

Panitumumab in metastatic colorectal cancer

The first fully human monoclonal antibody for chemotherapy-refractory disease

What's new, what's important

Panitumumab (Vectibix) is the first fully human monoclonal antibody approved for use in cancer. It differs from cetuximab (Erbix), which is a chimeric mouse/human monoclonal antibody that binds to the extracellular domain of the epidermal growth factor receptor (EGFR). Panitumumab blocks both epidermal growth factor (by binding to the EGFR) and tumor growth factor- α (TGF- α) from binding to the extracellular domain of EGFR.

The drug is currently approved by the US Food and Drug Administration for the treatment of EGFR-expressing metastatic colorectal carcinoma with disease progression on or following treatment with fluoropyrimidine, oxaliplatin (Eloxatin), and irinotecan (Camptosar) regimens. Patients enrolled on the clinical trial that led to panitumumab's approval had EGFR-expressing tumors that were documented by immunohistochemistry (Dako EGFR pharmDx®).

The side effects of this drug are principally dermatologic reactions and diarrhea. These side effects are similar to those observed with other agents that target the EGFR. Infusion reactions are uncommon with panitumumab.

Panitumumab is a valuable addition to the treatment of colorectal cancers that are refractory to standard cytotoxic chemotherapy. Studies are progressing with panitumumab in combination with novel chemotherapy regimens and in other tumor types. There is no direct comparison between panitumumab and cetuximab in clinical setting, but some of the pre-clinical evidence suggests that panitumumab may be more potent than cetuximab. But clinical trials are needed to confirm this finding.

— Jame Abraham, MD
Section Editor

Panitumumab (Vectibix) is a fully human immunoglobulin G2 monoclonal antibody directed against the extracellular domain of the epidermal growth factor receptor (EGFR). It is the first such monoclonal antibody to be approved for use in cancer treatment. Human monoclonal antibodies are expected to result in reduced immunogenic reactions (including systemic reactions and development of antimonoal antibody antibodies) compared with prior generations of humanized or chimeric monoclonal antibodies, such as cetuximab (Erbix) or bevacizumab (Avastin).

Thus far, it appears that no human antihuman antibodies have occurred in patients treated with panitumumab.¹ In comparison, human antichimeric antibodies are observed in a small proportion of patients (~3%) treated with cetuximab, which contains a high percentage (34%) of mouse proteins. Allergic reactions appear to occur in < 1% of patients receiving panitumumab, and few infusion reactions have been reported to date. It appears

that no pretreatment with an antihistamine or corticosteroid is necessary.

Pivotal phase III evidence

Panitumumab currently is indicated for the treatment of EGFR-expressing metastatic colorectal cancer (mCRC) with disease progression on or following fluoropyrimidine-, oxaliplatin (Eloxatin)-, and irinotecan (Camptosar)-containing regimens. In the pivotal phase III trial resulting in US Food and Drug Administration approval for use of panitumumab in this setting, a dose of 6 mg/kg every 2 weeks was compared with best supportive care in 463 patients in whom standard chemotherapy had failed. Panitumumab treatment was associated with a highly significant improvement in the primary endpoint of progression-free survival (PFS), reducing the risk of disease progression or death by 46% ($P < 0.000000001$).¹⁻³

The benefit of panitumumab in improving PFS was evident in all patient subsets. The overall response rate was 8%, with a median time to response of 8 weeks and a median duration of re-

sponse of 17 weeks. Among the 174 patients in the best supportive care group who were crossed over (per protocol) to panitumumab salvage therapy, the overall response rate was 10%, with 32% of the patients having stable disease. Interim analysis of the study data did not indicate an overall survival benefit with panitumumab; however, an analysis excluding those patients in the best supportive care arm who responded to crossover panitumumab salvage therapy showed a trend toward improved survival in the panitumumab arm (hazard ratio, 0.78).

The major toxicity of panitumumab observed in the trial was skin toxicity, usually occurring as acneiform dermatitis similar to that seen with cetuximab therapy; other skin reactions included erythema, pruritus, and paronychia. Skin toxicity was observed in 90% of panitumumab recipients in the trial, with grade 3 or 4 toxicity occurring in 14%.

