#EHA-1269, Abstract PF961
Topic: Aggressive Non-Hodgkin lymphoma – Clinical

Robust Single Agent Activity of BI-1808, a Tumor Necrosis Factor Receptor 2 (TNFR2) Blocker/Depleter, in Cutaneous T-cell Lymphoma (CTCL) Patients

Stefan K. Barta[A], Christiane Querfeld[B], Sean Lim[C], Ana Carneiro[D], Stephen Morris[E], Jeffrey Yachnin[F], Marica Vaapil[G], Susanne Gertsson[G], Petra Holmkvist[G], Ingrid Karlsson[G], Linda Mårtensson[G], Dmytro Piliuhin[G], Anette Sundstedt[G], Johan Wallin[G], Ingrid Teige[G], Danijela Lindahl[G], Björn Frendeus[G,H], Andres McAllister[G]

[A]University of Pennsylvania Hospital, Philadelphia, PA, USA; [B]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [C]University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom; [D]Skåne University Hospital, Department on Hematology, Oncology and Radiation Physics, Lund, Sweden; [E]Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom; [F]Karolinska Comprehensive Cancer Center, Solna, Sweden; [G]BioInvent International AB, Lund, Sweden; [H]Centre for Cancer Immunology, University of Southampton, Southampton, United Kingdom

Background

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 targets TNFR2 by inhibiting its interaction with 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 solid tumor patients. Consequently, targeting TNFR2 through this method represents a promising and innovative cancer treatment paradigm for patients.

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, more often demonstrating a relatively indolent course, while Sezary syndrome (SS) is characterized by widespread erythroderma, involvement of lymph nodes, blood compartment and extranodal lesions, commonly exhibiting 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.

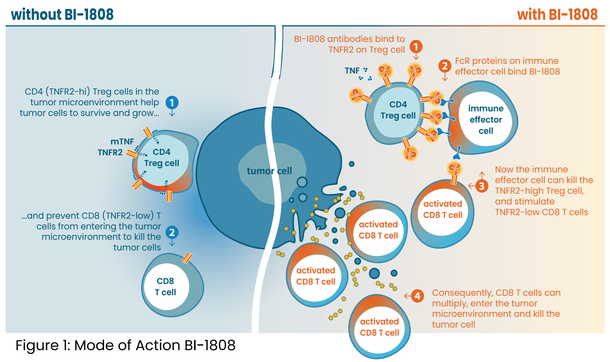


Figure 1: Mode of Action BI-1808

The Study

Safety and preliminary efficacy of BI-1808 as single agent is currently investigated in subjects with T-cell lymphomas including CTCL in a sub-cohort of the ongoing Phase 2a clinical trial 19-BI-1808-01. 20 subjects will be enrolled for signal seeking, whereafter a dose optimization phase will open.

Results

As of May 15, 2025, 9 evaluable subjects with CTCL received BI-1808 as single agent Q3W. All treatment related adverse events were classified as mild or moderate with no potentially related Gr3+ 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 multiplex staining of skin biopsies showed evidence of signficant increase in CD8+ infiltration and accompanying granzyme B elevation at 5 weeks after start of treatment.

Out of 9 evaluable CTCL cases, 1 SS subject exhibited complete response (CR), 3 subjects (1 MF, 2 SS) exhibited partial response (PR) as best clinical response; the remaining 5 subjects showed stable disease (SD).

In addition, 2 subjects with peripheral T-cell lymphoma (PTCL) were evaluable. 1 Subject showed PR as best response, while the other showed SD.

Case Study 1: CTCL

Subject A (CTCL MF, Best response: PR)

Female subject in her late 20s, presented with Mycosis Fungoides stage IIb at diagnosis, with skin involvement across head; neck; anterior and posterior trunk. Previous treatments include retinoids, radiotherapy, methotrexate, mechlorethamine and durvalumab.

The subject tolerated the treatment well, and received full intended dose intensity. At first assessment on trial after 9 weeks the subject exhibited a partial response, with a reduction in mSWAT of 68%. This response was maintained up until month 9.

