5. Carobbio A, Ferrari A, Masciulli A, Ghirardi A, Barosi G, Barbui T. Leukocytosis and thrombosis in essential thrombocythemia and polycythemia vera: a systematic review and meta-analysis. *Blood Adv*. 2019;3(11):1729-1737.
6. Shahneh F, Grill A, Klein M, et al. Specialized regulatory T cells control venous blood clot resolution through SPARC. *Blood*. 2021;137(11):1517-1526.
7. Kambas K, Mitroulis I, Apostolidou E, et al. Autophagy mediates the delivery of thrombogenic tissue factor to neutrophil extracellular traps in human sepsis. *PLoS One*. 2012;7(9):e45427.
8. Gadomska G, Stankowska K, Boinska J, Bartoszewska-Kubiak A, Haus O, Rość D. Activation of the tissue factor-dependent extrinsic pathway and its relation to *JAK2 V617F* mutation status in patients with essential thrombocythemia. *Blood Coagul Fibrinolysis*. 2016;27(7):817-821.
9. Maugeri N, Giordano G, Petrilli MP, et al. Inhibition of tissue factor expression by hydroxyurea in polymorphonuclear leukocytes from patients with myeloproliferative disorders: a new effect for an old drug? *J Thrombosis Haemostasis*. 2006;4(12):2593-2598.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

Received: 10 September 2021 | Revised: 3 November 2021 | Accepted: 5 November 2021

DOI: 10.1002/ajh.26404

Eltrombopag in adult patients with immune thrombocytopenia in the real-world in France, including off-label use before 6 months of disease duration: The multicenter, prospective ELEXTRA study

To the Editor:

Immune thrombocytopenia (ITP) is a rare autoimmune disease responsible for platelet destruction, impaired platelet production, and resulting in spontaneous bleeding.[1] First-line treatment is based on corticosteroids. Intravenous immunoglobulin (IVIg) is added in case of serious bleeding.[2,3] In 60%–70% of adult patients, ITP becomes persistent (lasting >3 months) and chronic (>12 months).[4] In such cases, second-line treatments are indicated, including rituximab, splenectomy, immunossupressants, thrombopoietin receptor agonists (TPO-RAs), and recently fostamatinib.[2,3] The two first TPO-RAs, romiplostim and eltrombopag, have been marketed in USA and Europe in 2008–2010. Eltrombopag binds to the transmembrane domain of the thrombopoietin receptor, inducing proliferation and differentiation of megakaryocytes. In randomized controlled trials, eltrombopag had a high efficacy rate, with the achievement of sustained response in >80% of patients. Safety signals were hepatitis, thromboembolism, and reversible myelofibrosis.[5] Eltrombopag was initially marketed for adult patients with chronic ITP, refractory or contraindicated to splenectomy. In the late 2010s, the indication was extended to patients aged ≥1 year, with ITP lasting ≥6 months, and refractory to at least one other treatment (e.g., corticosteroids, IVIg). In Europe, the use of eltrombopag before 6 months of disease duration is off-label, while it has been labeled in the USA in patients with persistent ITP (duration >3 months) in February 2021. Indeed, guidelines suggest that TPO-RAs, including eltrombopag, could be used early in the disease course as second-line treatment.[2,3]

Real-world data about eltrombopag use, effectiveness, and safety are scarce. They are based on retrospective series, with study periods ending before the publication of guidelines recommending TPO-RAs as second-line treatments early in the disease course (File S1). Therefore, real-world data about eltrombopag effectiveness and safety are needed, particularly in patients treated off-label before 6 months of ITP duration.

The study population consisted of all adult patients with incident ITP prospectively included and followed in the CARMEN-France registry from June 2013 to December 2019 who were exposed to eltrombopag during the disease course. Information about this registry is indicated in File S1. The Follow-up ended on December 31, 2019.

Exposure to eltrombopag was assessed describing the time from ITP diagnosis to first exposure to eltrombopag and the duration of first exposure to eltrombopag. Patients' characteristics were described, including previous lines of treatments. Concomitant treatment was defined by ongoing treatment at the time of eltrombopag initiation, IVIg in the previous month or rituximab in the previous 6 months.

Responses were assessed in the subgroup of patients with a platelet count $<30 \times 10^9$/L. Overall response was defined by achievement of platelet count $\geq 30 \times 10^9$/L, complete response by platelet count $\geq 100 \times 10^9$/L, partial response by platelet count between $30–100 \times 10^9$/L, and no response by platelet count $<30 \times 10^9$/L. We also described the time from eltrombopag initiation to overall response and complete response achievement; and the number of patients with no bleeding during exposure to eltrombopag.

