Treatment Patterns and Outcomes Among Patients with Warm Autoimmune Hemolytic Anemia Receiving Rituximab in the United States: A Retrospective Database Study

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Key Takeaways

- **RTX dosing patterns were variable, with many patients receiving >4 administrations per cycle**
- **A high relapse frequency was observed, highlighting the considerable burden that remains among patients with wAIHA initiating RTX**
- **Relapses were largely characterized by wAIHA hospitalizations and blood transfusions, both of which may suggest clinically meaningful hemolysis**
- **Overall, an unmet need remains for improved control of wAIHA, particularly among patients experiencing relapses after RTX initiation**

Background

Warm autoimmune hemolytic anemia (wAIHA) is the predominant subtype of autoimmune hemolytic anemia (AIHA); it is characterized by the presence of autoantibodies that react optimally at body temperature (37°C), leading to premature destruction of red blood cells[1,2]

While there are no targeted therapies approved for wAIHA, rituximab (RTX) is often used as a first- or second-line treatment option[1,2]

- Recommended dosing is cyclical, with patients receiving either four doses of 375 mg/m^2 every week or two doses of 1,000 mg on days 1 and 15[2]
- Initiation of a new cycle may be considered after subsequent treatment relapse[2]
- Other recommended treatment options after relapse are limited[2]

RTX real-world utilization and treatment outcomes, including relapse events, have not been well established among a US patient population

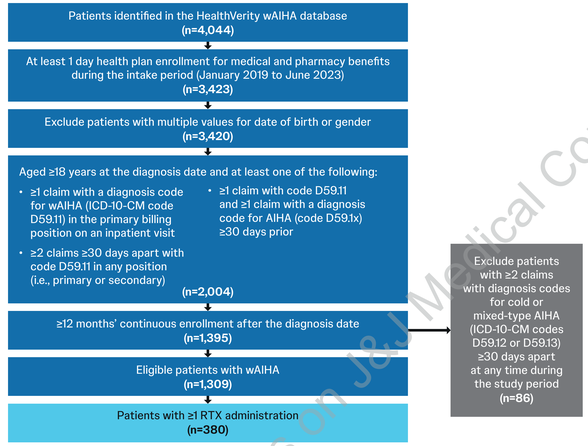
Objective

To describe treatment patterns and relapse events among US patients with wAIHA receiving RTX

Methods

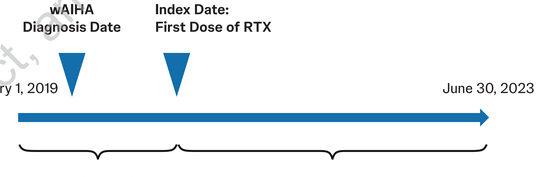
- This retrospective cohort study used data from HealthVerity, comprising large, de-identified US closed medical and pharmacy insurance claims databases and data collected from diagnostic laboratories[3]
- Patients were required to have had one of the following between January 2019 and June 2023 (**Figure 1**):
  - ≥1 claim with a wAIHA diagnosis code (International Classification of Diseases, 10th Revision, Clinical Modification [ICD-10-CM] code D59.11) in the primary position during an inpatient visit
  - ≥2 claims with a wAIHA diagnosis code in any position (i.e., primary or secondary) ≥30 days apart
  - ≥1 claim with a wAIHA diagnosis code plus one AIHA diagnosis code (ICD-10-CM code D59.1x) ≥30 days prior
- The date of the first diagnosis meeting the above criteria was defined as the diagnosis date
- Included patients were aged ≥18 years on the diagnosis date and had ≥12 months' continuous enrollment after the diagnosis date
- Patients receiving ≥1 RTX infusion after wAIHA diagnosis were classified as RTX users, and the date of the first infusion was designated as the index date (**Figure 2**)
  - Post-index analyses included RTX treatment cycles and relapse events

Figure 1. ***Patient selection***



***AIHA**=autoimmune hemolytic anemia, **ICD-10-CM**=International Classification of Diseases, 10th Revision, Clinical Modification, **RTX**=rituximab, **wAIHA**=warm autoimmune hemolytic anemia.*

Figure 2. ***Study design***



[a]*Relapse events occurring within 30 days of the previous event were counted as part of the same event, and a gap of ≥30 days between RTX doses was used to define the start of a new RTX cycle.*

***AIHA**=autoimmune hemolytic anemia, **ESA**=erythropoiesis stimulating agent, **RTX**=rituximab, **wAIHA**=warm autoimmune hemolytic anemia.*

Results

Baseline Characteristics

- Of 1,309 patients with wAIHA identified, 380 (29.0%) received ≥1 administration of RTX (**Table 1**)
  - The mean age for RTX users was 51.5 (standard deviation [SD] 17.8) years, and 60.5% were female
  - The mean baseline Quan-Charlson Comorbidity Index score for RTX users was 2.6 (SD 2.4)

