



POST-ORLANDO 2025  
Novità dal Meeting della Società Americana di Ematologia

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Torino  
Centro Congressi Lingotto  
19-21 febbraio 2026

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## Citopenie Autoimmuni

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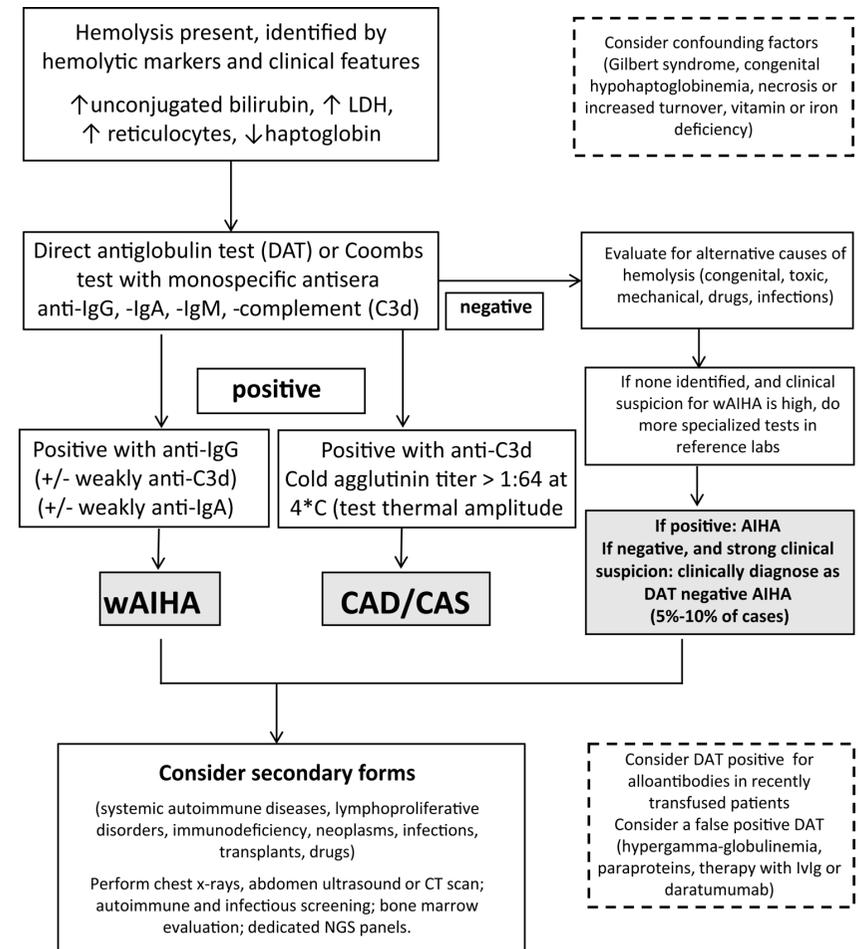
## DICHIARAZIONE NOME COGNOME

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Alexion					X	X	
Amgen			X				
Janssen			X			X	
Novartis					X	x	
Roche						X	
Sanofi			x		X		
Sobi					X		
Zenas	x						



## Autoimmune hemolytic anemias (AIHAs)

- Incidence of 0.6-1.3/100.000/year.
- Include warm (**wAIHA**) and cold (cold agglutinin disease, **CAD**) forms.
- The pathogenesis is complex involving IgG or IgM autoantibodies, antibody-dependent cellular cytotoxicity in the reticuloendothelial system, complement activation, and bone marrow compensatory response.
- The disease is diagnosed through the **Direct Antiglobulin test (DAT) with monospecific anti-sera and detection and titration of cold agglutinins in the serum for CAD.**
- **Further work-up** with bone marrow evaluation, CT-scan, and serologies indicated **on a case by case basis to exclude secondary forms.**