In the whole population, the withdrawal of concomitant treatment present at eltrombopag initiation was described (except rituximab). The frequencies of eltrombopag withdrawal were also described. The reasons of eltrombopag withdrawal were retrospectively assessed.

Safety outcomes were the occurrence of adverse drug reactions (ADRs) during eltrombopag exposure, which were collected by investigators. Causality was then assessed by two investigators (G. Moulis. and M. Lafaurie) according to the World Health Organization causality assessment scale.[6] All ADRs with a causality score at least as "possible" were described.

All outcomes were measured for the first exposure to eltrombopag. Detailed statistical analyses are presented in File S1.

Out of 799 adult patients with incident ITP included in the CARMEN-France registry during the study period, 156 (19.6%) had been exposed to eltrombopag, including 95 (60.9%) before 6 months of ITP duration. Patients' characteristics are detailed in Table 1 (Table S1 for secondary ITP). In the whole cohort, eltrombopag was mostly used as second-line and third-line treatment (33.3% and 35.9%, respectively) with a median time from ITP diagnosis to eltrombopag initiation of 3.3 months. Patients' characteristics were similar between patients who initiated eltrombopag <6 months of ITP duration and those who initiated eltrombopag ≥6 months of ITP duration, except a higher frequency of patients with comorbidities of the Charlson's comorbidity index in the first group (46.2% vs. 27.9%) (Table 1).

Effectiveness outcomes among the patients with a platelet count $<30 \times 10^9$/L at eltrombopag initiation ($n = 75$) are presented in Table S2. Overall response was achieved in 86.7% of patients and complete response in 70.7%. These rates were similar between groups of disease duration, with a slightly higher rate of complete response rate in the <6 months group (Table S2). The median time to overall response was 8 days, and the median time to complete response was 19 days. The rates of overall response and complete response were similar by groups of age, sex, Charlson's comorbidity index, and number of previous lines of treatments (Table S3). During exposure to eltrombopag, 111 (71.2%) patients had no bleeding (74.7% and 65.6% in the groups with a disease duration <6 months and ≥6 months at eltrombopag initiation, respectively).

Out of 126 patients with concomitant treatment at eltrombopag initiation, 77 (60.1%) had the concomitant treatment permanently withdrawn during eltrombopag exposure (58.0% in the group with a disease duration <6 months at eltrombopag initiation).

In total, 91 (58.3%) patients stopped eltrombopag with a median duration of exposure of 1.8 months. The most frequent reasons were the absence or loss of response (34.1%), ADRs (24.2%) and sustained complete response (18.7%) (Table S4). The median duration of exposure to eltrombopag in the patients who stopped eltrombopag due to sustained response was 164 days.

Thirty-eight ADRs scored at least "possible" were reported in 35 patients (22.4%) (Table S5). Thromboembolism occurred in eight patients (Table S6).

In this French real-world prospective study of eltrombopag use in adult patients with ITP, the population was more severe than the general ITP population with 84.2% having experienced bleeding before eltrombopag initiation.[6] In clinical practice in France, eltrombopag was mostly used off-label before 6 months of ITP duration (60.9%) and as second- and third-line treatment, as suggested by recent guidelines.[2,3] No patient was splenectomized before eltrombopag, in contrast with the first retrospective series in the real-world (File S1). The Charlson's comorbidity index score was higher in patients exposed to eltrombopag in the first 6 months of ITP. We can hypothesize that this higher number of comorbidities resulted in an earlier prescription of eltrombopag instead of immunosuppressive drugs (higher risk of bleeding or of infection reflected a higher Charlson's index score).

The rates of response/complete response achievement, overall and without bleeding, as well as the time to response/complete response were similar to that observed in clinical trials and previous retrospective real-world series.[5] These rates must be taken with caution in real-world analysis, since concomitant treatment was frequently used either as acute rescue therapy until eltrombopag achieves effectiveness (i.e., corticosteroids or IVIg), or as exposure to previous second-line treatment with delayed effectiveness such as rituximab. In addition, 60.1% of the patients had definitively withdrawn a concomitant treatment during eltrombopag exposure, which is an additional strong outcome to assess real-world effectiveness. The fact that the rates of overall response and complete response were quite similar by subgroups of age, sex, Charlson's comorbidity index groups, previous lines of treatments, as well as by subgroups of disease duration is an important finding, arguing for the same effectiveness of TPO-RAs in patients in early phase of the disease.[5]

Among the 156 patients, 58.3% stopped eltrombopag. Among them, the reason was sustained response for 18.7%, corresponding to previous retrospective reports (Supporting Information S1).