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TABLE 1

Efficacy and toxicity of panitumumab plus IFL or FOLFIRI as first-line treatment in metastatic colorectal cancer

Parameter	Panitumumab + IFL (n = 19)	Panitumumab + FOLFIRI (n = 24)
Efficacy, n (%)		
Objective response	9 (47%)	8 (33%)
Complete response	0 (0%)	0 (0%)
Partial response	9 (47%)	8 (33%)
Stable disease	5 (26%)	11 (46%)
Progressive disease	1 (5%)	3 (13%)
No assessment	4 (22%)	2 (8%)
Median (95% CI) PFS, months*	5.6 (4.4, 8.3)	10.9 (6.0, -)
Median (95% CI) survival, months*	16.8 (13.7, -)	-†
Major toxicities, n (%)		
Diarrhea, grade 3/4	10 (53%)/1 (5%)	6 (25%)/0 (0%)
Skin toxicity		
Any grade	19 (100%)	24 (100%)
Grade 3	3 (16%)	4 (17%)
Hypokalemia, grade 3	3 (16%)	0 (0%)
Fatigue, grade 3	2 (11%)	0 (0%)
Nausea, grade 3	1 (5%)	0 (0%)
Hypomagnesemia, grade 4	1 (5%)	1 (4%)

IFL = 5-fluorouracil (5-FU), leucovorin, and irinotecan; FOLFIRI = folinic acid, 5-FU, and irinotecan; CI = confidence interval; PFS = progression-free survival; - = not estimable

* Kaplan-Meier estimate † At the time of this analysis, 23 of 24 patients remained alive.

Adapted from Hecht et al⁴

Current studies

In a phase II trial,⁴ 19 patients with mCRC and EGFR expression in $\geq 10\%$ of tumor cells received panitumumab (2.5 mg/kg weekly via a 1-hour infusion) in combination with 5-fluorouracil (5-FU), leucovorin (LV), and irinotecan (IFL regimen). Owing to IFL toxicity, the protocol was amended to substitute folinic acid, 5-FU, and irinotecan (FOLFIRI) for IFL; in all, 24 patients were treated with panitumumab plus FOLFIRI. The primary objective of the study was to assess the incidence of grade 3 or 4 diarrhea with panitumumab in combination with chemotherapy. Major findings are summarized in Table 1. Grade 3 or 4 diarrhea was more common with IFL than with FOLFIRI. Skin toxicity occurred in all patients, with no grade 4 skin toxicity being observed. Grade 3 hypokalemia, fatigue, and nausea were seen with

IFL but not with FOLFIRI, and grade 4 hypomagnesemia occurred in one patient in each part of the study. No severe infusion reactions and no formation of human antihuman antibodies were observed in any patient.

An objective response (all partial) occurred in 47% of patients receiving panitumumab plus IFL and 33% of those treated with panitumumab plus FOLFIRI; stable disease was observed in 26% and 46% of patients, respectively. These findings suggest that combining panitumumab with FOLFIRI is well tolerated and active in the first-line treatment of mCRC and that the regimen should be evaluated in a larger trial.

FOLFOX (5-FU/LV/oxaliplatin) plus bevacizumab has recently become the most commonly used regimen for first-line treatment of mCRC. The randomized phase III Panitumumab Advanced

Colorectal Cancer Evaluation (PACCE) trial is examining the addition of panitumumab to FOLFOX/bevacizumab as first-line treatment in a target population of 800 patients.⁵ A second part of this trial is examining the addition of panitumumab to FOLFIRI/bevacizumab as first-line treatment in a planned population of 200 patients. The primary endpoint is PFS in the part of the trial studying FOLFOX/bevacizumab with or without panitumumab. Preliminary data from the PACCE trial are expected in the near future.

Finally, a phase Ib trial is under way evaluating various combinations of panitumumab with AMG 706, a novel tyrosine kinase inhibitor targeting the vascular endothelial growth factor, platelet-derived growth factor, and Kit receptor, and FOLFOX or FOLFIRI in patients with mCRC.⁶