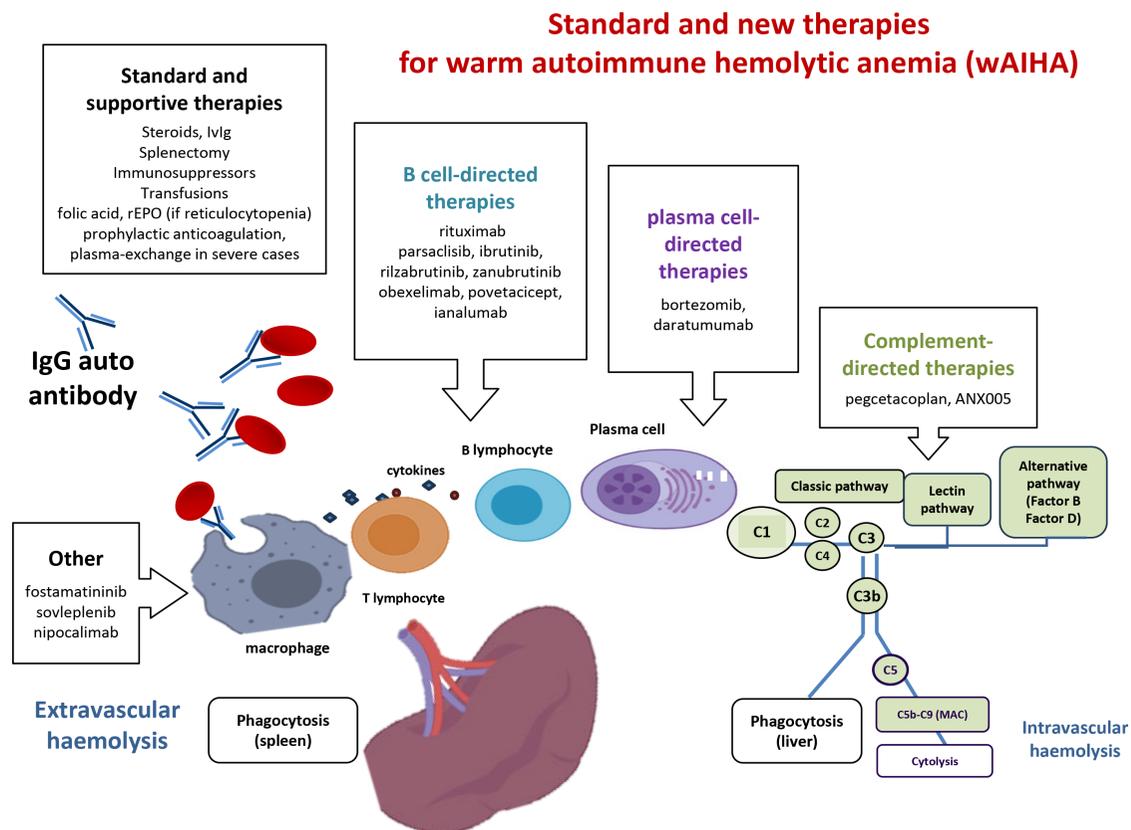




## Educational Session 5 Nov 2025 Immune Cytopenias: Addressing Challenges and Advancing Treatments

### Wilma Barcellini – wAIHA

- IgG mediated, reactivity at 37°C
- DAT pos for IgG or IgG+C3d
- ADCC in the spleen as the main pathogenic mechanism
- Forms with C3d positivity show more severe phenotype



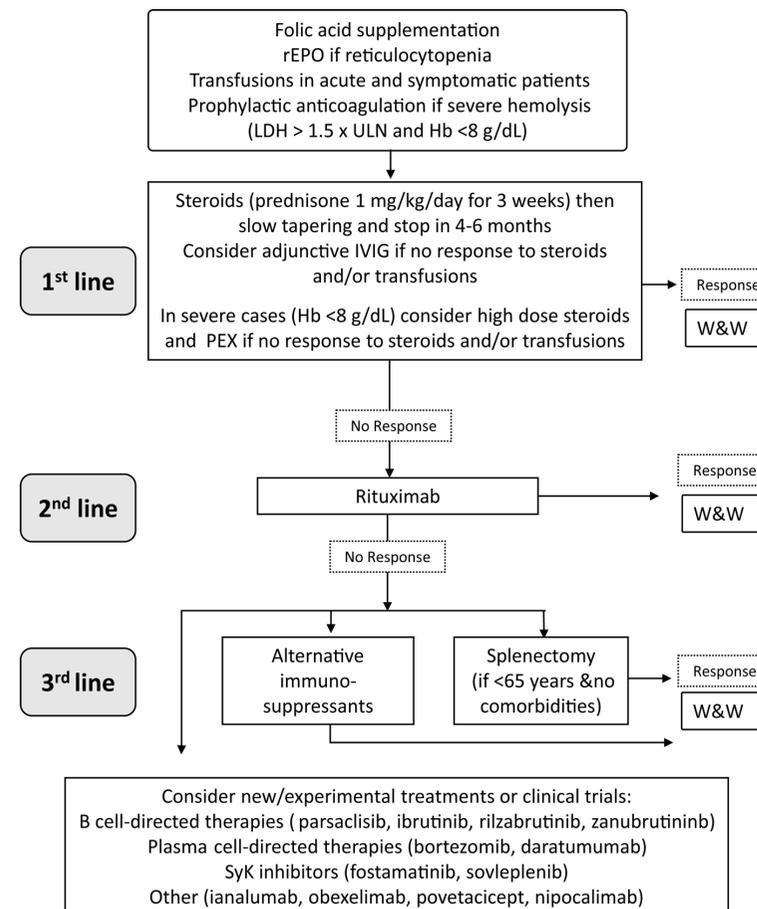


## Educational Session 5 Nov 2025

### Immune Cytopenias: Addressing Challenges and Advancing Treatments

#### Wilma Barcellini – wAIHA

- Steroids +/- IVIG as frontline, effective in >80% of cases
- Rituximab as second line/early first line if no response after 2-3 weeks of steroids
- Clinical trials if available as third line vs IST (MMF?) vs plasma cells inhibitors (bortezomib or daratumumab) off label