Treatment Patterns

- In total, 274 (72.1%) RTX users received only one cycle of RTX, and the remaining 106 (27.9%) received ≥2 cycles (**Table 2**)
- Mean post-index follow-up time for the analyses of treatment patterns and relapse events was 20.6 (SD 8.6) months
- Overall, patients received a mean of 2.4 (SD 1.5) RTX doses per cycle
- The 106 patients who received >1 cycle of RTX received a mean of 2.5 (SD 1.9) doses per cycle, with 16 (15.1%) receiving >4 doses for ≥1 cycle during the follow-up period (reasons not recorded)

Relapse Events

- During post-index follow-up, 197 (51.8%) RTX users experienced ≥1 relapse event (**Table 3**)
- Individual events that made up the composite of relapse events before and after RTX treatment are shown in **Table 4**
  - Overall, 70 (18.4%) RTX-treated patients experienced ≥1 wAIHA-related hospitalization during follow-up, with 222 wAIHA-related hospitalization events observed in total
  - Additionally, 40 (10.5%) RTX-treated patients received a total of 79 blood transfusions

Table 1. ***Demographics and baseline clinical characteristics***

Characteristic	All Patients (n=1,309)	RTX Users (n=380)
Age at diagnosis, years, mean (SD)	50.3 (18.4)	51.5 (17.8)
Age group, n (%)		
18–34 years	289 (22.1)	78 (20.5)
35–49 years	325 (24.8)	80 (21.1)
50–64 years	306 (23.4)	90 (23.7)
≥65 years	389 (29.7)	132 (34.7)
Sex, female, n (%)	862 (65.9)	230 (60.5)
Race, n (%)		
White	410 (31.3)	113 (29.7)
African American or Black	141 (10.8)	33 (8.7)
Asian	32 (2.4)	10 (2.6)
Hispanic	125 (9.5)	39 (10.3)
Other	48 (3.7)	19 (5.0)
Missing/unknown	553 (42.2)	166 (43.7)
Quan-CCI score, mean (SD)	2.5 (2.6)	2.6 (2.4)
Quan-CCI score, n (%)		
0	381 (29.1)	92 (24.2)
1	199 (15.2)	58 (15.3)
2	231 (17.6)	66 (17.4)
3	122 (9.3)	53 (13.9)
≥4	376 (28.7)	111 (29.2)
Elixhauser comorbidities, n (%)		
Hypertension, uncomplicated	619 (47.3)	177 (46.6)
Chronic pulmonary disease	283 (21.6)	75 (19.7)
Liver disease	304 (23.2)	115 (30.3)
Coagulation deficiency	416 (31.8)	135 (35.5)
Obesity	451 (34.5)	140 (36.8)
Fluid and electrolyte disorders	393 (30.0)	115 (30.3)
Depression	267 (20.4)	64 (16.8)

***Quan-CCI**=Quan-Charlson Comorbidity Index, **RTX**=rituximab, **SD**=standard deviation.*

Table 2. ***Number of RTX cycles***

RTX Cycles, n (%)	RTX Users (n=380)
1	274 (72.1)
2	67 (17.6)
3	10 (2.6)
4	14 (3.7)
≥5	15 (3.9)

***RTX**=rituximab.*

Table 3. ***Timing of relapse events during follow-up***

Parameter	RTX Users (n=380)
Patients with ≥1 relapse during follow-up, n (%)	**197 (51.8)**
0–6 months post-index	80 (21.1)
6–12 months post-index	42 (11.1)
≥12 months post-index	75 (19.7)
Patients without relapse during follow-up, n (%)	**183 (48.2)**

***RTX**=rituximab.*

Table 4. ***Relapse events before and after RTX treatment***

Parameter	RTX Users (n=380)	
	Before RTX treatment	After RTX treatment
Patients with ≥1 relapse, n (%)	**156 (41.1)**	**197 (51.8)**
Initiation of new RTX cycle	–	106 (27.9)
wAIHA hospitalization	88 (23.2)	70 (18.4)
Blood transfusion	53 (13.9)	40 (10.5)
IV or SC immunoglobulin administration	14 (3.7)	21 (5.5)
ESA administration	11 (2.9)	16 (4.2)
Splenectomy	2 (0.5)	5 (1.3)
Relapse events, n	**246**	**614**
Initiation of new RTX cycle	–	218
wAIHA hospitalization	128	222
Blood transfusion	80	79
IV or SC immunoglobulin administration	25	64
ESA administration	11	26
Splenectomy	2	5

***ESA**=erythropoiesis stimulating agent, **IV**=intravenous, **RTX**=rituximab, **SC**=subcutaneous, **wAIHA**=warm autoimmune hemolytic anemia.*

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