A single administration of 186RNL was delivered by CED utilizing 1-5 catheters at a maximum flow rate of up to 20 ml/min. Delivery parameters (i.e., number of catheters (1-5), infusion rates, drug volumes, and drug concentrations) to determine the maximum tolerated dose (MTD), feasible maximum dose (FMD), safety, and efficacy of 186RNL in recurrent adult glioma (NCT116117). CED Planning, Catheter Placement, and Drug Administration. Brachial Plexus Block was used to place the catheter to deliver the treatment. For each 10% increase in the Ratio of Treated to Total Tumor Volume, the risk of death decreases by 60% (95% CI 0.35 to 0.74). For each 100 Gy increase of Total Dose in Distribution Volume, the risk of death decreases by 66.9% (p=0.002).

### RESULTS

#### Patients

- Twenty-eight adult recurrent glioma patients in the Phase 1 study, across the 8 dosing Cohorts, were treated from March 2012 to May 2013. Five patients in Cohort 1-4 received prior temozolomide.
- Five adult recurrent glioma patients in the Phase 2 study were treated in 2023. 2 females and 4 males. All 5 patients were treated for tumor sizes ≤20 cm³, 1 recurrence, bevacizumab-naïve, and histologically confirmed glioblastoma.
- The average tumor volume across all 20 patients was 105.4 cm³ (range 0.88-630.5).

#### Phase 1

- Twenty-eight patients in the Phase 1 (10 cohort) received 186RNL in doses ranging from 0.0-4.5 mCi in volume ranging from 0.6-163 mL. Five patients in the Phase 2 received 186RNL doses of 22.3 mCi in volume of 8.8 mL.
- The maximum CED administration was 5-20 µl/min and 1-5 catheters were used per patient. An average absorbed dose in the tumor for all Phase 1 patients was 304 Gy (range 8.7-747 Gy) while exposure outside the brain was negligible. Absorbed average dose to the brainstem was 0.3 Gy.
- An average absorbed dose of 100 Gy was achieved in 5/12 (42%) patients in Phase 1, Cohorts 1-4.
- An average absorbed dose of 100 Gy was achieved in 17/18 (94%) patients in Phase 2, Cohorts 5-8.
- An average absorbed dose of 100 Gy was achieved in all Phase 2 patients (100%).

#### Dosage Escalation Scheme

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dose (mCi)</th>
<th>Volume (mL)</th>
<th>Number of Patients</th>
<th>Absorbed Dose (Gy)</th>
<th>Median OS (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.32</td>
<td>2.64</td>
<td>3</td>
<td>8.8</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>4.0</td>
<td>8.0</td>
<td>3</td>
<td>22.3</td>
<td>6</td>
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<tr>
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<td>137</td>
<td>258</td>
<td>4</td>
<td>41.5</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>22.3</td>
<td>462</td>
<td>3</td>
<td>22.3</td>
<td>7</td>
</tr>
</tbody>
</table>

#### Thermochemistry

- In preclinical models of glioma, 186RNL eradicated transplanted tumor cells when >100 Gy of radiation was delivered, with no evidence of neurologic compromise or other safety and toxicity markers. Furthermore, a study in beagles to assess toxicity of an intracranial, single dose administration of 186RNL showed no test article-related pathologic changes at the highest administered amount (6 mCi).

#### Immunology

- Methylated 186RNL is an ongoing, first-in-human, open-label, Phase 1/2 study investigating dose escalation and other clinical parameters in 33 patients with recurrent glioma (ReSPECT-GBM).

### Case Studies

1. **Recurrent glioma patients** 1: pre-treatment MRI, 24 h post-treatment, SPECT, and post-treatment MRI. 1-Phase 1, cohort 4; 2-Phase 1, cohort 5; 3-Phase 1, cohort 6. Overall survival ranged from 730-1333 days. One patient remains alive.

### Summary

- A single dose of 186RNL was generally well-tolerated, with no dose limiting toxicities and no radiation exposure across 28 Phase 1 patients /8 dose points.
- For each 10% increase in the Ratio of Treated to Total Tumor Volume, the risk of death decreases by 60% (95% CI 0.35 to 0.74).
- For each 100 Gy increase of Total Dose in Distribution Volume, the risk of death decreases by 66.9% (p=0.002).

### Conclusions

- Most common AEs were pre-existing GBM related signs and symptoms (e.g., weakness, fatigue, headache, seizure, scap discomfort after CED) and 70% of AEs had the unrelated or unlikely attribution. For The Median absorbed radiation dose to the tumor (MARDT) was 308.4 Gy (95% CI 73.5 Gy).
- Patients were stratified by MARDT (<100 Gy, 100 Gy ≤ MARDT). In all patients (n=27), the median overall survival (OS) was 8 months (95% CI 13 to 13). Patients receiving >100 Gy (n=15), the median OS was 9 months (95% CI 11 to 24) and in those with MARDT ≤100 Gy (n=12), the median OS was 12 months (95% CI 3 months to 30). For those with 100 Gy Increase of Total Dose in Distribution Volume, the risk of death decreases by 45.6% (p=0.005).

For each 10% increase in the Ratio of Treated to Total Tumor Volume, the risk of death decreases by 60% (95% CI 0.35 to 0.74). For each 100 Gy increase of Total Dose in Distribution Volume, the risk of death decreases by 66.9% (p=0.002).

### Acknowledgments

The study was supported by an NCI award 1R01CA235800, a pilot award from Mays Cancer Center P30CA054174, a Commercialization Award from CPRIT DP150021, and Plus Therapeutics. 186RNL is an investigational treatment.

### References


### Disclosures

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### ClinicalTrials.gov Identifier

NCT01906385

https://www.respect-trials.com/gbm/