Robust and Durable Clinical Responses Observed Following Treatment with AB-101, an Allogeneic NK Cell Therapy, Combined with Rituximab in Patients with Severe Rheumatoid Arthritis and Inadequate Response to Multiple Prior Targeted Therapies

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IRIS Research + Development

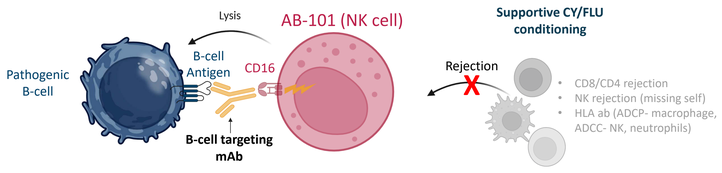
Background

Deep B-cell depletion achieved with CAR T-cell therapy has produced high rates of durable remission across multiple autoimmune diseases. However, CAR T-cell therapy is associated with significant safety risks, including cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS), as well as inpatient administration, manufacturing complexity, high cost, and limited accessibility.

AB-101 is a non-genetically modified, allogeneic, off-the-shelf, cryopreserved natural killer (NK) cell therapy that, in combination with B-cell–targeting monoclonal antibodies (mAbs), has the potential to induce profound B-cell depletion via antibody-dependent cellular cytotoxicity (ADCC) without the risks inherent to CAR T-cell therapy. This approach has recently demonstrated deep and durable B-cell depletion in outpatient clinical trials combining AB-101 with anti-CD20 mAbs.

IRIS-RD-01 is an investigator-initiated study evaluating AB-101 in combination with anti-CD20 mAbs in subjects with B-cell driven rheumatologic diseases. Here, we characterize safety, efficacy, and peripheral B-cell depletion and reconstitution kinetics as pharmacodynamic markers of AB-101 activity in 6 subjects with rheumatoid arthritis.

Mechanism of Action



Study Design

IRIS-RD-01 (*NCT06581562*) is an open-label single center study sponsored by Artiva that is assessing the safety and preliminary activity of combining AB-101 and rituximab in B-cell associated autoimmune diseases.

Key Inclusion Criteria
- Meet 2010 ACR/EULAR classification criteria for RA
- Refractory to ≥2 b/tsDMARDs

Endpoints:
- Safety and tolerability
- Pharmacodynamics
- Efficacy: CDAI, DAS28-ESR

AB-101 Treatment Regimen

AB-101 Dose: 1 x 10^9 cells X 3, weekly

Conditioning: Cy/Flu*

Rituximab: 1000 mg x 2, 2 weeks apart

*Fludarabine: 25 mg/m² x 3
Cyclophosphamide: 1000 mg/m² x 1

Abbreviations:
* Biologic / targeted synthetic (b/tsDMARDs), MTX: methotrexate; LEF: leflunomide; pred: prednisone, *MCII: Minimal Clinically Important Improvement*

Baseline Demographics & Disease Characteristics

Subject	RA-IIT-1	RA-IIT-2	RA-IIT-3	RA-IIT-4	RA-IIT-5	RA-IIT-6
Age (y) / Sex	37 / F	39 / F	52 / F	68 / F	42 / F	57 / F
Disease Duration (y)	9	22	7	32	22	22
SJC; TJC	24; 24	13; 10	19; 16	24; 28	7; 11	18; 19
CDAI	57	36	52.5	71	34	55.5
DAS28-ESR	7.8	5.9	7.6	8.9	5.5	7.1
Concomitant medications at baseline	MTX, LEF, pred	MTX, pred	LEF, HCQ, pred	-	pred	MTX, pred
Prior Targeted Therapies (b/tsDMARDs)						
Anti-TNF (#)	2	2	1	1	2	4
JAK inhibitor (#)	1	-	-	-	-	-
Anti-IL-6 (#)	-	1	-	-	-	1
Abatacept (#)	-	-	1	1	-	1
Anti-CD20 (#)	-	1[a]	-	-	1	1
# Distinct Targeted Classes*	**2**	**3**	**2**	**2**	**2**	**4**

Biologic/targeted synthetic (b/tsDMARDs) of separate MoA, e.g. anti-TNF; anti-IL-6; abatacept; anti-CD20; JAK inhibitor. [a]imvotamab (CD20 x CD3 bispecific antibody)

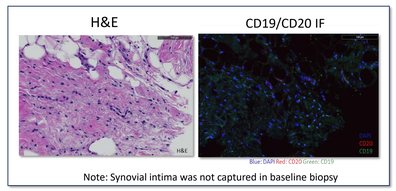
Safety

- No CRS, ICANS, or GvHD reported.
- No SAEs or Grade ≥3 AEs reported.
- Adverse events (AEs) were consistent with those expected with the conditioning regimen and/or rituximab infusion.
- Serum IgG, IgA, and IgM levels were reduced (median ~8%, 19%, and 47%, respectively, at 6 months) but remained within the normal range.
- Vaccine antibody titers (measles, mumps, rubella and tetanus) remained unchanged from baseline.

