

# Targeting TNFR2 with BI-1808 with or without Pembrolizumab: Immune Activation and Promising Responses in Advanced Cutaneous T-Cell Lymphomas

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## A Novel Immunotherapy Approach in CTCL: TNFR2 Blockade Shows Durable and Meaningful Responses

### Introduction

CTCL represents biologically well-defined lymphomas with pronounced immune dysregulation and limited durable treatment options in the relapsed/refractory setting.

Targeting TNFR2 addresses one of immunosuppressive mechanism in CTCL by modulating regulatory T-cell-driven tumor immune evasion.

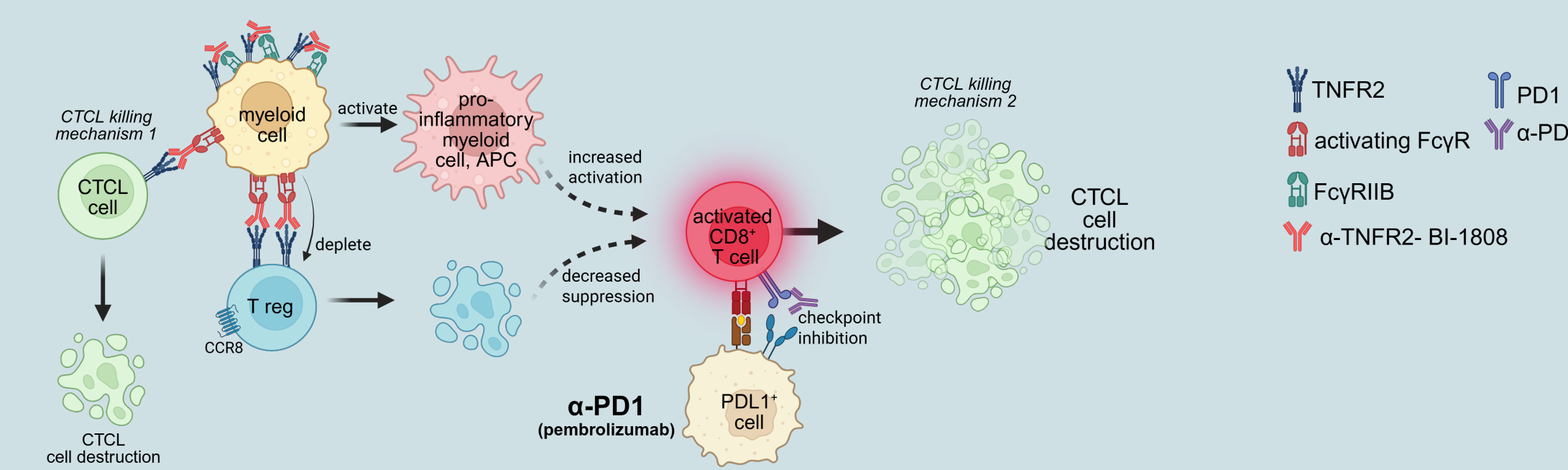
BI-1808 demonstrates clinically relevant immune activation and disease control, supporting CTCL as a suitable indication for early immuno-oncology development.

Combination with pembrolizumab was explored based on the hypothesis that TNFR2-mediated immune modulation may enhance sensitivity to PD-1 blockade.

### Background

Cutaneous T-cell lymphomas (CTCL) are rare non-Hodgkin's lymphomas arising from malignant skin-homing T cells. 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<sup>+</sup>CD26<sup>+</sup> 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<sup>+</sup> T-cell activity.

