatment, periodically during Vectibix® treatment, and for up to 8 weeks after the completion of treatment. Other electrolyte disturbances, including hypokalemia, have also been observed. Replete magnesium and other electrolytes as appropriate.
- In Study 20020408, 4% of patients experienced infusion reactions and 1% of patients experienced severe infusion reactions (NCI-CTC grade 3-4). Infusion reactions, manifesting as fever, chills, dyspnea, bronchospasm, and hypotension, can occur following Vectibix® administration. Fatal infusion reactions occurred in postmarketing experience. Terminate the infusion for severe infusion reactions.
- Severe diarrhea and dehydration, leading to acute renal failure and other complications, have been observed in patients treated with Vectibix® in combination with chemotherapy.

IMPORTANT SAFETY INFORMATION *(continued)*

- Fatal and nonfatal cases of interstitial lung disease (ILD) (1%) and pulmonary fibrosis have been observed in patients treated with Vectibix®. Pulmonary fibrosis occurred in less than 1% (2/1467) of patients enrolled in clinical studies of Vectibix®. In the event of acute onset or worsening of pulmonary symptoms interrupt Vectibix® therapy. Discontinue Vectibix® therapy if ILD is confirmed.
- In patients with a history of interstitial pneumonitis or pulmonary fibrosis, or evidence of interstitial pneumonitis or pulmonary fibrosis, the benefits of therapy with Vectibix® versus the risk of pulmonary complications must be carefully considered.
- Exposure to sunlight can exacerbate dermatologic toxicity. Advise patients to wear sunscreen and hats and limit sun exposure while receiving Vectibix®.
- Keratitis and ulcerative keratitis, known risk factors for corneal perforation, have been reported with Vectibix® use. Monitor for evidence of keratitis or ulcerative keratitis. Interrupt or discontinue Vectibix® for acute or worsening keratitis.
- In an interim analysis of an open-label, multicenter, randomized clinical trial in the first-line setting in patients with mCRC, the addition of Vectibix® to the combination of bevacizumab and chemotherapy resulted in decreased OS and increased incidence of NCI-CTC grade 3-5 (87% vs 72%) adverse reactions. NCI-CTC grade 3-4 adverse reactions occurring at a higher rate in Vectibix®-treated patients included rash/acneiform dermatitis (26% vs 1%), diarrhea (23% vs 12%), dehydration (16% vs 5%), primarily occurring in patients with diarrhea, hypokalemia (10% vs 4%), stomatitis/mucositis (4% vs < 1%), and hypomagnesemia (4% vs 0).
- NCI-CTC grade 3-5 pulmonary embolism occurred at a higher rate in Vectibix®-treated patients (7% vs 3%) and included fatal events in three (< 1%) Vectibix®-treated patients. As a result of the toxicities experienced, patients randomized to Vectibix®, bevacizumab, and chemotherapy received a lower mean relative dose intensity of each chemotherapeutic agent (oxaliplatin, irinotecan, bolus 5-FU, and/or infusional 5-FU) over the first 24 weeks on study compared with those randomized to bevacizumab and chemotherapy.
- Vectibix® can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment, and for at least 2 months after the last dose of Vectibix®.
- In monotherapy, the most commonly reported adverse reactions (≥ 20%) in patients with Vectibix® were skin rash with variable presentations, paronychia, fatigue, nausea, and diarrhea.
- The most commonly reported adverse reactions (≥ 20%) with Vectibix® + FOLFOX were diarrhea, stomatitis, mucosal inflammation, asthenia, paronychia, anorexia, hypomagnesemia, hypokalemia, rash, acneiform dermatitis, pruritus, and dry skin. The most common serious adverse reactions (≥ 2% difference between treatment arms) were diarrhea and dehydration.

Please see Vectibix® full Prescribing Information, including **Boxed WARNING**.

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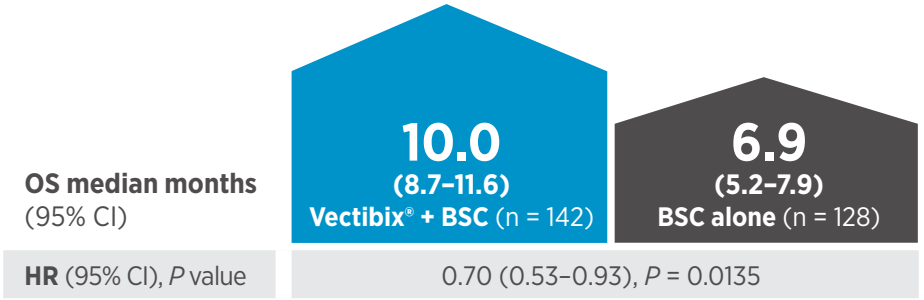
(panitumumab)
100mg/5ml | 20mg/ml for injection

VECTIBIX® + BSC SIGNIFICANTLY IMPROVED MEDIAN OS VS BSC ALONE IN THIRD-LINE PATIENTS WITH WT *RAS** mCRC (*P* = 0.0135)[1]

STUDY 20100007 WAS A PHASE 3, OPEN-LABEL, MULTICENTER, RANDOMIZED (1:1) STUDY OF 377 PATIENTS WITH CHEMOREFRACTORY WT *KRAS*† mCRC TREATED WITH VECTIBIX® Q2W + BSC OR BSC ALONE[1,2]

- OS in the subgroup of patients with WT *RAS* mCRC was a prespecified key secondary endpoint[1]

WT *RAS* mCRC (n = 270)



- 30% reduction in the risk of death with Vectibix® + BSC vs BSC alone[1]

44.9% increase (3.1-month absolute difference) in median OS[1]

*Defined as wild type in both *KRAS* and *NRAS*.[1]
†Exon 2 in codons 12 and 13.[1]
BSC = best supportive care; CI = confidence interval; HR = hazard ratio; mCRC = metastatic colorectal cancer; OS = overall survival; Q2W = every 2 weeks; WT = wild type.

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References: 1. Vectibix® (panitumumab) prescribing information, Amgen. **2.** Kim TW, Elme A, Kusic Z, et al. A phase 3 trial evaluating panitumumab plus best supportive care vs best supportive care in chemorefractory wild-type *KRAS* or *RAS* metastatic colorectal cancer. *Br J Cancer*. 2016;115(10):1206-1214.

AMGEN®

Please visit Vectibix.com/hcp for more information.

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