Ethnicity affects relapse-free survival in immune-mediated thrombotic thrombocytopenic purpura

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Abstract

Immune-mediated thrombotic thrombocytopenic purpura (iTTP) is caused by a severe, antibody-mediated deficiency of ADAMTS13 activity. The B-cell depleting agent rituximab is effective in restoring ADAMTS13 activity and therefore preventing relapses. However, the risk of relapse appears heterogeneous among patients, although the underlying causes are elusive. Preliminary reports suggested that African ancestry could be associated with decreased relapse-free survival (RFS). Data from the registry of the French National Thrombotic Microangiopathy Reference Center were used to further address the role of ethnicity on response and RFS after rituximab administration in the acute as well as in the preemptive setting. A total of 790 patients (134 patients of African ancestry and 656 patients of European ancestry) were included in the study. Time from rituximab administration to ADAMTS13 recovery was comparable between the two cohorts. Patients of African ancestry had inferior 3-year RFS after the first rituximab-treated episode compared to patients of European ancestry (P<0.05). In multivariate analyses, African ancestry was identified as an independent risk factor for relapse (hazard ratio [HR]=1.36; P<0.05), as well as male sex (HR=1.21; P<0.05) and type of index episode treated by rituximab (relapsed disease *vs*. initial episode, HR=1.62; P<0.05). Moreover, time to relapse shortened progressively after consecutive courses of rituximab, regardless of ethnicity (P<0.05). These results indicate that ethnicity affects RFS with patients of African ancestry relapsing earlier, suggesting that a closer ADAMTS13 monitoring might be necessary in high-risk patients.

Introduction

Immune-mediated thrombotic thrombocytopenic purpura (iTTP) is a rare disease characterized by a severe, antibody-mediated deficiency in the von Willebrand factor-cleaving protease ADAMTS13 (a disintegrin and metalloproteinase with thrombospondin-1 motifs, 13th member) activity. ADAMTS13 activity deficiency leads to microangiopathic hemolytic anemia, severe thrombocytopenia and ischemic end-organ damage.[1,2] The evolving knowledge on the pathogenesis of iTTP provided a rationale for using B-cell depleting therapies such as rituximab in the acute phase, as well as in the preemptive setting in patients who experience a severe decrease in ADAMTS13 activity during follow-up while otherwise in remission, an event now termed ADAMTS13 relapse.[3-6] Rituximab therapy rapidly induces B-cell depletion, thereby effectively preventing relapse in most patients.[3,4] However, about 40% of patients will need further treatment due to a clinical or ADAMTS13 relapse, whereas others maintain a normal ADAMTS13 activity.[3,4,7] The cause of this heterogeneity in patients' response to rituximab is unclear, while its understanding could lead to a more personalized follow-up with personalized immunomodulation. Recent studies in other autoimmune diseases identified ethnical disparities after rituximab treatment that might play a role in the heterogeneity of rituximab response.[8] More specifically for iTTP, the USTMA group assessed the possible role of ethnicity in the different response of iTTP to rituximab, and showed that rituximab may be less effective in preventing relapse for patients of African ancestry.[9] Furthermore, the same group reported that clinical and/or ADAMTS13 relapses occur significantly sooner for patients of African ancestry from the second course of rituximab treatment.[10] However, these studies typically did not involve regular ADAMTS13 monitoring, and only a small prospective cohort was evaluated for ADAMTS13 relapses, while since the routine use of preemptive therapies clinical relapses are rare. In this context, ADAMTS13 relapses might better reflect long-term outcomes.[10] Furthermore, these data originate exclusively from the United States, where medico-social factors may differ from those in other geographical regions and might influence access to regular diagnostic procedures, follow-up measurements (e.g., ADAMTS13 monitoring) and novel treatment options. In contrast, the French healthcare system provides universal coverage; therefore, social and economic factors might have a limited role compared to previous studies. Here, we report the results of a large cohort of French patients in which we explored the role of ethnicity in iTTP relapse.

Methods

Patients and treatment

Data on adult patients with a diagnosis of iTTP included from October 2000 to July 2023 in the registry of the French TMA Reference Center (CNR-MAT; www.cnr-mat.fr) have been collected according to a predefined computerized dataset.[3,4] For the present study, all episodes of iTTP treated with rituximab were included. iTTP diagnosis was considered in patients with features of TMA and a confirmed severe, immune-mediated ADAMTS13 deficiency (<10%). ADAMTS13 activity and anti-ADAMTS13 antibodies were assessed as previously described.[11] Non-inclusion criteria, clinical response, remission, and relapse definitions were based on previous studies and are detailed in the *Online Supplementary Appendix*.

Patients were classified based on self-reported ancestry. Two groups were defined: patients of African ancestry (including Sub-Saharan and West-Indies origins) and patients of European ancestry. This classification was chosen to

reflect genetic and epidemiological relevance in the context of iTTP. Both groups were compared for the outcome following the administration of rituximab in the acute phase, in the preemptive setting or both. The primary endpoint was relapse-free survival (RFS) from the first course of rituximab according to ethnicity. Secondary endpoints included RFS from ≥2nd course of rituximab according to ethnicity and the assessment of risk factors of relapse. Assessment of response was performed as previously described.[5,12] ADAMTS13 response was defined by an ADAMTS13 activity of ≥20%. ADAMTS13 RFS (i.e., time to next ADAMTS13 relapse), clinical RFS (i.e., time to next clinical relapse) and combined RFS (i.e., time to next clinical and/or ADAMTS13 relapse) were calculated. We used the combined relapse endpoint for risk analysis.