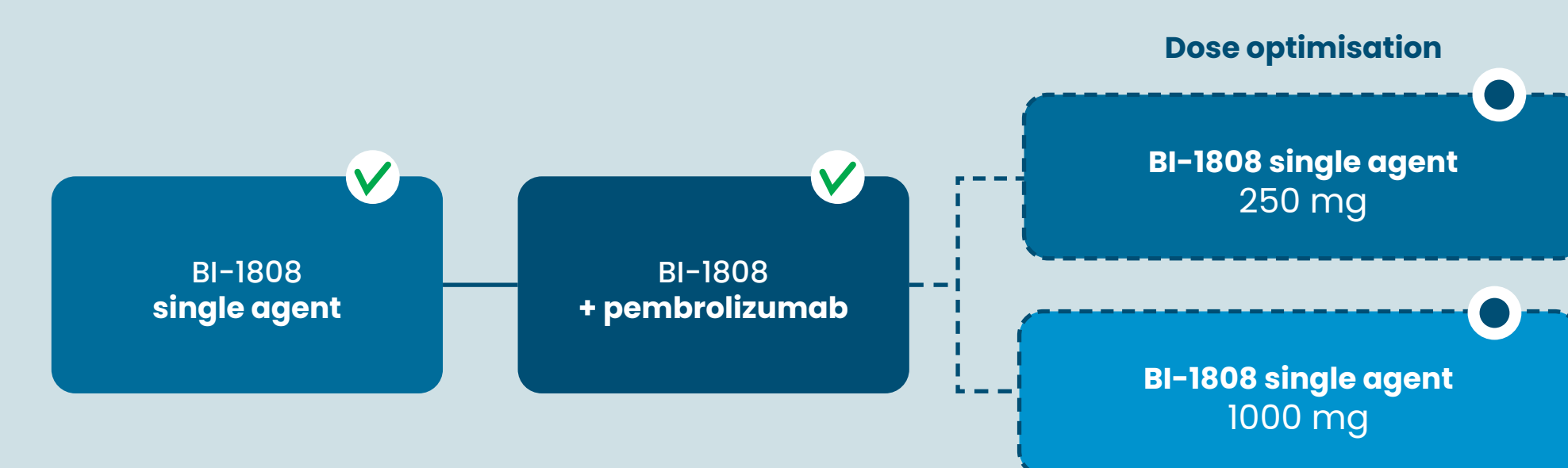


### Study Overview

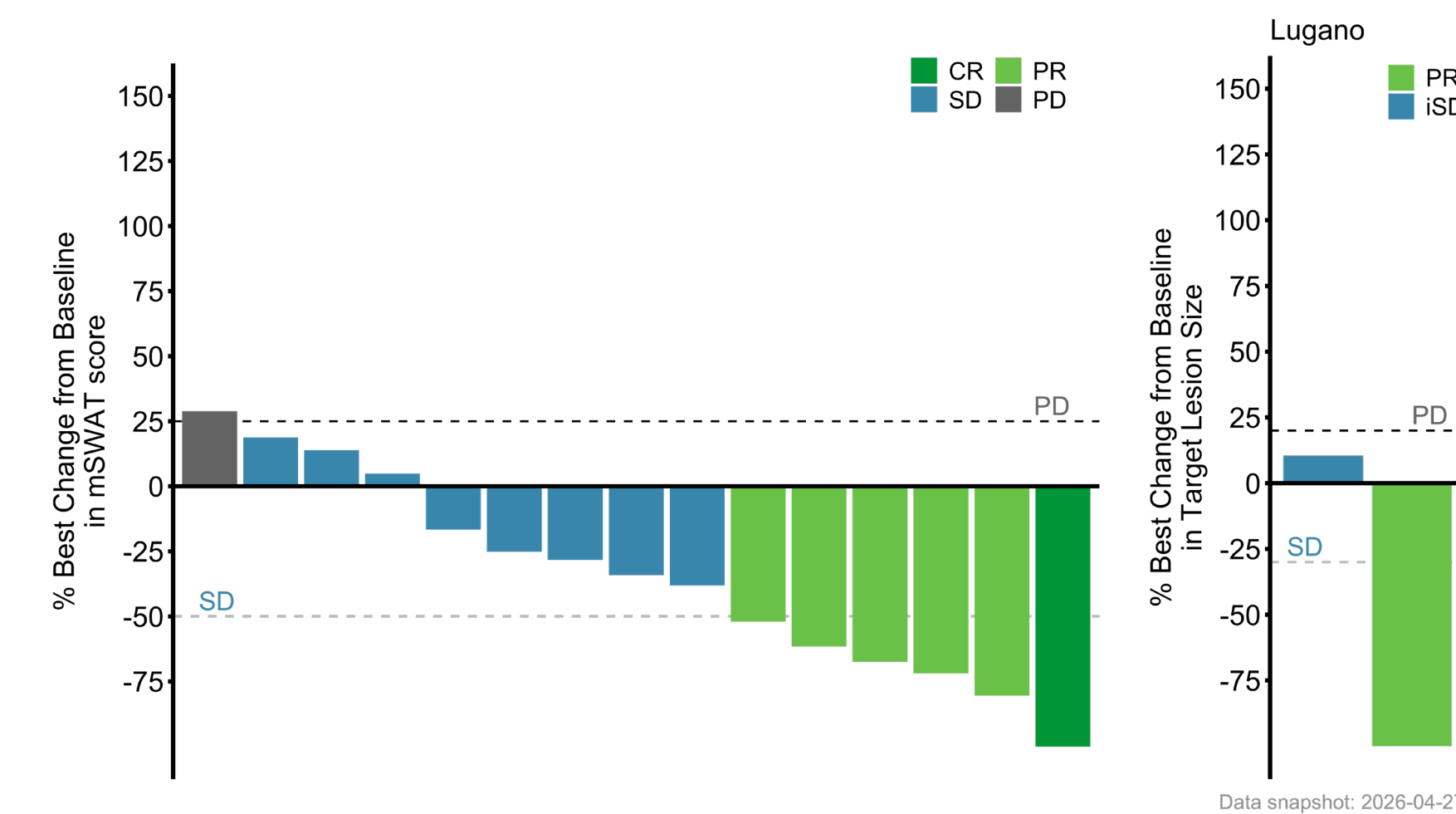
Safety and preliminary efficacy are currently investigated in CTCL patients, in a sub-cohort of the ongoing Phase 2a clinical trial 19-BI-1808-01.

