Journal of Clinical Oncology
jco.ascopubs.org

Published online before print January 22, 2013, doi: 10.1200/JCO.2012.42.5215
JCO **February 20, 2013** vol. 31 no. 6 **724-730**

Phase II Study of Gemcitabine, Carboplatin, and Bevacizumab in Patients With Advanced Unresectable or Metastatic Urothelial Cancer

Arjun V. Balar, Andrea B. Apolo, Irina Ostrovnaya, Svetlana Mironov, Alexia Iasonos, Alisa Trout, Ashley M. Regazzi, Ilana R. Garcia-Grossman, David J. Gallagher, Matthew I. Milowsky and Dean F. Bajorin

+ Author Affiliations

Corresponding author: Dean F. Bajorin, MD, Genitourinary Oncology Service, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY 10021; e-mail: bajorind@mskcc.org.

Presented at the 2011 Genitourinary Cancers Symposium, Orlando, FL, February 17-19, 2011, and the 47th Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, June 3-7, 2011.

Abstract

Purpose Although gemcitabine and carboplatin (GCa) is a standard option for patients with advanced urothelial cancer (UC) who are ineligible for cisplatin, outcomes remain poor. This trial evaluated the efficacy and safety of bevacizumab with GCa in advanced UC.

Patients and Methods Patients with Karnofsky performance status of 60% to 70%, creatinine clearance less than 60 mL/min, visceral metastasis, or solitary kidney were eligible and received a lead-in dose of bevacizumab 10 mg/kg followed 2 weeks later by gemcitabine 1,000 mg/m^2 on days 1 and 8 and carboplatin at area under the [concentration-time] curve (AUC) 5.0 or 4.5 and bevacizumab 15 mg/kg on day 1 every 21 days for six cycles. Patients achieving at least stable disease (SD) continued bevacizumab 15 mg/kg every 21 days for 18 additional cycles. The study was powered to detect a 50% improvement in median progression-free survival (PFS) over a historical control.

Results Fifty-one patients, median age 67 years (range, 42 to 83 years), were enrolled onto the study and were evaluable for toxicity. Twenty (39%) experienced grade 3 to 4 toxicity, and 10 (20%) had thromboembolic events (deep venous thrombosis or pulmonary embolism). Four received one or fewer cycles leaving 47 evaluable for outcomes. Twenty-three (49%) achieved response (three complete; 20 partial), and 11 had SD. Median PFS was 6.5 months (95% CI, 4.7 to 7.8 months); PFS was greater in the carboplatin AUC 5.0 group (P = .04). Median overall survival (OS) was 13.9 months.

Conclusion The 95% one-sided lower confidence bound of 4.77 months for median PFS did not meet the predesignated PFS of more than 4.8 months considered sufficient for further study. Median OS was greater than expected. An ongoing phase III trial in patients who are eligible for therapy with cisplatin will define the role of bevacizumab in UC.

Footnotes

See accompanying article on page 670

Supported in part by Genentech and by Grant No. NIH T32 CA009207 (D.F.B.).

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

Clinical trial information: NCT00588666.

Related Article

ONCOLOGY GRAND ROUNDS:
Antiangiogenic Agents, Chemotherapy, and the Treatment of Metastatic Transitional Cell Carcinoma
Nicholas J. Vogelzang
JCO Feb 20, 2013:670-675; published online on January 22, 2013;
[Abstract] [Full Text] [PDF]

Articles citing this article

Antiangiogenic Agents, Chemotherapy, and the Treatment of Metastatic Transitional Cell Carcinoma
JCO Feb 20, 2013:670-675
[Abstract] [Full Text] [PDF]