

BI-1808 + pembrolizumab induces durable responses in heavily pretreated ovarian cancer

Targeting TNFR2 depletes Tregs and remodels the tumor microenvironment to enhance antitumoral immune response in ovarian cancer.

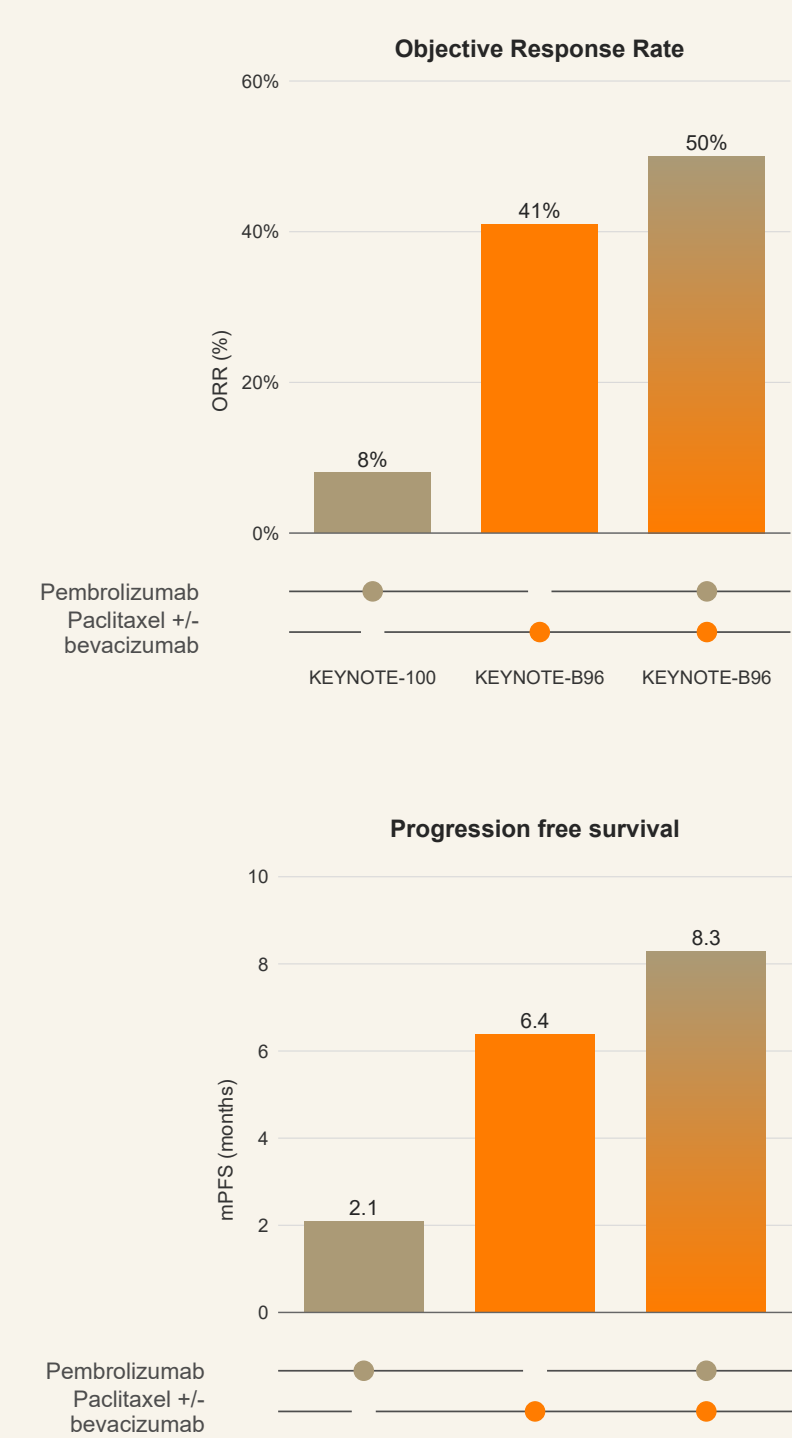
Results

- As of September 14, 2026, cohort enrollment of Part B had completed. Out of 34 subjects eligible for disease response assessment, 1 CR and 7 PRs were recorded (ORR 24%), and a disease control rate of 53% with several stable disease cases exceeding 10 months.
- An early readout of progression free survival suggests a mPFS of 4.1 months as compared to previously reported 2.1 months with pembrolizumab monotherapy assessed through RECIST.
- mPFS assessed per IRECIST (mPFS) was 10.3 months, highlighting the impact of delayed but durable response previously reported for BI-1808.
- Responses were seen in both HGSA and clear cell histology, including patients with active liver metastases.
- Patients were heavily pretreated, with a median of 4 prior regimens. 14.7% of patients had received prior anti-PD-(L)1 therapy. One patient with PR had received pembrolizumab as regimen 4 of 10, with PD as best response to it.
- Immune biomarkers confirmed significant Treg depletion and robust CD8⁺ T-cell activation.