Treatments administered in the acute phase and in the preemptive setting are detailed in the *Online Supplementary Appendix*. In the acute phase, rituximab was administered intravenously at a dose of 375 mg/m^2 on a day-1-4-8-15 schedule. In the preemptive setting, rituximab was started after detection of ADAMTS13 deficiency (<10%). The dose and administration regimen in the preemptive setting was usually of 375 mg/m^2/week for 4 weeks until 2012; thereafter, after evaluation of the risk-benefit balance (i.e., the potential infectious risk of repeated rituximab administrations in up to 50% of iTTP patients while a single administration improves efficiently ADAMTS13 activity in >85% of cases), one single administration of 375 mg/m^2 was performed.[4]

Statistics

Descriptive statistics were performed on the overall cohort and stratified by ethnic groups. Continuous variables were summarized as medians with interquartile ranges (interquartile range [IQR], 25-75%) and compared using the Wilcoxon-Mann-Whitney test. Categorical variables were described as counts and percentages and compared using χ^2 or Fisher's exact tests, as appropriate. Further details of statistical analyses are added in *Online Supplementary Appendix*.

All statistical analyses were conducted using R version 4.4.2 for macOS® (https://www.r-project.org, accessed October 2024). All *P* values were two-sided, with a significance threshold set at $P<0.05$.

Ethics and patient consent statement

This study was part of the Thrombotic Microangiopathy program study approved by the Ethics Committee of Hospital Pitié-Salpêtrière (Paris, France) (*clinicaltrials gov. Identifier: NCT00426686*), the Health Authority and the French Ministry of Health (P051064/PHRC AOM05012), and the French Data Protection Authority. Ethnicity data collection and analysis was approved by the Ethical Committee of Hospital Avicenne, Bobigny, France (CLEA-2025-469). All study procedures were performed in accordance with the Declaration of Helsinki.

Results

Baseline characteristics

At the time of the study, 3,565 patients with TMA were involved in the French National TMA registry, including 1,141 iTTP patients; among them, 942 received rituximab during

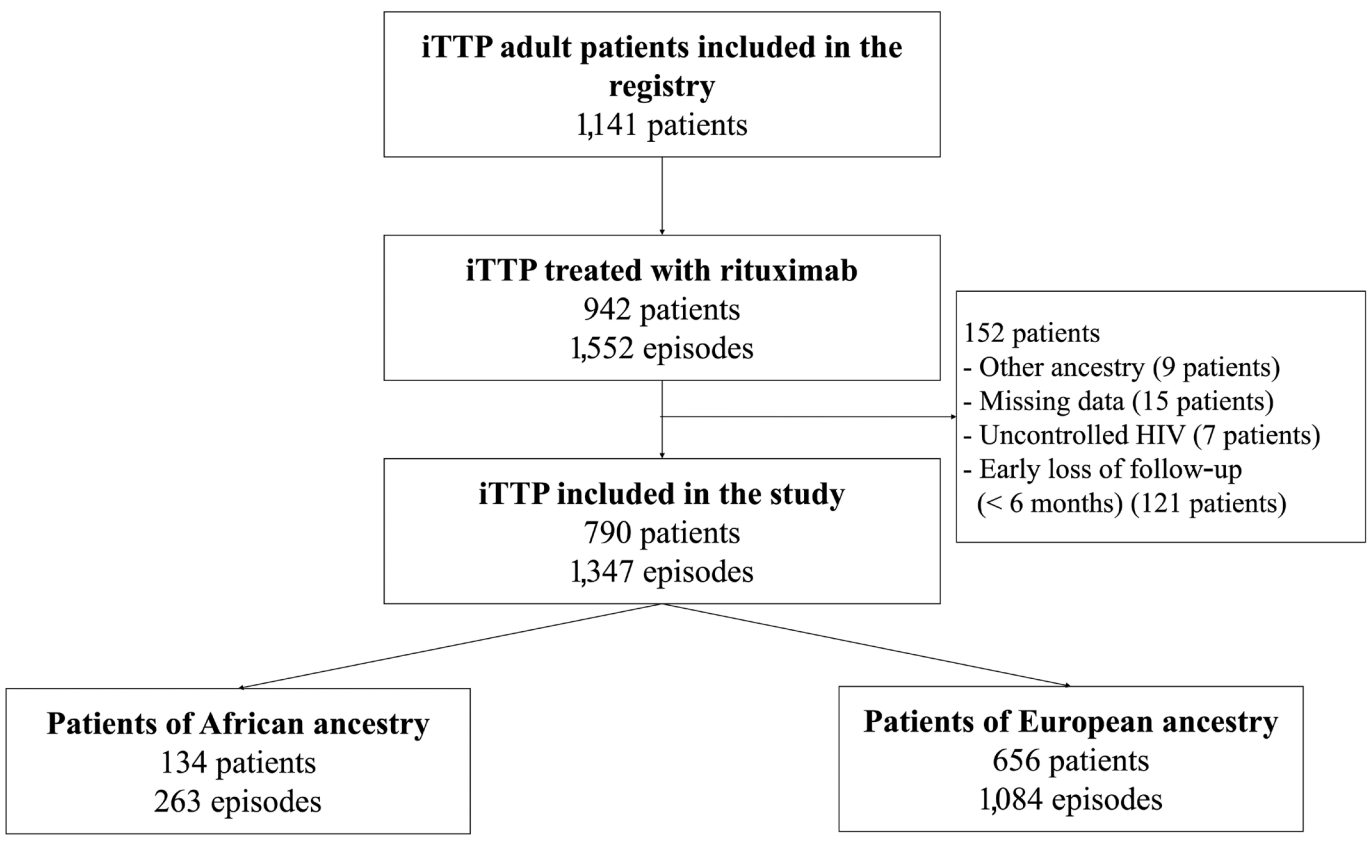


Figure 1. Flowchart of the study. iTTP instead of Ittp: immune-mediated thrombotic thrombocytopenic purpura; RTX: rituximab; HIV: human immunodeficiency virus.

Table 1. Baseline characteristics of patients.

