# $^{186}$Rhenium-Nanoliposome ($^{186}$RNL) Remodels the Tumor Microenvironment in Preclinical Ovarian Cancer Models

**Henriette Balinda PhD, Jinangely Martinez Garcia, Zhiyuan Ning, Niannian Ji PhD, Zaineb Hassouneh, Funan He PhD, Siyuan Zheng PhD, Neelam Mukherjee PhD, and Andrew Brenner MD PhD**

University of Texas Health San Antonio, San Antonio, TX, USA

16TH BIENNIAL RIVKIN OVARIAN CANCER RESEARCH SYMPOSIUM
October 16-18, 2026
Philadelphia, PA

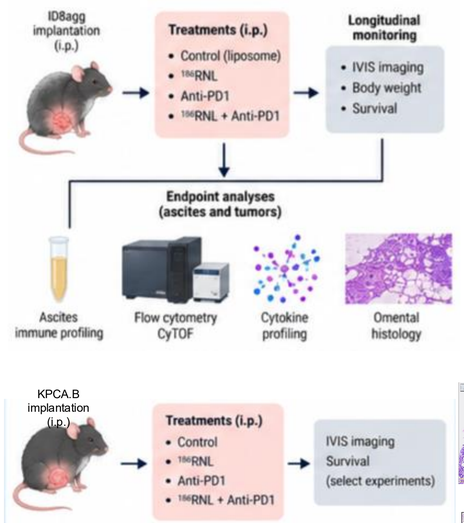
## BACKGROUND

Epithelial ovarian cancer remains poorly responsive to immune checkpoint inhibition alone, in part because of an immunosuppressive tumor microenvironment. $^{186}$Re-nanoliposome ($^{186}$RNL) is a locoregional radionuclide therapy with the potential to directly control tumor while modifying the tumor immune microenvironment and potentially enhancing response to PD-1 blockade.

## Objective

Our objective was to evaluate the dose-dependent antitumor efficacy of $^{186}$RNL and determine whether combination with anti-PD1 improves therapeutic outcomes and remodels the ovarian tumor immune microenvironment.

## METHODS




## RESULTS

### 1. $^{186}$RNL improves survival in a dose-dependent manned in ID8agg mouse model

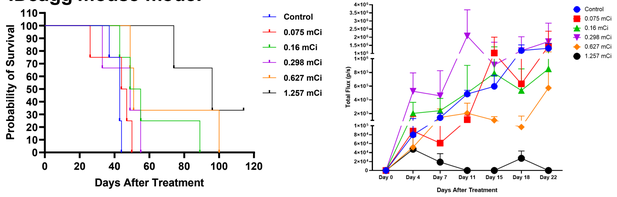
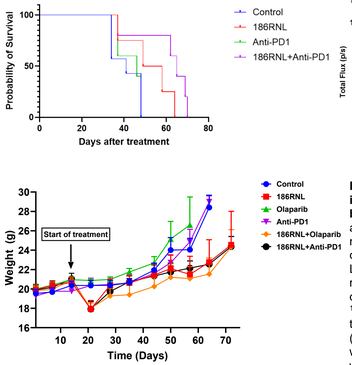



**Figure 1:$^{186}$RNL improves survival and suppresses tumor growth in a dose-dependent manner in a preclinical ovarian cancer model.** Kaplan–Meier survival analysis (left) demonstrates improved survival with increasing doses of $^{186}$RNL (0.075–1.257 mCi) compared with untreated controls, with a significant dose-dependent survival effect ($p$ = 0.0003). Longitudinal IVIS bioluminescence imaging (right), shown as total flux (photons/s), demonstrates reduced tumor burden following $^{186}$RNL treatment, with the greatest and most sustained suppression observed at the highest dose (1.257 mCi). Data are presented as mean ± error bars where applicable.

### 2. $^{186}$RNL + Anti-PD1 improves survival and reduces tumor burden without added toxicity



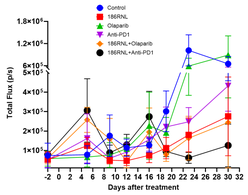




**Figure 2. $^{186}$RNL combined with anti–PD-1 improves survival and reduces tumor burden without added toxicity.** Kaplan–Meier analysis (top left) shows prolonged survival in mice treated with $^{186}$RNL plus anti–PD-1 compared with control and either monotherapy. Longitudinal IVIS bioluminescence imaging (top right), expressed as total flux (photons/s), demonstrates reduced tumor burden in the $^{186}$RNL + anti–PD-1 combination group over the treatment period. Body-weight monitoring (bottom left) shows weight loss in mice treated with $^{186}$RNL, but the quickly recover. The weight gain from ~Day 50 is due to ascites accumulation. Data are presented as mean ± error bars where applicable.

