TRILACICLIB PRESERVES AND ENHANCES IMMUNE SYSTEM FUNCTION IN EXTENSIVE-STAGE SMALL CELL LUNG CANCER (SCLC) PATIENTS RECEIVING FIRST-LINE CHEMOTHERAPY

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BACKGROUND
- Chemotherapy-induced damage of hematopoietic stem and progenitor cells (HSPCs) causes multi-lineage myelosuppression, including depletion of lymphocytes, a hallmark of the immune system, potentially diminishing the activity of chemotherapy treatment.
- The myelopreservation benefits of trilaciclib demonstrated here, in addition to the preclinical murine data, suggest the potential to preserve HSPCs and immune system function during chemotherapy.

STUDY OBJECTIVE
To assess the immunological changes in peripheral blood during E/P vs trilaciclib treatment.

METHODS
- More comprehensive clinical trial data can be found in a poster (1666PD).
- Paternal IgG1 THERAPEUTICS; 2LINEBERGER COMPREHENSIVE CANCECER CENTER AT THE UNIVERSITY OF NORTH CAROLINA; 3NORRISCOTTON CANCECER CENTER; 4EMORY UNIVERSITY

RESULTS
- TRILACICLIB preserves and enhances immune system function in extensive-stage small cell lung cancer (SCLC) patients receiving first-line chemotherapy.
- This randomized, double-blind, placebo-controlled, two-part, Phase 1b/2 trial in SCLC demonstrated proof-of-concept for the potential of trilaciclib to preserve HSPCs and immune system function during chemotherapy.
- With the addition of trilaciclib to E/P, the increase in number of circulating CD8+ T cells in the effecter cell population and, to a lesser extent, in the central memory T cell population.
- The myelopreservation benefits of trilaciclib including reduced multi-lineage myelosuppression and reduced supportive care requirements and dose reductions (Dragnev et al ESMO 2018, Poster 1666PD).
- The addition of trilaciclib to ICI treatment results in an enhanced anti-tumor immune response and improved overall survival.

CONCLUSIONS
- Trilaciclib is a first-in-class therapy with demonstrated proof-of-concept for the potential to preserve HSPCs and immune system function during chemotherapy/maintenance therapy, including extended treatment with immunotherapy.
- The addition of trilaciclib to ICI treatment results in an enhanced anti-tumor immune response and improved overall survival.

Table 1: Evaluation of Immune Subpopulations

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<th>Cell Population</th>
<th>Treatment Group</th>
<th>Mean Value</th>
<th>p-value</th>
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<tr>
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<td>Trilaciclib</td>
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Figure 1: Study Schema

Figure 2: Lymphocyte Assessment Over Time

Figure 3: CD8+ T Cell Subpopulations

Figure 4: CD4+ T Cell Subpopulations

Figure 5: T Cell Subpopulations

Figure 6: Functional Status of T Cell Subpopulations

Figure 7: Combination Chemotherapy/ICI/Trilaciclib Treatment in Preclinical Models

*ICJ: immunotherapy checkpoint inhibitor; PD-L1: programmed death-ligand 1; *T: trilaciclib; #1671P

**Table 2:** Immunophenotyping analysis of CD8+ T cells in peripheral blood of SCLC patients receiving E/P chemotherapy and E/P plus trilaciclib treatment. Analyses were completed at Fios Genomics. Only data from C1D1, C3D1, C5D1 and post-treatment visit (PTV) were graphed.

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**Figure 3:** Immunophenotyping analysis of CD8+ T cells in peripheral blood of SCLC patients receiving E/P chemotherapy and E/P plus trilaciclib treatment. Analyses were completed at Fios Genomics. Only data from C1D1, C3D1, C5D1 and post-treatment visit (PTV) were graphed.

**Figure 4:** Immunophenotyping analysis of CD8+ T cells in peripheral blood of SCLC patients receiving E/P chemotherapy and E/P plus trilaciclib treatment. Analyses were completed at Fios Genomics. Only data from C1D1, C3D1, C5D1 and post-treatment visit (PTV) were graphed.

**Figure 5:** Immunophenotyping analysis of CD8+ T cells in peripheral blood of SCLC patients receiving E/P chemotherapy and E/P plus trilaciclib treatment. Analyses were completed at Fios Genomics. Only data from C1D1, C3D1, C5D1 and post-treatment visit (PTV) were graphed.

**Figure 6:** Immunophenotyping analysis of CD8+ T cells in peripheral blood of SCLC patients receiving E/P chemotherapy and E/P plus trilaciclib treatment. Analyses were completed at Fios Genomics. Only data from C1D1, C3D1, C5D1 and post-treatment visit (PTV) were graphed.

**Figure 7:** Immunophenotyping analysis of CD8+ T cells in peripheral blood of SCLC patients receiving E/P chemotherapy and E/P plus trilaciclib treatment. Analyses were completed at Fios Genomics. Only data from C1D1, C3D1, C5D1 and post-treatment visit (PTV) were graphed.