ASH # 5349

Session: 623

Mantle Cell, Follicular, Waldenstrom's, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological: Poster III

Promising efficacy of BI-1206, an Antibody targeting FcγRIIB, in Combination with Rituximab and Acalabrutinib in R/R NHL Patients

L. M. Fogliatto[1], A.C. Cordeiro[2], E. Domingo Domenéch[3], D. Morillo[4], A Penedo[5], E. Bågeman[5], D. Lindahl[5], I. Karlsson[6], L. Mårtensson[6], Z. P Parra-Guillen[6], D. Piliuhin[6], K Risberg Handeland[6], I. Teige[6], J. E. Wallin[5], B. Frendeus[5], A. McAllister[6]

[1] Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; [2] A.C. Camargo Cancer Center, São Paulo, Brazil; [3] Hospital Duran i Reynals, Institut Catala d'Oncologia, Barcelona, Spain; [4] University Hospital Fundacion Jimenez Diaz, Madrid, Spain; [5] University Hospital HM Sanchinarro, START Madrid CIOCC, Madrid, Spain; [6] BioInvent, Lund, Sweden

Background

Anti-CD20 antibodies like rituximab are crucial for treating non-Hodgkin's B-cell lymphoma. However, 15% of patients do not respond to treatment, and 25% relapse within 3 years following treatment.

One contributing resistance mechanism is through the inhibitory Fc receptor FcγRIIB. Activation of this receptor triggers rituximab internalization, and high intratumoral FcγRIIB expression correlates with markedly lower response rates in FL, MCL, and DLBCL.

BI-1206, an anti-FcγRIIB IgG1 antibody, blocks rituximab internalization and enhances its efficacy. In R/R FL patients, BI-1206 combined with rituximab showed promising results, with a 59% ORR (CRR 41%, DCR 86%, n=22) and excellent tolerability when administered subcutaneously.

Rationale

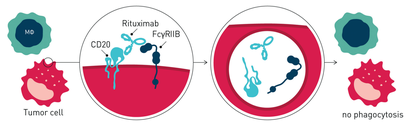
The combination of obinutuzumab + zanubrutinib in the ROSEWOOD[1] trial demonstrated a beneficial effect of adding BTK inhibition to CD20 blockade for the treatment of FL. Obinutuzumab vs obinutuzumab + zanubrutinib, showed an ORR increase from 45% to 69%.

Addition of BTKi to rituximab (Strati et al[2]) did not provide a similar additional value, speaking to the need to adress rituximab resistance.

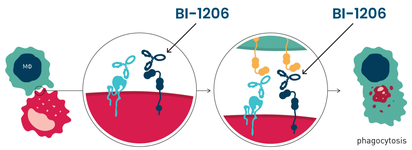
As BI-1206 specifically targets the mechanism of resistance to rituximab, the combination of BI-1206 with rituximab and the next-generation BTKi acalabrutinib is expected to provide a safe and effective treatment for NHL patients.

Overcoming rituximab resistance

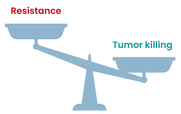
FcγRIIB-receptor removes rituximab from CD20 so immune cells fail to attack the tumor



With blockade of the FcγRIIB-receptor, the immune effector cells can kill the tumor cell



FcγRIIB blockade (BI-1206) may overcome rituximab resistance by several mechanisms acting on tumor and immune effector cells.



	CD20 internalization	Activating FcγR-dependent Tumor cell killing
rituximab	+++	-
Fc-engineered aCD20 (e.g. obinutuzumab)	+	+ (FcγRIIIa)
rituximab + FcγRIIB blockade (BI-1206)	-	+++ (FcγRI/IIa/IIIa)

Comparison of rituximab, Fc-engineering, and FcγRIIB blocking strategies to counteract resistance and enhance tumor B cell killing.

References

[1] Zinzani et al JCO 2023 41(33), [2] Strati et al Br J Hem 2024 205(6)

Combination treatment of BI-1206, rituximab and acalabrutinib shows impressive response rates in R/R NHL, resetting one of the main resistance mechanisms to rituximab

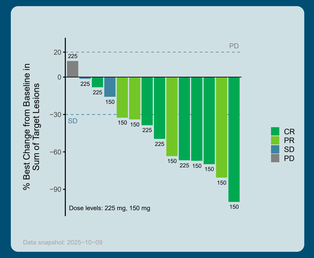
Preliminary efficacy

With the completion of the safety run-in portion of the Study 17-BI-1206-02 triplet, 14 patients were evaluable for disease assessment. A high number of responses have been observed (ORR=79%) and warrants continuation trial into the expansion phase of up to 30 patients at 225 mg SC.

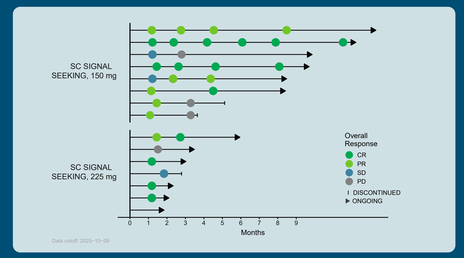
50% of patients showed complete response, and the absolute majority of patients are still on treatment at this date.

There was no apparent difference in safety or efficacy between the two studied dose levels of BI-1206.