The rate and pattern of ADRs observed in the ELEXTRA study are also in accordance with previous real-world retrospective studies.[5] Importantly, 8 (5.1%) patients experienced venous thrombosis, including 7 (4.5%) deep vein thrombosis and/or pulmonary embolism. The mechanisms inducing a higher rate of thrombosis (about 5 per 100 patient-years) in patients with ITP treated with TPO-RAs are unknown.[5] Of note, 6 of the 8 venous thromboses occurred in patients with a disease duration <6 months. This high incidence rate of thrombosis during the early phase of the disease must be taken with caution due to the low number of events. Almost all patients had other risk factors for thrombosis. No arterial event attributable to eltrombopag was reported in this study. This may be due to a causality assessment disfavoring eltrombopag in older, comorbid patients with a high prevalence of cardiovascular risk factors except age and sex. Myelofibrosis was not systematically searched in this real-world study but no ADR of central cytopenia was observed.

The limitations of this study are the inclusion of patients from mostly referral centers (except in the Midi-Pyrénées region) that may limit the representativeness of the population with more severe patients and an earlier use of eltrombopag in comparison with the entire population of ITP patients treated with eltrombopag in France. Only 75 patients (48.1%) had a platelet count $<30 \times 10^9$/L at eltrombopag initiation, allowing the measurement of response achievement. The presence of concomitant treatment makes the assessment of the true role of eltrombopag in response/complete response achievement difficult.

In conclusion, eltrombopag was used early in the ITP course in the French real-world practice. Effectiveness and safety profile identified in clinical trials and previous retrospective real-world series were confirmed, even in the subgroup of disease duration <6 months.

TABLE 1 Characteristics of patients exposed to eltrombopag

Characteristics	Total ($n = 156$)	ITP duration at eltrombopag initiation	
		<6 months ($n = 95$)	≥6 months ($n = 61$)
Age at ITP diagnosis, mean (±SD), years	60.2 (±20.9)	60.5 (±21.4)	59.7 (20.4)
Women, *n* (%)	77 (49.4%)	45 (47.4%)	34 (55.7%)
Cardiovascular risk factors[a], *n* (%)	89 (57.1%)	56 (58.9%)	33 (54.1%)
History of venous thrombosis, *n* (%)	9 (5.8%)	6 (6.3%)	3 (4.9%)
Charlson's Comorbidity Index score[b]			
0, *n* (%)	94 (61.0%)	50 (53.8%)	44 (72.1%)
1–2, *n* (%)	41 (26.6%)	28 (30.1%)	13 (21.3%)
≥3, *n* (%)	19 (12.3%)	15 (16.1%)	4 (6.6%)
Median platelet count at ITP diagnosis (Q1–Q3), $\times 10^9$/L	8.0 (5.0–33.0)	7.0 (5.0–17.0)	20.0 (5.0–38.0)
Bleeding at ITP diagnosis, *n* (%)	118 (75.6%)	76 (80.0%)	42 (68.9%)
Median time from ITP diagnosis to eltrombopag initiation (range), months	3.3 (0.1–82.2)	1.6 (0.1–5.9)	12.5 (6.0–82.2)
Median platelet count at eltrombopag initiation (Q1–Q3), $\times 10^9$/L	26.0 (12.0–41.0)	24.0 (11.0–41.0)	29.0 (15.0–41.0)
Bleeding before eltrombopag initiation, *n* (%)	132 (84.6%)	80 (84.2%)	52 (85.2%)
Lines of ITP treatments before eltrombopag initiation, median (range)	2 (0–5)	2 (0–4)	2 (0–5)
Eltrombopag in ITP treatment history			
1st line, *n* (%)	4 (2.6%)	3 (3.2%)	1 (1.6%)
2nd line, *n* (%)	52 (33.3%)	41 (43.2%)	11 (18.0%)
3rd line, *n* (%)	56 (35.9%)	32 (33.7%)	24 (39.3%)
4th line, *n* (%)	26 (16.7%)	14 (14.7%)	12 (19.7%)
>4th line, *n* (%)	18 (11.5%)	5 (5.3%)	13 (21.3%)
Previous treatments before eltrombopag initiation			
Corticosteroids, *n* (%)	150 (96.2%)	91 (95.8%)	59 (96.7%)
Intravenous immunoglobulin, *n* (%)	106 (67.9%)	66 (69.5%)	40 (65.6%)
Dapsone, *n* (%)	28 (17.9%)	11 (11.6%)	17 (27.9%)
Danazol, *n* (%)	8 (5.1%)	2 (2.1%)	6 (9.8%)
Rituximab, *n* (%)	26 (16.7%)	5 (5.3%)	21 (34.4%)
Romiplostim, *n* (%)	12 (7.7%)	5 (5.3%)	7 (11.5%)
Azathioprine, *n* (%)	2 (1.3%)	0	2 (3.3%)
Mycophenolate, *n* (%)	0	0	0
Ciclosporin, *n* (%)	1 (0.6%)	1 (1.1%)	0
Hydroxychloroquine, *n* (%)	14 (9.0%)	6 (6.3%)	8 (13.1%)
Vinblastine, *n* (%)	5 (3.2%)	5 (5.3%)	0
Splenectomy, *n* (%)	0	0	0
Concomitant ITP treatment at eltrombopag initiation			
Corticosteroids	76 (48.7%)	52 (54.7%)	24 (39.3%)
Intravenous immunoglobulin (IgIV)[c]	76 (48.7%)	57 (60.0%)	19 (31.1%)
Dapsone	5 (3.2%)	3 (3.2%)	2 (3.3%)
Danazol	3 (1.9%)	2 (2.1%)	1 (1.6%)
Hydroxychloroquine	8 (5.1%)	5 (5.3%)	3 (4.9%)
Immunosuppressors	2 (1.3%)	1 (1.0%)	1 (1.6%)
Romiplostim	5 (3.2%)	1 (1.0%)	4 (6.6%)
Rituximab[c]	20 (12.8%)	5 (5.3%)	15 (24.6%)