The subject exhibited a substantial decrease in CD4/CD8 ratio indicative of a beneficial immune response.

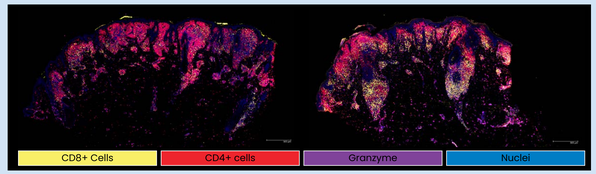


Figure 6: Immunoflorescence staining of of CTCL skin biopsy at baseline (left) compared to week 5 (right)

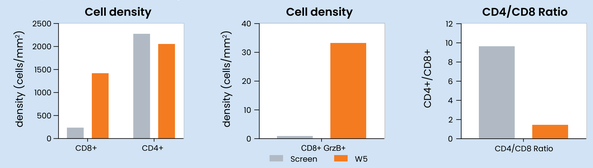


Figure 7: Change in T cell density from baseline to week 5

Subject

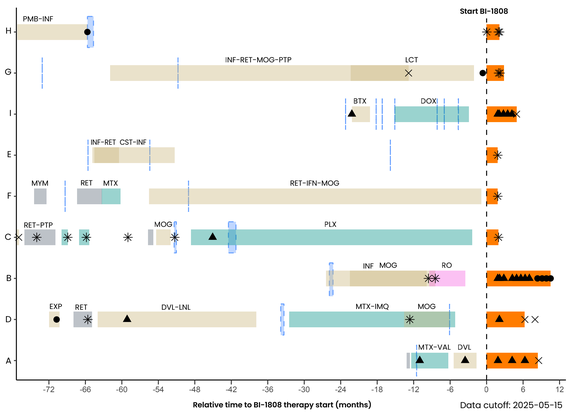


Table 1: Evaluable CTCL patients in BI-1808 monotherapy

Subject	Cancer Type	Sex, Age (yrs.)	Stage at Diagnosis
H	SS	F, 71	IIA
G	SS	M, 77	IIIB
I	SS	M, 66	unk
E	SS	M, 75	IV
F	SS	M, 75	IIIB
C	SS	M, 64	IV
B	SS	M, 66	IV
D	MF	M, 68	IIB
A	MF	F, 28	IIB

Class Treatment: Others, BI-1808, Radiotherapy, Biologic Therapy, Targeted Therapy, Chemotherapy
Response: Stable Disease, Complete Response, Progressive Disease, Partial Response

Figure 2: CTCL Patient Characteristics, Prior Systemic Therapies, and Swimmer Plot

T cell clonality analysis by RNA-based TCR sequencing

RNA-based TCR sequencing and analytics including clone characterization and clonality score of skin biopsies were performed by Personalis.

Results demonstrate the dominance of one malignant T cell clone and a clear reduction upon BI-1808 treatment.

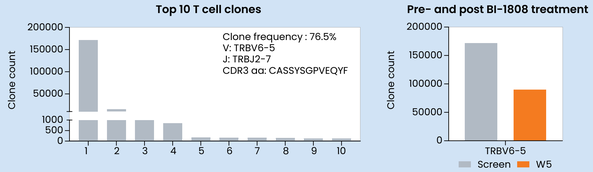
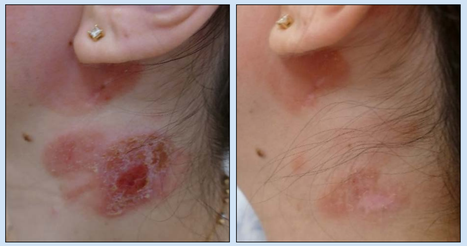


Figure 8: Expression of top 10 most frequent T cell clones at baseline (left) Reduction of the most frequent clone from baseline to week 5 (right)



Subject A
MF, PR ongoing
week 25, near CR

Figure 9: Photograph of neck and facial skin lesions at baseline (left) compared to Cycle 7 (21 weeks) (right)