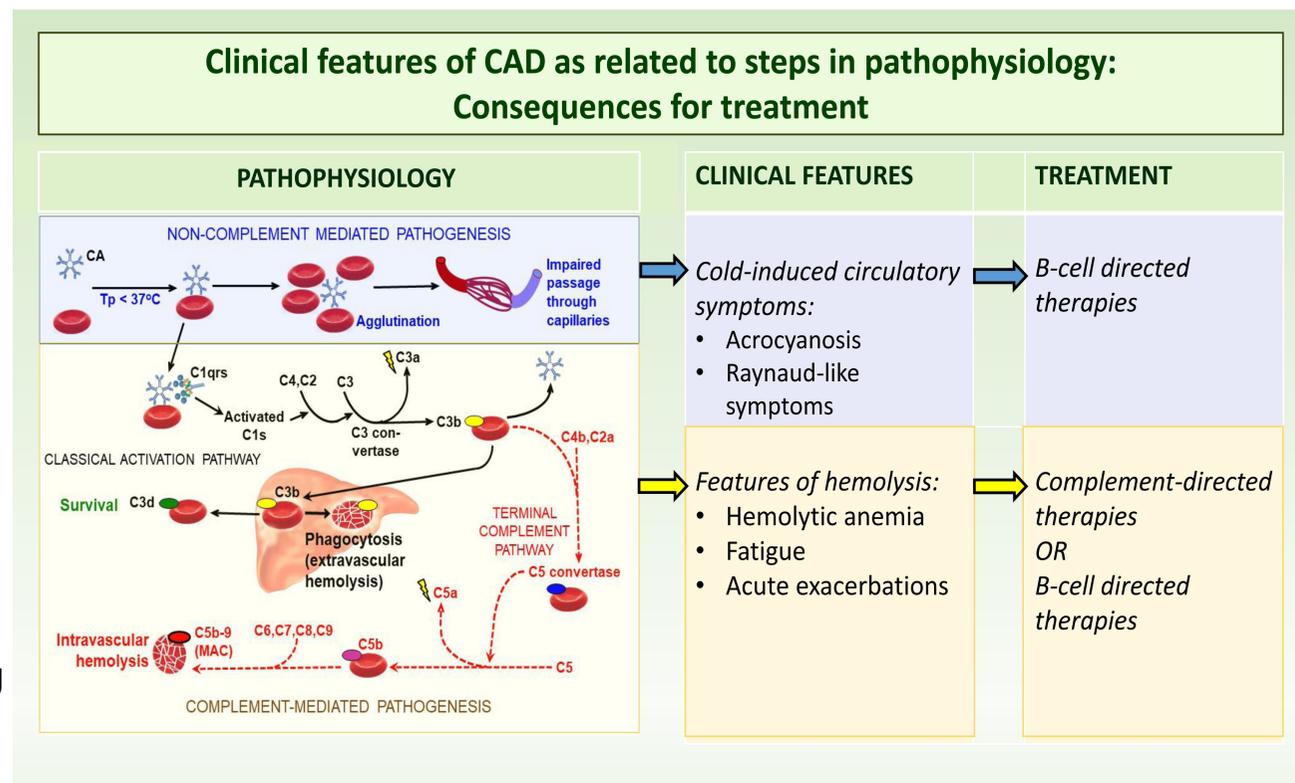




## Educational Session 5 Nov 2025 Immune Cytopenias: Addressing Challenges and Advancing Treatments

### Sigbjorn Berentsen – CAD

- IgM mediated, reactivity at 0-34°C
- DAT pos for C3d and CA titer >1:64
- C3d mediated extravascular hemolysis mainly in the liver
- CA mediated peripheral signs/symptoms
- Cold exposure and complement amplifying conditions may exacerbate the disease.

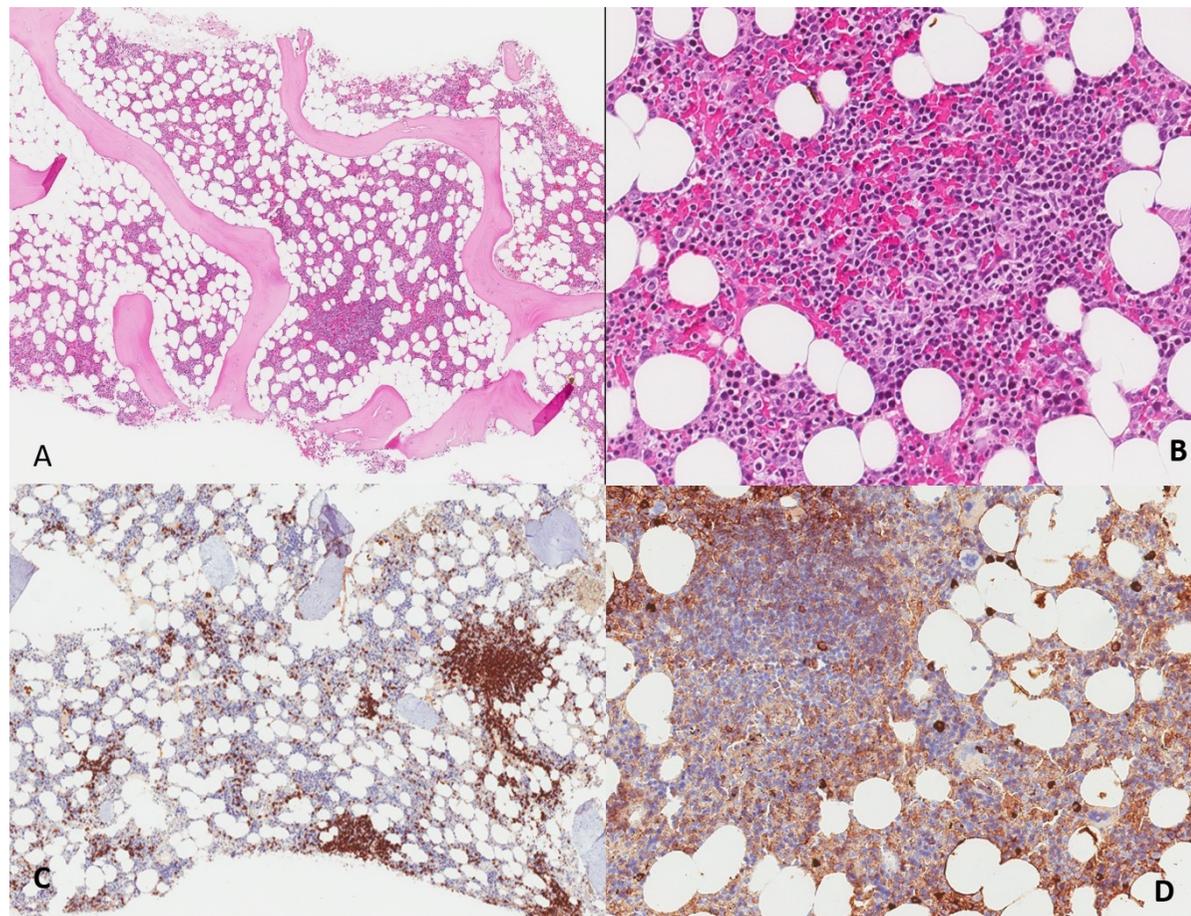




## Educational Session 5 Nov 2025 Immune Cytopenias: Addressing Challenges and Advancing Treatments

### Sigbjorn Berentsen – CAD

- Cold agglutinin–associated lymphoproliferative bone marrow disorder present in >80% of cases along with serum IgM MGUS, mainly k.
- MYD88 neg
- A, B - hematoxylin-eosin
- C. CD20 staining
- D. IgM-positive B cells within the infiltrate