### 3. Histologic evidence of reduced omental tumor burden

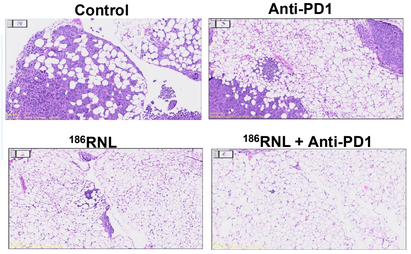



**Figure 3. Histologic evidence of reduced omental tumor burden following $^{186}$RNL and anti–PD-1 treatment.** Representative H&E-stained sections of omental tissue from control, anti–PD-1, $^{186}$RNL, and $^{186}$RNL + anti–PD-1–treated mice. Control and anti–PD-1 groups show prominent tumor involvement, whereas $^{186}$RNL treatment is associated with reduced tumor burden. The $^{186}$RNL + anti–PD-1 combination shows minimal residual tumor involvement, supporting enhanced tumor control with combination therapy.

### 4. Combination therapy enhances immune cell infiltration

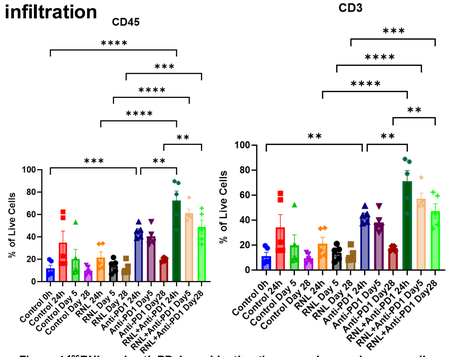



**Figure 4.$^{186}$RNL and anti–PD-1 combination therapy enhances immune cell infiltration.** Flow cytometric analysis of immune cells collected at baseline (0 h), 24 h, Day 5, and Day 28 following treatment. The percentage of **CD45⁺ leukocytes** (left) and **CD3⁺ T cells** (right) among live cells increased following combination treatment, with the highest levels observed in the $^{186}$RNL + anti–PD-1 group at 24 h. Elevated immune-cell frequencies were maintained at later time points, indicating that combination therapy promotes recruitment and/or accumulation of immune cells, including T cells, within the tumor-associated compartment. Bars represent group means with error bars; individual symbols represent biological samples. Statistical significance is indicated as **p < 0.01, ***p < 0.001, and ****p < 0.0001.

### 5. Combination therapy drives a CD-8-dominant immune response

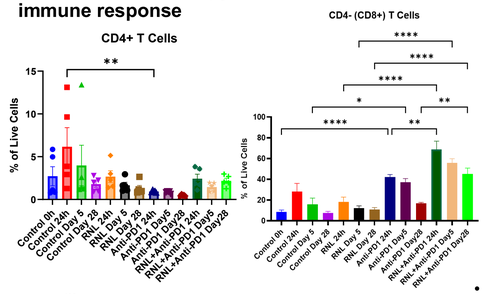



**Figure 5. $^{186}$RNL and anti–PD-1 combination therapy drives a CD8-dominant T-cell response.** Flow cytometric analysis of T-cell populations at baseline (0 h), 24 h, Day 5, and Day 28 following treatment. CD4⁺ T-cell frequencies (left) remained relatively low across treatment groups and time points. In contrast, CD4⁻ (CD8⁺) T cells (right) were markedly increased following anti–PD-1 treatment and were highest in the $^{186}$RNL + anti–PD-1 combination group, particularly at 24 h. The elevated CD8⁺ T-cell population persisted through Day 28, supporting a sustained, CD8-dominant immune response following combination therapy. Bars represent group means with error bars; individual symbols represent biological samples where shown. Statistical significance is indicated as $p$ < 0.05, p < 0.01, and **p < 0.0001.

### 6. Trend towards T-cell activation with combination therapy

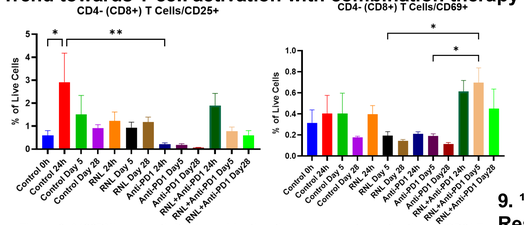



**Figure 6. ^186RNL and anti–PD-1 combination therapy promotes activation of CD8⁺ T cells.** Flow cytometric analysis of activated CD4⁻ (CD8⁺) T-cell populations at baseline (0 h), 24 h, Day 5, and Day 28 following treatment. CD25⁺ CD8⁺ T cells (left) show an early increase following treatment, including with the ^186RNL + anti–PD-1 combination. CD69⁺ CD8⁺ T cells (right) are increased with combination therapy, with elevated levels observed at 24 h and Day 5 relative to anti–PD-1 monotherapy. Together, these findings indicate enhanced CD8⁺ T-cell activation following ^186RNL + anti–PD-1 treatment. Bars represent group means with error bars. Statistical significance is indicated as $p$ < 0.05 and **p** < 0.01.

