TPS2672 Poster Session

EGL-121, a first-in-human phase 1/2 trial of EGL-001 in adult patients with selected advanced and/or metastatic solid tumors.

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Background: Regulatory T cells (Tregs) play a key role in the resistance to immune checkpoint inhibitors therapy (ICI). Disarming Tregs could therefore restore/enhance anti-tumor responses and increase the number of patients benefiting from these treatments. EGL-001, a novel therapeutic agent, is designed to provide checkpoint inhibition by antagonizing the CTLA-4-CD80/86 interaction while selectively depleting intratumoral Tregs by downregulating CD25 and inhibiting IL-2 signaling specifically within these cells. This dual mechanism of action effectively unleashes potent anti-tumor immunity even in anti-PD-1 resistant models, independent of FcgR activity. In murine models, EGL-001 shows preferential distribution and persistence in the tumor until Treg get depleted/inactivated. Our data demonstrated complete anti-tumor activity of EGL-001 as a single agent across various tumor models and it overcomes resistance to anti-PD-1 treatment in many tumor models, highlighting its broad therapeutic potential. Additionally, EGL-001 effectively depletes Tregs and exhibits activity in ex-vivo human tumor samples, where other ICI showed no significant effect. In NHPs, EGL-001 was well tolerated across all tested doses, with rapid peripheral clearance preventing lymphoid tissue hyperplasia in the spleen and lymph nodes. **Methods:** A Phase I/II clinical trial (NCT06622486) is currently underway in eight sites in France and Spain to evaluate EGL-001 as monotherapy and in combination with checkpoint inhibitors in selected tumor types characterized by tumor Treg implication in induction of mechanism of resistance to ICI. The selective targeting of tumor-infiltrating Tregs could effectively improve anti-tumor immune response and limit systemic immune-related toxicities. This first-in-human, multicenter, open label Phase 1/2 study evaluates the safety, tolerability, and initial activity of EGL-001 in adult patients with selected advanced and/or metastatic solid tumors. The study consists of a Part 1 (Phase 1) dose escalation of EGL-001 administered as a single agent (from 0.3 mg/kg to 12 mg/kg), and in combination with pembrolizumab treatment, according to a BOIN design, followed by a Part 2 (Phase 2) dose expansion of EGL-001 administered at the selected doses as monotherapy and/or in combination therapy with anti-PD(L)1. Eligible patients are those who have initially benefited (secondary resistance) from an ICI treatment as monotherapy or in combination as SoC as defined by a CR, PR, or SD $\geq$3 months as best response by RECIST Version 1.1. As of January 2025, the first 3 Cohorts of EGL-001 (0.03, 0.1, 0.3 mg/kg) have been completed. EGL-001 was well tolerated with no DLTs reported. Clinical trial information: NCT06622486. Research Sponsor: None.