ASH # 3633

Session: 625

T Cell, NK Cell, or NK/T Cell Lymphomas: Clinical and Epidemiological: Poster II

BI-1808, a Tumor Necrosis Factor Receptor 2 (TNFR2) Blocker/Depleter, Shows Promising Efficacy in T Cell Lymphoma Patients

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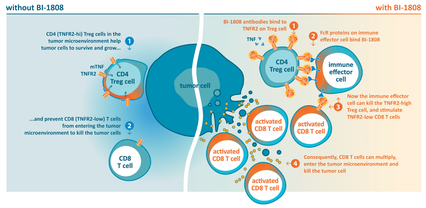
Rationale

TNFR2 is a potential oncogene in TCL, characterized by recurrent point mutations and gain-of-function alterations, leading to its abnormal expression on CD4+CD26- tumor cells. BI-1808 is an IgG1 monoclonal antibody that directly targets T cell lymphoma cells; in addition, it inhibits TNFR2 binding to the ligand TNF-α, enabling FcγR-dependent depletion of regulatory T cells (Treg), and promoting the expansion of intratumoral CD8+ T cells, and has shown single agent activity in several indications including patients with solid tumors. Consequently, targeting TNFR2 through this method represents a promising and innovative cancer treatment.

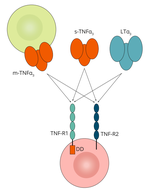
Cutaneous T-cell lymphomas (CTCL) encompass a group of diseases characterized by the infiltration of malignant T lymphocytes in the skin. Mycosis fungoides (MF) is the most prevalent form of CTCL, often demonstrating a relatively indolent course. Sézary syndrome (SS) is characterized by widespread erythroderma, involvement of lymph nodes, blood compartment, and extra nodal lesions, and commonly exhibitsing more aggressive behavior. Survival is poor in advanced MF and SS, with a 5-year survival range of 20–60%.

Peripheral T-cell lymphomas (PTCL) is a group of cancers that arises in the lymphoid tissues outside of the bone marrow. Most PTCL subtypes are aggressive, and treatment options are sparse, and limited to chemotherapy.



About TNFR2

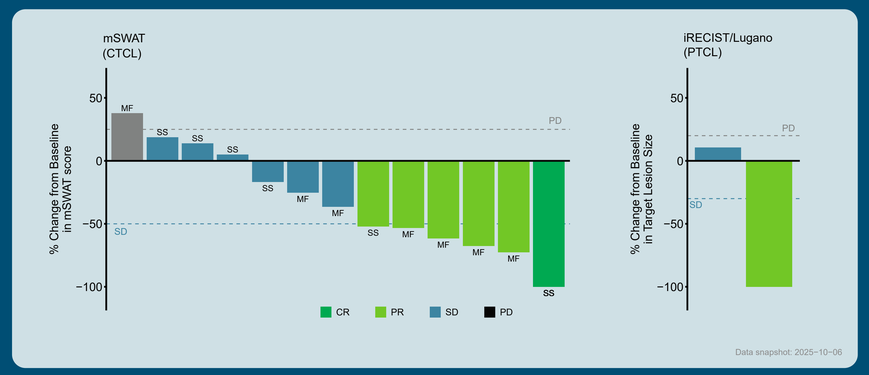
- High expression on T regs, activated/ memory CD8+ T cells, NK cells, also DC's and several myeloid cells, e.g. monocytes
  - Shares ligands with TNFR1
  - Membrane bound TNF-α binds and signals through TNFR2
- TNFR2 has been shown to be critical for T reg proliferation and survival
- Proposed as a co-stimulatory factor for T cells proliferation and activation (similar to e.g. OX40 or 4-1BB)



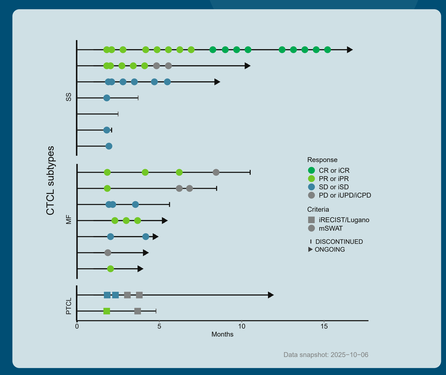
BI-1808 targets TNFR2, a novel immunomodulatory target with potential for therapeutic efficacy across many tumor types, with early clinical data showing responses in patients with CTCL/PTCL and several various solid cancers.

