Oxaliplatin: Practical Guidelines for Administration

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Colorectal cancer (CRC) accounts for about 11% of all new cancers in the United States and kills approximately 56,000 people each year. Although the use of antineoplastic agents has demonstrated palliation of symptoms, increased survival, and improved quality of life when compared with best supportive care, improved therapies still are needed. Oxaliplatin, released in August 2002, offers an effective expansion of the CRC treatment armamentarium. Proper dosage and administration of oxaliplatin are vital to maximizing its efficacy and safety. This article reviews administration guidelines, adverse events, side effects, and key areas for patient education.

Key Words: colorectal neoplasms, antineoplastic combined chemotherapy protocols

In 2004, nearly 150,000 adults in the United States will be diagnosed with colorectal cancer (CRC), accounting for 11% of all new cancers and causing an estimated 56,000 deaths (American Cancer Society, 2004). Chemotherapy has yielded palliation of symptoms, increased survival, and improved quality of life compared with best supportive care in the treatment of CRC (Cunningham et al., 1998; Rougier et al., 1998), yet greater understanding of the biology of CRC, coupled with recent developments in cancer research, can propel the treatment of this disease beyond standard strategies.

Until recently, cisplatin and its analog carboplatin were the only platinum agents available to treat malignancies. Oxaliplatin (Eloxatin®, Sanofi-Synthelabo Inc., New York, NY), a third-generation cisplatin analog and a member of the diaminocyclohexane family of platinum compounds, has partial noncross-resistance with cisplatin (Armand et al., 2000; Maindrault-Goebel et al., 2000). This drug is somewhat similar to cisplatin and carboplatin in its direct intracellular target and mechanism of action by binding to DNA and causing the cross-link of DNA bases (Armand et al.; Raymond, Chaney, Taamma, & Cvitkovic, 1998). However, unlike cisplatin and carboplatin, oxaliplatin shows activity in the treatment of patients with advanced CRC and, according to the National Cancer Institute's Anticancer Drug Screen panel, has had in vitro activity in six of eight colon cancer cell lines that were resistant to cisplatin and carboplatin (Rixe et al., 1996).

Researchers have found that, as a single agent, oxaliplatin has efficacy in chemotherapy-naive patients with advanced CRC (Becouarn et al., 1998; Diaz-Rubio et al., 1998), as well as those whose disease is refractory to previous treatment with 5-fluorouracil (5-FU) (Levi et al., 1993; Machover et al., 1996). Treatment with oxaliplatin was well tolerated, and response was attained with acceptable toxicity. These nonrandomized studies support the activity of oxaliplatin in disease that is resistant to 5-FU. However, despite these relatively good results, single-agent use of oxaliplatin is not recommended as standard therapy in most patients with advanced CRC because single-agent 5-FU and some combination regimens may be more effective (Becouarn et al.). Numerous phase II and III studies of oxaliplatin, in combination with 5-FU and leucovorin (LV) for the treatment of advanced CRC in patients previously treated with 5-FU, found a synergistic effect between oxaliplatin and 5-FU (Andre et al., 1999; de Gramont et al., 1997, 2000; Gerard et al., 1998; Giacchetti et al., 2000; Levi et al., 1992; Maindrault-Goebel et al., 2000). In another phase III trial, patients who had failed prior 5-FU, LV, and irinotecan chemotherapy were randomized to receive 5-FU, LV, and oxaliplatin; single-agent oxaliplatin; or 5-FU and LV as second-line treatment of their metastatic CRC (National Cancer Institute, 2002). Accrual to this study has been completed, and 821 patients have been enrolled. In an interim analysis of 459 patients, those treated with the 5-FU, LV, and oxaliplatin combination had an increased response rate and an increased median time to tumor progression compared with those who received either oxaliplatin or 5-FU and LV alone (Sanofi-Synthelabo Inc., 2003) (see Table 1).

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