EHA-1227

Targeting the Resistance to Rituximab Through FcγRIIB Blockade: BI-1206 + Rituximab + Acalabrutinib Shows Powerful Activity in R/R NHL

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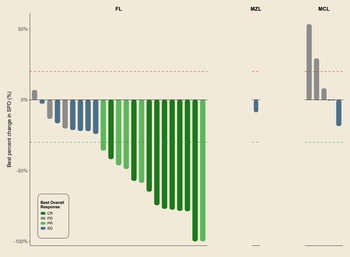
Introduction

Anti-CD20 antibodies remain central to the management of NHL, yet a substantial proportion of patients exhibit primary resistance or early relapse. FcγRIIb-mediated rituximab internalization is a known resistance-mechanism, and higher tumor FcγRIIb levels correlate with poor responses.

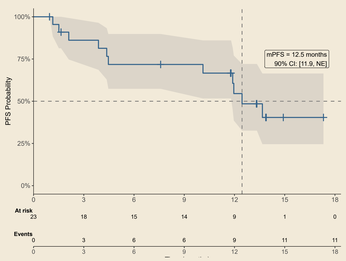
BI-1206, an anti-FcγRIIb IgG1 antibody, blocks this internalization and preserve/restore rituximab activity. In relapsed/refractory FL patients, BI-1206 plus rituximab achieved a 61% ORR, 39% CRR and mPFS of 12.5 months.

In this poster we present 23 disease evaluable patients treated with BI-1206 in combination with rituximab + acalabrutinib, a.k.a. BI-1206 triplet, as per data cut-off May 6, 2026.

Previously observed efficacy in BI-1206 + rituximab doublet



Waterfall plot of BI-1206 + rituximab doublet across NHL subtype. Response assessed through FDG-PET according to Lugano criteria.



Progression free survival probability in FL subset after treatment with BI-1206 + rituximab doublet.

Rationale

The ROSEWOOD trial[1] showed that adding the BTK inhibitor zanubrutinib (Z) to the Fc-engineered anti-CD20 antibody obinutuzumab (O) increased ORR from 45% to 69%, and mPFS from 10.4 to 28 months.

In contrast, adding the BTK inihibitor acalabrutinib to rituximab resulted in only 31% ORR and mPFS of 8.3 months[2], despite similar kinase profiles for acalabrutinib and zanubrutinib.

These findings suggest that the greater activity of the OZ regimen resulted from improved CD20-targeting, highlighting the need to overcome rituximab resistance.

Tumor FcγRIIB-mediated internalization is a principal driver of rituximab resistance. Because BI-1206 directly targets this mechanism, and obinutuzumab shows reduced but not blunted FcγRIIB-mediated internalization, combining BI-1206 with rituximab + acalabrutinib has the potential to further improve treatment responses.

Study Overview

This single-arm study evaluates BI-1206 with rituximab and acalabrutinib in up to 30 patients with relapsed or refractory NHL, with a focus on FL.

The design compares two subcutaneous (SC) BI-1206 doses of 150 and 225 mg. BI-1206 plus rituximab is administered QW during a 4 week induction. Patients with disease control at week 6 may receive a 2nd induction, then maintenance every eight weeks for up to six cycles. Acalabrutinib is given at 100 mg twice daily for 1 year.

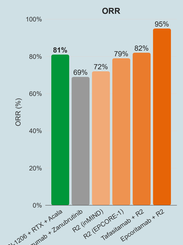
During safety run-in (first six patients per dose level), patients with mantle cell lymphoma (MCL) and marginal zone lymphoma (MZL) subtype were also eligible for enrollment.

Disease response is assessed per Lugano criteria, i.e. through metabolic response assessment through CT guided FDG-PET when possible.

BI-1206 has previously demonstrated capacity to restore rituximab sensitivity in NHL, and follicular lymphoma (FL) in particular.

Addition of BTK inhibition through acalabrutinib leads to an additional boost in efficacy, and the triplet combination provides an ORR of >80%.

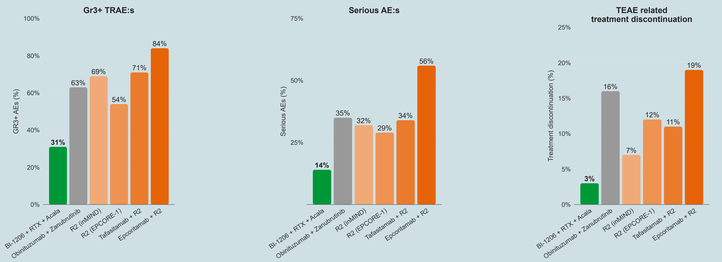
Efficacy



BI-1206 triplet compared to standard and emerging treatments in R/R FL

- When comparing to recent trials with similar inclusion criteria[2,3,4], this early study readout show that BI-1206 triplet results in a robust ORR signal, on par with R2, and even the recently approved tafasitamab + R2 combination[3].
- The BI-1206 triplet exhibit a very favorable safety comparison to R2-based therapies, with low rate of serious AE:s and TEAE related discontinuation.
- Addition of acalabrutinib to BI-1206 + rituximab adds to the efficacy, without inflating toxicity.