Characteristics	Patients of African ancestry* N=134	Patients of European ancestry N=656	All N=790	*P*
Age, years at first rituximab administration, median (IQR)	41 (31-51)	42 (31-54)	43 (33-54)	0.3
Males, N (%)	29 (22)	193 (29)	222 (28)	0.068
First episode, N (%)	106 (79)	500 (76)	606 (77)	-
Indication of rituximab Acute episode, N (%) Preemptive therapy, N (%) 4-infusion regimen, N (%)**	 122 (91) 12 (9) 13 (9.7)	 604 (92) 52 (8) 63 (9.6)	 726 (92) 64 (8) 76 (9.6)	 0.7 - 0.97

IQR: interquartile range. *Including 33 patients from West-Indies; **performed until 2012.

the acute phase of the disease and/or as a preemptive treatment. We excluded 152 patients (9 had an ancestry other than African or European, 7 had an uncontrolled HIV infection, and 15 patients had no sufficient data; 121 additional patients were not considered in this study due to a follow-up of less than 6 months). A total of 1,347 episodes from 790 patients managed from 2000 to 2023 were finally analyzed (detailed flowchart in Figure 1). One hundred and thirty-four (17%) patients were of African ancestry (including 33 patients from West-Indies) and 656 were of European ancestry. Baseline characteristics of patients, including rituximab regimens (4-infusion *vs.* single course), were comparable (Table 1).

ADAMTS13 response to rituximab according to ethnicity

ADAMTS13 response (i.e., ADAMTS13 activity ≥20%) was achieved in up to 96% of patients following rituximab administration, regardless of ethnicity (Table 2). There was no difference in time to ADAMTS13 response between patients of African ancestry and those of European ancestry (median 36 *vs.* 37 days, respectively; *P*=0.99) (Table 2; Figure 2). After a comparable median follow-up between both groups (47 months; IQR, 25-95; and 41 months; IQR, 20-85, respectively; *P*=0.25), the rate of relapses did not significantly differ between groups (*P*=0.083) (Table 2), although the total number of relapses tended to be higher in patients of African ancestry (*P*=0.053) (Table 2). Following the first course of rituximab, we found that 3-year combined RFS was significantly lower for patients of African ancestry than for patients of European ancestry (*P*=0.015) (Figure 3A).

Risk factors for relapse

To further assess if ethnicity had a cumulative impact in relapse risk, we performed a multivariate Prentice-Williams-Peterson analysis stratified by episode number, to identify risk factors for combined relapse. This analysis identified African ancestry as an independent risk factor for cumulative combined relapse (hazard ratio [HR]=1.50; 95% confidence interval [CI]: 1.20-1.88; *P*<0.001). Other independent risk factors for combined relapse were male sex (HR=1.24; 95% CI: 1.01-1.54; *P*=0.043) and the type of index episode treated by rituximab (relapse *vs.* first episode, for all cumulative episodes, HR=1.61; 95% CI: 1.20-2.17; *P*=0.002) (Table 3, Figure 3B).

In a second approach, we investigated the contribution of episode number to subsequent relapse risk. Using a Cox regression model, we confirmed that a relapsing episode, male sex and African ancestry were associated with a higher risk of relapse; in addition, we found that the risk of relapse progressively increased with episode number, regardless of ethnicity (Table 4; Figure 4). Accordingly, and regardless ethnicity, patients with a first iTTP episode experienced a relapse in 37% of cases, whereas patients who had a first or a second relapse experienced a further relapse in 46% and 59% of cases, respectively.

Table 2. Response to rituximab (preemptive treatment) or to rituximab-containing regimens (acute phase treatment).

Response	African ancestry N=134	European ancestry N=656	*P*
Clinical refractoriness, N (%)	2 (2)	6 (1)	0.6
Exacerbation, N (%)	22 (18)	122 (20)	0.6
ADAMTS13 refractory, N (%)	3 (2)	30 (5)	0.2
Any type of relapse, N (%)	58 (43)	232 (35)	0.083
Clinical relapse, N (%)	22 (16)	95 (14)	0.6
Number of clinical relapses, median (IQR)	1 (1-2)	1 (1-2)	0.5
ADAMTS13 relapse, N (%)	47 (35)	187 (29)	0.13
Number of ADAMTS13 relapses, median (IQR)	0 (0-1)	0 (0-1)	0.078
Death, N (%)	0 (0)	11 (2)	0.2

ADAMTS13: a disintegrin and metalloporteinase with thrombospondin-1 motifs, 13th member; IQR: interquartile range.