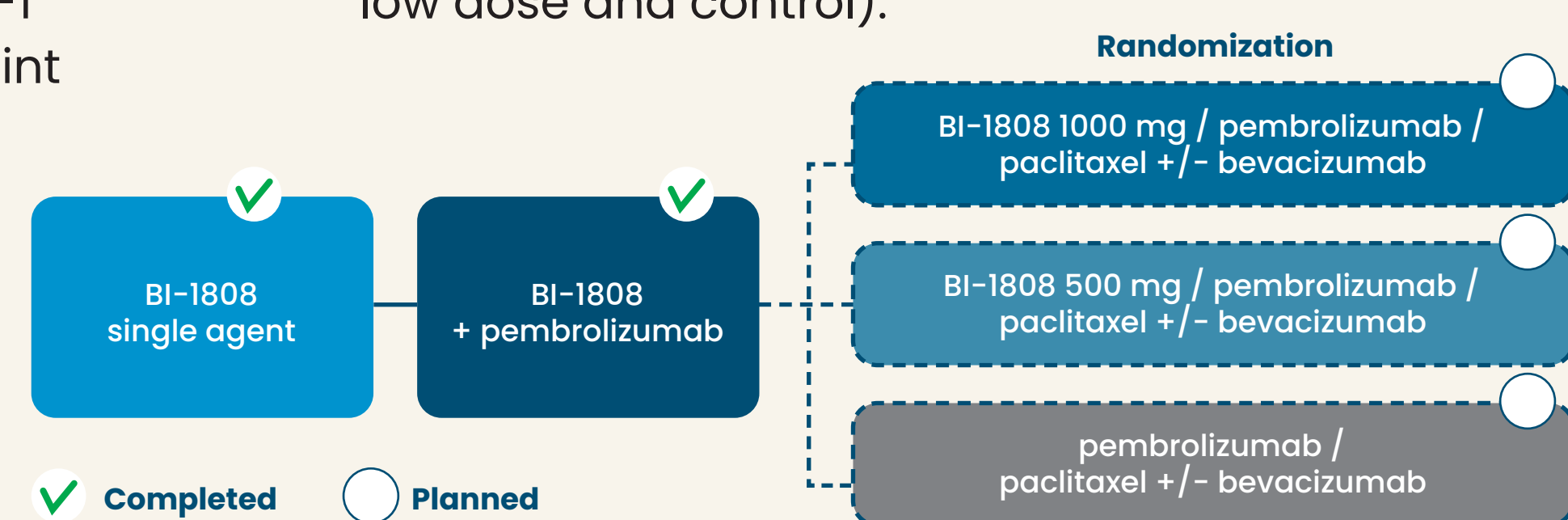
Next Step

Addition of paclitaxel +/- bevacizumab

- Weekly paclitaxel, often with bevacizumab, has been standard of care in PRROC. KEYNOTE-B96³ recently added an immunotherapy option to this backbone: in the over all population, pembrolizumab plus paclitaxel +/- bevacizumab improved median PFS (8.3 vs 6.4 months) and OS (17.7 vs 14.0 months) versus chemotherapy alone — the longest survival reported to date in this setting, and a rare positive result after decades of largely negative trials in PRROC. This establishes an immunotherapy-based chemotherapy backbone for further development, and pembrolizumab + paclitaxel +/- bevacizumab is now a natural platform for testing novel agents in this indication.