References

1. Saif MW, Cohenuram M. Role of panitumumab in the management of metastatic colorectal cancer. *Clin Colorectal Cancer* 2006;6:118-124.
2. Chu E. Panitumumab: a new anti-EGFR antibody for the treatment of advanced colorectal cancer [editorial]. *Clin Colorectal Cancer* 2006;6:13.
3. Peeters M, van Cutsem E, Siena S, et al. A phase 3, multicenter, randomized controlled trial of panitumumab plus best supportive care (BSC) vs. BSC alone in patients with metastatic colorectal cancer. Presented at the 97th Annual Meeting of the American Association of Cancer Research, April 1-5, 2006; Washington, DC. Abstract CP-1.
4. Hecht J, Posey J, Tchekmedyan S, et al. Panitumumab in combination with 5-fluorouracil, leucovorin, and irinotecan (IFL) or FOLFIRI for first-line treatment of metastatic colorectal cancer (mCRC). Presented at the 2006 Gastrointestinal Cancers Symposium, January 26-28, 2006; San Francisco, Calif. Abstract 237.
5. Wainberg Z, Hecht JR. A phase III, randomized, open-label, controlled trial of chemotherapy and bevacizumab with and without panitumumab in the first-line treatment of patients with metastatic colorectal cancer. *Clin Colorectal Cancer* 2006;5:363-367.
6. Burris HA, Stephenson J, Hurwitz H, et al. Safety and pharmacokinetics (PK) of AMG 706 with panitumumab and FOLFIRI for the treatment of patients (pts) with metastatic colorectal cancer (mCRC). Presented at the 2006 Gastrointestinal Cancers Symposium, January 26-28, 2006; San Francisco, Calif. Abstract 354.

A welcome addition to the therapeutic armamentarium against colorectal cancer

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Colorectal cancer continues to be a major public health problem. It is the third most common cancer in both men and women, comprising 10% of the 710,040 newly diagnosed cancers in men and 11% of the 662,870 new cancers in women. From 15%–25% of patients have metastatic disease at diagnosis, and up to 50% of all patients will eventually develop metastatic disease. If the disease is localized to the bowel mucosa, it is usually curable, with a 93% 5-year survival rate. In patients with widespread metastatic disease, however, the 5-year survival rate is only 8%.¹

For decades, effective treatment for metastatic colorectal cancer (mCRC) was limited to 5-fluorouracil (5-FU). The best results with this agent in combination with leucovorin (LV) demonstrated a response rate of 23% with a median survival of 10–12 months.²

The past decade has witnessed the development of many new agents for the treatment of colorectal cancer. Newer chemotherapeutic agents include irinotecan (Camptosar) and oxaliplatin (Eloxatin). These agents have significant antitumor activity, and their use has already led to improvement in the median survival time for patients with mCRC. The addition of irinotecan to 5-FU/LV produces a significant improvement in overall survival, from 14.1 months to 17.4 months, and an increase in response rate from 22% to 35%.³ The addition of oxaliplatin to 5-FU/LV resulted in improvement of the response rate from 22% to 50% and prolongation of progression-free survival from 6 months to 8.2 months.⁴

Sequential use of regimens containing irinotecan and 5-FU/LV and regimens containing 5-FU/LV/irinotecan and 5-FU/LV/oxaliplatin resulted in further improvement of the median survival to 20 months.⁵

Targeted agents in mCRC

Further improvement in the survival for patients with mCRC is expected to come from the development of targeted biologic agents. These agents are designed specifically to inhibit the biochemical processes involved in carcinogenesis. At present, three such agents are approved by the US Food and Drug Administration (FDA) for use in mCRC, either alone or in combination with chemotherapy. These agents include bevacizumab (Avastin), which binds and inhibits the vascular endothelial growth factor (VEGF), and two other agents, cetuximab (Erbix) and panitumumab (Vectibix), which target the epidermal growth factor receptor (EGFR) on the surface of colorectal cancer cells.

Largely on the showing of a significant improvement in survival, from 15.6 months to 20.3 months, among mCRC patients treated with bevacizumab in addition to irinotecan and bolus 5-FU/LV (IFL regimen),⁶ bevacizumab was approved for use in combination with intravenous 5-FU-based chemotherapy. Regimens containing 5-FU, LV, irinotecan, oxaliplatin, or bevacizumab have now become the first line of treatment of mCRC in the United States.

EGFR is a transmembrane glycoprotein that functions to promote cell growth, development, and differentiation

in a variety of normal and transformed tissues. The expression of EGFR is frequently associated with malignant transformation in prostate, breast, ovarian, lung, kidney, and colorectal carcinomas, as well as many others. In mouse xenograft models of human tumors, anti-EGFR antibodies were demonstrated to inhibit tumor growth and eradicate established human tumors.⁷ These observations led to the further development of anti-EGFR monoclonal antibodies in the treatment of cancer.

Colorectal cancer cells have been shown to express both EGFR and its ligand, epidermal growth factor (EGF). EGF is secreted in an autocrine fashion and binds to the EGFR, resulting in the activation of signaling pathways that sustain the malignant phenotype. From 70%–80% of advanced colorectal cancers have been shown to express EGFR.⁸ Therefore, anti-EGFR agents are exciting novel agents in the management of this disease.

