**Poster #194**

**Characterization of the Pharmacodynamic Activity of CLN-619, an Anti-MICA/B Monoclonal Antibody, in Cancer Patients from an Ongoing Phase 1 Trial**

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**CLN-619 Engages Both Innate & Adaptive Immune Cells**

CLN-619 binds to, depletes, and downregulates the expression of MICA/B in tumor cells, thereby reactivating tumor cells to innate and adaptive immune attack.

**Biomarker Plan**

- Preclinical and clinical evaluation of target engagement for the CLN-619 Phase 1 study
- Assessment of tumor PD biomarkers for CLN-619 in the antitumor and the tumor-responding immune cell populations

**Intratumoral MICA/B Expression Increased On-treatment**

Increased MICA/B-positive staining in the majority of paired biopsies On-treatment (Cycle 2 Day 8) as compared to baseline (Screening).

**Responding Endometrial Tumors Are Microsatellite-Stable (MSS) and Have Low TMB and Low Neoantigen Presentation Index**

- High CD4 (1000-3000 cells/mm²) and CD8 T-cell infiltration (300-1000 cells/mm²)
- Objective responses and prolonged stable disease (≥ 6 months) were observed in tumors
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**Tumor Microenvironment Analysis in Patients with Stable Disease Lasting 26 Months**

<table>
<thead>
<tr>
<th>Tumor Biopsies from Patients with Stable Disease Lasting 26 months</th>
<th>Low Tumor Mutation Burden (TMB) and Low Neoantigen Presentation Index in Tumors with Prolonged SD</th>
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</thead>
<tbody>
<tr>
<td>MSS- and HLA-A2 analyzed for neo-antigen burden (TMB) and NKG2D expression at baseline and on-treatment.</td>
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<tr>
<td>Tumor type</td>
<td>Time of biopsy collection</td>
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<tr>
<td>Adenoid Cystic H&amp;N</td>
<td>Screening</td>
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<tr>
<td>Sensing</td>
<td>On-treatment</td>
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</tbody>
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MICA/B membrane localization was assessed (as percentage of tumor cells) and quantified by a pathologist as % of Ctrl.

**Sustainable MICA in Patient Serum is a Pharmacodynamic Biomarker for CLN-619**

- CLN-619 Biinds to sMICA in Human Serum
- CLN-619 binding to sMICA in human serum
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**Conclusions**

- Intratumoral MICA/B expression is increased on-treatment with CLN-619 in paired tumor biopsies demonstrating the proof of biology
- Increased MICA/B levels are associated with higher tumor responses in patients with highest sMICA levels
- Peripheral blood MICA levels are measured by a sandwich ELISA assay

**References**

- [3] Available at: https://clinicaltrials.gov/ct2/show/NCT05117476

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