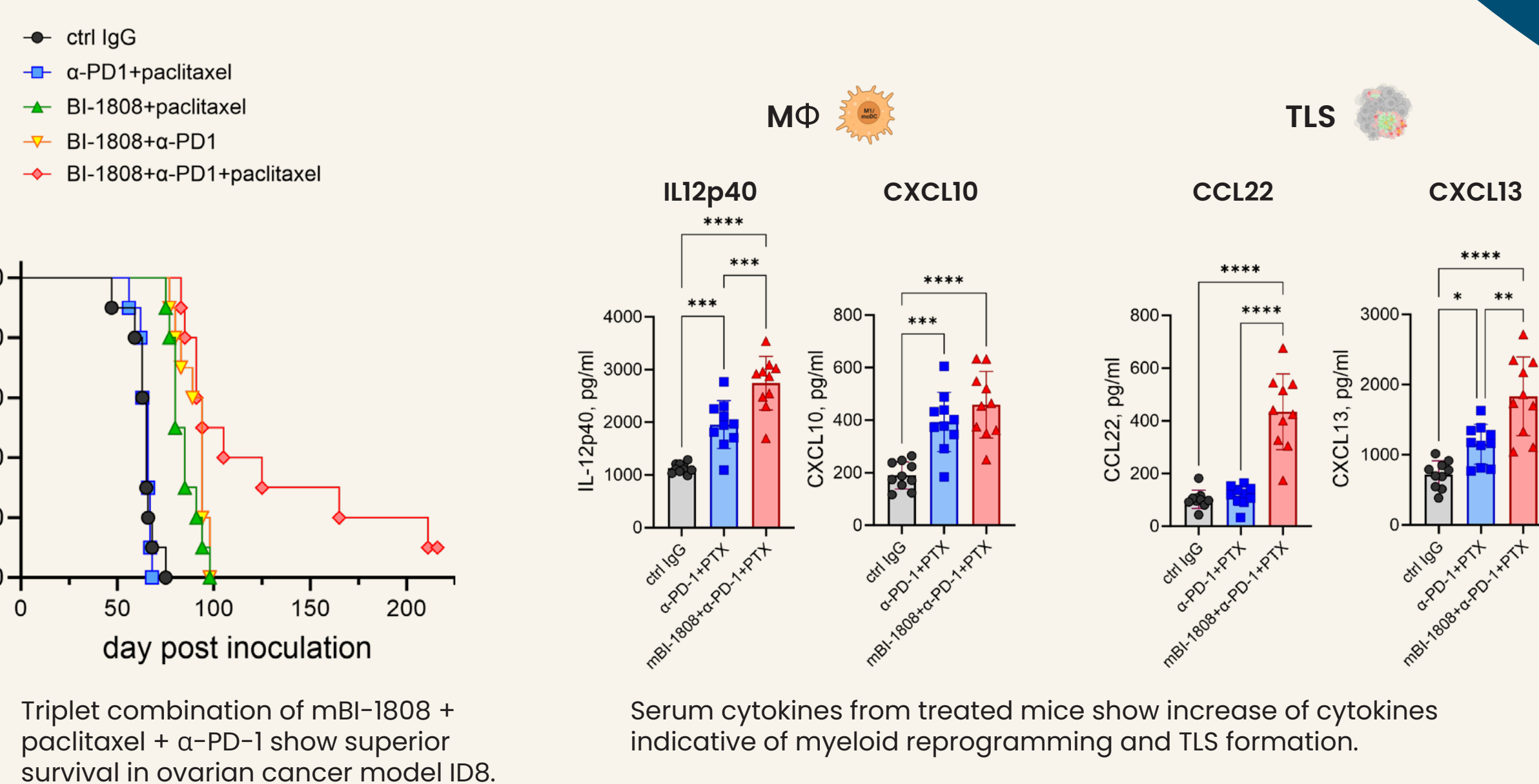
- The next question is whether targeting an additional, complementary mechanism of immune suppression can further enhance this activity. BI-1808 is a TNFR2-directed agent that modulates the tumor microenvironment; BI-1808 + pembrolizumab has shown promising early clinical activity in recurrent ovarian cancer (ORR 24%, mPFS 4.1 months) — a marked improvement over single agent pembrolizumab in KEYNOTE-100⁴ (ORR 8%, mPFS 2.1 months) — providing an initial signal that combining TNFR2-directed TME modulation with PD-1 blockade adds activity beyond checkpoint inhibition alone.



- Building on both signals, BI-1808 + pembrolizumab + paclitaxel +/- bevacizumab will be explored as a next-generation, mechanism-driven regimen combining T-cell checkpoint activation, TME modulation, and tumor-directed chemotherapy — a logical next step to further improve outcomes in this population. Preclinical data combining BI-1808 with paclitaxel show promising additive or synergistic effects. Part C of the current study will investigate addition of weekly paclitaxel +/- bevacizumab. This cohort will enroll 20 patients in each of three arms (high dose, low dose and control).