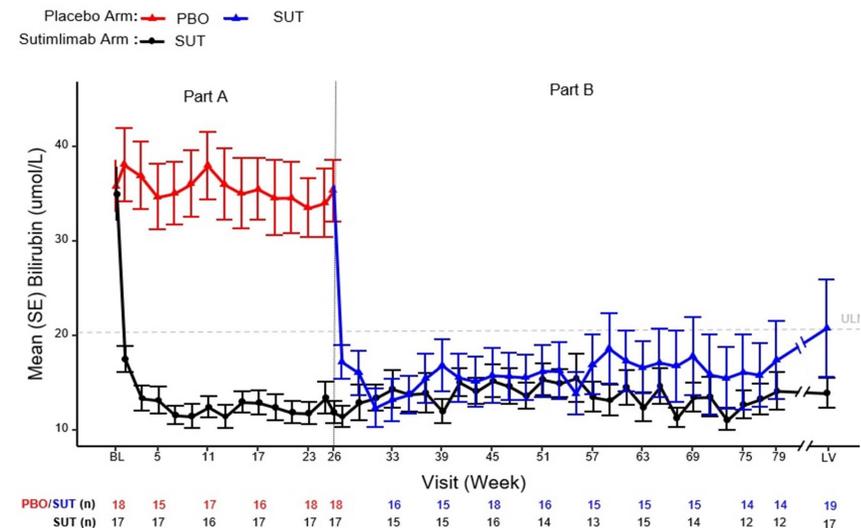
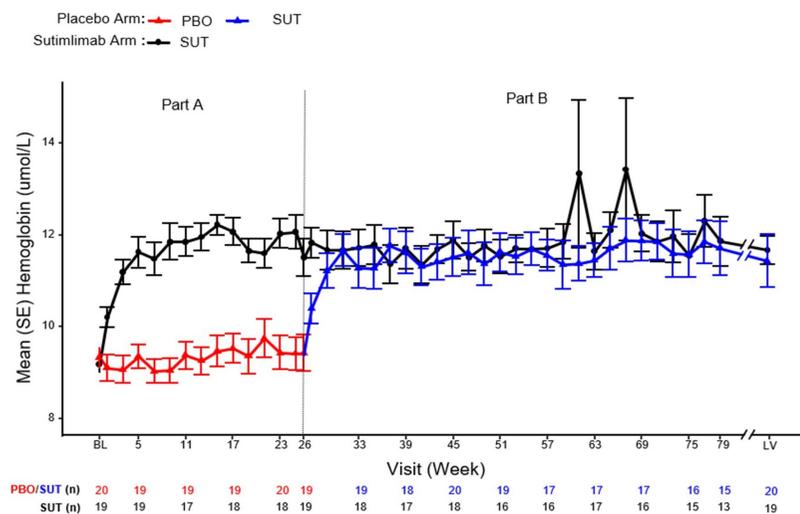


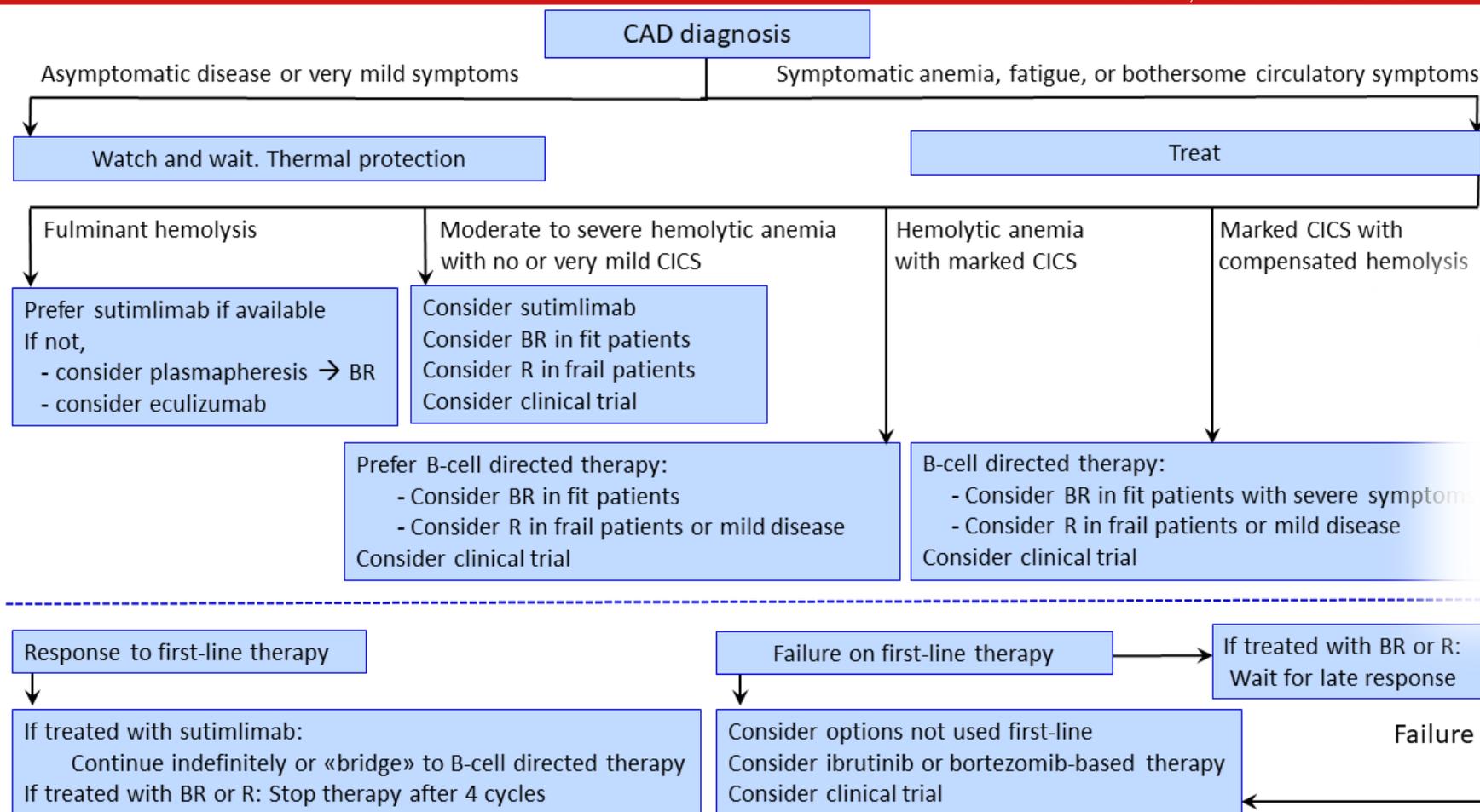


Treatment with sutimlimab vs placebo in 42 patients with CAD in a randomized controlled trial. Marked and rapid improvements in hemoglobin and bilirubin levels were observed in the sutimlimab arm, compared to no changes in the placebo arm.

