**Intrallesional Administration of the CD47 Antagonist TTI-621 (SIRPaFc) Induces Responses in Both Injected and Non-injected Lesions in Patients with Relapsed/Refractory Mycosis Fungoides and Sézary Syndrome: Interim Results of a Multicenter Phase I Trial**

Christiane Querfeld¹, John A. Thompson², Matthew Taylor³, Raju K. Pillai¹, Lisa D.S. Johnson⁴, Tina Catalano⁵, Penka S. Petrova⁶, Theresa Thompson⁷, Robert A. Uger⁷, Yaping Shou⁸, Oleg Akilov⁹

¹City of Hope, Duarte, CA, USA; ²University of Washington/Seattle Cancer Care Alliance, Seattle, WA, USA; ³Oregon Health & Science University, Portland, OR, USA; ⁴Trillium Therapeutics Inc., Mississauga, Ontario, Canada; ⁵University of Pittsburgh Medical Center, Pittsburgh, PA, USA

**BACKGROUND**

CD47 is an immune checkpoint that binds signal regulatory protein alpha (SIRPa) and delivers a “do not eat” signal to suppress macrophage phagocytosis. Tumor cells, including T-cell lymphomas, frequently overexpress CD47 to escape immune surveillance. TTI-621 (SIRPaFc) is a fusion protein consisting of the CD47 binding domain of human SIRPa linked to the Fc region of human IgG1, designed to enhance phagocytosis and antitumor activity by blocking the CD47-SIRPa interaction between antigen-presenting cells and macrophages, and engaging activating Fc receptors (Figure 1). It is hypothesized that direct intraleional (SI) administration of TTI-621 may enhance both local and systemic antitumor activity.

**RESULTS**

**Patients**

- At the data cut-off (Nov 5, 2018), 27 patients with CTCL were enrolled. MF (n=22), MF with transformation (n=3), primary cutaneous anaplastic large cell lymphoma (pALCL) (n=3), and Sézary Syndrome (SS) (n=1).
- Demographic and baseline disease characteristics are shown in Table 2.

**Study Schema and Enrollment**

- Enrolled: MF (n=22), MF with transformation (n=3), primary cutaneous anaplastic large cell lymphoma (pALCL) (n=3), and Sézary Syndrome (SS) (n=1).
- CAILS scores were available in 22 patients (Figure 1).

**Efficacy**

- Overall CAILS scores were available in 22 patients (Figure 1).
- Nine patients had reduced CAILS scores, with a more pronounced reduction with continuous therapy (n=3).

**Individual Responses**

- Five patients received weekly continuous therapy with TTI-621 beyond the 2 week induction period (ranging: 1-26 weeks of further treatment).

**CONCLUSIONS**

- Single and multiple IL injections of up to 10 mg TTI-621 were well tolerated.
- The phase II study of heavily pre-treated MF/SS patients had a reduction in CAILS scores in treated lesions; 41% (9/22) had ≥50% CAILS score decrease.
- Responses were rapid and occurred across all disease stages following single and multiple TTI-621 injections of varying doses.
- Similar CAILS-based changes were seen in adjacent non-injected lesions, suggesting local regional effects that were not confined to the site of injection.
- Continuous therapy led to further reductions in CAILS scores in 3/4 evaluable patients and evidence of systemic effects in one patient. Additional clinical benefit beyond the two-week induction and rolling injections may provide additional clinical benefit.

**TRANSLATIONAL ASSESSMENTS**

- Emerging translational data demonstrate that IL-2T621 administration leads to a rapid influx of macrophages and CDB+ T cells.