Preclinical data on combination

Triplet combination of BI-1808 + paclitaxel + α -PD-1 show superior survival in ovarian cancer model and increase of MoA-reflective cytokines



About the model: Disseminated intraperitoneal ID8 resembles HGSA ovarian cancer. ID8 cells and spheroids initially disseminate through the peritoneal fluid and engraft in omental spots where TGF- β and VEGF support angiogenesis, matrix remodeling, adhesion, and invasion. Over 2-3 weeks, tumors develop across the peritoneum, liver capsule, mesentery, pancreas, spleen, reproductive tract, and bowel. Over time, impaired lymphatic drainage can lead to malignant ascites; mice typically die from tumor burden between 8 and 12 weeks. ID8 is regarded as modestly susceptible to paclitaxel. In this study a high dose intensity of 20 mg/kg was utilized.

From Modest to Meaningful: Targeting TNFR2 with BI-1808 to Unlock Checkpoint Inhibitor Efficacy in Platinum-Resistant Recurrent Ovarian Cancer (PRROC)

Introduction

The Problem: Checkpoint blockade alone is insufficient when the tumor microenvironment remains immunosuppressive. In solid tumors, antitumor T-cell activity is constrained by multiple suppressive mechanisms, including TNFR2-expressing regulatory T cells and suppressive myeloid populations.

The Opportunity: BI-1808 targets the immunosuppressive microenvironment, not just the T cell. It is a ligand-blocking, Fc γ R-engaging TNFR2 antibody designed to deplete highly suppressive intratumoral Tregs and remodel the myeloid compartment, thereby promoting recruitment, activation and expansion of tumor-reactive CD8⁺ T cells.

The Clinical Translation: Ovarian cancer (OC) offers a clinically relevant first setting to test this mechanism. TNFR2⁺ immunosuppressive cells, e.g. Tregs and TAMs are enriched in the ovarian cancer tumor microenvironment and associated ascites, where they exhibit potent immunosuppressive activity — supporting TNFR2 as a biologically relevant target in this disease.

The clinical benefit of pembrolizumab + paclitaxel +/- bevacizumab (KEYNOTE-B96) in platinum-resistant recurrent ovarian cancer (PRROC) further supports the rationale for combining T-cell activation with strategies that address additional mechanisms of immune suppression.

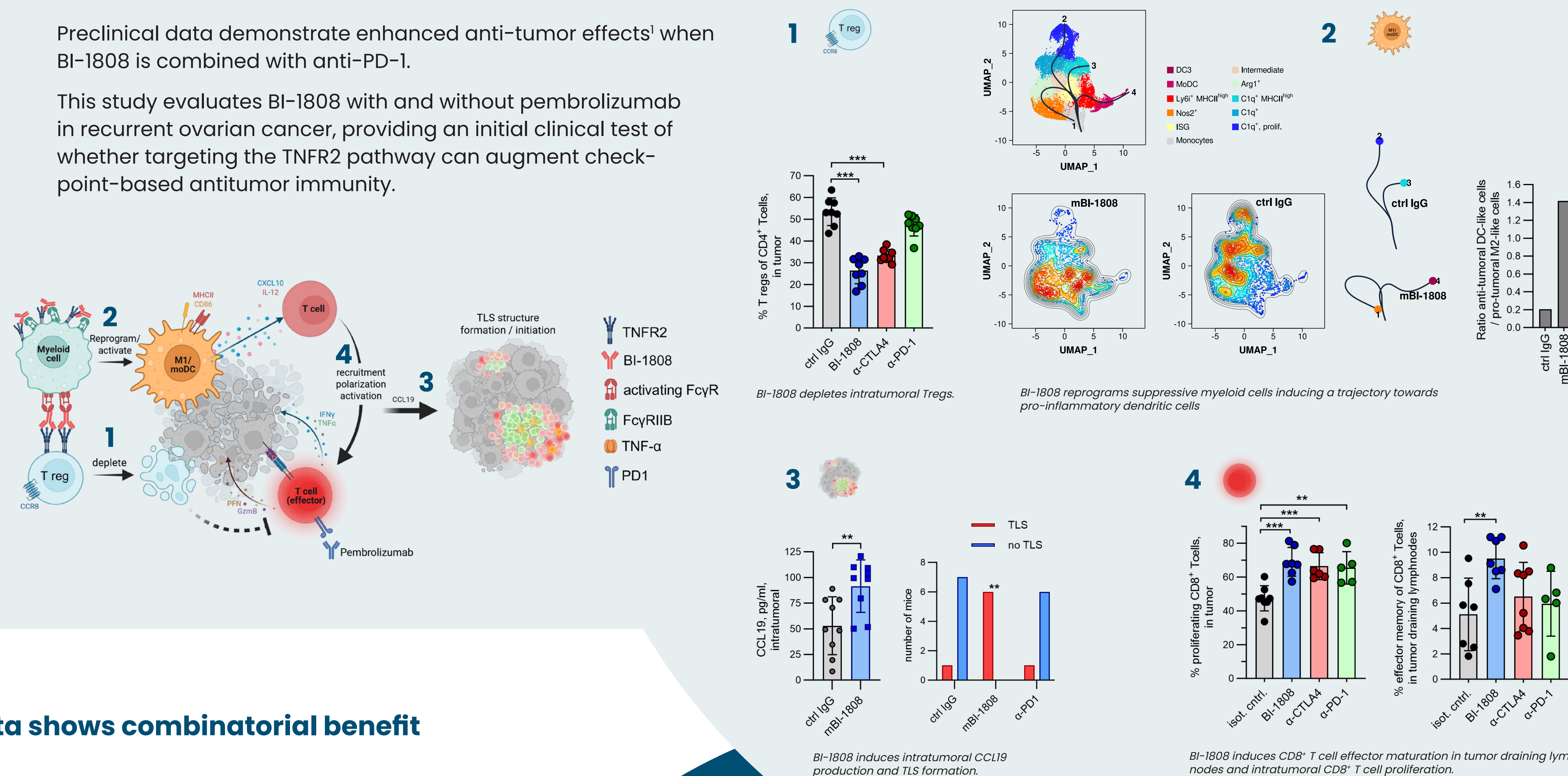
We are evaluating whether targeting TNFR2-driven immune suppression with BI-1808 can remodel the tumor microenvironment and enhance the antitumor activity of established immunotherapy-based regimens in ovarian cancer.