Röth et al. Blood 2023

- **No effective on CA induced peripheral symptoms**
- **Need for continuous indefinite treatment IV every 2 weeks**







### Long-Term Efficacy and Safety of Rilzabrutinib, an Oral Bruton Tyrosine Kinase (BTK) Inhibitor in Patients With Warm Autoimmune Hemolytic Anemia (wAIHA) in the LUMINA Phase 2b Part B Study: A 74-Week Follow-Up

Bruno Fattizzo,<sup>1</sup> Henrik Frederiksen,<sup>2</sup> Alessandro Lucchesi,<sup>3</sup> Bing Han,<sup>4</sup> Catherine M. Broome,<sup>5</sup> Nichola Cooper,<sup>6</sup> Joan Cid,<sup>7</sup> Frederick Chen,<sup>8</sup> Amitabha Mazumder,<sup>9</sup> Miriam Vara Pampliega,<sup>10</sup> Deepthi Jayawardene,<sup>11</sup> Heidi Krenz,<sup>12</sup> Jing Zhao,<sup>11</sup> Ahmed Daak,<sup>11</sup> David J. Kuter<sup>13</sup>

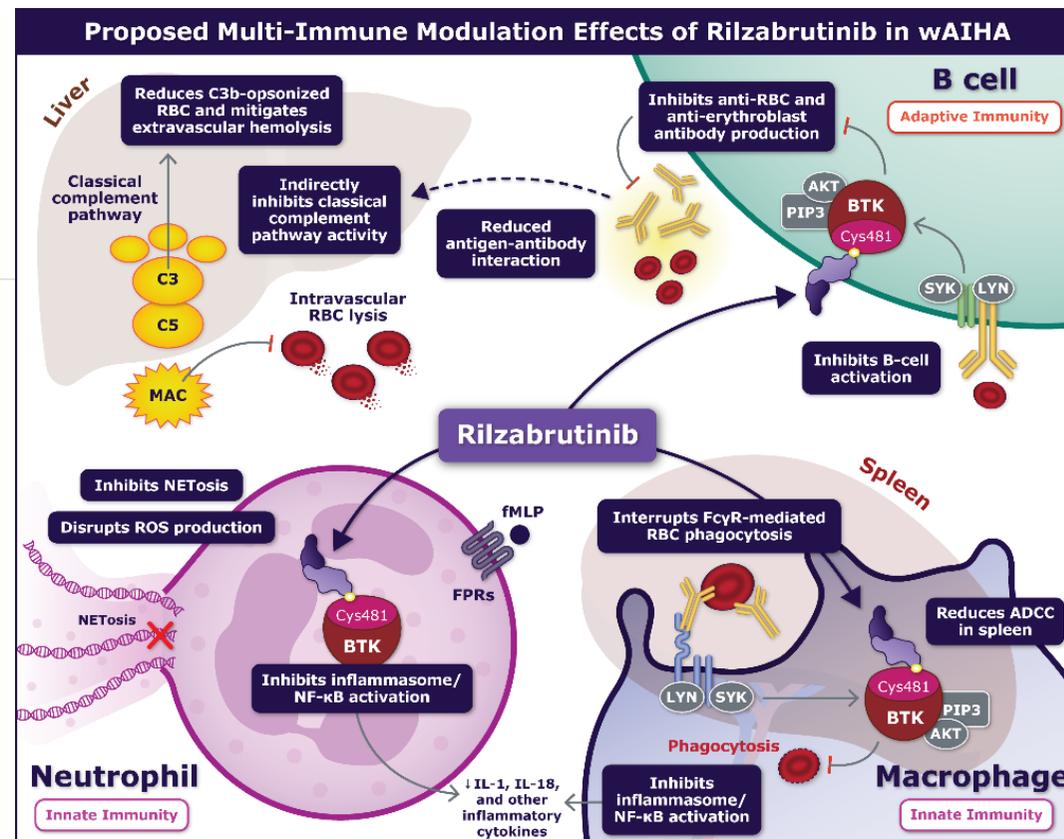
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ASH Poster: #4655

## Rilzabrutinib is an oral, reversible, covalent Bruton tyrosine kinase (BTK) inhibitor

### BTK inhibition is expected to increase Hb in wAIHA through multi-immune modulation:

- Reduced production of pathogenic autoantibodies
- Reduction of antibody-dependent cell-mediated cytotoxicity in spleen
- Reduced inflammation and complement activation

