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Clinical Trial Results

A Phase I/II Study of XELIRI Plus Bevacizumab as Second-Line Chemotherapy for Japanese Patients With Metastatic Colorectal Cancer (BIX Study)

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Author Summary

Abstract

Background. Capecitabine is used mainly with oxaliplatin to treat metastatic colorectal cancer (mCRC). Results from capecitabine plus irinotecan (XELIRI) with or without bevacizumab (BV) have been reported in Europe but not in Japan. Consequently, the safety and efficacy of XELIRI plus BV in Japanese patients with mCRC were assessed in a single-arm phase II study.

Methods. Eligible patients had had prior chemotherapy containing BV for mCRC and wild-type or heterozygous UGT1A1. Therapy in each 21-day treatment cycle consisted of capecitabine (800 mg/m^2 twice daily on days 1–15), irinotecan (200 mg/m^2 on day 1), and BV (7.5 mg/kg on day 1). The primary endpoint was dose-limiting toxicity in phase I and progression-free survival (PFS) in phase II.

Results. A total of 34 patients (6 in phase I, 28 in phase II) were enrolled from May 2010 to June 2011. Baseline characteristics included a median age of 60 years (range: 22–74 years) for 24 men and 10 women. No dose-limiting toxicities appeared in phase I. Median PFS was 240 days (95% confidence interval: 179–311 days). Overall response rate was 18.1%, and the disease-control rate was 90.9%. The incidence of adverse events frequently associated with irinotecan and capecitabine were neutropenia (any grade, 55.9%; grade 3 or 4, 11.8%), diarrhea (any grade, 50%; grade 3 or 4, 5.9%), and hand-foot syndrome (any grade, 61.8%; grade 3 or 4, 5.9%).

Name	*NC/NA	1	2	3	4	5	All Grades
Leukocytes (total WBC)	41%	23%	35%	0%	0%	0%	58%
Neutrophils/granulocytes (ANC/AGC)	44%	8%	35%	11%	0%	0%	55%
Hemoglobin	29%	50%	17%	2%	0%	0%	70%
Platelets	52%	41%	5%	0%	0%	0%	47%
Diarrhea	50%	14%	29%	5%	0%	0%	50%
Anorexia	47%	32%	14%	5%	0%	0%	52%
Nausea	47%	32%	11%	8%	0%	0%	52%
Vomiting	70%	20%	5%	2%	0%	0%	29%
Fatigue (asthenia, lethargy, malaise)	61%	11%	23%	2%	0%	0%	38%
Mucositis/stomatitis (clinical exam)	82%	11%	5%	0%	0%	0%	17%
Dizziness	94%	0%	0%	5%	0%	0%	5%
Neuropathy: sensory	70%	17%	8%	2%	0%	0%	29%
Hair loss/alopecia (scalp or body)	67%	17%	14%	0%	0%	0%	32%
Rash: hand-foot skin reaction	38%	44%	11%	5%	0%	0%	61%
Renal/genitourinary, other	52%	20%	23%	2%	0%	0%	47%
Hypertension	67%	5%	17%	8%	0%	0%	32%

Figure 1. Adverse events during phase I/II treatment. No serious adverse events were reported.

Abbreviations: *, no change from baseline/no adverse event; AGC, absolute granulocyte count; ANC, absolute neutrophil count; WBC, white blood cells.

Conclusion. Our results suggest that XELIRI plus BV is well tolerated and effective as a second-line treatment for mCRC in Japanese patients. This regimen could be especially

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appropriate for patients resistant to oxaliplatin-based regimens. ***The Oncologist*** 2014;19:1131–1132

Discussion

In this prospective trial for Japanese patients with metastatic colorectal cancer, capecitabine plus irinotecan (XELIRI) plus bevacizumab as a second-line regimen achieved longer progression-free survival (240 days) and a higher overall response rate (18.1%) than other reported regimens, with an acceptable tolerability profile (Fig. 1). Unlike FOLFIRI, XELIRI doses do not require a long infusion process or an infuser pump, providing a great advantage to patients. The key finding in this study was that XELIRI plus bevacizumab demonstrated promising results beyond progression in Japanese patients.

Author disclosures available online.

For Further Reading:

Herbert I. Hurwitz, Niall C. Tebbutt, Fairooz Kabbinavar et al. Efficacy and Safety of Bevacizumab in Metastatic Colorectal Cancer: Pooled Analysis From Seven Randomized Controlled Trials. ***The Oncologist*** 2013;18:1004–1012.

Implications for Practice:

Several randomized trials of bevacizumab have been conducted to address specific questions regarding its use for patients with metastatic colorectal cancer (mCRC); however, because of their sample size limitations, subgroup analyses are frequently of limited power. By pooling individual patient data from seven randomized trials, more comprehensive analyses of the efficacy and safety of bevacizumab were made possible because of the large number of included patients. In addition, outcomes in clinically relevant subgroups were examined, and the data from these subgroups were consistent with those reported in the overall analyses. The results of this pooled analysis help further the clinician's understanding of the overall risks and benefits associated with adding bevacizumab to chemotherapy for patients with mCRC.