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POSTER ABSTRACTS

508.BONE MARROW FAILURE: ACQUIRED

Atgam Efficacy and Safety in Moderate-to-Very Severe Acquired Aplastic Anemia: Outcome of a Large Multicenter Cohort of 634 Children and Adults from the French Authorization for Temporary Use Surveillance Program

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Introduction

Acquired aplastic anemia (AA) is a rare immunological disease leading to bone marrow failure. First-line treatment in patients aged >40 years or without a matched related donor is immunosuppressive therapy (IST) based on anti-human T lymphocyte immunoglobulin (ATG) plus cyclosporine.

This ATGAM Temporary Use Authorization program was a retrospective, multicenter study to report safety and efficacy surveillance data on ATGAM use in patients with AA.

Methods

This study collected surveillance data from the ATGAM Named Patients Program for French authorities ahead of ATGAM registration. Patients were treated with ATGAM 40 mg/kg for 4 days in addition to cyclosporine. Safety and efficacy data were collected from patients treated from September 2011 to August 2022 and reported to the French authority every 6 months.

Patients were classified as severe AA if they had 2 of the following criteria: neutrophil count $<0.5\times10^9$/L, platelet count $<20\times10^9$/L, or reticulocyte count $<60\times10^9$/L. Very severe AA: same as severe except neutrophil count $<0.2\times10^9$/L. Patients not meeting criteria for very severe/severe AA were classified as moderate.

Patient response was evaluated using the RACE study criteria (Peffault de Latour, et al [2022]), for severe AA: complete response was defined as: hemoglobin >100g/L, neutrophil count $>1.0\times10^9$/L, and platelet count $>100\times10^9$/L; partial response: no longer meeting criteria for severe disease; no response: still severe AA and/or transfusion dependent. For moderate AA (Marsh, et al [1999]), complete response was defined as: neutrophil count $>2.0\times10^9$/L and platelet count $>100\times10^9$/L; partial response: neutrophil count $>1.0\times10^9$/L and platelet count $>30\times10^9$/L; no response: transfusion dependent.

Patients were classified as receiving first-line treatment (never received ATG), refractory (failed to respond to previous IST with ATG within 12 months before initial ATGAM), or relapse (recurrence of AA after a positive response to IST with ATG), regardless of AA severity.

Results

In total, 634 patients with moderate-to-very severe AA were treated with ATGAM (n=537 first-line; n=68 refractory/relapse; n=29 not classified) in addition to cyclosporine (40 first-line patients also received eltrombopag) from January 2012 to August 2022. By severity, n=124 were moderate, n=317 severe, n=133 very severe, and n=60 severity unknown. Patient demographics are shown in Table 1. Overall response (partial+complete) in patients on first-line therapy at 3, 6, and 12 months was 22.5% (n=78), 50.6% (n=156), and 79.2% (n=164), respectively.

By severity, overall response rates in first-line therapy for moderate and severe/very severe cohorts, respectively, were: 25.0% (n=20) and 21.7% (n=58) at 3 months; 56.8% (n=42) and 48.7% (n=114) at 6 months; and 74.1% (n=40) and 81.0% (n=124) at 12 months.

Overall response at 6 and 12 months by age and AA severity in patients on first-line treatment is shown in Table 2.

Median duration of follow-up was 12.4 months. Overall survival (95% confidence interval) at 12 months for all patients was 91.5% (88.8-93.6). The treatment was well tolerated, and no new safety signals were observed with ATGAM. Cumulatively, 1,087 adverse events were reported in 364 patients over the entire program period, the majority of which were disease related.

Conclusion

This real-world, retrospective study utilizing surveillance data showed response rates in line with the recent RACE study (Peffault de Latour, et al [2022]) for patients with first-line severe AA treated with a combination of ATGAM and cyclosporine. No new safety risks were identified in this large cohort of patients. Treatment with ATGAM remains of benefit in patients with moderate-to-very severe AA.

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Table 1. Demographic and baseline characteristics

Characteristic	First-line Treatment (n=537)	Refractory (n=33)	Relapse (n=35)	All Treated Patients (n=634)
Age, year				
Mean ± SD	40.5 ± 23.4	39.4 ± 21.0	44.2 ± 21.1	40.8 ± 23.2
Minimum; maximum	0.8; 88	6; 80	9; 77	0.8; 88
Age <18 years, n (%)	138 (25.9)	5 (15.6)	4 (11.4)	148 (24.5)
Sex, n (%)				
Male	284 (53.3)	17 (53.1)	19 (54.3)	323 (53.4)
Female	249 (46.7)	15 (46.9)	16 (45.7)	282 (46.6)
Weight, kg				
Mean ± SD	63.2 ± 23.6	63.3 ± 18.8	71.4 ± 17.9	63.6 ± 23.1
PNH clone >1%, n (%)	117 (34.4)	7 (38.9)	9 (37.5)	135 (35.1)
Karyotype, n (%)				
Normal	378 (93.3)	23 (88.5)	29 (93.5)	433 (93.1)
Abnormal	2 (0.5)	1 (3.8)	-	3 (0.6)
Failure	5 (1.2)	-	-	5 (1.1)

PNH, paroxysmal nocturnal hemoglobinuria

Table 2. Overall response at 6 and 12 months, by age and AA severity in patients on first-line treatment

Visit	Moderate	Severe + Very Severe	Severity Unknown	Total
Age <18 years, n	17	117	4	138
6 months overall, n (%)	7 (53.8)	36 (43.4)	0	43 (44.8)
12 months overall, n (%)	8 (80.0)	46 (92.0)	0	54 (90.0)
Age 18-<40 years, n	28	72	5	105
6 months overall, n (%)	11 (64.7)	21 (45.7)	0	32 (50.8)
12 months overall, n (%)	9 (69.2)	22 (84.6)	0	31 (79.5)
Age 40-<60 years, n	37	92	7	136
6 months overall, n (%)	17 (58.6)	21 (50.0)	0	38 (53.5)
12 months overall, n (%)	16 (72.7)	23 (82.1)	0	39 (78.0)
Age ≥60 years, n	23	121	10	154
6 months overall, n (%)	7 (46.7)	33 (55.0)	0	40 (53.3)
12 months overall, n (%)	7 (77.8)	32 (68.1)	0	39 (69.6)

Overall response combines complete and partial responses.
AA, aplastic anemia

Figure 1

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