This data show BI-1808 emerging as a safe and efficacious treatment option in advanced T-cell lymphoma.

Ph2a signal seeking cohort in TCL in Study 19-BI-1808-01



Waterfall plot of best response to BI-1808 treatment in CTCL (left) and PTCL (right)



Swimmer plot of CTCL and PTCL patients

Preliminary efficacy

As of October 6, 2025, 21 patients with TCL received BI-1808 as single agent Q3W. All treatment related adverse events were classified as mild or moderate with no potentially related grade 3+ AE reported.

Disease "flares" characterized by increased skin peeling, erythema, and pruritis were observed during first weeks of treatment in several cases, considered related to immune activation associated with depletion of T reg and influx of CD8+ T cells.

Immunofluorescence staining of skin biopsies showed evidence of significant increase in CD8+ infiltration and accompanying granzyme B elevation at 5 weeks after start of treatment.

Out of 13 disease evaluable CTCL cases, 1 SS patient exhibited complete response (CR), 5 participants (4 MF, 1 SS) exhibited partial response (PR) as best clinical response; and 6 participants showed stable disease (SD).

In addition, 2 patients with peripheral T-cell lymphoma (PTCL) were evaluable according to Lugano critera. One patient showed PR as best response, while the other showed stable disease.

Safety findings

14 subjects with CTCL and 2 subjects with PTCL, received BI-1808 as 1000 mg single agent IV every 3 weeks.

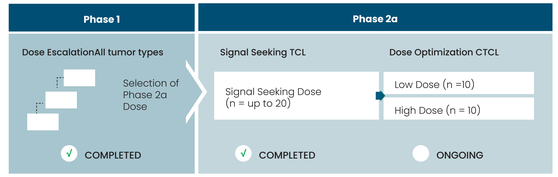
TEAE were mainly classified as a mild or moderate, apart from one Gr3 event (skin reaction followed by pyrexia).

Safety summary for BI-1808 in TCL	Phase 2a
Number of safety evaluable subjects	14 CTCL+2PTCL
Subjects with at least 1 TEAE any grade	13 (81%)
Subjects with any ≥Grade 3 TEAEs	4 (25%)
Subjects with any TEAEs related to BI-1808	6 (38%)
Subjects with ≥Grade 3 TEAEs related to BI-1808	1 (6%)
Subjects with serious TEAEs related to BI-1808	1 (6%)
Subjects with related AE:s that led to discontinuation	0

Study overview

Safety and preliminary efficacy of BI-1808 as single agent is currently investigated in patients with T-cell lymphomas in a sub-cohort of the ongoing Phase 2a clinical trial 19-BI-1808-01.

The study was designed to enroll 20 subjects at signal seeking dose, whereafter a dose optimization phase will open.



Patient characteristics

Sex	Age	CTCL subtype	Stage at diagnosis	Previously treated with Mogamulizumab	Best response to BI-1808
M	66	SS	IV	YES	CR
M	64	SS	IV	YES	SD
M	75	SS	IV	NO	SD
M	75	SS	IIIB	YES	SD
M	77	SS	IIIB	YES	SD
F	71	SS	IIA	NO	SD
M	66	SS	Unknown	NO	PR
F	28	MF	IIB	NO	PR
M	68	MF	IIB	YES	PR
M	72	MF	IB	NO	PR
M	51	MF	IB	NO	SD
F	71	MF	IIB	NO	PD
F	39	MF	IB	NO	PR

Conclusions

The signal seeking cohort of BI-1808 as single agent therapy for the treatment of TCL show highly promising efficacy associated with strong immune activation.

An objective response rate of 46% in heavily pretreated patients with advanced CTCL warrants the study to proceed to next stage of dose optimization.

BI-1808 was well tolerated, allowing the exploration also of combination with other agents. A separate cohort investigating the combination of BI-1808 and pembrolizumab in CTCL is currently recruiting.

Contact information

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Study identifier: NCT06205706

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