The study is designed to enroll 20 patients at BI-1808 1000 mg Q3W,

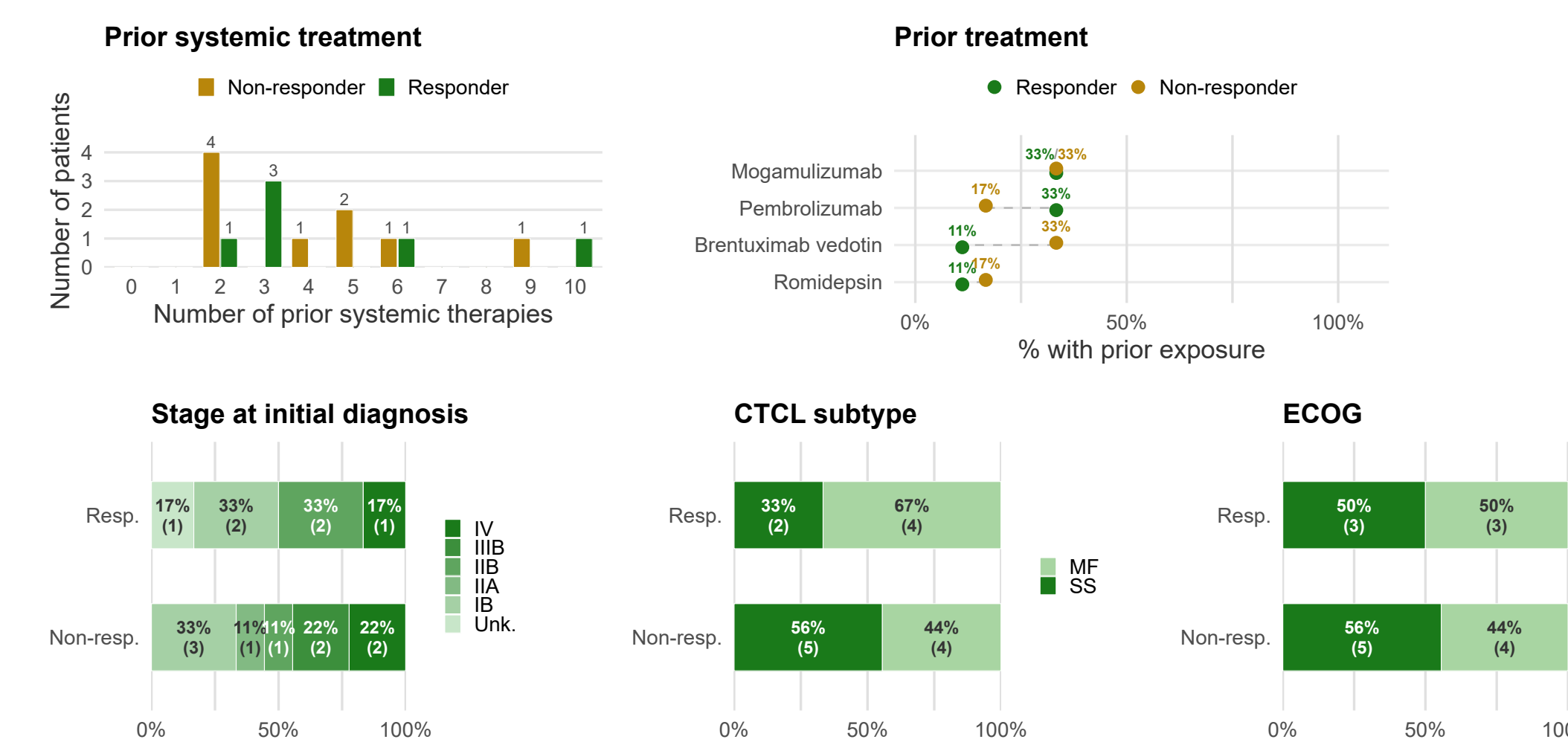
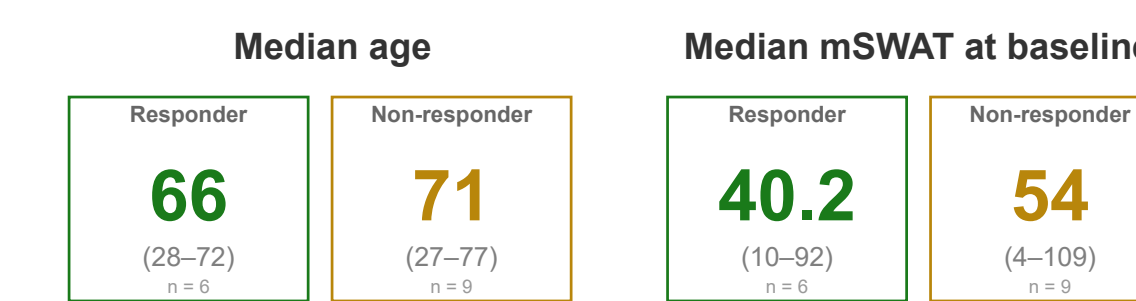
followed by 10 patients to receive the combination with 200 mg Q3W pembrolizumab. The study also includes a dose optimization phase enrolling 10+10 patients evaluating BI-1808 at 250 mg vs 1000 mg Q3W currently ongoing.