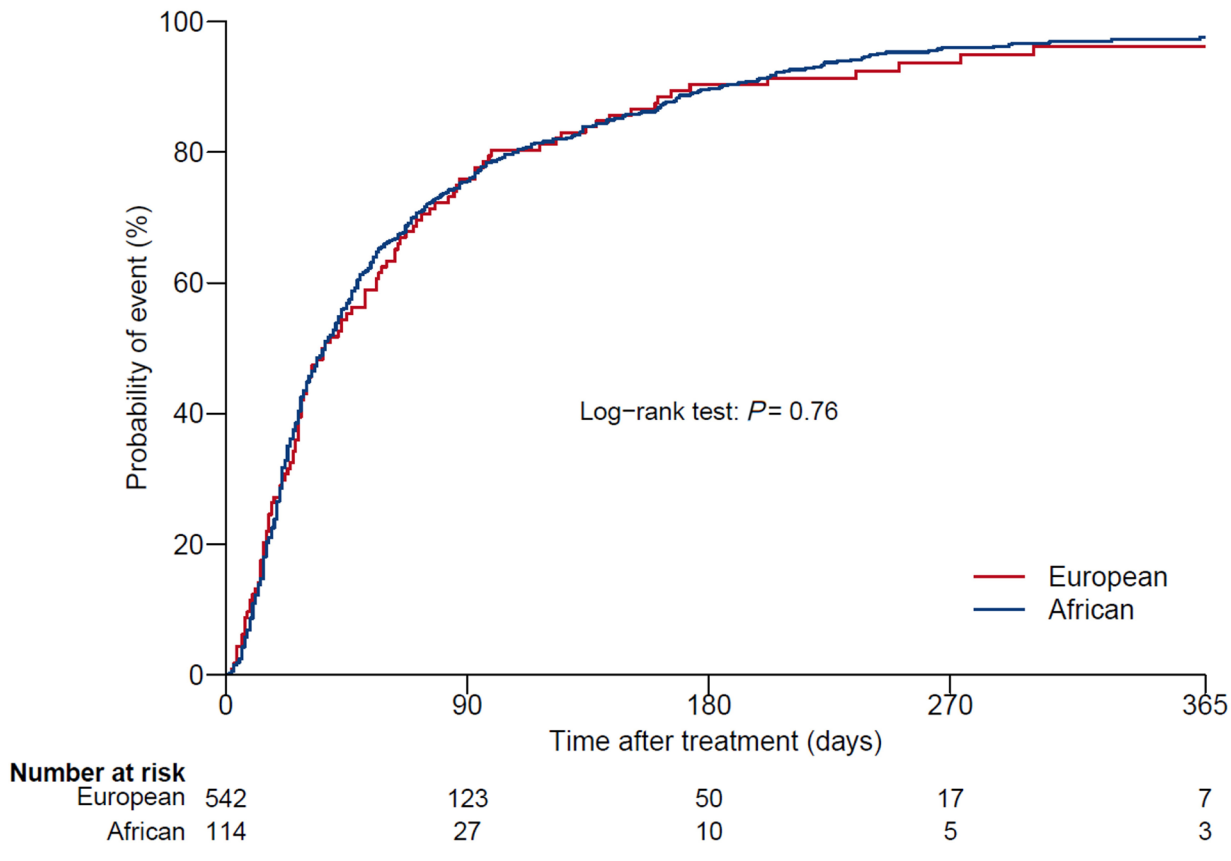


Figure 2. ADAMTS13 response (ADAMTS13 activity ≥20%) after rituximab administration in patients according to ethnicity. ADAMTS13: a disintegrin and metalloporteinase with thrombospondin-1 motifs, 13th member.

Discussion

In this large, nationwide cohort of closely monitored French iTTP patients, we found that African ancestry is associated with a significantly shorter RFS following rituximab treatment compared to patients of European ancestry. This association persisted after adjusting for confounders and was observed across both initial and subsequent courses of rituximab. Importantly, the time to ADAMTS13 recovery following rituximab did not differ between ethnic groups, highlighting that early therapeutic response is preserved, but durability of remission may be compromised in patients of African ancestry. Additionally, the time to relapse progressively shortened with the number of rituximab courses regardless of ethnicity, underscoring the cumulative burden of disease recurrence in relapsing patients.

Our findings provide robust confirmation of prior observations from US cohorts suggesting ethnic disparities in RFS following rituximab in iTTP.[9,10] By replicating and expanding these findings in a distinct healthcare and social context with systematic ADAMTS13 monitoring, we validate the association between African ancestry and increased relapse risk. Nevertheless, in contrast to a previous report, we show that the progressive shortening of the time to relapse is independent of ethnicity.[10] This discrepancy is most likely explained by the greater statistical power of our study, which included a larger number of patients. In that regard, the association between the number of consecutive therapeutic lines and shorter ADAMTS13 RFS highlights the importance of a personalized approach and a tailored ADAMTS13 monitoring during follow-up to prevent clinical relapses.

Table 3. Risk factors of cumulative combined (clinical and/or ADAMTS13) relapse.

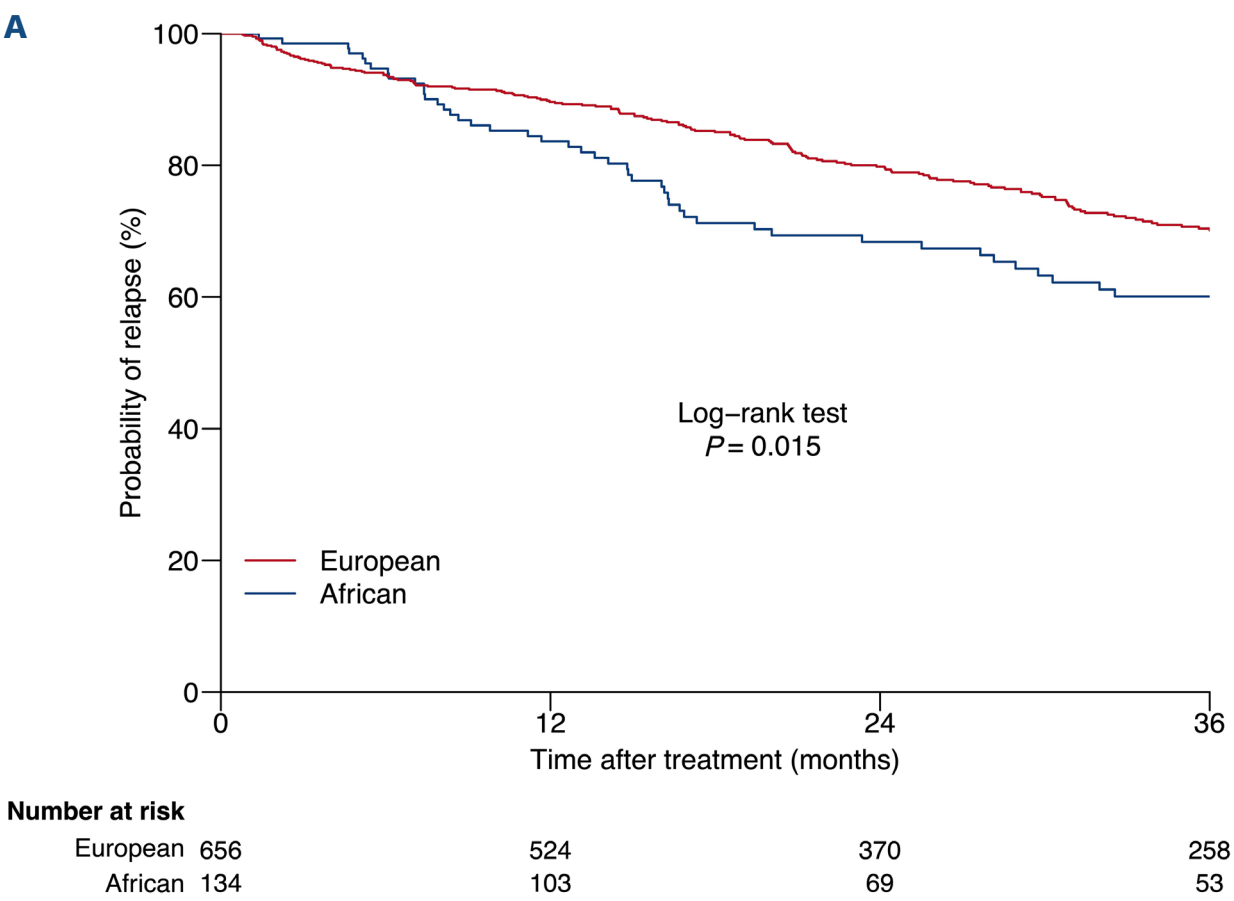
Variable	Hazard ratio (CI)	*P*
African ancestry	1.50 (1.20-1.88)	<0.001
Age	1.00 (1.00-1.01)	0.58
Male sex	1.24 (1.01-1.54)	0.043
Initial relapse	1.61 (1.20-2.17)	0.002