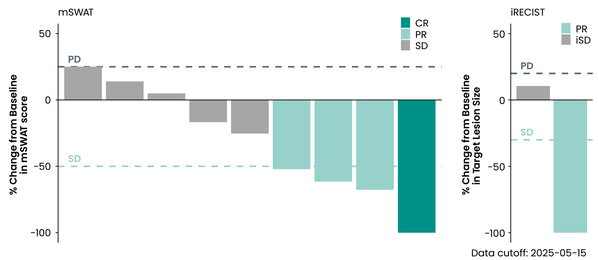


Figure 3: Waterfall plot of best overall response assessed by mSWAT for CTCL (left) or iRECIST for PTCL (right)

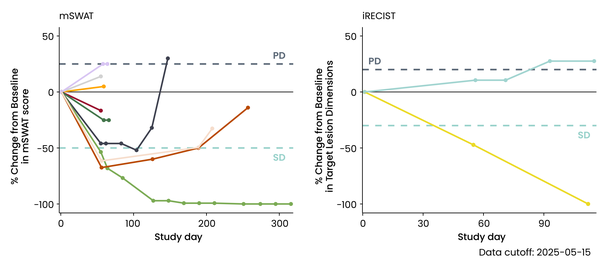


Figure 4: Spider plot of CTCL (left) and PTCL (right) subjects treated with BI-1808 monotherapy

Case Study 2: PTCL

Subject K is a 47 year old male that presented with Stage IV metastatic PTCL approximately two years prior to enrollment. During these two years, subject received 6 prior lines of treatment, including various permutations of brentuximab vedotin + chemotherapy, and one line of autologus stem cell transplantation. The subject showed an initial partial response to BI-1808 as assessed by CT and FDG-PET at first assesment, with target lesions eventually being completely cleared.
After 4 months on trial, the subject progressed with multiple new lesions.

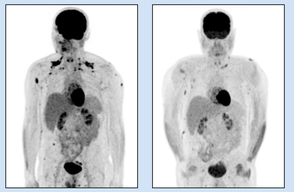


Figure 10: FDG-PET assessment at baseline (left) compared to week 9 (right)

Table 3: Subject Characteristics

Subject	Cancer Type	Sex, Age (yrs.)	Stage at Diagnosis
K	PTCL	M, 47	IV
L	PTCL	F, 76	IV

Table 2: Safety Profile for TCL Subjects

BI-1808 Monotherapy	Phase 2a
Administration route	IV
Dose	1000mg
Number of subjects	9 CTCL + 2 PTCL
Subjects with at least 1 TEAE any grade	11 (100%)
Subjects with any ≥Grade 3 TEAEs	4 (36%)
Subjects with mild and moderate TEAEs related to BI-1808	4 (36%)
Subjects with ≥Grade 3 TEAEs related to BI-1808	0
Subjects with serious TEAEs related to BI-1808	0
Subjects with treatment related AE:s that led to discontinuation	0

As of May 15, 2025, 9 subjects with CTCL and 2 subjects with PTCL, received BI-1808 as single agent Q3W.

All treatment related adverse events were classified as a mild or moderate with no related grade ≥ 3 AE reported.

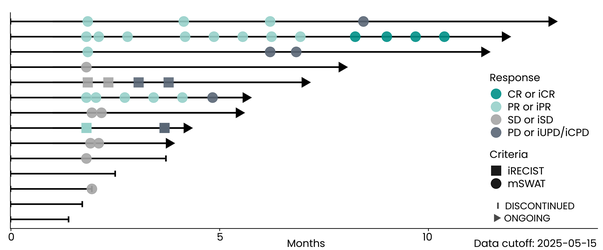


Figure 5: Swimmer lane plot of CTCL+PTCL subjects treated with BI-1808 monotherapy

Conclusions

Early data from the signal seeking cohort of BI-1808 in TCL show promising efficacy associated with strong immune activation in subjects with advanced CTCL, leading to a preliminary objective response rate of 45% and a 100% disease control rate.

Acknowledgements

We extend our deep appreciation to study participants, their families and clinical research staff.

Contact information: clinicaltrials@bioinvent.com
Study identifier: NCT06205706