(PF1058) TARGETING TNFR2 WITH BI-1808 WITH OR WITHOUT PEMBROLIZUMAB: IMMUNE ACTIVATION AND PROMISING RESPONSES IN ADVANCED CUTANEOUS T-CELL LYMPHOMAS

Topic: 20. Other aggressive lymphomas

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Background

Cutaneous T cell lymphomas (CTCL) are rare nonHodgkin lymphomas arising from malignant skinhoming T cells. The most common subtypes are mycosis fungoides (MF), typically an indolent skin-limited disease, and Sézary syndrome (SS), an aggressive leukemic variant characterized by circulating malignant T cells and erythroderma.Outcomes for advanced CTCL subtypes remain poor, with limited 20-60% 5-year survival.
TNFR2 has emerged as a pathogenic driver in CTCL through gain-of-function alterations that increase expression in malignant $CD4^+CD26^-$ cells. BI-1808, an IgG1 monoclonal antibody directed against TNFR2, blocks ligand engagement and induces FcγR-mediated depletion of regulatory T cells, leading to enhanced intratumoral $CD8^+$ T-cell activity. Clinical studies have demonstrated antitumor activity in CTCL and solid tumors, supporting TNFR2 targeting as a promising broad immunotherapeutic approach.
Preclinical data indicates a positive combinatorial effect of BI-1808 and pembrolizumab. Pembrolizumab has shown promising results in clinical trials in CTCL.

Aims

Safety and preliminary efficacy are currently investigated in CTCL patients, in a sub-cohort of the ongoing Phase 2a clinical trial 19-BI-1808-01.

Methods

The study is designed to enroll 20 patients at 1000 mg BI-1808 Q3W, followed by 10 patients to receive 1000 mg BI-1808 + 200 mg Q3W pembrolizumab. The study also includes a dose optimization phase enrolling 10+10 patients evaluating BI-1808 at 250 mg vs 1000 mg Q3W currently ongoing.

Results

As of February 19, 2026, the signal-seeking portion of the study has been fully enrolled. 20 patients with advanced stage CTCL received BI-1808 as single-agent Q3W (13 MF, 8 SS), and 9 patients received BI-1808 in combination with pembrolizumab (6 MF, 3 SS). MF patients had previously received a median of 5 (2-13) prior systemic treatments, and SS patients 3 (1-14).
Treatment related AEs were classified as mild or moderate. G3 TEAEs included one skin reaction in the monotherapy arm, and in the combination arm one instance of pulmonary embolism, and one case of colitis were observed. Disease "flares" (characterized by increased skin peeling, erythema, and pruritus) were observed early during treatment in several cases, and were shown to be related to immune activation, depletion of T regs and influx of CD8+ T cells.
Immunofluorescence multiplex staining of skin biopsies showed a significant increase in CD8+ infiltration and accompanying granzyme B elevation in responding patients at 5 weeks after start of treatment. Serum analysis showed rapid and sustained induction of IL-12. IL-12 is crucial for counteracting the protumor Th2 cytokine profile and switching the balance in favor of Th1 $CD8^+$ T cells and NK cells.

Out of 15 CTCL mSWAT evaluable cases in the single agent arm, 1 SS patient exhibited complete response (CR) lasting approximately 2 years to date and ongoing, 5 participants (3 MF, 2 SS) exhibited confirmed partial response (PR) as best clinical response, and 8 participants showed stable disease (SD). Out of 8 evaluable patients in the combination arm, 4 patients exhibited PR at first assessment (3 MF, 1 SS), and 2 patients SD.
More complete data will be disclosed in the poster.

Summary/Conclusion

Current data from the signal seeking cohort of BI-1808 in CTCL show promising efficacy associated with strong immune activation in patients with advanced CTCL, leading to an impressive objective response rate of 40% in BI-1808 single agent, and 50% in combination with pembrolizumab.