Abbreviation: ITP, immune thrombocytopenia.

[a]Excluding age (>50 years for men and >60 years for women) and sex.

[b]Missing data for 2 patients.

[c]Patients were considered as concomitantly exposed to intravenous immunoglobulin in case of infusion during the previous month, and to rituximab in case of infusion during the previous 6 months.

ACKNOWLEDGEMENTS

The ELEXTRA was funded by Novartis SAS. The CARMEN-France registry is sponsored by Toulouse University Hospital and also received grants from CSL Behring, Amgen, Grifols, Novartis, the French Society of Internal Medicine and French referral centers for autoimmune cytopenias. See Conflict of interest statement for the role of the funder.

CONFLICT OF INTEREST

This study was granted by Novartis SAS. The design of the ELEXTRA study, protocol, and statistical analyses plan were made by GM, MA, and SLT. Novartis SAS had no access to data and no role in analysis, interpretation of results and manuscript writing. The present manuscript has been sent to Novartis SAS representatives before submission, with no substantial modification requested from the authors. GM received meeting attendance grants from Amgen and Novartis, is coordinator of research studies granted by Amgen, CSL Behring, Novartis and Grifols. He participated in educational sessions funded by Amgen and Novartis, and to boards for Amgen, Novartis and Sobi. TC received honoraria and/or research or educational support from AbbVie, AstraZeneca, Bristol Myers Squibb (Celgene), Novartis and Takeda. SC is investigator of research studies granted by Bioverativ, Novartis, Protalex, Rigel and participated to boards for Novartis and Sobi. ME received meeting attendance grants from Novartis, Octapharma and Sobi, and participated to educational sessions for Amgen, Grifols, Novartis and to boards for Grifols and Novartis. MMi participated to educational sessions and boards for Amgen, Argenx, Novartis, Sobi, and UCB. BG participated to educational sessions and boards Amgen, Grifols, Novartis, Roche and Sobi. All other authors declare having no conflict of interest.

