Single versus Multiple Dose Radiopharmaceutical Injections: Dosimetry Analysis of Intracavitary ^{131}I-TM601 in High-grade Glioma Patients

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Introduction: TM601, or synthetic chlorotoxin, is a peptide specifically targeting tumor cells. Radiolabeled TM601 can deliver localized radiation to tumor with the potential to reduce the incidence of normal brain radionecrosis. We report the difference in Biological Equivalent Dose (BED) between single and multiple injections based on a dosimetry sub-study of a phase II trial in which intracavitary ^{131}I-TM601 was given weekly for either 3 or 6 weeks.

Methods: As part of a dosimetry sub-study, 5 out of 76 patients treated in this phase II trial underwent additional imaging after receiving 1, 3, or 6 doses of 40 mCi/0.8 mg ^{131}I-TM601 intracavitarily. For each imaging study, 5 sequential SPECT images were registered with MRI to determine the radiation dose to the 2-cm tumor cavity margin. BED was calculated based on measured dose rate and clearance half-life for ^{131}I-TM601 in the 2-cm cavity margin, assuming an alpha/beta of 3 and repair time of 1.5 hours for normal tissue.

Results: In 11 imaging studies from 5 subjects, median effective clearance half-life for ^{131}I-TM601 in the 2-cm margin was 48 hours (range 35-74 hours). Median radiation dose to the cavity margin was 1.2 Gy/mCi (range 0.5- 3.4 Gy/mCi), and its median intra-patient variation was 14.7% (range 7.1-18.9%). Median total dose to the cavity margin was 278 Gy (range 72-396 Gy). Median BED to the cavity margin was 414 Gy (range 96-709 Gy). If the same dose were administered as a single injection, the BED to the cavity margin would increase 1.5-2.0 times for 3 injections and 2.6 times for 6 injections.

Conclusion: For multiple dose delivery, the intra-patient variation in ^{131}I-TM601 dosimetry demonstrated less variability than that of inter-patient variation. Fractionation in future studies will minimize the risk of normal tissue toxicity.