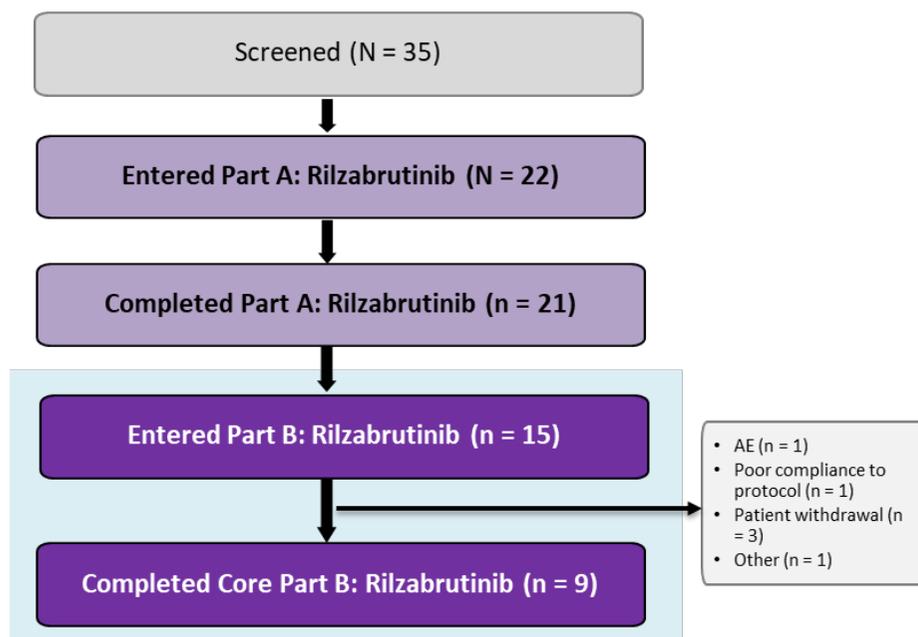




**22 AIHAs received Rilza 400 mg BID in a phase 2 trial**

**15 respondents continued treatment in part B**

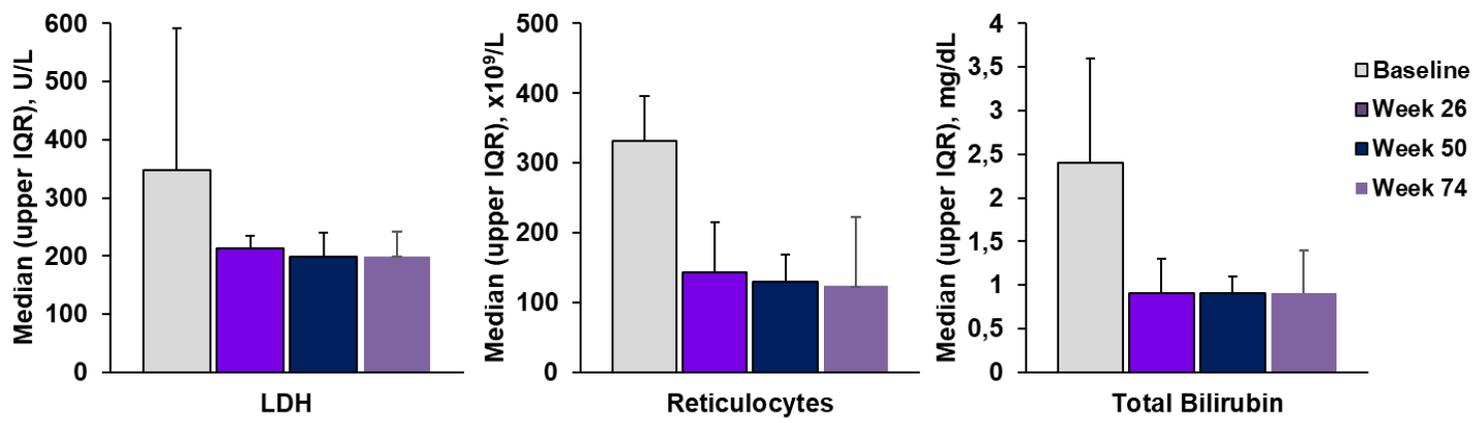
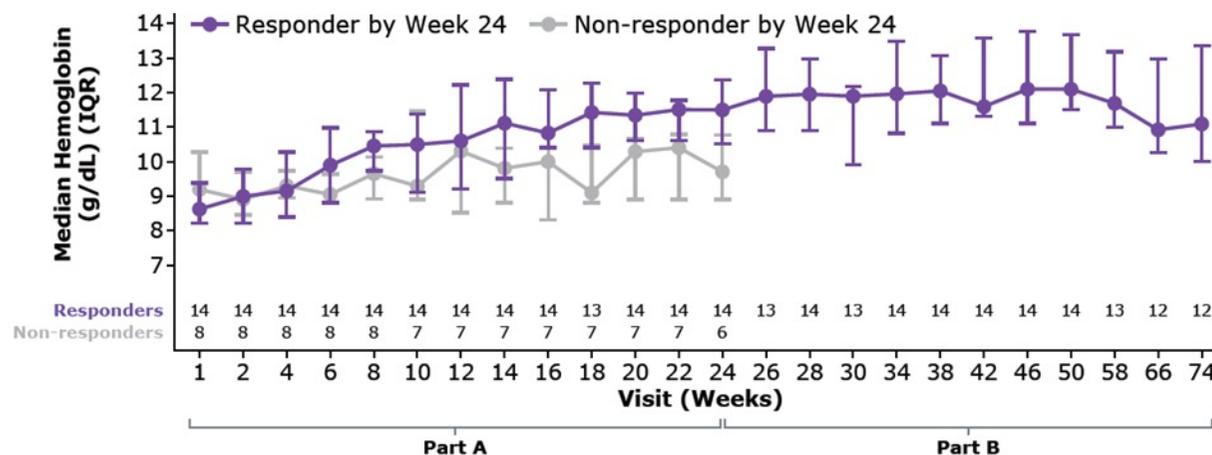
**Notably they had received more than 3 prior AIHA therapies in more than 50% of cases**



Characteristic	Part B (n = 15)
≥3 prior wAIHA medications, n (%)	9 (60)
Prior splenectomy, n (%)	2 (13)
Prior response to wAIHA treatment,* n responded/n received (%)	
Corticosteroids	12/15 (80)
Rituximab	6/9 (67)
Immunosuppressants	3/8 (38)
Rilzabrutinib study treatment, n (%)	
Standalone rilzabrutinib	6 (40)
Rilzabrutinib plus concomitant corticosteroids	9 (60)