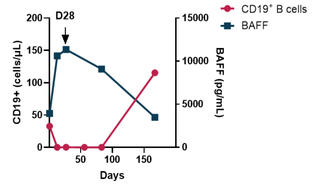
AEs in ≥ 2 Participants	Grade 1-2, n (%)	Grade ≥3 n (%)
Nausea	Gr1: 2 (33.3) Gr2: 4 (66.7)	0
Headache	Gr1: 3 (50.0) Gr2: 1 (16.7)	0
Urinary tract infection	Gr2: 3 (50)	0
Diarrhoea	Gr1: 1 (16.7) Gr2: 1 (16.7)	0
Vomiting	Gr1: 2 (33.3)	0

Pharmacodynamics

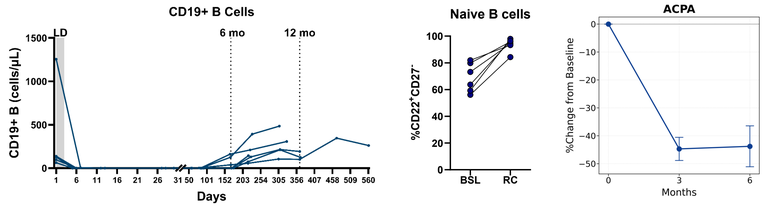
A No CD19+ B cells in synovial biopsy post-treatment



Elevated BAFF levels with B-cell depletion



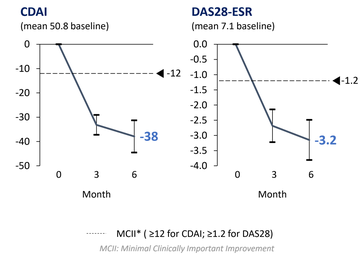
B Deep B-cell depletion, reconstitution with naïve B cells, and reduction in ACPA

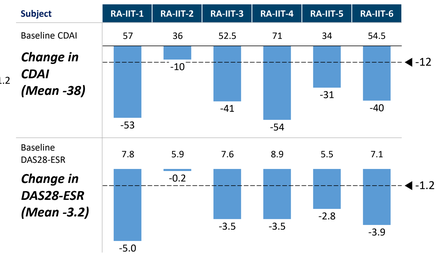


A) Synovial biopsy shows absence of B cells at Day 28 (left) and elevated BAFF associated with tissue depletion (right) in the same subject. B) CD19+ B-cell depletion in RA subjects (n=6), percent change from baseline (Mean ± SEM) at 0, 3, and 6 months and reconstitution with naïve/transitional B cells, Anti-CCP (ACPA). BSL: Baseline, RC: reconstitution

Efficacy

CDAI and DAS28-ESR substantially improved, with 5 of 6 subjects meeting MCII in both scores at 6 months



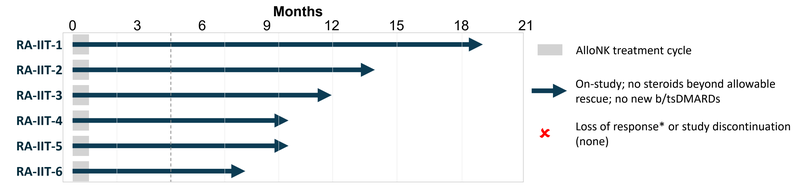


Majority of disease parameters assessed showed ≥ 70% Improvement at 6 months

% Change vs Baseline						
Subject	**RA-IIT-1**	**RA-IIT-2**	**RA-IIT-3**	**RA-IIT-4**	**RA-IIT-5**	**RA-IIT-6**
# Distinct Targeted Classes*	2	3	2	2	2	4
Swollen Joint Counts	-87.5	-7.7	-78.9	-87.5	-100	-100
Tender Joint Counts	-100	-10	-81.3	-71.4	-100	-78.9
Physician Global Assessment	-90.9	-92.9	-88.9	-77.8	-68.8	-70.6
Patient Global Assessment	-71.4	-25	-52.9	-60	-87.5	-11.1
hs-CRP	-29.7	-75.4	-67.4	-56.5	0	-75.8

* Biologic / targeted synthetic (b/tsDMARDs) of separate MoA, e.g. anti-TNF; anti-IL-6; abatacept; anti-CD20; JAK inhibitor
Subject RA-IIT-2: Responded well at Week 12 with 69% reduction in SJC and % 60% reduction in TJC but abruptly discontinued low dose chronic steroids on her own before Week 24 visit leading to a flare at Week 24. This subject had normal ESR (<28mm/hr) and CRP (<3mg/L) at baseline.

No patients discontinued or started a new b/tsDMARD as of data cutoff



* Loss of response = patient requires rescue steroids beyond "soft rescue" rules similar tothose applied in RA registrational trials (up to 20mg/d x 5d or equivalent), and/or started new b/tsDMARD, as of data cutoff (03 April 2026)

Summary

- In the first clinical study with the AB-101 treatment regimen in RA, low-dose (1B) therapy demonstrated encouraging biological activity and a favorable safety profile, supporting the initiation of a Phase 2a basket trial.
- Data are consistent with results in 15 refractory RA patients in the Phase 2a basket trial (*see **late-breaker abstract # LB003***).
- No subjects discontinued or started new b/tsDMARDs, with first subject followed for >18 months.
- Treatment well tolerated with no CRS, ICANS, GvHD, hypogammaglobulinemia, SAEs, or Grade ≥3 AEs.
- Complete peripheral B-cell depletion observed in all patients, with reconstitution of naïve B cells and reduction in ACPA levels.

Conclusion

These data support the AB-101 treatment regimen as a potential off-the-shelf, outpatient alternative to CAR T therapies with comparable depth of B-cell depletion and clinical responses, but without associated risks.

Disclaimer: Data presented reflect a data cutoff of 03APR2026 and are subject to change.

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