Cetuximab vs panitumumab

Cetuximab and panitumumab are monoclonal antibodies that target the EGFR. They are both approved for use in chemotherapy-refractory mCRC.

Cetuximab

Cetuximab is a chimeric monoclonal antibody that binds to the extracellular domain of the EGFR of cancer cells, preventing ligand binding and activation of the receptor. This action effectively blocks the downstream signaling of EGFR, resulting in impaired cell growth and proliferation. Cetuximab has single-agent activity as well as activity in combination with irinotecan with

patients with EGFR-positive, irinotecan-refractory mCRC. Among patients receiving cetuximab plus irinotecan, the overall response rate was 23%, with a median time to disease progression of 4.1 months. In the cohort receiving cetuximab alone, the overall response rate was 10.8%, with a median time to disease progression of 1.5 months.⁹ In an open-label study involving 57 patients, single-agent cetuximab produced a partial response in 9% of patients with irinotecan-refractory colorectal cancer, with a median survival of 6.4 months.⁹ Cetuximab, in combination with irinotecan, is approved for the treatment of mCRC in patients refractory to irinotecan and for use as a single agent in the treatment of recurrent mCRC in patients who cannot tolerate irinotecan-based chemotherapy.

Early data also suggest promising activity for cetuximab in combination with oxaliplatin-based regimens. In preliminary trials, combining weekly cetuximab with an oxaliplatin-containing regimen resulted in an 81% response rate in patients with irinotecan-refractory disease.¹⁰

Panitumumab

Panitumumab is a fully humanized immunoglobulin (Ig)G2 monoclonal antibody directed against the extracellular domain of the EGFR. Panitumumab blocks both EGF and tumor growth factor- α (TGF- α) from binding to EGFR, inhibits tumor growth, and elicits tumor regression and eradication of established tumors in animal models. Panitumumab was recently approved by the FDA for treatment of EGFR-expressing mCRC in patients whose disease has progressed on or following treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing regimens.

This approval was based on a randomized trial that compared single-agent panitumumab with best supportive care in 463 patients in whom standard chemotherapy had failed.¹¹ Treatment with panitumumab significantly pro-

longed progression-free survival compared with best supportive care. The overall response rate of mCRC patients receiving panitumumab monotherapy was 8%, and the median duration of response was 17 weeks. During the study, 174 patients in the group receiving best supportive care crossed over to salvage therapy with panitumumab. In these patients, a response rate of 10% was noted. An overall survival benefit for panitumumab could not be established in the trial, although a trend toward improved survival was observed when crossed-over patients were excluded.

Panitumumab is now being evaluated in combination with chemotherapy. Two trials have been conducted. In one, panitumumab is being combined with 5-FU/LV and irinotecan. In the other, panitumumab is being used in combination with 5-FU/LV and oxaliplatin. Data from these trials are eagerly awaited.

Structural differences

Although both cetuximab and panitumumab are directed against the same target, they have significant structural differences. Cetuximab is a chimeric monoclonal antibody with a significant amount of mouse protein. The presence of this foreign protein increases the chance of antibody development against the monoclonal antibody. It may also increase the chance of infusion reactions. Panitumumab, on the other hand, is a fully humanized antibody; therefore, its use poses a low risk of antipanitumumab antibody formation and infusion reactions. Furthermore, cetuximab is an IgG1 monoclonal antibody, whereas panitumumab is an IgG2 monoclonal antibody. These differences may have some clinical significance, as dissimilar Ig subtypes may affect complement activation and antibody-mediated cytotoxicity differently.¹²

Toxicity profiles

The toxicity profiles of cetuximab and panitumumab are similar, not only

to each other but also to those of other anti-EGFR molecules, such as erlotinib (Tarceva). The main side effects of both cetuximab and panitumumab are diarrhea and skin rash. These reactions appear to be a class effect of anti-EGFR agents in general and are seen in small-molecule anti-EGFR inhibitors as well.