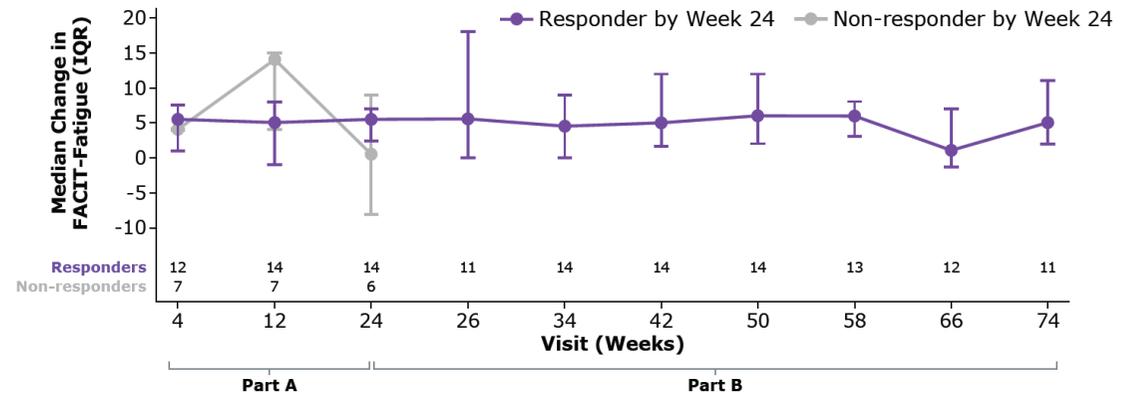


- Baseline Hb level was 8.2 g/dL (5.8-11.4)
- Hb levels were maintained through Week 74
- Hb at week 74 was 11.7 g/dL ( 6.6-14.7)
- Hemolytic markers consistently decreased





- **FACIT-Fatigue score improved by a median of 5 points** from baseline – clinically significant improvement



AEs (N = 15), n (%)	Any Cause	Related AEs
<b>Any AE</b>	<b>12 (80)</b>	<b>5 (33)</b>
Diarrhea	5 (33)	1 (7)
Upper respiratory tract infection	4 (27)	0
Back pain	3 (20)	0
Headache	3 (20)	0
Anemia	2 (13)	1 (7)
Cellulitis	2 (13)	0
Cough	2 (13)	1 (7)
Fatigue	2 (13)	0
GERD	2 (13)	0
Hemolytic anemia	2 (13)	0
Pneumonia	2 (13)	0
Herpes zoster	1 (7)	1 (7)
Lymphopenia	1 (7)	1 (7)
Decreased neutrophil count	1 (7)	1 (7)
Decreased WBC count	1 (7)	1 (7)

## Conclusions

LUMINA phase 2 study through week 74 showed:

**Continued efficacy with sustained Hb response**

2 patients achieved drug-free remission

**Clinically meaningful improvement in fatigue score**

**Well-tolerated safety profile**

**Phase 3, randomized, placebo-controlled study (LUMINA3; NCT07086976) is actively recruiting**



## Real world use of sutimlimab in patients with cold agglutinin disease: An international study

Fattizzo B, Sambruna E, Miyakawa Y, Michel M, Visco C, Fillitz M, Kannourakis G, Greve MB, Kleemiss M, Cid J, Patriarca A, Pavan L, Dizdari A, Maschio N, Sau A, Bitetti C, Curreli L, Lame D, Markovic U, Solimando A, Pedone GL, Versino F, Bortolotti M, Rapezzi D, Sammartano V, Tumedei N, Fianchi L, Khwaja J, De Vivo A, Lanza F, Vianello F, Oliva EN, Jaeger U, Jilma B, Moulis G, Barcellini W.

### Baseline features

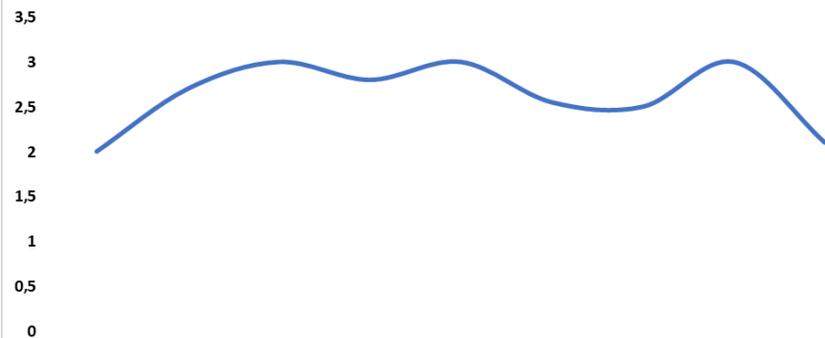
- The median age was 66 years (range 45-88) and 31 (57%) patients were females.
- The direct antiglobulin test (DAT) was positive for C3 alone in 35 patients, for IgG and C3 in 8, and for IgM and C3 in 10.
- The median CA titer was 1:1,024 (range, 1:4 to >1:25,000).

### History of CAD patients pre-sutimlimab

- Prior CAD treatments (median 3, 1-4)
- Pre- Sutimlimab complications included 8  $G \geq 3$  infections and 12 thrombotic events.
- The median number of RBC transfusions in the 6 months pre-Sutimlimab was 2 (0-18).



