IT-05. ADMINISTRATION OF TOCA 511 TO SUBJECTS WITH RECURRENT HGG UNDERGOING REPEAT RESECTION

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INTRODUCTION: Recurrent high grade glioma (rHGG) remains one of the most deadly cancers. Investigational agents Toca 511, a retroviral replicating vector, and Toca FC (extended-release 5-FC) are used in combination to target residual tumor at the time of resection. METHODS: This study (NCT01470794) is primarily designed to identify the highest safe and well tolerated dose of Toca 511 administered to subjects undergoing resection for rHGG. The starting dose was $1.4 \times 10^7$ Transducing Units (TU). Using a standard 3+3 design, doses have been escalated at half-log intervals to $4.8 \times 10^9$ TU. Following tumor resection, multiple injections of vector are administered into the walls of the resection cavity. Starting approximately 6 weeks post-surgery cyclic oral Toca FC is administered. RESULTS: 36 patients across 6 vector dose cohorts have been studied. In evaluable patients the largest cross-sectional area of tumor ranged from 0 (unmeasurable) to 14.57 cm². The combination treatment has been safe and well tolerated with 1 grade 3 possibly treatment related AE of transient generalized weakness. Subsequent resection of tumor from subjects who previously received Toca 511 confirmed virus can selectively infect residual tumor cells. Preliminary data based on investigator assessment show 14/32 evaluable patients achieved best overall response of SD or better (from baseline MRI 5-7 weeks post-surgery, prior to 5-FC). Treatment related pseudoprogression has been observed by MRI and supported by histopathology of re-resected tumor. Independently reviewed response data and PFS will be presented. The median survival by Kaplan Meier analysis in the first 4 cohorts is 11.8 months. CONCLUSION: Toca 511 administered at the time of tumor resection and followed by cycles of Toca FC has been safe and well tolerated to date. In addition to continued dose escalation of Toca 511 and Toca FC in patients with rHGG, a randomized trial in patients with newly diagnosed glioma is now planned.