

From Anti-CD38 Interference to Diagnosis:

Real-World Multicenter Experience with DaraEx^{plus}

BACKGROUND

DaraEx^{plus} contains a Fab fragment of an anti-CD38 antibody designed to block CD38 epitopes on red blood cells (RBCs), thereby preventing the binding of therapeutic anti-CD38 antibodies (e.g., daratumumab, isatuximab) and mitigating their interference in the indirect antiglobulin test (IAT) (**Figure 1**). DaraEx^{plus} was introduced to the market in 2022. Here, we present **multicenter data on the performance of DaraEx^{plus}** in routine IAT diagnostics.

METHODS

Data from routine immunohematological testing using DaraEx^{plus} were collected via a **structured survey from four European transfusion centers between April 2025 and April 2026**. Participants generated data either prospectively or retrospectively, by recording data with the beginning of the survey or by using historical data from their laboratory information management system, respectively. The collected dataset was analyzed with respect to inhibition efficiency and detection of alloantibodies.

RESULTS

Four transfusion centers contributed data generated between 2023 and 2026, comprising 1,325 individual test reactions using DaraEx^{plus}-treated RBCs. Of these, 1,054 (79.5%) were performed with specimens from patients receiving daratumumab, 22 (1.7%) from isatuximab-treated patients, 237 (17.9%) from patients with unknown, and 12 (0.9%) from patients with suspected anti-CD38 antibodies. All samples were EDTA plasmas. Overall, 1,263 (95.3%) results were consistent with expectations. Complete inhibition using the express protocol (10µl DaraEx^{plus}) was achieved in 1,258 (94.9%) reactions, while 10 (0.8%) of the remaining positive reactions were escalated into the alternative protocol (25µl DaraEx^{plus}). 5 of these reactions became negative, amounting to a success rate of 50% of the alternative protocol (**Table 1**). One laboratory changed the lot of the red blood cells and repeated the express protocol with the new lot instead of using the alternative protocol, which yielded satisfactory results in 5 of 6 cases (83.3%, data not shown). **No new alloantibodies were identified, and no known alloantibodies were missed** in the antigen masking IAT.

CONCLUSION

With an **inhibition rate of 95.3%**, DaraEx^{plus} demonstrates robust performance for mitigating anti-CD38 antibody mediated therapeutic biologics interference in IAT routine diagnostics. No evidence of masking of alloantibodies was found, and no contraindications or interfering substances were identified.