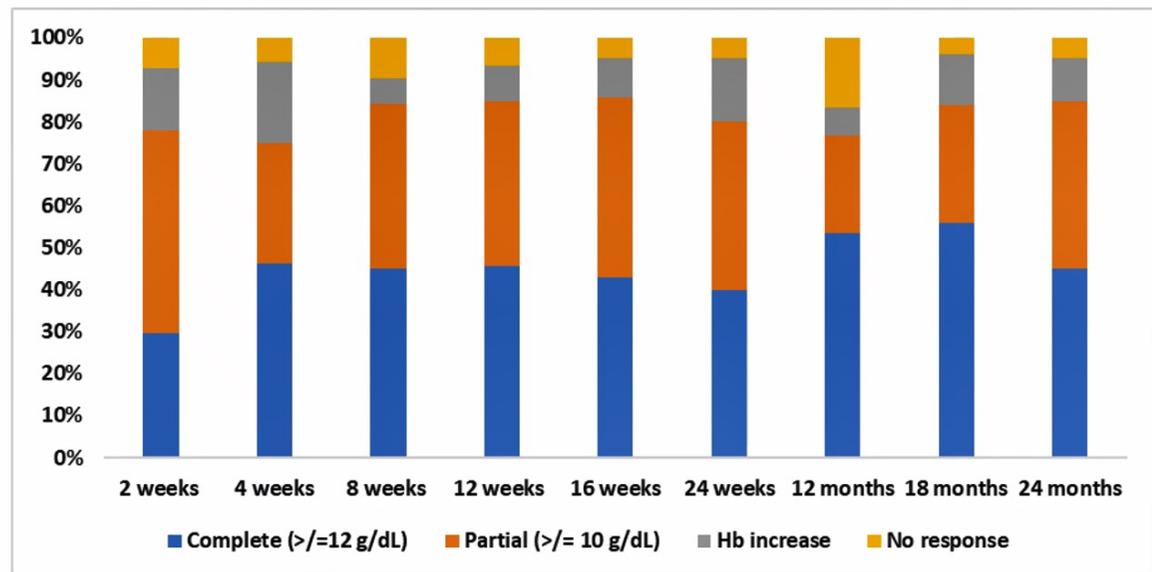
Median  $\Delta$ Hb at different timepoints



- Hb increased over time: **+2.0 g/dL at 2 weeks, +2.7 g/dL at 4 weeks, and +3 g/dL at 8 weeks, followed by sustained levels up to 24 months.**
- Overall response rates (PR + CR) were **78%, 75%, 84%, 85%, 86%, 80%, 77%, 84%, and 85%** at the respective timepoints.
- **48/54 became transfusion-independent.**

### Treatment with sutimlimab

- At baseline, median Hb was 8.4 g/dL (2.9–10.8), unconj bilirubin 1.9 mg/dL (0.8–7.49), and rets  $107 \times 10^9/L$  (10–340).
- Sutimlimab was administered as monotherapy (n=42) or in combination with erythropoietin (8), corticosteroids (2), or both (2).
- The median follow-up was 28 months (6–81).





## Safety assessment of sutimlimab assessment

- Sutimlimab was discontinued in 2 patients due to lack of response, in 1 due to overt Waldenström's macroglobulinemia, and in 7 based on their own decision with maintenance of good CAD control.
- **13 patients had an infection (G3 in 7, 1 H. influenzae pneumonia),**
- **1 thrombosis (DVT of basilic vein),**
- **8 hemolytic exacerbations mostly during infections.**
- At the last follow up only one patient had died due to progressive WM with sepsis.

## Conclusions

- **Sutimlimab confirmed to be an effective treatment in improving anemia and resolving transfusion dependence in more than 70% patients in the real world.**
- **Median Hb increased by more than 2 g/dL at 2 weeks** and throughout the follow up.
- Most patients became transfusion independent.
- **7 patients experienced a G3 infection, including a H.Influenzae pneumonia despite vaccination.**
- **8 patients experienced breakthrough hemolysis** mostly during infectious episodes.



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Novità dal Me

704. CELLULAR IMMUNOTHERAPIES: EARLY PHASE CLINICAL TRIALS AND TOXICITIES | NOVEMBER 3, 2025

## Allogeneic dual-target CD19/BCMA CAR T-cell therapy (QT-019B) for refractory autoimmune hemolytic anemia

Lele Zhang, Ruonan Li, Yucan Shen, Jianping Li, mengze hao, Jing Zhang, Xingxin Li, Neng Nie, Jingyu Zhao, Zhexiang Kuang, Xiao Yu, Liyun Li, Yanan Yue, Jiapan Hu, xu feng, xiaohui ding, li he, hao wang, Zhenkun wang, Hongwei Dou, xuqiang kong, Shanshan Xu, yiwen dong, Xin Zhao, yingyong xu, Luhan Yang, Jun Shi

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Allogeneic CAR-T cell product targeting both CD19 and BCMA, aiming to achieve an immune reset via comprehensive eradication of autoantibody-producing cells.

Investigator-initiated trial (NCT06733610), 4 rAIHA were administered QT-019B after standard lymphodepletion with fludarabine and cyclophosphamide.

DLT evaluation: dosing levels of  $3 \times 10^5$ /kg (n=1),  $1 \times 10^6$ /kg (n=2), and  $3 \times 10^6$ /kg (n=1).

The initial four patients follow-up durations of 7, 5, 4, and 2 months, respectively.

- Patient 1 received a dose of  $3 \times 10^5$  cells/kg, did not exhibit robust in vivo PK expansion, no safety concerns
- Patient 2 reached a Cmax of 37,749 copies/ $\mu$ g DNA on Day 14 and fell below the lower limit of quantification (LLOQ; 100 copies/ $\mu$ g DNA) by Day 21. At baseline, his hemoglobin was 68 g/L, hemolysis improved from Day 18, CR by Day 26, sustained through Day 150 without recurrence of hemolysis.
- Patient 3, diagnosed with rAIHA,  $1 \times 10^6$  cells/kg, did not exhibit robust in vivo PK expansion.
- Patient 4 attained a Cmax of 322,186 copies/ $\mu$ g DNA on Day 17, Grade 1 CRS. At baseline, Hb was 66 g/L, hemolysis improved from Day 14, by Day 60 Hb was 110 g/L.

In summary, the allogeneic dual-target anti-CD19/BCMA CAR T-cell therapy (QT-019B) has shown promising clinical outcomes in the treatment of rAIHA.

Underlying causes of suboptimal in vivo PK expansion needs further investigation.



## Conclusions

- **Treatment armamentarium** of wAIHA and CAD is **enriching** with novel therapies.
- **Sutimlimab is approved for CAD** to treat hemolytic anemia after rituximab failure, is not effective on acrocyanosis and needs long-term infusion.
- B-cell targeting with **BTKi** has the potential of inducing long term remissions **in wAIHA, phase 3 rilza study ongoing.**
- Novel immunotherapies such as **auto- and allo- CAR-T cells** in immune mediated cytopenias are intriguing, toxicity, in vivo expansion, and response duration needs further investigation.