Cetuximab. Nonsuppurative acneiform rash has been reported in 87% of patients receiving cetuximab alone or in combination with radiation therapy or irinotecan.⁹ The rash most commonly occurs on the face, upper chest, and back but can also extend to the extremities; it is characterized by multiple follicular or pustular lesions. Skin drying and fissuring, as well as superadded infections, are seen. Cases of *Staphylococcus aureus* skin infections have been reported.⁹ Grade 3 or 4 rash is reported in 8% of patients on cetuximab alone and 14% of patients on cetuximab and irinotecan.⁹ The onset of rash is generally within the first 2 weeks of therapy. The majority of affected patients recover within 28 days of stopping treatment. Paronychia inflammation is a related disorder seen in up to 12% of patients treated with cetuximab (grade 3 in 0.4% of patients).⁹

The other side effects of cetuximab include infusion reactions in 3% of patients and rare instances of interstitial lung disease and fever.⁹ Diarrhea is common, affecting 72% of cetuximab-treated patients.⁹ Severe diarrhea has been reported in 22% of patients on cetuximab and irinotecan.⁹ Ten percent of patients receiving cetuximab plus irinotecan discontinued therapy due to side effects, whereas 4% of patients receiving cetuximab alone discontinued the drug because of side effects.⁹

Panitumumab. The side effects of panitumumab include rash, which is seen in up to 90% of patients treated with the drug and is severe in 16%.¹¹ The rash is similar to that seen with cetuximab. Conjunctivitis and increased lacrimation, as well as eyelid irritation, are seen in up to 4% of patients on panitumumab.¹¹ Paronychia has been described in 25% of patients and was severe in 2%.¹¹ The

median time to development of skin- and eye-related toxicity was 14 days. Eleven percent of panitumumab patients required discontinuation of therapy due to side effects, mainly rash.¹¹ Diarrhea is observed in 21% of patients and is severe in 2%. Infusion reactions are exceedingly rare in patients treated with panitumumab.¹¹

Hypomagnesemia is seen with both cetuximab and panitumumab and therefore should be monitored in patients receiving either drug. Approximately 15% of patients on cetuximab experienced hypomagnesemia; 10%–15% of these patients had severe hypomagnesemia.¹¹ In some cases, intravenous replacement is required. Experience with panitumumab is limited; however, the magnesium level should be monitored in patients on this agent as well.

Immunogenicity is a concern with all monoclonal antibodies. Non-neutralizing anticetuximab antibodies were detected in 5% of patients who were evaluated. The median time to onset was 44 days.⁹ There does not appear to be a clear relationship between the appearance of antibodies and the safety or antitumor activity of cetuximab. The incidence of binding antibodies to panitumumab is less

than 1% by one assay and up to 4% by a different assay.¹¹ Again, no evidence of altered pharmacokinetic profile or toxicity was noted in patients who developed antibodies to panitumumab.

Conclusion

Anti-EGFR agents are a welcome addition to the therapeutic armamentarium against colorectal cancer. These agents show considerable promise by themselves and in combination with previously approved agents for treatment of colorectal cancer. They provide the clinicians caring for these patients with another line of defense against this disease. As further research into their role in earlier stages of the disease is carried out, these agents may contribute significantly to making mCRC a manageable chronic disease associated with long survival and good quality of life.

References

1. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2006. *CA Cancer J Clin* 2006;56:106–130.
2. Expectancy of primary chemotherapy in patients with advanced asymptomatic colorectal cancer: a randomized trial. Nordic Gastrointestinal Tumor Adjuvant Therapy Group. *J Clin Oncol* 1992;10:904–911.
3. Douillard JY, Cunningham D, Roth AD, et al. Irinotecan combined with fluorouracil compared with fluorouracil alone as first-line treatment for metastatic colorectal cancer: a multicentre randomised trial. *Lancet* 2000;355:1041–1047.
4. de Gramont A, Figer A, Seymour M, et al. Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer. *J Clin Oncol* 2000;18:2938–2947.
5. Tournigand C, Andre T, Achille E, et al. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: a randomized GERCOR study. *J Clin Oncol* 2004;22:229–237.
6. Hurwitz H, Fehrenbacher L, Novotny W, et al. Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. *N Engl J Med* 2004;350:2335–2342.
7. Baselga J, Mendelsohn J. Receptor blockade with monoclonal antibodies as anti-cancer therapy. *Pharmacol Ther* 1994;64:127–154.
8. Tong WM, Ellinger A, Sheinin Y, Cross HS. Epidermal growth factor receptor expression in primary cultured human colorectal carcinoma cells. *Br J Cancer* 1998;77:1792–1798.
9. Erbitux [package insert]. New York, NY: ImClone Systems Incorporated and Princeton, NJ: Bristol-Myers Squibb Company; 2006.
10. Tabernero JM, van Cutsem E, Sastre J, et al. An international phase II study of cetuximab in combination with oxaliplatin/5-FU/folinic acid (FOLFOX-4) in the first-line treatment of patients with metastatic colorectal cancer expressing epidermal growth factor receptor (EGFR): preliminary results. *J Clin Oncol* 2004;22(14S):3512.
11. Vectibix [package insert]. Thousand Oaks, CA: Amgen Inc; 2006.
12. Yan L, Davis HM. Pharmacogenetics and pharmacogenomics of therapeutic monoclonal antibodies. *Pharmacogenomics* 2006;7:961–964.

