(PF953) TARGETING RESISTANCE TO RITUXIMAB THROUGH FCGRIIB (CD32B) BLOCKADE: BI-1206 + RITUXIMAB + ACALABRUTINIB SHOWS POWERFUL ACTIVITY IN R/R NHL

Topic: 18. Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

Laura Fogliatto*[1], Eduardo Munhoz[2], Ana Costa Cordeiro[3], Guilherme Fleury Perini[4], Don Stevens[5], Mariana Bastos-Oreiro[6], Eva Domingo[7], Daniel Morillo[8], Agustin Penedo Coello[9], Erika Bågeman[10], Danijela Lindahl[10], Ingrid Karlsson[10], Linda Mårtensson[10], Zinnia Parra-Guillen[10], Dmytro Piliuhin[10], Karianne Risberg Handeland[10], Anette Sundstedt[10], Ingrid Teige[10], Johan Wallin[10], Björn Frendeus[10], Andres McAllister[10]

[1]Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil;[2]Hospital Erasto Gaertner - Liga Paranaense de Combate ao Câncer, Curitiba, Brazil; [3]A.C. Camargo Cancer Center, São Paulo, Brazil; [4]Hospital Israelita Albert Einstein, São Paulo, Brazil; [5]Norton Cancer Institute - Saint Matthews, Louisville, United States of America; [6]Hospital General Universitario Gregorio Marañón, Madrid, Spain; [7]Hospital Duran i Reynals- Institut Catala d'Oncologia, Barcelona, Spain;[8]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; [9]University Hospital HM Sanchinarro. START Madrid CIOCC, Madrid, Spain; [10]BioInvent International AB, Lund, Sweden;

Background

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 restores rituximab activity. In relapsed/refractory FL patients, BI-1206 plus rituximab achieved a 59% ORR with good tolerability.
The ROSEWOOD trial showed that adding the BTKi zanubrutinib (Z) to the Fc-engineered anti-CD20 antibody obinutuzumab (O) increased ORR from 45% to 69%. In contrast, adding the BTKi acalabrutinib to rituximab resulted in only 31% ORR, 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 plus acalabrutinib has the potential to further improve treatment responses.

Aims

Assess safety and efficacy of BI-1206 in combination with rituximab and acalabrutinib in R/R NHL.

Methods

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

Results

As of Jan 26, 2026, 23 patients were treated with BI-1206 in combination with rituximab and acalabrutinib. Nineteen patients experienced treatment-related AEs, the majority of which were mild or moderate (86%). Nine patients had Gr 3 events considered related or possibly related to study treatment: three patients with neutropenia, two with lymphopenia, two patients with IRR related to rituximab. The following Gr 3 events were recorded once: thrombocytopenia, headache, increased transaminases, urticaria and maculo-papular rash.
No treatment-related serious AEs and no Gr 4/5 events were observed.
The overall response rate observed was 80%. Among 20 evaluable patients, 7 achieved complete responses, 9 partial responses, and the remaining patients all exhibited stable disease as best response. In the FL subset (n=13), ORR was 77%. At cut-off date, average treatment duration reached was 4 months. Five patients completed the study duration of one year. Study is still ongoing and data is expected to mature.

Summary/Conclusion

The combination treatment was well tolerated and demonstrates a highly promising therapeutic effect in R/R FL, achieving an ORR of 77%. Taken together with the approximately 80% ORR usually observed with SoC R2 therapy, these data suggest that the BI-1206 triplet may offer at least comparable efficacy with a highly manageable safety profile.
In this heavily pretreated R/R NHL population with limited therapeutic options, the BI-1206 triplet delivers robust, durable responses and a beneficial, manageable safety profile, making it a compelling future treatment option for patients with R/R FL.
We acknowledge AstraZeneca for providing acalabrutinib.

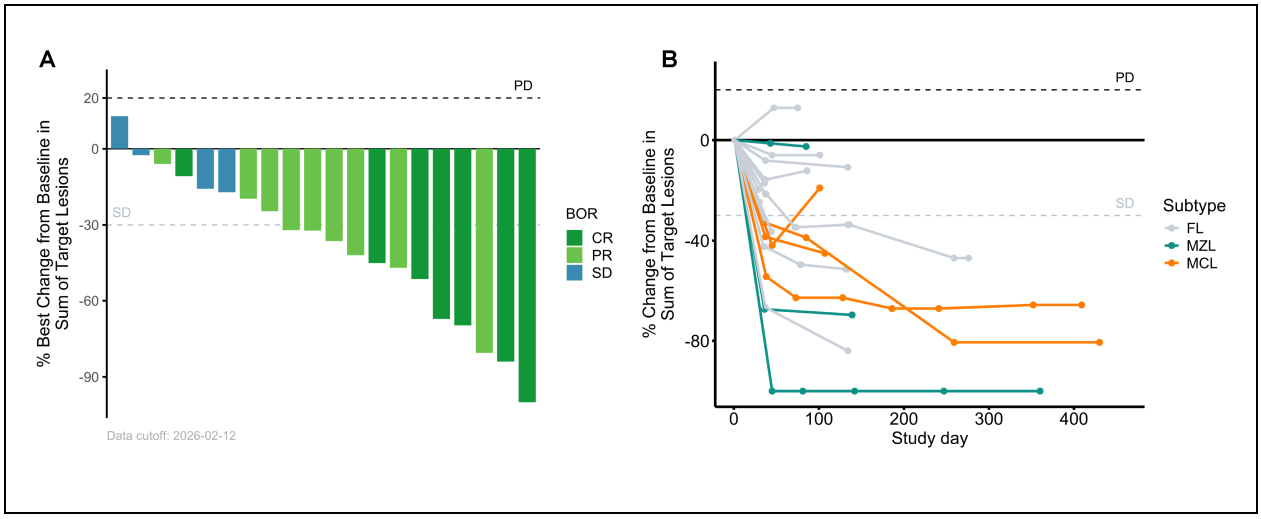

Figure 1 A) Waterfall plot depicting best response as assessed by Lugano criteria (FDG-PET if available, else CT) and largest decrease in tumor burden as assessed by CT. B) Spider plot depicting tumor burden (sum of perpendicular diameter) versus time from treatment start. Color indicate NHL subtype.