Rationale

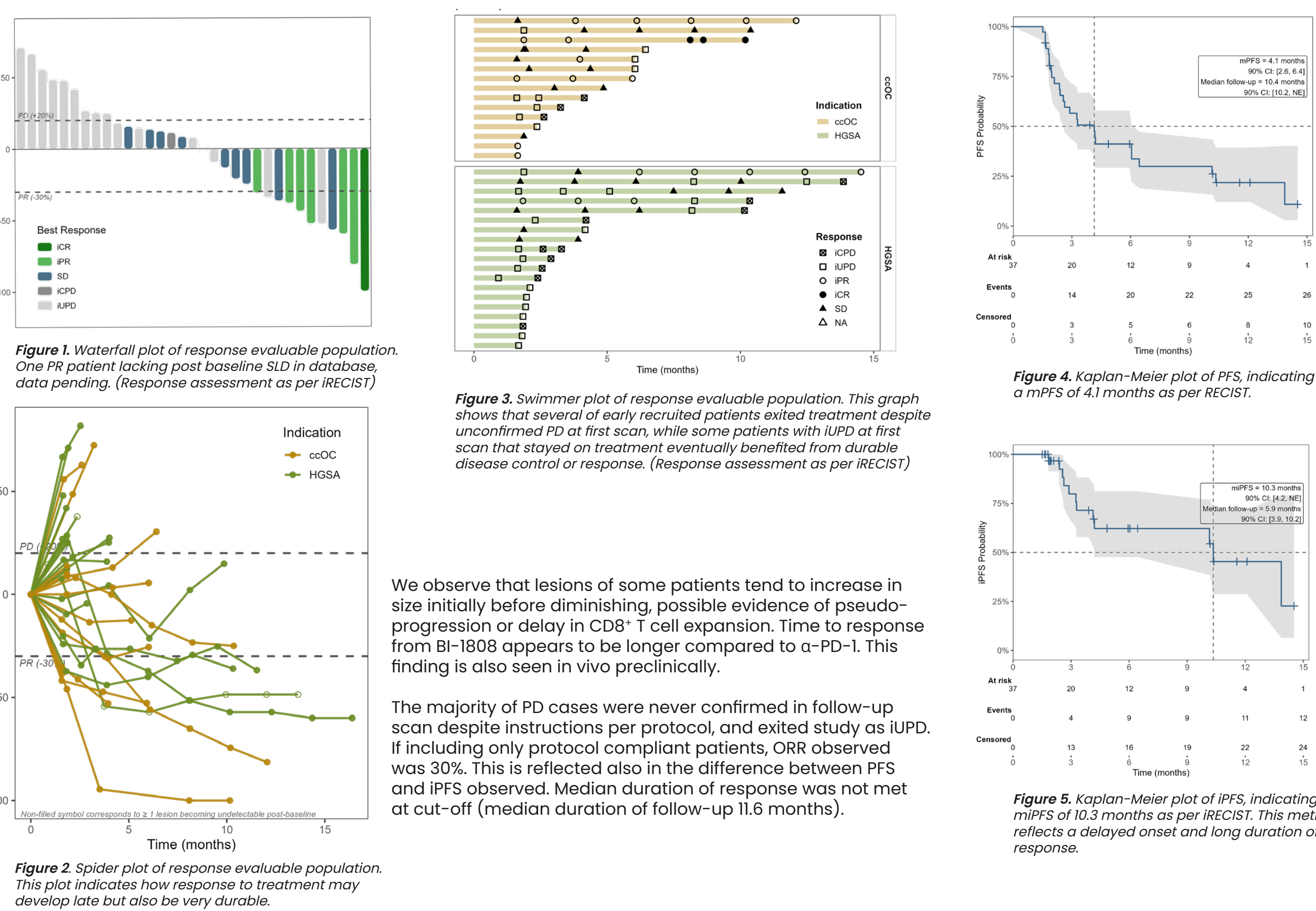
PD-1 blockade can activate antitumor T cells, but its activity may remain constrained by the suppressive tumor microenvironment. BI-1808 targets this immune resistance through TNFR2-directed depletion of suppressive Tregs, modulation of the myeloid compartment, TLS induction and CD8⁺ T-cell activation.