CI: confidence interval.

The mechanisms underlying the different RFS by ethnicity remain incompletely understood. By analogy with other immune-mediated diseases, hypotheses include faster B-cell repletion after anti-CD20 therapy, differences in B-cell subset distribution, HLA-related genetic predispositions and more frequent immunization against rituximab.[8,13-15] Notably, a lower prevalence of protective alleles such as HLA-DRB1*04 has been described in patients of African ancestry.[16] Further prospective studies with integrated immunophenotyping, pharmacokinetics, and genomics are warranted. In the meantime, intensified ADAMTS13 monitoring and tailored preemptive strategies may be justified in patients of African ancestry to mitigate relapse risk. Patient education and improved compliance are crucial in optimal follow-up. In that regard, we believe our results should help treating physicians better understand potential risk factors associated with shorter ADAMTS13 RFS, and tailor ADAMTS13 monitoring to improve outcome. The potential role of alternative or next-generation immunomodulatory

agents, such as obinutuzumab or anti-CD38 antibodies, should also be explored in this population.

Our study has several strengths. It is the largest to date to examine the role of ethnicity in iTTP relapse and the first to explore this question within a European context. The current analysis relies on data from a well-characterized, prospective national registry. Importantly, all patients underwent regular ADAMTS13 monitoring, allowing precise determination of both clinical and ADAMTS13 relapses. This approach contrasts with prior studies limited to clinical relapses alone. Nonetheless, some limitations should be acknowledged. Ethnicity was self-reported and dichotomized into broad categories, potentially obscuring intra-group heterogeneity. Moreover, although the French healthcare system provides universal coverage, unmeasured social determinants of health, may still influence outcomes. Lastly, rituximab regimen changed during the study period, with a 4-weekly infusion course of rituximab in the first years and a single infusion from 2012. However, the 4-weekly infusion course only involved a minority of patients (<10%)



