AT-37. PHASE I STUDY OF PLERIXAFOR AND BEVACIZUMAB IN RECURRENT HIGH-GRADE GLIOMA

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Although anti-angiogenic therapy for high-grade glioma is promising, responses are not durable. The SDF-1/CXCR4 axis may help mediate resistance to VEGFR inhibition. Plerixafor is a reversible CXCR4 inhibitor that has demonstrated growth inhibition in glioblastoma xenografts. We conducted a Phase I study to determine the safety and tolerability of plerixafor in combination with bevacizumab in patients with recurrent HGG. A 3 x 3 dose escalation design to a maximum planned dose level of plerixafor 320 μg/kg on Days 1-21 and bevacizumab 10 mg/kg on Days 1 and 15 of each 28 day cycle was used. DLTs were determined during the initial 4 weeks of therapy and included drug-related Grade ≥ 3 non-hematologic toxicities and Grade ≥ 4 hematologic toxicities. Part 1 of the study has been completed with a total of 23 patients enrolled with the following characteristics: median age 58 (23-72), median KPS 90 (70-100), 11 women (47.8%). One DLT (grade 3 rectal fistula) was seen at a dose level of plerixafor 240 μg/kg + bevacizumab and the cohort was expanded. Because no further DLTs were seen at the 240 μg/kg dose level, the maximum planned dose level of plerixafor 320 μg/kg + bevacizumab opened and a total of 12 patients were treated with no DLTs. Treatment was well tolerated with one grade 3 hypophosphatemia and one grade 3 rectal fistula. Preliminary pharmacokinetic data on plerixafor from the first two cohorts compares well with historical PK data. Combination treatment with bevacizumab and plerixafor was well tolerated in the studied HGG patients. No DLTs were encountered at the maximum planned dose level. The study will now expand to a surgical cohort to examine tumor tissue penetration as well as a separate non-surgical cohort with patients treated with continuous daily dosing of plerixafor 320 μg/kg and bevacizumab. Updated results will be presented.