### BI-1808 single agent

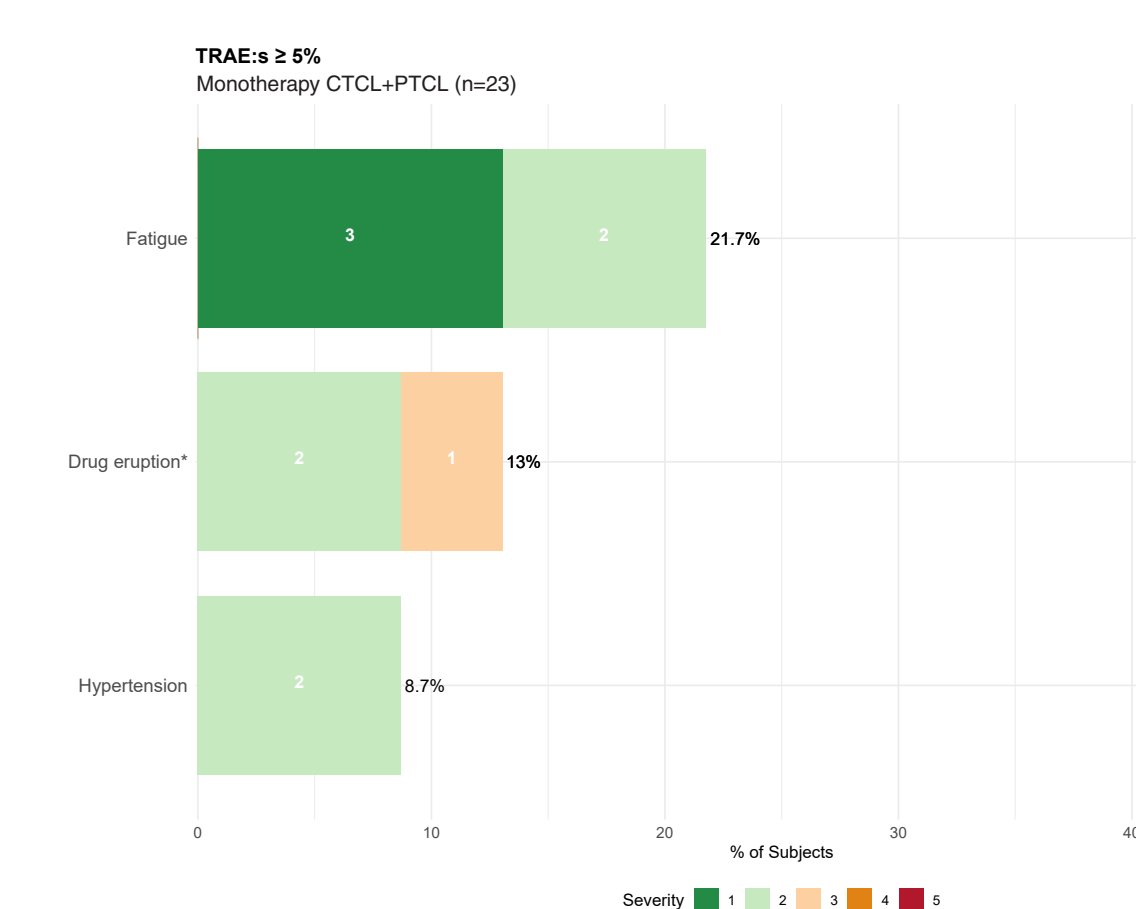


- As of April 27, 2026, the signal-seeking portion of the study has been fully enrolled.
- 20 patients with advanced stage CTCL received 1000 mg BI-1808 as single agent Q3W (12 MF, 8 SS).
- 15 CTCL subjects were mSWAT evaluable, and out of these 15 patients exhibited complete response (CR) lasting 2 years to date and ongoing.
- 5 patients (3 MF, 2 SS) exhibited confirmed partial response (PR), corresponding to an ORR of 40%. 8 patients exhibited SD as best clinical response, corresponding to DCR of 93%.
- 2 enrolled PTCL patients were evaluable. 1 subject exhibited PR, and the other SD as best response.



