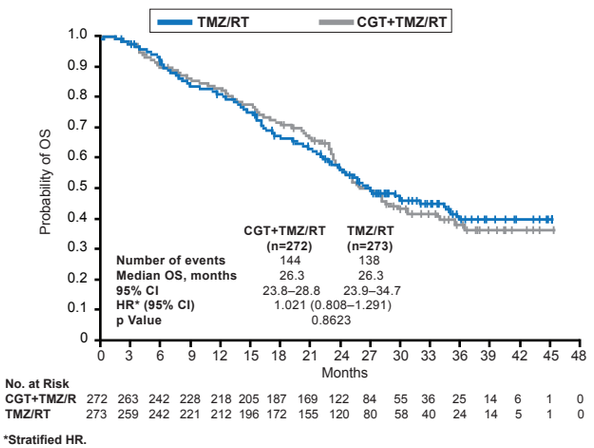
to 13.4; median control PFS, 7.9 months; 95% CI, 5.9 to 12.5; HR, 0.918; 95% CI, 0.750 to 1.124; p=0.4102).

Toxicity in both arms was mainly related to TMZ and RT. The marginally increased incidence of pulmonary embolism in the CIL-treated patients (12 vs 5 patients) was not considered clinically relevant. Other adverse events in the two study arms were similar in the two treatment arms.

Figure 1. Overall Survival: Intent to Treat



CIL=cilengitide; RT=radiotherapy; TMZ=temozolomide.

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The researchers concluded that CIL applied with the standard therapeutic combination of TMZ and RT did not prolong survival, with no patient subgroup exhibiting a clinical benefit. No new safety concerns were evident.

Bevacizumab Monotherapy Improves DFI in Melanoma Patients at High Risk of Recurrence

Written by Maria Vinall

Results of the preplanned interim analysis of the Adjuvant Avastin Trial in High-Risk Melanoma trial [AVAST-M; ISRCTN81261306; EudraCT 2006-005505-64; Corrie P et al. *J Clin Oncol* 2013 (suppl; abstr LBA9000)] of melanoma patients at high risk of recurrence has shown that adjuvant bevacizumab (BEV) monotherapy is well tolerated and improved disease-free interval (DFI). Longer follow-up is required to determine an impact on the primary endpoint of 5-year overall survival (OS).

BEV is a recombinant humanized monoclonal antibody to vascular endothelial growth factor shown to improve survival in several advanced solid tumors. Modest activity has been reported in advanced melanoma [Kim KB et al. *J Clin Oncol* 2012]. AVAST-M is Phase 3 trial evaluating single-agent BEV as adjuvant therapy following histologically confirmed completely resected stage IIB, IIC, and III cutaneous melanoma (American Joint Committee on Cancer staging). Participants were randomized within 12 weeks of surgery to receive BEV 7.5 mg/kg Q3W for 1 year (maximum of 17 infusions over 1 year or until disease progression; n=671) or to observation only (n=672). Subjects will be followed for 10 years or until death.

The primary study endpoint is OS. Secondary endpoints are DFI, distant metastasis-free interval (DMFI), safety and toxicity, and quality of life (QoL). Pippa Corrie, PhD, University of Cambridge, Cambridge, United Kingdom, presented the results of the first preplanned interim analysis.

Participants (56% men; median age ~56 years) were recruited from 48 sites across the United Kingdom between July 2007 and March 2012. Most (~88%) subjects were ECOG PS 0. Nearly 75% of patients had resected stage III disease (15% stage IIIA, ~36% IIIB, and 21% IIIC). Ulceration status of the primary melanoma was ~38% present, ~47% absent, ~15% unknown. About one third of the patients had undergone sentinel lymph node biopsy; 21% had microscopic lymph node involvement. Median follow-up for survival was 25 months.

The median duration of treatment was 51 weeks (range, 21 to 52 weeks); median dose intensity was 86% (range, 41% to 96%). In all, 54% of BEV-treated patients completed planned treatment. The most common reasons for discontinuation were disease recurrence (38% of cases) and toxicity (33%). Grade 3/4 adverse events (AEs) occurred in 15% of BEV patients and 5% of observation patients. The most common Grade 3/4 AE was hypertension, which occurred in 6% of BEV-treated patients. There was one potential treatment-related death—a hemopericardium associated with an aortic aneurysm dissection in a BEV-treated patient with a history of cardiac events.

On the primary outcome, the 1-year OS was the same in both groups (HR, 0.97; 95% CI, 0.78 to 1.22; p=0.76).

There was a difference on the secondary endpoint of disease recurrence; 39% of patients in the BEV group had a recurrence of disease compared with 44% of patients in the observation group. There were no differences in either locoregional or first distant recurrence. Patients in the treatment arm has significantly improved DFI (HR, 0.83; 95% CI, 0.70 to 0.98; p=0.03) compared with observation patients. DFI at 1 and 2 years were 77% and 59% in the BEV group versus 70% and 57% for observation only.

The treatment effect for DFI was consistent and remained significant after adjustment for disease stage and ulceration. The benefit of BEV appears to be less apparent in patients with stage II disease.