REFERENCES

1. Cooper N, Ghanima W. Immune thrombocytopenia. *N Engl J Med*. 2019;381:945-955.
2. Provan D, Arnold DM, Bussel JB, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. *Blood Adv*. 2019;3:3780-3817.
3. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv*. 2019;3:3829-3866.
4. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood*. 2009;113:2386-2393.
5. Ghanima W, Cooper N, Rodeghiero F, Godeau B, Bussel JB. Thrombopoietin receptor agonists: ten years later. *Haematologica*. 2019;104:1112-1123.
6. Piel-Julian M-L, Mahévas M, Germain J, et al. Risk factors for bleeding, including platelet count threshold, in newly diagnosed immune thrombocytopenia adults. *J Thromb Haemost*. 2018;16:1830-1842.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

APPENDIX A: COLLABORATORS: CARMEN INVESTIGATORS GROUP

Daniel ADOUE, Laurent ALRIC, Baptiste ANDRE, Sophie ARISTA, Laurent BALARDY, Delphine BONNET, Bernard BONNOTTE, Odile BEYNE-RAUZY, Cécile BOREL, Delphine BRECHEMIER, Antoine BRIANTAIS, Natacha BRUN, Miguel CARREIRO, Brice CASTEL, Thibault COMONT, Pierre COUGOUL, Carine COURTAULT, Alina DANU, Karen DELAVIGNE, Xavier DELBREL, Samuel DESHAYES, Claire DINGREMONT, Jérémie DION, Pierre DUFFAU, Jean-Marc DURAND, Jean ESTELLE, Benoît FAUCHER, Francis GACHES, Clément GAUDIN, Patrick GIRAUD, Aurélie GODEL-LABOURET, Julie GRAVELEAU, Sondess HADJ-KHELIFA, Jean-Robert HARLE, Benjamin HEBRAUD, Hélène HENNIQUE, Sarah KHATIBI, Maryse LAPEYRE-MESTRE, Kamel LARIBI, Lorraine LEPLAY, Yann LEVENEUR, François LIFERMANN, Nicolas LIMAL, Bertrand LIOGER, Sylvie OLLIER, Irène MACHELART, Serge MADAULE, Gwenola MAIGNE, Clothilde MARTEL, Guillaume MARTIN-BLONDEL, Martin MICHAUD, Julia MOEGLIN, Aline MOIGNET-AUTREL, Morgane MOURGUET, Philippe MONTANE DE LA ROQUE, Fanny NUCCIO, Corentin ORVAIN, Laurent PRUDHOMME, Grégory PUGNET, Christian RECHER, Véronique REMY, Patrick RISPAL, Frédérique ROY-PEAUD, Laurent SAILLER, Arnaud SAINT-LEZER, Benjamin de SAINTE MARIE, Aurélie SAUNIER, Gaëtan SAUVETRE, Nicolas SCHLEINITZ, Julie SEGUIER, Stéphane SIRE, Caroline SOUBRIER, Laure SWIADER, Suzanne TAVITIAN, Geoffrey URBANSKI, Willy VAILLANT, Véronique VEIT.

DATA AVAILABILITY STATEMENT

Data available upon request to corresponding author and after regulatory approval.

FUNDING INFORMATION

French referral centers for autoimmune cytopenias; the French Society of Internal Medicine; Novartis; Grifols; Amgen; CSL Behring; Toulouse University.

Guillaume Moulis[1,2], Johanne Germain[2], Manuela Rueter[2], Margaux Lafaurie[2,3], Myriam Aroichane[4], Thibault Comont[5], Matthieu Mahévas[6], Jean-François Viallard[7], Stéphane Chèze[8], Mikaël Ebbo[9], Sylvain Audia[10], Soraya Leclerc-Teffahi[4], Agnès Sommet[2,3], Odile Beyne-Rauzy[4], Marc Michel[5], Bertrand Godeau[5], Maryse Lapeyre-Mestre[2,3], the CARMEN investigators group

[1]*Department of Internal Medicine, Toulouse University Hospital, Toulouse, France*
[2]*Clinical Investigation Center, Toulouse University Hospital, Toulouse, France*
[3]*Department of Clinical Pharmacology, Toulouse University Hospital, Toulouse, France*
[4]*Novartis SAS, Rueil-Malmaison, France*
[5]*Department of Internal Medicine, Toulouse Cancer University Hospital, Toulouse, France*

[6]Department of Internal Medicine, National Referral Center for Autoimmune Cytopenias, Créteil University Hospital, Créteil, France
[7]Department of Internal Medicine, Bordeaux University Hospital, Bordeaux, France
[8]Department of Haematology, Caen University Hospital, Caen, France
[9]Department of Internal Medicine, Marseille University Hospital, Marseille, France
[10]Department of Internal Medicine, Dijon University Hospital, Dijon, France

Correspondence
Guillaume Moulis, Service de Médecine Interne, CHU Purpan, URM, place du Dr Baylac, 31059 Toulouse cedex 9, France.
Email: moulis.g@chu-toulouse.fr

List of Collaborators: CARMEN investigators group is available in the Appendix.

