Labetuzumab govitecan in metastatic colorectal cancer

Labetuzumab govitecan monotherapy might be safe and effective in patients with relapsed or refractory metastatic colorectal cancer previously treated with irinotecan-containing therapy.

Irinotecan-containing chemotherapy yields impressive results in metastatic colorectal cancer, but is associated with substantial toxicity. In a phase 1–2 trial, Efrat Dotan (Fox Chase Cancer Center, Philadelphia, PA, USA) and colleagues assessed the use of labetuzumab govitecan, based on the rationale that this antibody–drug conjugate would directly deliver cytotoxic agents to the tumours, thereby reducing systemic toxicities. They enrolled 86 patients with relapsed or refractory metastatic colorectal cancer who had been heavily pretreated, including with an irinotecan-containing regimen. They primarily assessed the safety and tolerability of labetuzumab govitecan in two dosing schedules; their secondary objectives were to assess the drug's immunogenicity, efficacy, and pharmacokinetics.

The patients were enrolled into one of four dosing cohorts: the first and second cohorts received labetuzumab govitecan twice weekly at a dose of either 4 mg/kg (n=23) or 6 mg/kg (n=20), and the third and fourth cohorts received the drug once weekly at a dose of either 8 mg/kg (n=21) or 10 mg/kg (n=22), on weeks 1 and 2 of 3-week repeated cycles. Of 86 patients, tumour response following treatment was not assessable in 14 patients. 27 (38%) of 72 patients had a significant decrease in tumour size and plasma carcinoembryonic antigen concentration following treatment. 42 patients achieved stable disease as their best overall response and one patient had a partial response. Median progression-free survival was 3·6 months (95% CI 2·0–4·0) and median overall survival was 6·9 months (5·7–7·8). In 86 patients, grade 3 or worse adverse events included neutropenia (n=14 [16%]), leukopenia (n=9 [11%]), anaemia (n=8 [9%]), and diarrhoea (n=6 [7%]). The two once-weekly dosing schedules showed similar efficacy and safety.

According to study coauthor Jordan D Berlin (Vanderbilt-Ingram Cancer Center, Nashville, TN, USA), labetuzumab govitecan has the "potential to be studied in a combination therapy in a frontline setting." Hans-Joachim Schmoll (Martin-Luther-Universitat Halle-Wittenberg, Halle, Germany) commented, "These data show at least that this targeted approach has efficacy, low toxicity and [it] is very likely representing the beginning of a targeted drug–conjugate era, now also in colorectal cancer."

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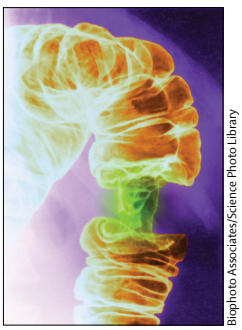

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For the **study by Dotan and colleagues** see *J Clin Oncol* 2017; published online Aug 17. DOI:10.1200/JCO.2017.73.9011