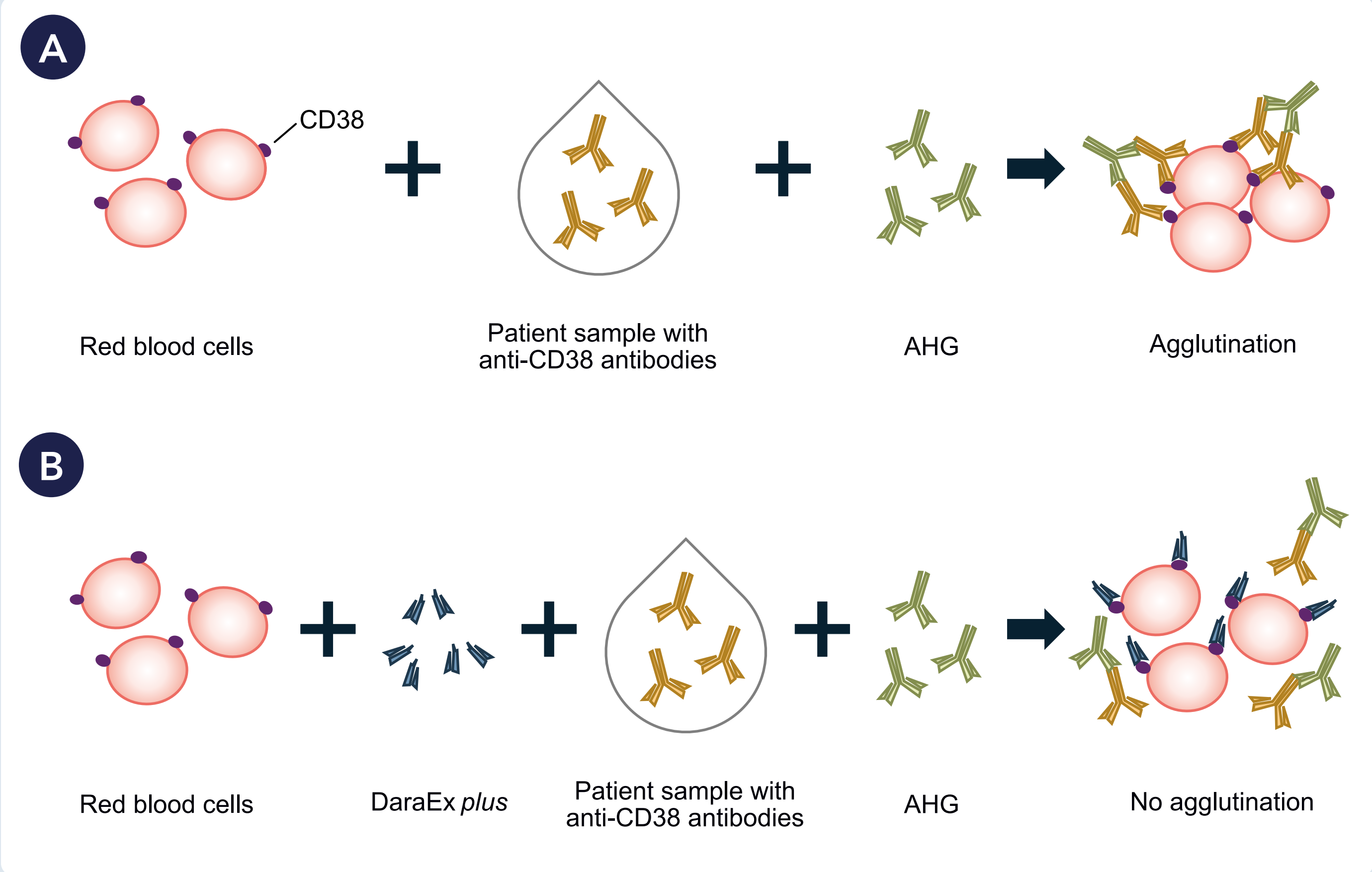


Figure 1. Principle of CD38 Antigen Masking IAT with DaraEx^{plus}.
A: Red blood cells, which are bearing CD38, are agglutinated by anti-CD38 antibodies contained in the patient sample, when performing an IAT with anti-human globulin (AHG). **B:** CD38 on the red blood cells is masked by DaraEx^{plus}, preventing the red blood cells from becoming agglutinated by AHG via anti-CD38 antibodies in the IAT.

Table 1. Results of the Survey.

	Lab 1	Lab 2	Lab 3	Lab 4	Total
Number of tests	240	284	350	451	1,325
Number of samples	106	78	°	108	292 (3/4 labs)
Number of patients	16+	59	°	28	103+ (3/4 labs)
Anti-CD38 drug: Daratumumab	#	89% (253)	100% (350)	100% (451)	79.5% (1,054)
Anti-CD38 drug: Isatuximab	#	7.7% (22)	0% (0)	0% (0)	1.7% (22)
Specific anti-CD38 drug unknown	98.8% (237)	0% (0)	0% (0)	0% (0)	17.9% (237)
Anti-CD38 treatment suspected	1.3% (3)	3.2% (9)	0% (0)	0% (0)	0.9% (12)
Successful express protocols	95.8% (230)	84.9% (241)	100% (350)	96.9% (437)	94.9% (1,258)
Successful alternative protocols	50% (5)	N/A	N/A	N/A	---
Anti-CD38 interference inhibition rate	97.9% (235)	84.9% (241)	100% (350)	96.9% (437)	95.3% (1,263)
Alloantibody rate	0%	0%	0%	0%	0%

° No information provided. **N/A** Alternative protocol was not conducted (lab 2 stopped the testing and accepted residual agglutination in the express protocol, lab 4 repeated the test using another red blood cell).
 # Anti-CD38 drugs were not differentiated.

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Conflict of Interest
 CPH and CS are employees of imusyn GmbH & Co. KG. CS is designated inventor of a patent related to antigen masking IAT.



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