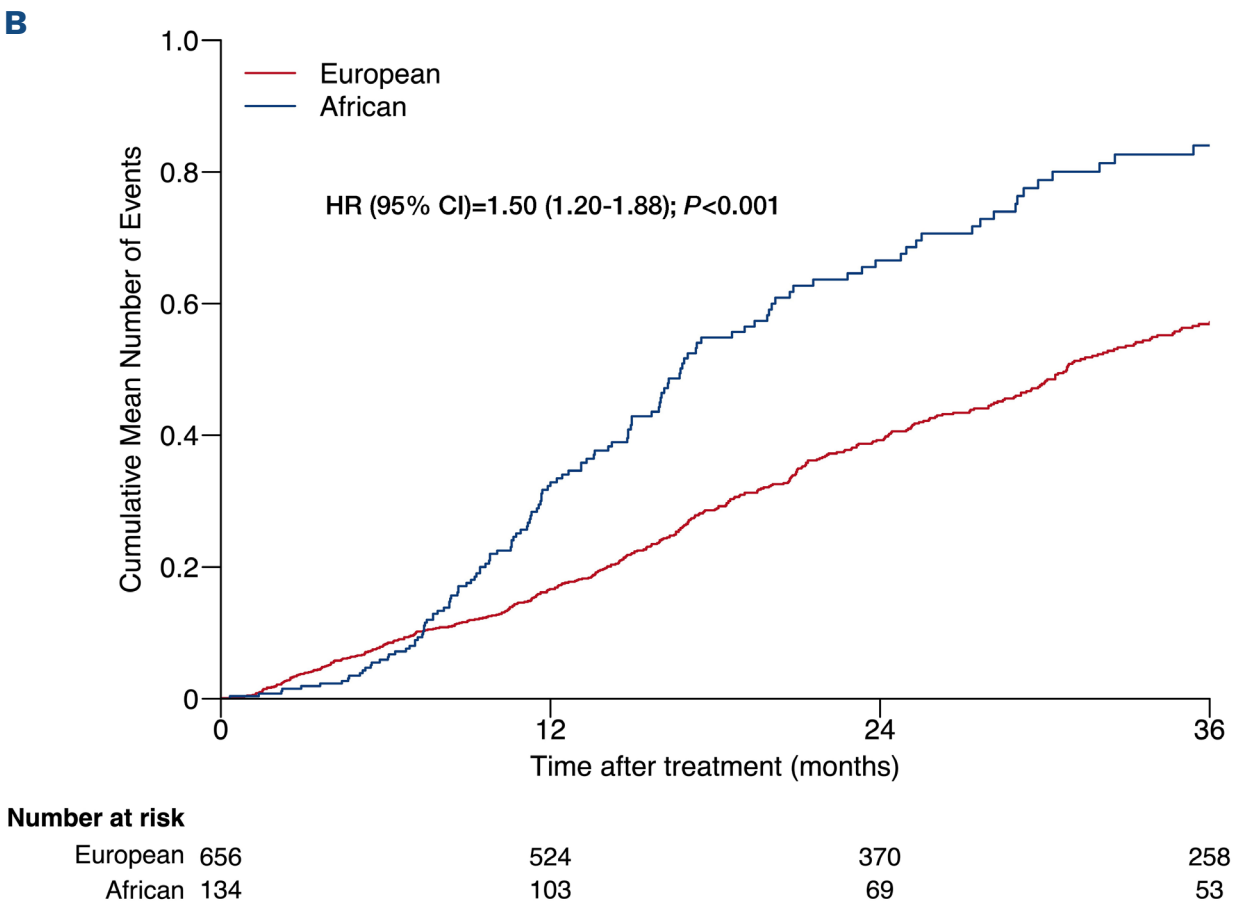
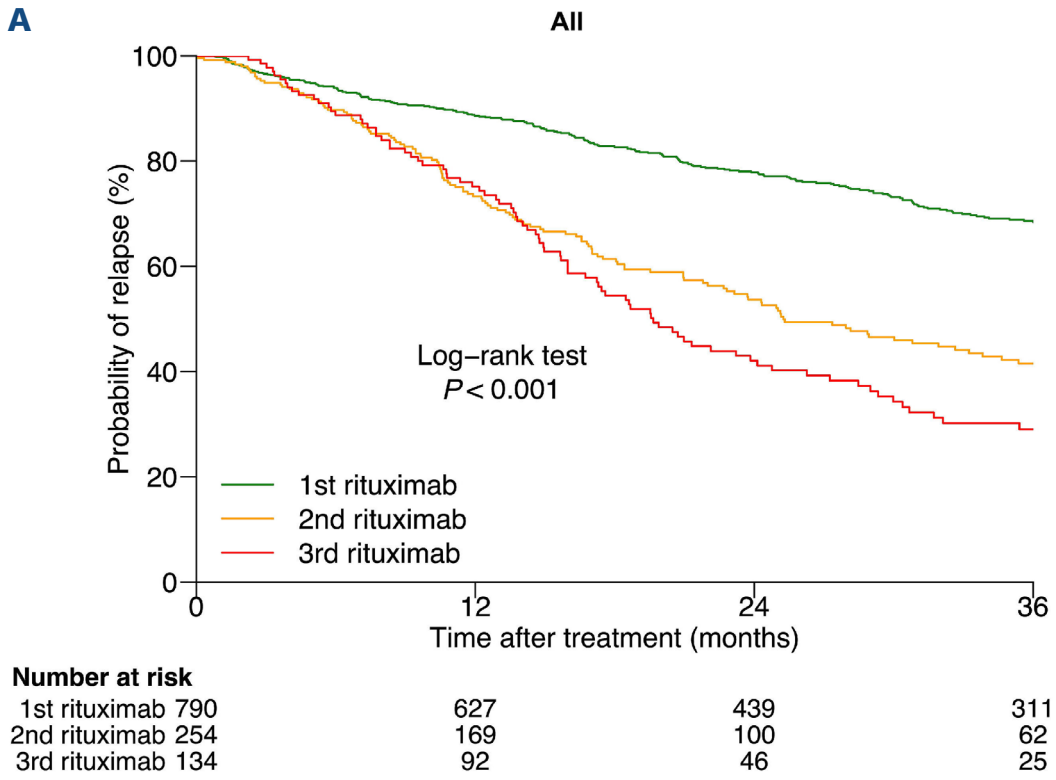
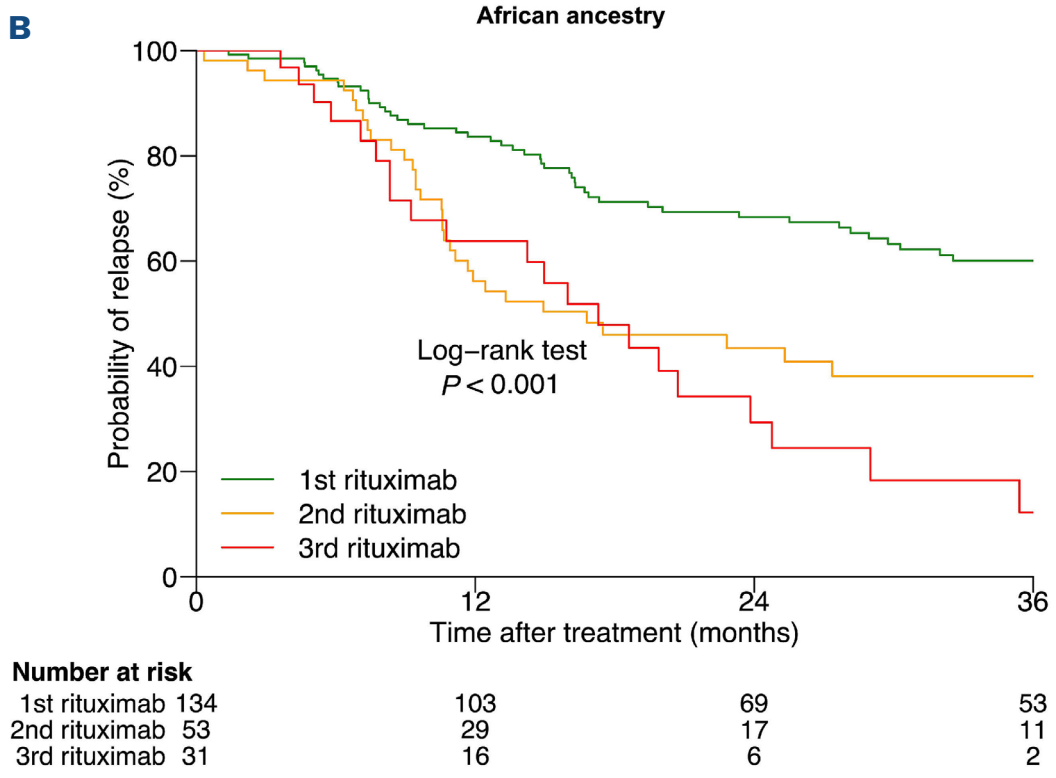


Figure 3. Relapse-free survival after rituximab administration. (A) Three-year combined relapse-free survival. (B) Mean cumulative function for combined relapse following rituximab according to ethnicity. HR: hazard ratio; CI: confidence interval.





