Gr 3+ non-heme toxicities were higher in pts receiving anemia in the TRC105+bev arm vs 0 in the bev only arm. 1.06 95% CI 0.66-1.69, p=0.83). Overall incidence of association between both PFS and OS, and initial hypophosphatemia (3 vs 0 pts). There was an NCT01648348.

Results:

1. TRC105+bev did not prolong median PFS versus bev alone (2.9 vs 3.2 mo, respectively; HR=1.14, 95% CI 0.90-1.45, p=0.29). There was a 3-fold change from baseline to Cycle 1 Day 11 in median CEC levels (p-value 0.0125 due to test adjustment). A higher percentage of patients in the bev only arm (60.4% vs. 36.1%, p=0.054) had anemia as compared to single agent bevacizumab in recurrent GBM patients, although it was associated with a higher incidence of hematological toxicities associated with a single agent bevacizumab.

2. The hazard ratio for PFS associated with the 3-fold change in median CEC levels 1.182 [98.75% CI (1.111, 1.596), alpha = 0.0125 due to test adjustment] compared with baseline to Cycle 1 Day 11 in CEC levels is 1.182 [98.75% CI (1.111, 1.596), alpha = 0.0125 due to test adjustment].

Conclusions

• The baseline levels for CECs associated with a 3-fold change in baseline CEC levels were performed. These data provide evidence that changes in median CEC levels can be used as a biomarker for clinical response and should be considered in future clinical trials.

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TRC105: Primary Endpoint: FPE

Overall Survival

- Demonstrated a significant difference in median CEC levels at baseline to Cycle 1 Day 11 (p=0.0012) (1.111, 1.596), alpha = 0.0125 due to test adjustment)

Analysis of Circulating Endothelial Cells (CECs)

- Patients were randomized to receive bevacizumab alone, bevacizumab plus TRC105, or placebo plus bevacizumab in a 1:1:1 ratio. CEC levels were evaluated at baseline and during treatment.

- The baseline levels for CECs associated with a 3-fold change in baseline CEC levels were performed. These data provide evidence that changes in median CEC levels can be used as a biomarker for clinical response and should be considered in future clinical trials.

- CECs were quantified using a commercial flow cytometry-based assay. CECs were defined as CD105+CD31+CD146+CD3- cells, which are characteristic of activated endothelial cells.

- CEC levels were monitored at baseline and during treatment, and a significant difference in median CEC levels at baseline to Cycle 1 Day 11 (p=0.0012) was observed.

- These data provide evidence that changes in median CEC levels can be used as a biomarker for clinical response and should be considered in future clinical trials.

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