Preclinical data demonstrate enhanced anti-tumor effects¹ when BI-1808 is combined with anti-PD-1.

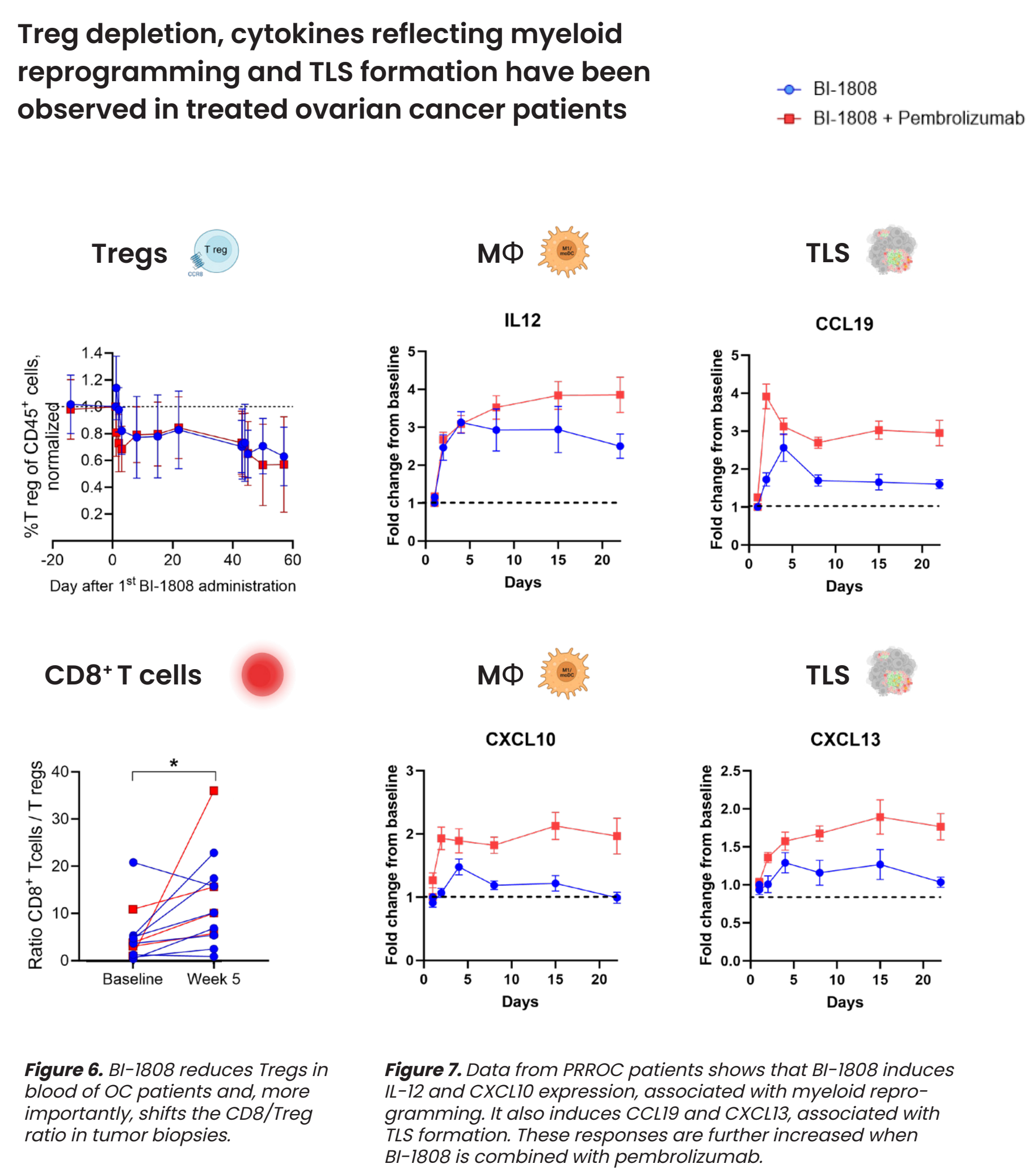
This study evaluates BI-1808 with and without pembrolizumab in recurrent ovarian cancer, providing an initial clinical test of whether targeting the TNFR2 pathway can augment checkpoint-based antitumor immunity.