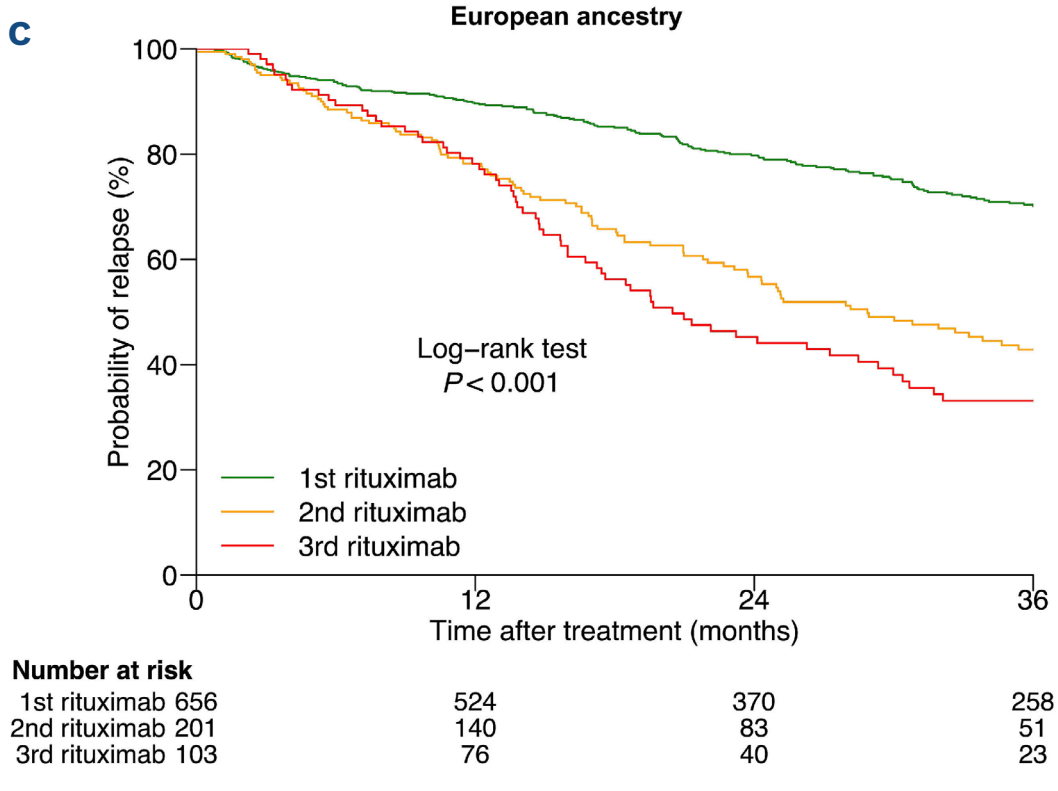


Figure 4. Combined relapse-free survival following consecutive rituximab treatment lines. (A) Combined relapse-free survival (RFS) in all patients, (B) in African ancestry patients, and (C) in patients of European ancestry.

equally distributed in both subgroups; therefore, the impact of this initially more intensive regimen on our conclusions is very unlikely. On the other hand, one could consider treating patients from African ancestry with more intensive rituximab regimens, as these were associated with better ADAMTS13 RFS.[4,17]

In conclusion, this study identifies African ancestry as an independent risk factor for relapse following rituximab treatment in iTTP, despite comparable initial responses. These findings underscore the importance of integrating ethnicity into risk stratification models and support regular ADAMTS13 monitoring as a cornerstone of long-term management, to facilitate a more personalized approach, particularly in high-risk groups, to prevent clinical relapse and optimize outcomes.

Table 4. Contribution of episode number to subsequent relapse risk.

Variable	Hazard ratio (CI)	*P*
Episode number		
1	1 (reference)	-
2	1.67 (1.27-2.19)	<0.001
3	2.25 (1.67-3.03)	<0.001
4 and subsequent	2.20 (1.64-1.66)	<0.001
African ancestry	1.36 (1.12-1.66)	0.002
Age	1.00 (1.00-1.01)	0.70
Male sex	1.21 (1.02-1.44)	0.031
Initial relapse	1.62 (1.24-2.11)	<0.001

CI: confidence interval.

Disclosures

PC is member of the clinical advisory board for Alexion, Sanofi and Takeda. AV is a member of the French clinical advisory board for Sanofi and Takeda. BJ has participated in advisory boards for Sanofi, Takeda and Alexion. FB discloses lecture fees from ASPEN. YD participated in advisory boards for Sanofi, Takeda, Samsung, Novartis and Alexion. All other authors have no conflict of interest to disclose.

Contributions

JW collected the data, prepared the datafile for statistical analyses and wrote the first version of the manuscript. BS, CD, JF, FP, PP, MM, DR, GC, YD, EA, YB, MG, JMH, MLQ, AS, TP, CL, CC, VC, JFA, SV, PP, LL, ML, AR, AH, VR, AJ, PZ, LG and NM treated the patients. SRP, RG, MTG, MD, DG TA and AAI participated in data collection. AP and FB performed the statistical analysis. RB organized the data collection from all centers. BJ and AV performed all ADAMTS13 explorations and critically reviewed the manuscript. AP and PC initiated the study, contributed to the data analysis, edited the manuscript and supervised the work.

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Data-sharing statement

Original data are available upon reasonable request to the corresponding author.