### Safety

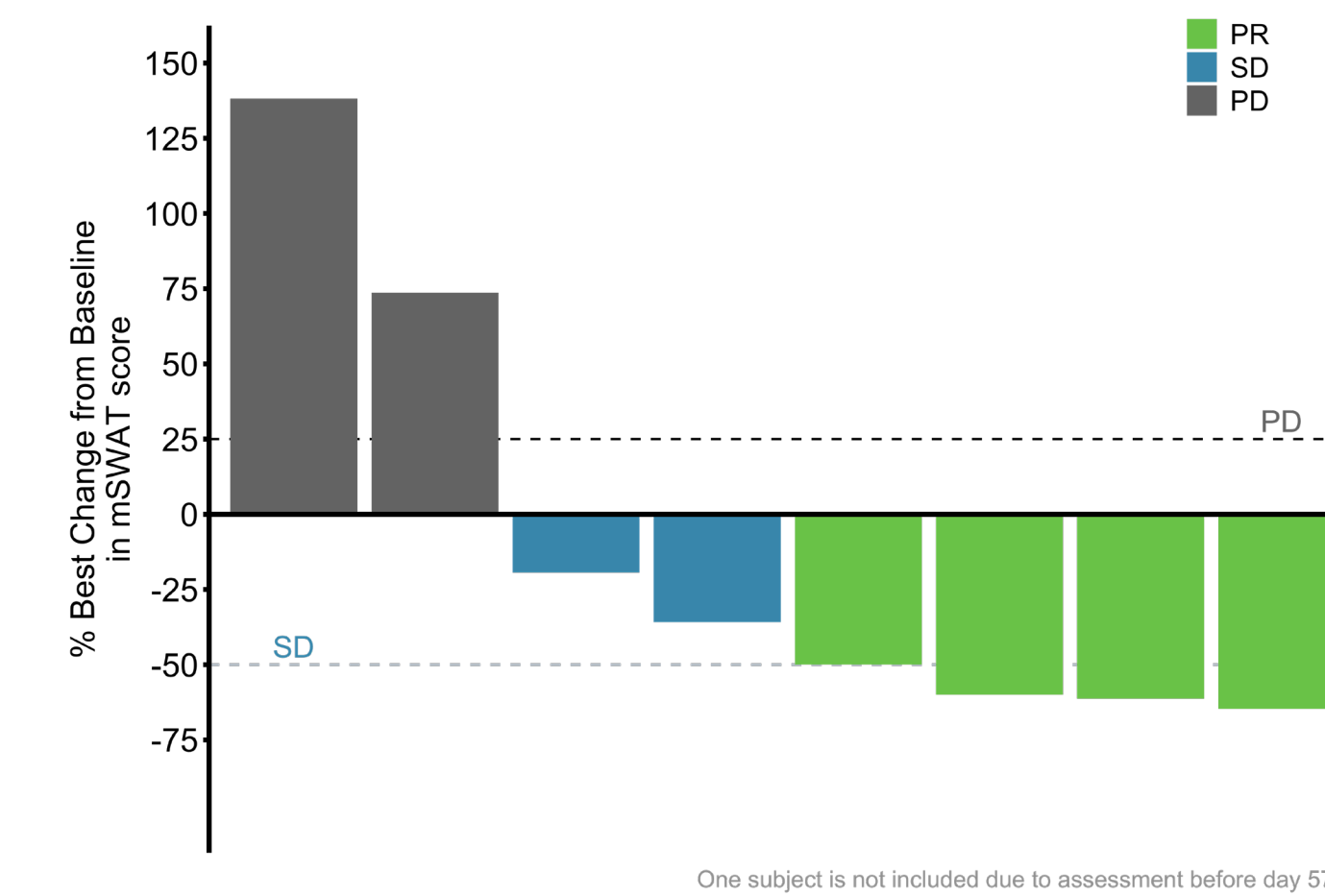
Single agent therapy very well tolerated with low occurrence of Gr3+ TRAE