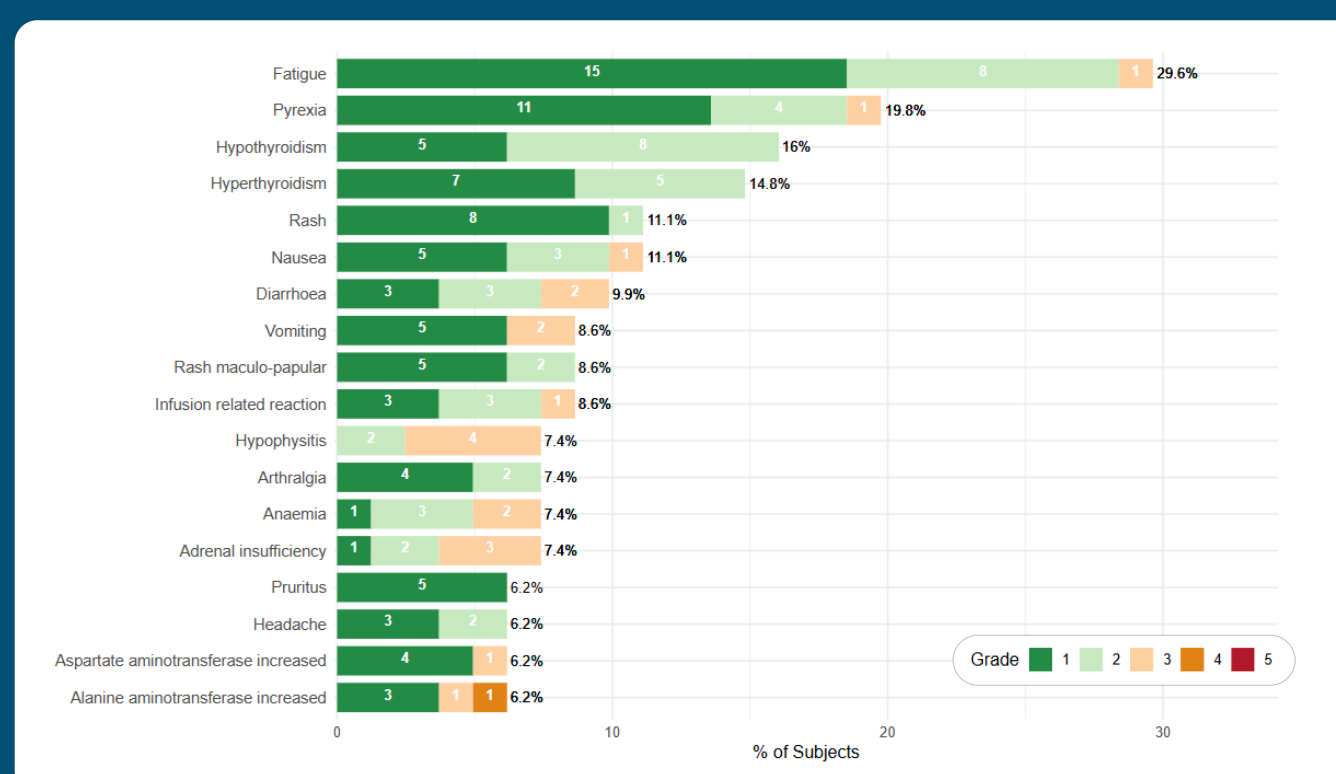
Phase 2a Part B (BI-1808 + pembrolizumab): Efficacy in ovarian cancer cohort



