

TREE STUDY
(Tree-2 Cohort):

TTP and TTF for Three Bevacizumab & Oxaliplatin – Fluoropyrimidine Regimens

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Background: The addition of bevacizumab (Bev) to fluorouracil (FU)-based combination chemotherapy results in statistically significant improvement in survival among patients (pts) with metastatic colorectal cancer (*Hurwitz H et al. NEJM 2004; 350:2335-2342*). The TREE study was designed to assess the safety, tolerability and efficacy of each of three oxaliplatin (OX) plus fluoropyrimidine (FP) regimens (bolus (b), infusional or oral FP; in the TREE-2 cohort, Bev 2.5 mg/kg/week was added to each regimen.

Methods: Eligibility: Measurable untreated mCRC; PS =1. Primary endpoint: Grade 3-4 toxicities in the first 12 weeks of treatment.

Secondary Endpoints: Response Rate (RR), Time to Progression (TTP), Survival (OS). The regimens in mg/m² were: **mFOLFOX+Bev** = 0 85mg, Leucovorin (LV) 350 mg, 5FU bolus 400 & 2400 CIV x 46 hrs and Bev 5mg/kg q2w; **bFOL+Bev** = 0 85 d1&15, LV 20 & bolus 5FU 500 d1,8,15 q4w and Bev 5 mg/kg q2w; **CapOx+Bev** = 0 130 d1, Capecitabine 850 x 14d and Bev 7.5 mg/kg q3w.

Results: 223 pts were randomized; 213 were treated. Selected grade 3-4 toxicity during first 12 weeks of treatment is shown in the table. The major reason for discontinuation in each arm was development of adverse events, but the time to discontinuation appears comparable to

other trials using similar OX-containing regimens. Overall RR was: **mFOLFOX+Bev** 52%, **bFOL+Bev** 34%, **CapOx+Bev** 45%. 5% of pts remain on study treatment. Median TTP is currently being analyzed.

Conclusions: Treatment with Bev + mFOLFOX is tolerable, with a promising RR as compared to the TREE-1 cohort (Proc ASCO GI, 2005). Grade 3- 4 toxicity with first line Bev plus OX based chemotherapy is less than that reported with Bev + IFL. All regimens of FP administration are active in combination with Bev but mFOLFOX may have the best balance of response and toxicity. TTP data for each regimens will be presented, confirming their relative utility. **OA**

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failure occurred 18 days later. Another death (76 YO) was reported 30 days after cycle 1 due to pneumonia/respiratory insufficiency. An 84 YO patient had treatment delayed after cycle 2, she died at home of an apparent MI. An 83 YO man was hospitalized 2 weeks after completing cycle 2. This patient was dehydrated as a result of gastroenteritis however he developed atrial flutter and died as a result of pulmonary edema. The last patient discontinued therapy after achieving CRu following 3 cycles. Three months later she died of sepsis and pneumonia.

Conclusions: This immunochemotherapeutic regimen is active in Grade III/IV CLL and the incidence of significant toxicities was low with deaths occurring in elderly patients. Future trials evaluating the use of R as maintenance therapy following this PCR regimen may also be warranted with an eye toward increasing the overall survival of patients with CLL. The use of combination therapy in elderly patients should be used with caution due to associated comorbidities. *Abstract #5045 appears in Blood, Volume 106, issue 11, November 16, 2005*

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62 (range 44-80) and the median number of prior regimens was 2 (range 1-7). The overall frequency of response was 75% with 25% achieving a complete response, 3% a nodular response, and 47% a partial response. We have compared these results to the recently reported MD Anderson FCR regimen. In terms of pre-treatment characteristics the patient groups in both studies appear comparable with the exception of a higher proportion of high-risk patients treated with PCR (78%) compared to FCR (50%) (P=0.003). The response frequencies are virtually identical in both studies with responses seen 75% of PCR treated patients and 73% of FCR treated patients and CR achieved in 25% in both studies. In terms of toxicity, however, PCR compares favorably to FCR in the following categories: Grade 3/4 neutropenia

PCR 53% vs FCR 81% (P=0.0007), thrombocytopenia PCR 16% vs FCR 34% (P=0.04), anemia PCR 9% vs FCR 24% (P=0.06), and grade 3/4 infections (including fever of unknown origin) PCR 28% vs FCR 47% (P=0.05). PCR also appeared to be better tolerated than FCR as indicated by the fraction of patients completing all planned cycles of chemotherapy at full dose 72% vs 38% (P=0.0004). An important caveat in these comparisons is that myeloid growth factor was routinely administered to patients on the PCR study but was not routinely administered to patients treated with FCR. In conclusion, PCR appears to be equivalent in activity to FCR but may be better tolerated and less toxic. These results indicate that a prospective randomized comparison is warranted. *Abstract #2127 appears in Blood, Volume 106, issue 11, November 16, 2005*

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pegfilgrastim 6mg, pegfilgrastim 12 mg, and filgrastim groups, respectively. Time to platelet recovery of at least 20x10⁹/L was 11 days for all groups. Safety profiles were similar for each group, and both treatments were well tolerated.

Conclusions: This study suggests pegfilgrastim is similar to filgrastim in the

setting of CT mobilization. Pegfilgrastim 6mg appears as effective as pegfilgrastim 12mg with respect to PBPC mobilization, collection, and engraftment. Further study with pegfilgrastim 6mg compared with filgrastim 5mcg/kg in this setting is warranted. *Abstract #1977 appears in Blood, Volume 106, issue 11, November 16, 2005*