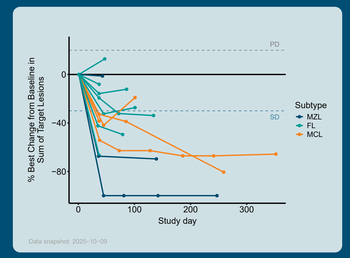
Study 17 BI-1206-02
BI-1206 + rituximab + acalabrutinib



Waterfall plot of safety run-in portion



Swimmer plot of safety run-in portion



Spider plot of sum of longest perpendicular diameter

Safety findings

We report here the results of the safety run-in portion of the study, whereas of October 9th, 2025, 16 patients have been treated with BI-1206 in combination with rituximab + acalabrutinib. 14 patients had recorded AE related to study medication.

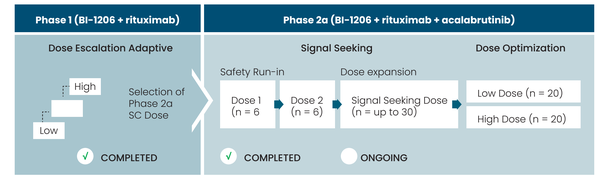
Most adverse events were classified as mild or moderate (87%). Seven subjects had Gr3 events considered related or possibly related to at least one of the study drugs: 4 subjects had Gr3 neutropenia, 2 subjects had Gr3 lymphopenia. The following Gr3 events were recorded in 2 subjects: urticaria and headache (1 subject), IRR, elevated GGT and maculopapular rash (1 subject).

Two serious adverse events were recorded: Gr2 pain in extremity, Gr3 neutropenia.

	SC for BI-1206 IV for rituximab PO for acalabrutinib	
BI 1206 Dose	150 mg	225 mg
Number of subjects	8 (100%)	8 (100%)
Subjects with at least 1 TEAE any grade	7 (86%)	7 (86%)
Subjects with ≥Grade 3 TEAEs	5 (63%)	3 (38%)
Subjects with TEAEs related to study drugs	7 (86%)	7 (86%)
Subjects with ≥Grade 3 TEAEs related to study drugs	5 (63%)	2 (25%)
Subjects with serious TEAEs related to study treatment	1 (13%)	1 (13%)
Subjects with treatment related AEs that led to discontinuation	0	0
Most common adverse events considered related to 1, 2 or all 3 drugs		
Subjects with any grade Neutropenia	3 (38%)	2 (22%)
Subjects with ≥Grade 3 Neutropenia	3 (38%)	1 (11%)
Subjects with any grade Thrombocytopenia	3 (38%)	3 (33%)
Subjects with ≥Grade 3 Thrombocytopenia	0	0
Subjects with any grade Lymphopenia	2 (25%)	0
Subjects with ≥Grade 3 Lymphopenia	2 (25%)	0

Study overview

This is a single arm study of BI-1206 in combination with rituximab and acalabrutinib, aiming to enroll 30 R/R NHL patients in total. It consists of a safety run-in with escalating SC doses of BI-1206 (150 & 225 mg) and an expansion phase at selected dose level. BI-1206 + rituximab is given weekly for a 4-week induction period, and patients exhibiting disease control at week 6 are eligible for an additional induction period, followed by maintenance therapy with dosing of BI-1206 and rituximab every 8 weeks for up to 6 cycles. Acalabrutinib is dosed at 100 mg BID throughout study duration (1 year).



Patient charachteristics

NHL subtype	OR	Sex	Age	Dose	Stage at diagnosis	Prior Treatment	POD24 status	ECOG	Bone marrow involvement
FL	SD	M	67	150	II	R-CHOP, R + copanlisib/placebo, R-GEMOX	NO	0	YES
FL	PR	M	56	150	III	R-CHOP	YES	1	YES
FL	CR	F	66	225	III	R-EPOCH, GemOX	YES	2	NO
FL	PD	F	46	225	IV	R-CHOP	YES	1	YES
FL	CR	F	49	225	III	R-CHOP, ICE, DHAX	YES	1	NO
FL	CR	F	56	225	III	R-CHOP	NO	1	YES
FL	PR	F	41	150	III	R-CHOP	YES	0	YES
MCL	CR	M	74	150	IV	R-CHOP, D-DHAP, Obinutuzumab + Glofitamab + Polatuzumab vedotin	YES	1	YES
MCL	PR	M	83	150	III	R-Bendamustine	NO	1	NO
MCL	PR	F	80	150	IV	R-CHOP, R, R-GemOX	YES	0	NO
MCL	CR	M	53	225	III	R-DHAOX, R	YES	0	YES
MZL	CR	M	61	150	II	R-Bendamustine	NO	1	NO
MZL	CR	F	52	150	UNKOWN	R-CVP, ICE	YES	0	YES
MZL	SD	F	41	225	IV	R-CHOP	UNKOWN	1	YES

OR = Best recorded objective response to current study treatment
POD24 = Patients who showed progress within 24 months after initial therapy

Conclusions

Combination treatment of SC BI-1206 + rituximab + acalabrutinib appears safe and well tolerated, and results in high response rates, with 50% of patients achieving a complete response.

The treatment combination shows promise to become the safest and most efficacious treatment option in subjects with indolent B-cell non-Hodgkin's lymphoma (NHL) who have relapsed or are refractory to rituximab.

Contact information

Contact information: clincialtrials@bioinvent.com
Study identifier: NCT03571568

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