Intratumoral G100 Induces Systemic Immunity and Abscopal Tumor Regression in Patients with Follicular Lymphoma: Results of a Phase 1/2 Study Examining G100 Alone and in Combination with Pembrolizumab

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I. RATIONALE / BACKGROUND
Local Treatment → Systemic Response
- Background: Follicular lymphoma (FL) is a B-cell non-Hodgkin lymphoma (NHL) subtype that is highly responsive to treatment; however, systemic failure is common with frequent relapses. In systemic NHL, immune checkpoint inhibitors (ICIs) are a treatment option with promising clinical activity. However, in FL, the systemic immune response to ICI-induced tumor regression is limited by the presence of dominant B cells that are a barrier to the development of systemic immunity.

II. STUDY DESIGN
- Phase 1 dose escalation (n=10), phase 2 efficacy study (n=20). Data from CRITICALITY (G100) in FL patients was presented at ASCO 2021.

III. RESULTS

A. G100 + Pembrolizumab Safety
- Table 2. Summary of Treatment Related TEAs

B. Efficacy of G100 and G100 + Pembrolizumab
- Table 3. Overall Response

C. Clinical Outcomes
- Figure 4. Progression-Free Survival

D. Exploratory Biomarker Results
- Table 6. Increased CD8+ TILs Are Associated With PR

IV. EXPLORATORY BIOMARKER RESULTS

Addition of pembrolizumab to G100 demonstrated a trend to a higher number of CD8+ TILs following treatment.

Figure 5. G100 + Pembrolizumab Treatment Resulted in Increased CD8+ Tumor Infiltrating Lymphocytes (TILs)

Figure 7. Association Of Baseline Tumor TLR4 Expression And PRs

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A strong association between baseline tumor TLR4 expression by IHC and objective clinical response (ORR) was observed (Figure 7) indicating the potential of patient selection and enrichment for responders.

Biomarker & Overall Conclusions
- Addition of pembrolizumab to G100 increases the CD8 T-cell infiltration of the tumor microenvironment (TME), as an indication of the pro-inflammatory activity of G100.

Baseline tumor TLR4 expression may serve as an enrichment biomarker for pembrolizumab in combination with pembrolizumab as a novel immunotherapy in pts with recurrent and refractory high risk indolent lymphomas.