### 7. Combination increases NK cells and reduces monocytes

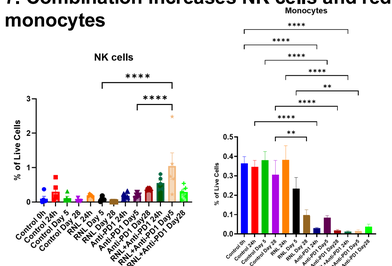



**Figure 7. ^186RNL and anti–PD-1 combination therapy alters immune-cell populations within the peritoneal tumor microenvironment.** Flow cytometric analysis of immune-cell populations collected at baseline (0 h), 24 h, Day 5, and Day 28 following treatment with ^186RNL, anti–PD-1, or the combination. Treatment produced time-dependent changes in the relative abundance of the analyzed immune-cell populations, with the ^186RNL + anti–PD-1 group showing distinct immune remodeling compared with control and monotherapy groups. Bars represent group means with error bars; individual symbols represent biological samples where shown. $p$ < 0.05.

### 8. $^{186}$RNL reduces the immunosuppressive cytokine IL-10

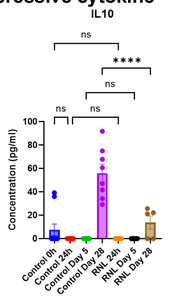



**Figure 8. 186RNL treatment reduces the immunosuppressive cytokine IL-10.** Cytokine profiling of samples collected from tumor-bearing mice demonstrates reduced IL-10 levels following ^186RNL treatment compared with control. IL-10 was elevated in the control group, whereas ^186RNL-treated mice showed substantially lower IL-10 levels, suggesting that ^186RNL may reduce immunosuppressive signaling within the tumor-associated peritoneal environment. Bars represent group means with error bars; individual symbols represent biological samples.

### 9. $^{186}$RNL Induces Early DNA-Damage Responses Followed by Immune Activation

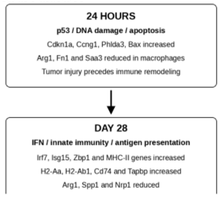



**Figure 9. $^{186}$RNL induces early tumor injury followed by immune remodeling in the ID8agg ovarian cancer model.** Single-cell RNA-seq of ascites/peritoneal lavage cells shows early activation of p53, DNA-damage, and apoptotic programs at 24 hours after $^{186}$RNL treatment, followed by increased interferon signaling, innate immunity, and antigen-presentation programs at Day 28. Reduced macrophage-associated immunosuppressive programs suggest remodeling of the tumor immune microenvironment over time.

### 10. $^{186}$RNL Reduces Tumor Burden in the KPCA Syngeneic Ovarian Cancer Model

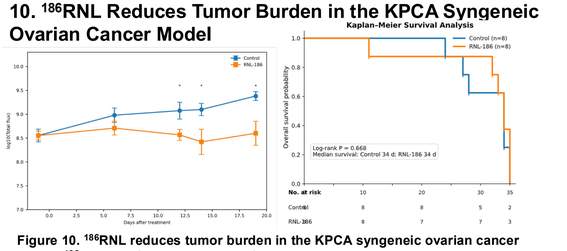



**Figure 10. $^{186}$RNL reduces tumor burden in the KPCA syngeneic ovarian cancer model.** $^{186}$RNL significantly reduced IVIS-measured tumor burden on Days 12, 14, and 19 compared with control. No significant difference in overall survival was observed (log-rank $p$ = 0.668; n = 8/group).

## CONCLUSION

- $^{186}$RNL produces dose dependent antitumor activity and prolongs survival in the ID8agg ovarian model.
- Combining $^{186}$RNL with ant-PD1 increases median survival to 65 days and reduces tumor burden without evidence of substantial added toxicity.
- Combination therapy remodels the ascites immune microenvironment toward an effector-dominant phenotype characterized by increased CD8+ T cells, CD4+ effector T cells and NK cells, with reduced monocytes.
- These findings support further investigation of 186RNL as a radioimmunotherapy platform for enhancing checkpoint blockade in ovarian cancer

## FUNDING

- V Foundation
- Plus Therapeutics/Ceronome

## REFERENCES

1. Brenner AJ, Patel T, Bao A, et al. Convection enhanced delivery of Rhenium ($^{186}$Re) Obisbemeda ($^{186}$RNL) in recurrent glioma: a multicenter, single arm, phase 1 clinical trial. *Nature Communications*. 2025;16:2079. doi: **10.1038/s41467-025-57263-1**.
2. Matulonis UA, Shapira-Frommer R, Santin AD, et al. Antitumor activity and safety of pembrolizumab in patients with advanced recurrent ovarian cancer: results from the phase II KEYNOTE-100 study. *Annals of Oncology*. 2019;30(7):1080–1087. doi: **10.1093/annonc/mdz135**.