ORCID
Guillaume Moulis https://orcid.org/0000-0001-9953-4640
Margaux Lafaurie https://orcid.org/0000-0001-6010-2891
Thibault Comont https://orcid.org/0000-0002-6891-9238
Matthieu Mahévas https://orcid.org/0000-0001-9182-1434

Received: 5 August 2021 | Revised: 3 November 2021 | Accepted: 5 November 2021

DOI: 10.1002/ajh.26405

Venetoclax plus hypomethylating agent for the salvage treatment of relapsing myeloid malignancies after hematopoietic stem cell transplantation: A multicenter retrospective study on behalf of the Zhejiang Cooperative Group for Blood and Marrow Transplantation

To the Editor:

Hematopoietic stem cell transplantation (HSCT) offers the highest possible curative potential for patients with hematological malignancies. However, the management of post-transplant relapse remains a challenging task. In general, the prognosis of patients with post-transplant relapse is extremely poor, since many of them cannot tolerate or are refractory to commonly used approaches. In view of this, the risks and benefits of salvage treatment must be weighed up, and novel, less toxic, more efficient treatment options are urgently needed.

Venetoclax (VEN), an oral selective inhibitor of anti-apoptotic protein B-cell leukemia/lymphoma-2 (BCL-2), has been approved for the treatment of a variety of hematologic malignancies.[1,2] In relapsed/refractory (R/R) myeloid malignancies, the combination of VEN and hypomethylating agent (HMA) has exhibited an encouraging treatment effect.[3] Nevertheless, research about VEN-HMA administration for post-transplant relapse is still in a preliminary stage.

Herein, we conducted a multicenter retrospective study, with the aim to evaluate the efficacy and side effects of VEN-HMA for post-transplant relapse and determine which patients may benefit from this combination therapy. Between July 2018 and June 2021, 44 consecutive patients with post-transplant relapse received VEN-HMA inpatient at 5 centers of Zhejiang province. The salvage treatment consisted of VEN for 28 consecutive days (100 mg of VEN for the first day and 200 mg for the second day, then increased to the final dose of 400 mg daily or equivalent to azole co-administration). Either azacytidine (AZA, 75 mg/m^2, d1-7) or decitabine (DEC, 20 mg/m^2, d1-5) was used as a VEN partner. During VEN-HMA treatment, hydration and alkalization were performed for the prophylaxis of tumor lysis syndrome (TLS). The response to VEN-HMA was determined according to the 2017 European Leukemia Net (ELN) response criteria. Adverse events were accessed by the Common Terminology Criteria for Adverse Events (CTCAE5.0)

Table S1 summarizes the patient baseline characteristics. Acute myeloid leukemia (AML) ($n = 34$) and myelodysplastic syndrome (MDS, $n = 7$) were the most common disease types. Each patient was analyzed for chromosomal and genetic abnormalities either at diagnosis and at post-transplant relapse. A complex/monosomal karyotype was seen in 10 (22.7%) patients. Ten patients (22.7%) had TP53 mutation or deletion, 6 (13.6%) exhibited IDH1/2 mutation (Figure 1A). Based on the 2017 ELN risk stratification, a total of 23 (52.3%) patients had adverse risk profiles. All patients experienced intramedullary relapse except two that relapsed at the chest wall and spine, respectively. Ten (22.7%) patients relapsed within 6 months, 18 (40.9%) relapsed between 6 months to 1 year, and 16 (36.4%) relapsed >1-year post-transplantation. Eighteen (40.9%) patients developed acute graft versus host disease (aGVHD) and 16 (36.4%) developed chronic graft versus host disease (cGVHD) before relapse.

Thirty-nine (88.6%) patients received VEN-HMA at first relapse after transplantation, while 5 (11.4%) received VEN-HMA at second relapse after transplantation. Twenty-six (59.1%) patients were treated with VEN-HMA directly after relapse (first-line therapy). For the remaining 18 (40.9%) patients, VEN-HMA was administrated as second-line therapy after failure of chemotherapy or DLI. Twenty-three (52.3%) patients had a higher tumor burden (bone marrow blasts >20%) at the initiation of VEN-HMA.