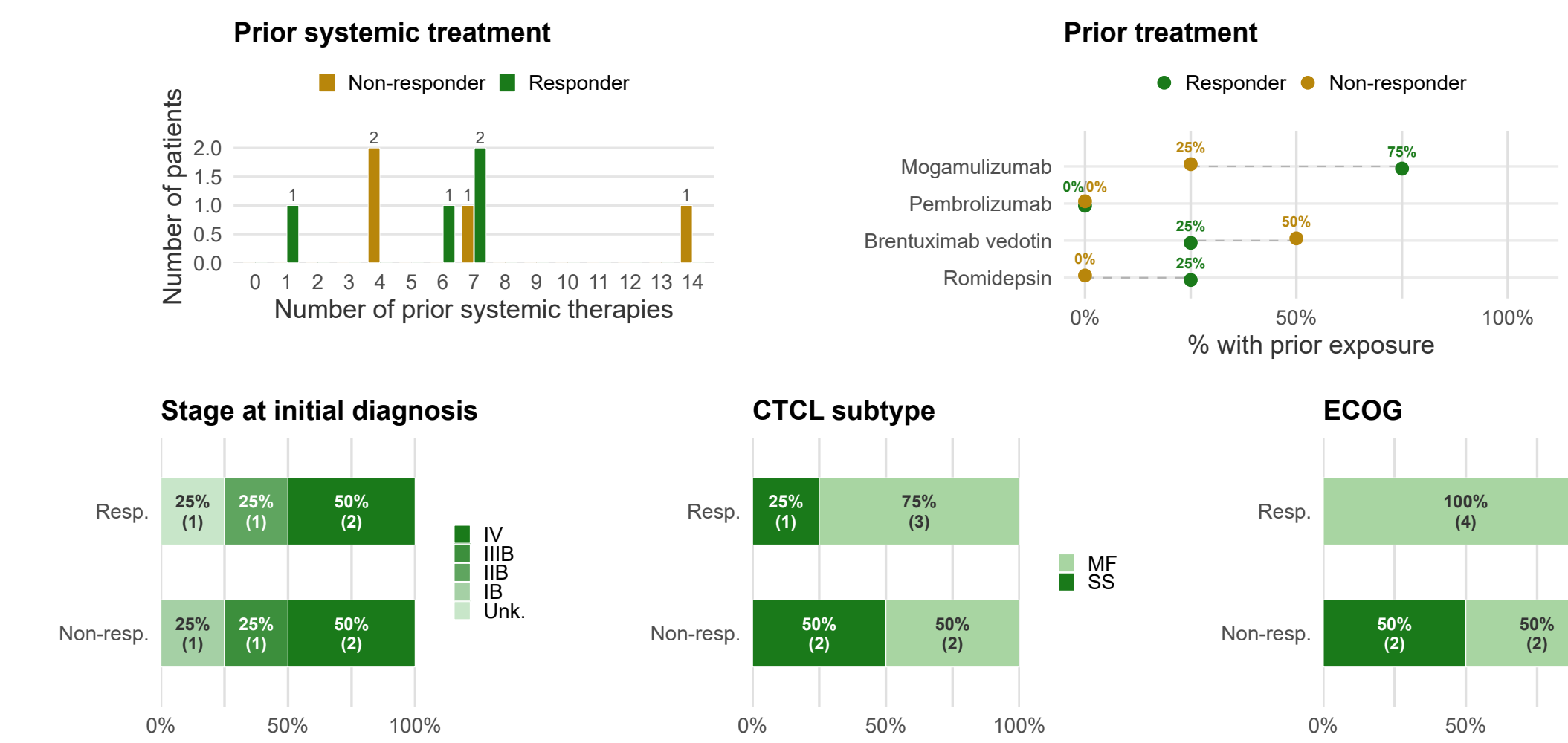
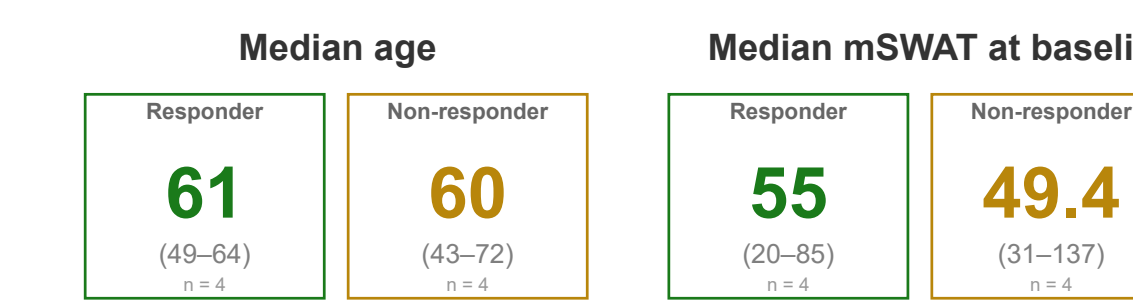
- Low rate Gr3+ TRAE:s (9%)
- Low rate treatment related SAE (13%)
- Only 1 patient experienced TRAE leading to discontinuation (4%)

\*drug eruption term is used for worsening of cutaneous symptoms (e.g., erythema, pruritus) shortly after the first dose