Safety



Conclusions

This BI-1206 triplet regimen drives formidable efficacy (ORR 81%) in R/R FL, coupled with an uncompromised tolerability profile.

The BI-1206 triplet exhibits response rates consistent with established clinical benchmarks, including standard of care R2 therapy and recent tafasitamab+R2 data, underscoring its potential as a highly competitive therapeutic option in this landscape.

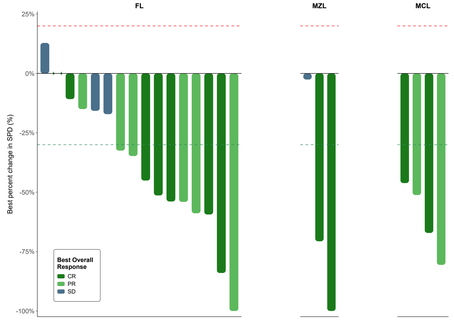
Anchored by an R2-matching mPFS of ~12.5 months (BI-1206 doublet), incorporating acalabrutinib creates a comprehensive triplet therapy. This regimen yields substantial response rates in R/R FL, demonstrating clear clinical efficacy and well-tolerated safety.

By targeting a critical gap in the management of relapsed/refractory NHL, the BI-1206 triplet represents a highly promising therapeutic intervention. Provided that late-stage clinical trials continue to validate its durable efficacy and favorable safety profile, this combination regimen is poised to secure a prominent role in the future treatment landscape.

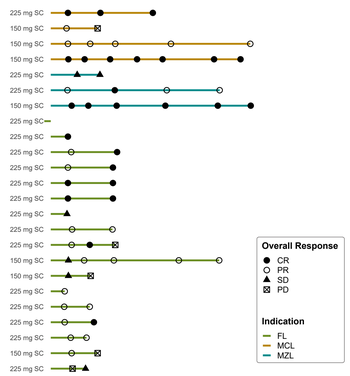
Preliminary Efficacy

As of data cut-off May 6, 2026 , objective response rate in total population was 83%. Among 23 evaluable patients, 11 achieved complete responses (CR), 8 partial responses (PR), and the remaining patients all exhibited stable disease as best response. In the FL subset (n=16), ORR was 81% and CRR 44%.

The cohort has been completely enrolled, but response assessment has not yet occurred for all patients. As majority of patients are still on treatment, any PFS calculation is yet premature.



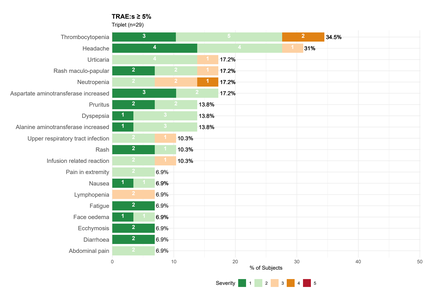
Waterfall plot of BI-1206 + rituximab + acalabrutinib triplet across NHL subtype. Response assessed through FDG-PET according to Lugano criteria.



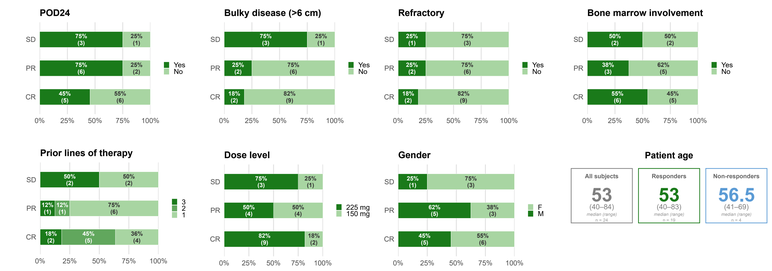
Swimmer plot of BI-1206 + rituximab + acalabrutinib triplet across NHL subtype. Response assessed through FDG-PET according to Lugano criteria.

Safety Overview

Treatment-related serious AEs were observed in 4 (14%) patients and discontinuation due to drug related AE in 1 patient. Thrombocytopenia was transient in nature with no associated bleeding.



Patient characteristics



1) Zinzani et al. **JCO** 2023 "ROSEWOOD: A Phase II Randomized Study of Zanubrutinib Plus Obinutuzumab Versus Obinutuzumab Monotherapy in Patients With Relapsed or Refractory Follicular Lymphoma"

2) Strati et al. **Br J Haem** 2024 "Acalabrutinib alone or in combination with rituximab for follicular lymphoma: An open-label study"

3) Sehn et al. **Lancet** 2026 "Tafasitamab, lenalidomide, and rituximab in relapsed or refractory follicular lymphoma (inMIND): a global, phase 3, randomised controlled trial"

4) Falchi et al. **Lancet** 2025 "Epcoritamab, lenalidomide, and rituximab versus lenalidomide and rituximab for relapsed or refractory follicular lymphoma (EPCORE FL-1): a global, open-label, randomised, phase 3 trial"

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