

Presented at the American Association for Cancer Research's Pancreatic Cancer: Progress and Challenges conference, Lake Tahoe, NV, June 18-21.

Phase I Trial of Radiotherapy with Concurrent Bevacizumab, Erlotinib and Capecitabine for Locally Advanced Pancreatic Cancer (LAPC). Heath D. Skinner, Christopher H. Crane, Sunil Krishnan, Milind M. Javle, Robert A. Wolff, Jason B. Fleming, Marilyn V. Clemons, Mark F. Munsell, Marc E. Delclos, Prajnan Das. University of Texas M. D. Anderson Cancer Center, Houston, TX.

Background: The addition of bevacizumab to chemoradiotherapy (CRT) for LAPC has been shown to be safe. The objective of this study was to determine the safety, tolerability and maximum tolerated dose (MTD) of the addition of erlotinib to this treatment regimen.

Methods: Seventeen patients with CT-staged biopsy-proven non-metastatic unresectable LAPC were enrolled between March 2008 and October 2010. Prior chemotherapy was permitted. All patients received 50.4 Gy (GTV only) in 28 fractions with concurrent capecitabine, bevacizumab and erlotinib. Dose was escalated using a continual reassessment method. Two patients each were enrolled at dose levels (DLs) 1-4 and 9 patients at DL 5. Bevacizumab was escalated from 5mg/Kg every two weeks (DLs 1-4) to 10mg/Kg (DL 5); erlotinib from 100 mg/day (DLs 1-2) to 150 mg/day (DLs 3-5); and capecitabine from 400mg/m² twice daily on days of radiation (DL 1) to 600mg/m² (DLs 2-3) to 825 mg/m² (DLs 4-5). Reassessment for potential resection was performed 6-8 weeks later.

Results: With a median follow-up of 10 months (range 3-23), no grade 3 toxicities were observed in DLs 1-4. Three (33%) patients at DL 5 developed a grade 3 acute toxicity (2 diarrheas and 1 rash). No grade 4 or 5 toxicities were seen. DL 4, with a posterior probability of 0.122 of dose limiting toxicity, was selected as the MTD. Median survival was 19.4 months and time to distant progression was 9.8 months. Patients treated at DLs 4 and 5 had a median survival of 24 months. Of 5 patients who underwent margin-negative resections, 4 were originally deemed unresectable and 1 was borderline; 4 were treated at DLs 4 or 5 (36% of patients treated at these dose levels); 3 patients had excellent pathological responses (complete response, 5% viable tumor, and 20% viable tumor) at pancreatectomy and are alive at 13, 21 and 22 months respectively with no local or distant failures.

Conclusions: The combination of erlotinib, bevacizumab and capecitabine with radiotherapy for LAPC is safe and tolerable. Both the promising survival and the high rate of resectability at the higher dose levels suggest that this strategy of dual inhibition of growth factor receptor pathways during CRT warrants continued evaluation.