### BI-1808 + pembrolizumab



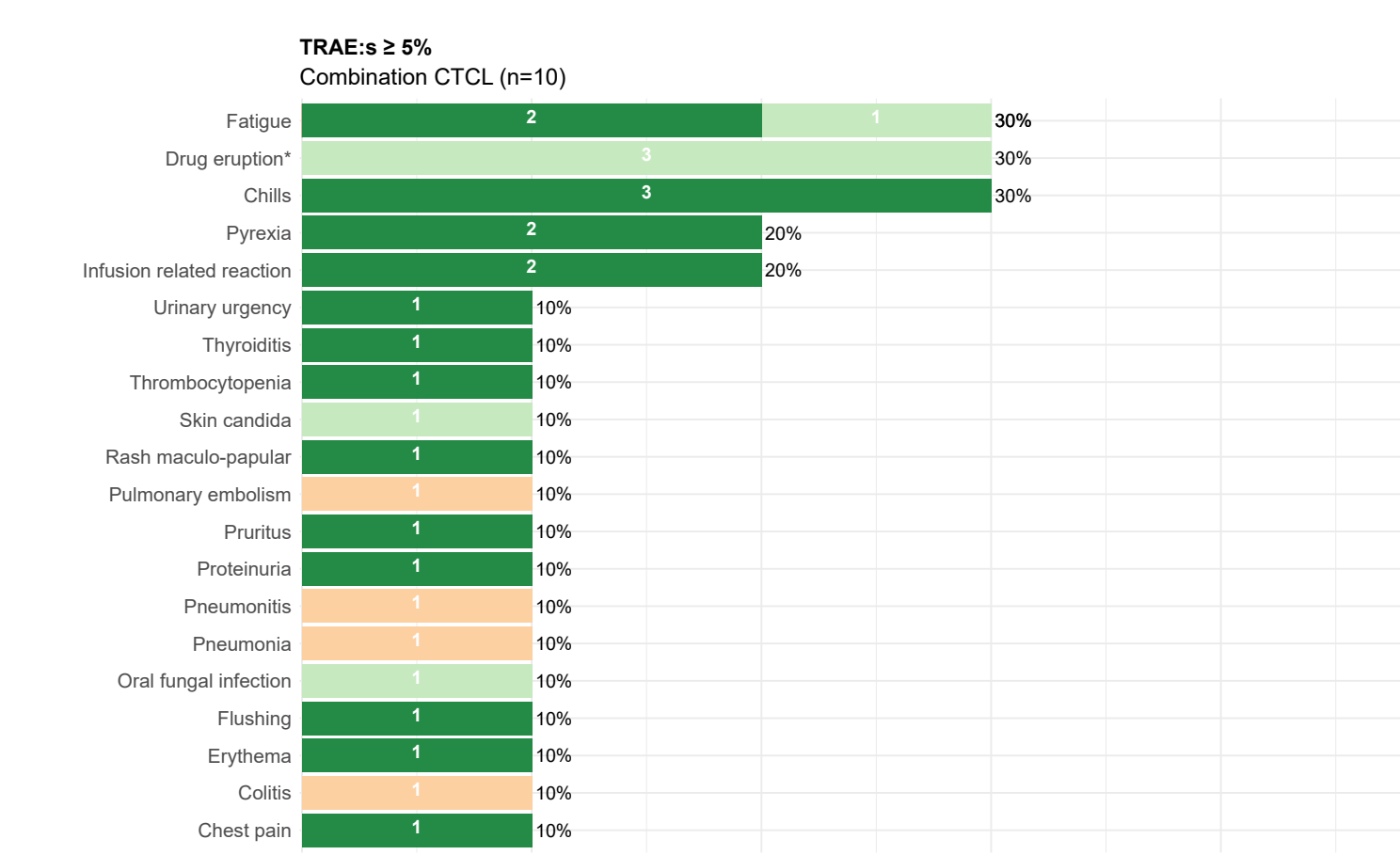
- 9 subjects received BI-1808 in combination with pembrolizumab (6 MF, 3 SS). Patients had received a median of 6 prior systemic lines (1-18), no prior anti-PD-1, and 4 subjects had received prior mogamulizumab.
- Out of 8 evaluable patients in the combination arm, 4 patients exhibited PR at first assessment, and 2 patients SD resulting in an ORR of 50% and DCR of 75%.



### Safety

Combination therapy well tolerated in a heavily pretreated population

- Grade 3+ TRAE observed in 4 patients (40%) which were SAEs at the same time
- One patient experienced TRAE leading to discontinuation (10%)



\*drug eruption term is used for worsening of cutaneous symptoms (e.g., erythema, pruritus) shortly after the first dose