Appendix

The members of the Reference Center for Thrombotic Microangiopathies (CNR-MAT) are: J-F. Augusto (Service de Néphrologie, dialyse et transplantation ; CHU Larrey, Angers); E. Azoulay (Service de Réanimation Médicale, Hôpital Saint-Louis, Paris); V. Barbay (Laboratoire d'Hématologie, CHU Charles Nicolle, Rouen); Y. Benhamou (Service de Médecine Interne, CHU Charles Nicolle, Rouen); B. Cador-Rousseau (Service de Néphrologie, Hôpital Pontchaillou, Rennes); C. Cartery (Service de Néphrologie, Centre Hospitalier de Valenciennes); Charvet-Rumpler Anne (Service d'Hématologie, CHU de Dijon); D. Chauveau and R. Davis (Service de Néphrologie et Immunologie Clinique, CHU Rangueil, Toulouse); G. Choukroun (Service de Néphrologie, Hôpital Sud, Amiens); J-P. Coindre (Service de Néphrologie, CH Le Mans); P. Coppo (Service d'Hématologie, Hôpital Saint-Antoine, Paris); Y. Delmas (Service de Néphrologie, CHU de Bordeaux, Bordeaux); A. Dossier (Service de Néphrologie, Hôpital Bichat, Paris); O. Fain (Service de Médecine Interne, Hôpital Saint-Antoine, Paris); L-M. Fornecker (Service d'Oncologie et d'Hématologie, Hôpital de Hautepierre, Strasbourg); V. Frémeaux-Bacchi (Laboratoire d'Immunologie, Hôpital Européen Georges Pompidou, Paris); L. Galicier (Département de Médecine Interne, CHU de Marseille - Hôpital de la Timone); M. Grall (Service de Réanimation Médicale, CHU Charles Nicolle, Rouen); S. Grangé (Service de Néphrologie, CHU Charles Nicolle, Rouen); J-M. Halimi (Service de Néphrologie Pédiatrique, Hôpital Bretonneau, Tours); A. Hertig (Service de Néphrologie, Hôpital de Foch-Suresnes); M. Hié (Service de Médecine Interne, Groupe Hospitalier Pitié-Salpétrière, Paris); A. Jaccard (Service d'Hématologie, CHU de Limoges);

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References

1. Joly BS, Coppo P, Veyradier A. Thrombotic thrombocytopenic purpura. Blood. 2017;129(21):2836-2846.
2. Kremer Hovinga JA, Coppo P, Lämmle B, Moake JL, Miyata T, Vanhoorelbeke K. Thrombotic thrombocytopenic purpura. Nat Rev Dis Primers. 2017;3(1):1-17.
3. Hie M, Gay J, Galicier L, et al. Preemptive rituximab infusions after remission efficiently prevent relapses in acquired thrombotic thrombocytopenic purpura. Blood. 2014;124(2):204-210.
4. Jestin M, Benhamou Y, Schelpe AS, et al. Preemptive rituximab prevents long-term relapses in immune-mediated thrombotic thrombocytopenic purpura. Blood. 2018;132(20):2143-2153.
5. Zheng XL, Vesely SK, Cataland SR, et al. ISTH guidelines for the diagnosis of thrombotic thrombocytopenic purpura. J Thromb Haemost. 2020;18(10):2486-2495.
6. Coppo P, Bubenheim M, Benhamou Y, et al. Caplacizumab use in immune-mediated thrombotic thrombocytopenic purpura: an international multicentre retrospective Cohort study (The Capla 1000+ project). EClinicalMedicine. 2025;82:103168.
7. Scully M, Yarranton H, Liesner R, et al. Regional UK TTP registry: correlation with laboratory ADAMTS 13 analysis and clinical features. Br J Haematol. 2008;142(5):819-826.
8. Saidenberg L, Arbini AA, Silverman GJ, Lotan I, Cutter G, Kister I. Faster B-cell repletion after anti-CD20 infusion in Black patients compared to white patients with neurologic diseases. Mult Scler Relat Disord. 2022;63:103830.
9. Chaturvedi S, Antun AG, Farland AM, et al. Race, rituximab, and relapse in TTP. Blood. 2022;140(12):1335-1344.
10. Fatola A, Evans MD, Brown J, et al. Relapse-free survival is progressively shortened in a subset of Black patients with immune-mediated TTP treated in the rituximab era. Blood Adv. 2025;9(2):417-424.
11. Coppo P, Bubenheim M, Azoulay E, et al. A regimen with caplacizumab, immunosuppression, and plasma exchange prevents unfavorable outcomes in immune-mediated TTP. Blood. 2021;137(6):733-742.
12. Cuker A, Cataland SR, Coppo P, et al. Redefining outcomes in immune TTP: an international working group consensus report. Blood. 2021;137(14):1855-1861.
13. Menard LC, Habte S, Gonsiorek W, et al. B cells from African American lupus patients exhibit an activated phenotype. JCI Insight. 2016;1(9):e87310.
14. Ritterhouse LL, Crowe SR, Niewold TB, et al. B lymphocyte stimulator levels in systemic lupus erythematosus: higher circulating levels in African American patients and increased production after influenza vaccination in patients with low baseline levels. Arthritis Rheum. 2011;63(12):3931-3941.
15. Combier A, Nocturne G, Henry J, et al. Immunization to rituximab is more frequent in systemic autoimmune diseases than in rheumatoid arthritis: ofatumumab as alternative therapy. Rheumatology (Oxford). 2020;59(6):1347-1354.
16. Martino S, Jamme M, Deligny C, et al. Thrombotic thrombocytopenic purpura in Black people: impact of ethnicity on survival and genetic risk factors. PLoS One. 2016;11(7):e0156679.
17. Westwood JP, Thomas M, Alwan F, et al. Rituximab prophylaxis to prevent thrombotic thrombocytopenic purpura relapse: outcome and evaluation of dosing regimens. Blood Adv. 2017;1(15):1159-166.