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From the Nurses' Station

Nursing considerations when administering panitumumab

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Panitumumab (Vectibix) is a new monoclonal antibody approved for use in metastatic colorectal cancer in patients who have disease progression on or following treatment with oxaliplatin (Eloxatin), irinotecan (Camp-

tosar), and fluoropyrimidines. In our clinic, we have treated patients with panitumumab as part of a clinical trial. From a nurse's perspective, panitumumab is a fairly user-friendly drug. Some practical considerations that should be kept in mind:

- Panitumumab is given as an intravenous (IV) infusion, never as a bolus or an IV push. It should be administered by an infusion pump, using a 0.22- μ m in-line filter.
- The dose of panitumumab is 6 mg/kg. It should be diluted to a total

volume of 100 mL of normal saline. If the dose is higher than 1,000 mg, the volume should be 150 mL.

■ The line should be flushed with normal saline before and after infusion. Panitumumab should not be mixed or co-administered with other medications.

■ Infusion time is 60 minutes through a peripheral or central line. Doses higher than 1,000 mg should be infused over 90 minutes.

■ Once mixed, panitumumab is stable for 6 hours at room temperature.

The main side effect of panitumumab is skin toxicity. Almost all patients have some degree of rash, but it is rarely severe enough to lead to discontinuation of treatment. Local measures that include cosmetics, emollients, and antibiotic creams help, although the management of this condition is still evolving. Acne

treatments do not help and can actually exacerbate the rash. Oral antibiotics may be needed to treat infectious complications.

The psychological aspects of panitumumab-related skin toxicity do need to be addressed, as some patients find it difficult to deal with a highly visible reminder of their cancer.

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From the Administrator's Desk

The economic concerns when new drugs become available

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The practice administrator should put quality of care as an executive priority. At the same time, the practice depends upon a healthy bottom line by optimizing the relationship between quality and costs. Our medical knowledge continues to evolve; therefore, the economics of the practice must keep up with the changes. This can be a difficult task, especially as new drugs become available for treatment.

Once the US Food and Drug Administration (FDA) approves a drug such as panitumumab (Vectibix), it then becomes available to practices from wholesalers. Prior to its becoming a part of the inventory, other factors must be considered and time will be of the essence in receiving correct reimbursement for the drug, including services rendered during the drug administration. New drugs are assigned a J code by Medicare that is used to report drugs that ordinarily cannot be self-administered. Drugs are sometimes initially given the assignment of J9999. This code reflects the

drug is newly FDA approved and has not been assigned an individual J code for reporting and billing.

Prior to administering panitumumab—or any new drug—the practice must do the following:

■ Establish that the drug is approved for diagnosis or treatment;

■ Receive authorization from the patient's insurance carrier, if required;

■ Evaluate the cost of the drug and the reimbursement; and

■ Counsel the patient in regard to the patient's financial responsibility.

Some insurance carriers will require a new drug to be presented to its review committee for predetermination, thereby delaying patient treatment. When the drug does not appear on the insurance carrier's already established fee schedule, the reimbursement is commonly paid at 50% or less of the attending physician's billed charges. This will inflate the amount customarily billed to receive appropriate reimbursement to cover the costs, making the physician appear greedy.

Therefore, to meet all of the aspects involved in providing treatment that is best suited for the patient, it is imperative that oncology practices train their staff to be patient advocates. This requires a significant investment of time and money, which, in general, is not factored into any reimbursements received from insurance carriers.

Financial counseling for patients is essential when a drug that has just been approved is prescribed, as they may be personally responsible for a significant portion of the drug cost. This is especially true in the current environment, where cost of care is being shifted to the beneficiaries through higher deductibles and co-insurance. Patients who do not have secondary insurance coverage or are self-paying have an even heavier financial burden and cannot afford some treatment plans, especially when new drugs, which tend to be more costly than long-established therapies, are involved.

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