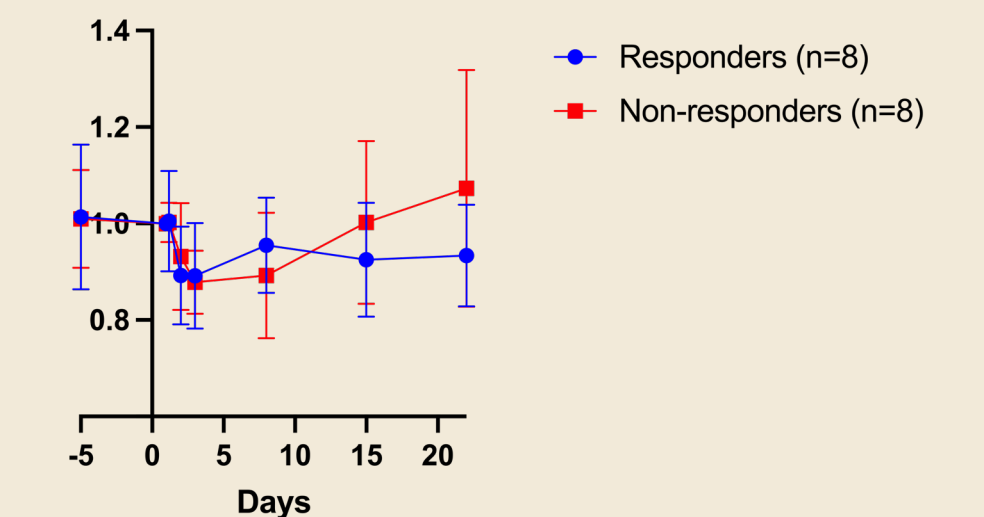
## Conclusions

- BI-1808 validates TNFR2 blockade as a powerful new therapeutic strategy, delivering efficacy that rivals current standards of care while driving robust, targeted immune activation in CTCL.
- In a population with historically poor outcomes, BI-1808 achieved objective responses across MF and SS, including a deep and ongoing complete response lasting ~2 years, confirmed partial responses, and a high rate of durable disease stabilization.
- BI-1808 stands out for its favorable safety profile and low rate of severe side effects allowing patients with advanced CTCL to stay on treatment long-term, effectively controlling the disease while protecting their daily quality of life.

### Translational

BI-1808 induces sustained CD4<sup>+</sup> T-cell depletion in patients with disease control

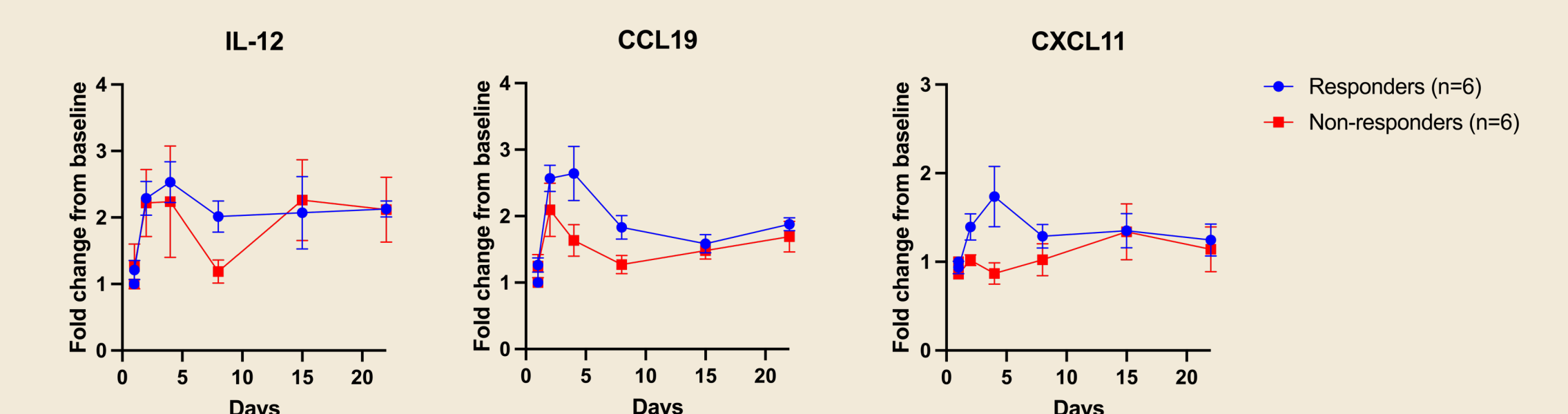
CD4<sup>+</sup> T-cell levels (measured as % CD4<sup>+</sup>CD3<sup>+</sup> of total CD45<sup>+</sup> cells) in blood of BI-1808 single agent (1000mg) treated patients during the first treatment cycle. Responders are defined as CR, PR and SD > 6 months; non-responders are defined as PD and SD < 6 months.



BI-1808 induces cytokines associated with CD8<sup>+</sup> T-cell activation, myeloid proinflammatory reprogramming and formation of tertiary lymphoid structures

Interleukin-12 (IL-12) is a potent immunomodulator in the tumormicro environment (TME), reversing the immunosuppressive activity of tumor-associated macrophages (TAMs), reducing the M2 phenotype while promoting the M1 phenotype and allowing more efficacious presentation of tumor antigens.

CXCL11 and CCL19 are key chemokines in the TME that promotes anti-tumor immunity by recruiting and activating immune cells. Elevated levels of CXCL11 and CCL19 are associated with increased CD8<sup>+</sup> T-cell infiltration and formation of Tertiary Lymphoid Structures (TLS), crucial for supporting and maintaining active anti-tumor T-cell responses.



Serum levels of IL12, CXCL11 and CCL19 in BI-1808 single agent patients during first treatment cycle. Responders are defined as CR, PR and SD > 6 months; non-responders are defined as PD and SD < 6 months.



Contact information  
Contact information: clinicaltrials@biolinvent.com  
Study identifier: NCT04752826

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