Translational data shows combinatorial benefit



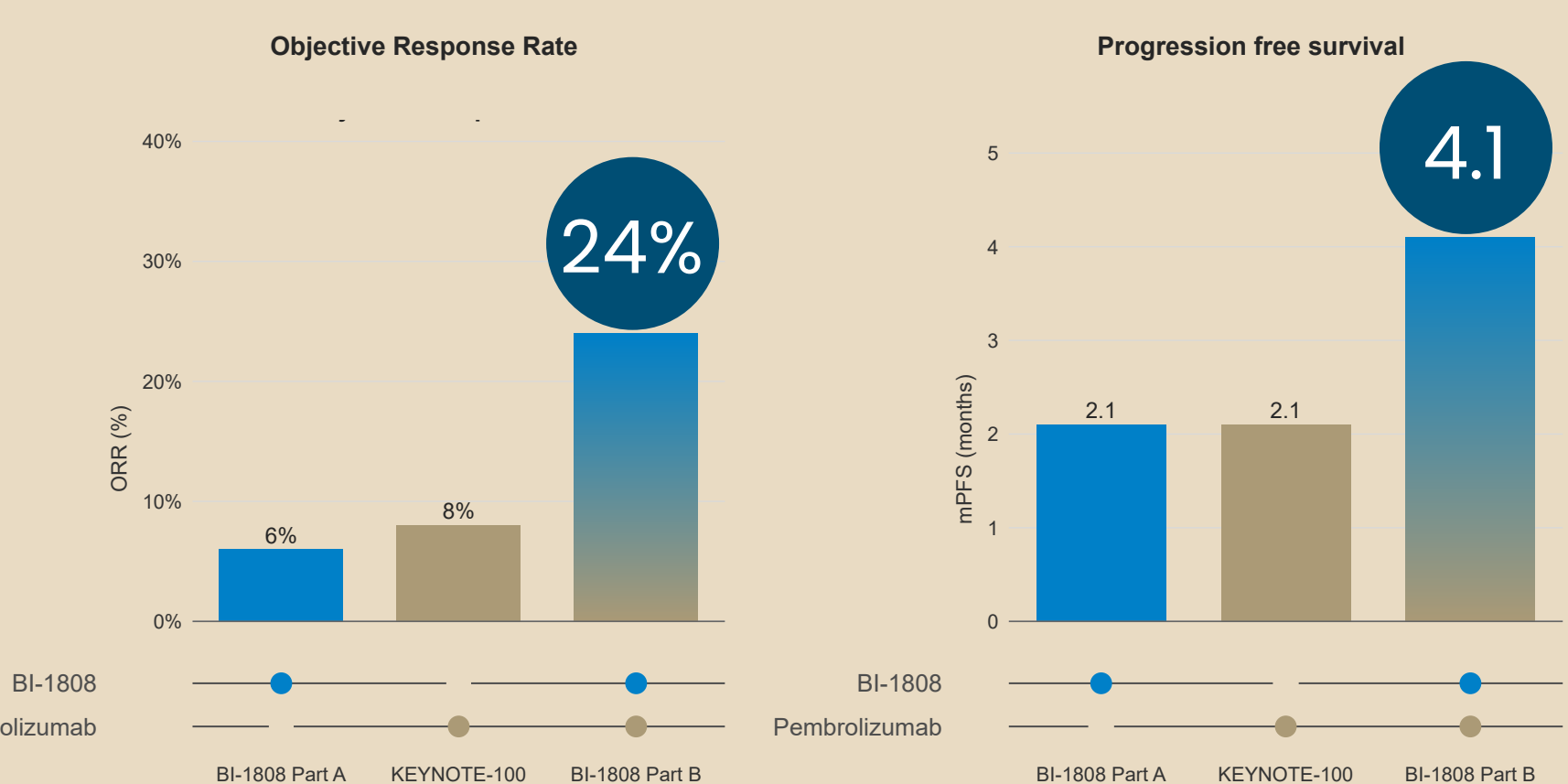
BI-1808 is well tolerated in combination with pembrolizumab in heavily pretreated patients across a range of solid cancer indications



- To date, 81 patients with solid cancer have been administered BI-1808 + pembrolizumab
- Manageable immune related AEs
- Low rate of Grade $\geq$ 3 AEs
- Low rate of treatment related discontinuations in combination arm (<5%)

Conclusions

BI-1808 in combination with pembrolizumab was very well tolerated and demonstrated clinical activity in patients with heavily pretreated PRROC, significantly exceeding efficacy of single agent therapy. Most importantly: disease control and response observed are durable, with 6 patients still on treatment at cut-off date.



The observed clinical signal, together with supportive preclinical findings, provides a rationale for further clinical evaluation of BI-1808 in combination with the pembrolizumab, weekly paclitaxel +/- bevacizumab backbone. Part C will investigate this regimen and include a randomization component, with first data expected H2 2027.



Contact information

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Study identifier: NCT04752825
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