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Treatment characteristics and outcomes in lower-risk, non-del(5q) myelodysplastic syndromes: findings from a medical record review in the USA, Canada and Europe

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ABSTRACT

Aim: To assess treatment patterns and outcomes in patients with non-del(5q) lower-risk myelodysplastic syndromes.

Methods: Patient medical records were reviewed in the USA, Canada (CAN), UK and the EU.

Results: Analysis included 119 patients in the USA/CAN (median age, 61.5 years) and 245 patients in the UK/EU (median age, 67.3 years). Most patients received erythropoiesis-stimulating agents (ESAs) as first-line (1L) therapy (USA/CAN: 89.0%; UK/EU: 90.2%). A substantial proportion of 1L erythropoiesis-stimulating agent-treated patients were transfusion dependent before 1L (USA/CAN: 37.1%; UK/EU: 51.2%); a small percentage of these patients achieved transfusion independence during 1L therapy (USA/CAN: 2.8%; UK/EU: 14.4%).

Conclusion: These findings highlight an unmet need for more effective treatments among patients with non-del(5q) lower-risk myelodysplastic syndromes.

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hematologic outcomes; lower-risk myelodysplastic syndromes; non-del(5q); real-world data; treatment patterns

1. Introduction

Myelodysplastic syndromes (MDS) are a group of clonal hematopoietic stem cell malignancies characterized by ineffective hematopoiesis, peripheral blood cytopenias and variable risk of progression to acute myeloid leukemia (AML) [1]. Most patients with MDS have lower-risk MDS (LR-MDS), which comprises the Very low, Low and Intermediate risk categories defined by the Revised International Prognostic Scoring System (IPSS-R) [2]. These patients carry less risk of AML progression compared with patients with higher-risk MDS and are primarily affected by symptomatic anemia, requiring them to receive frequent red blood cell transfusions (RBCTs) [3,4]. Although RBCTs are an essential component of supportive care and symptom management, transfusion dependence is associated with reduced survival and has a substantial impact on quality of life [5–8]. Therefore, the primary goal of LR-MDS treatment is to manage anemia and reduce transfusion burden [3].

Approximately 85%–90% of patients with LR-MDS are reported to have the non-del(5q) karyotype [9,10]. Erythropoiesis-stimulating agents (ESAs) are an established treatment for the non-del(5q) LR-MDS associated anemia in patients who are ESA-naive, alone or in combination with granulocyte colony-stimulating factor (G-CSF) [3]. Chelation therapy is also common in this patient population for the treatment of iron overload due to frequent RBCTs [11]. Treatment options are relatively limited for patients with non-del(5q) LR-MDS who are unresponsive to ESAs. Current treatments include erythroid maturation agent luspatercept, lenalidomide and oral azacitidine [3,12,13]. Luspatercept was shown to reduce the severity of anemia in patients with LR-MDS with ring sideroblasts (RS) who were transfusion dependent (TD) and refractory, intolerant or ineligible to receive ESAs [13]. Furthermore, in the phase 3, randomized controlled

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COMMANDS trial, luspatercept demonstrated clinically meaningful and statistically significant improvements in RBC transfusion independence (TI) and hematologic improvement-erythroid rates compared with ESAs, in ESA-naive patients with LR-MDS who require RBCTs (ClinicalTrials.gov Identifier: NCT03682536) [14,15].

Real-world treatment patterns and clinical outcomes in patients with non-del(5q) LR-MDS have not been well documented. Understanding how patients are managed in routine clinical practice is essential to identifying best practices and opportunities for further investigation. This study investigated real-world treatment patterns and hematologic outcomes in patients with non-del(5q) LR-MDS across North America and Europe.

2. Methods

2.1. Study design

This retrospective, noninterventional study used data collected from a review of medical records of patients diagnosed with non-del(5q) LR-MDS. Data were abstracted between June and November 2021 by practicing hematologists, oncologists and hematologist-oncologists recruited in the USA, Canada (CAN), UK and three countries in the EU (France, Germany and Spain) through an electronic case report form. To be eligible for study inclusion, physicians must have treated at least five patients with MDS in the year before data abstraction, practiced for at least 3 years after completion of their formal training or board certification and acted as a primary decision-maker regarding the patient's LR-MDS treatment. Physicians were recruited via a fieldwork partner agency who identified potential participants using physician directories maintained by local medical associations (i.e., the American Medical Association physician database); in-house databases; and telephone directories when supplemental recruitment efforts were needed. Physicians who participated in the study were compensated for their time spent on data abstraction according to a usual and customary rate. This study was reviewed by the RTI International Institutional Review Board (IRB) (Federal-Wide Assurance #3331). Countries requiring a local IRB were subjected to additional review by country- and site-specific IRBs, where applicable.

2.2. Patient selection criteria

Eligible patients were adults (≥18 years of age) with a histologically confirmed diagnosis of primary or *de novo* MDS, as documented in patient medical records, between 1 July 2013 and 30 September 2018 (Figure 1). The diagnoses were limited to September 2018, as at the time of initial study designing, this ensured availability of at least 24 months of *potential* follow-up duration to adequately assess therapy lines and clinical outcomes. Eligible patients were also required to have non-del(5q) mutation status and lower-risk status, as measured by the International Prognostic Scoring System (IPSS) or the IPSS-R at the time of diagnosis of MDS as follows: (1) Low or Intermediate-1 IPSS risk level or (2) Very low, Low or Intermediate IPSS-R risk level. Patients were excluded from the study if they had a history of AML or evidence of other malignant neoplasms prior to MDS diagnosis, with the following exceptions: disease-free status for ≥5 years at the time of MDS diagnosis; presence of basal or squamous cell carcinoma of the skin; presence of carcinoma *in situ* of the cervix; presence of carcinoma *in situ* of the breast; or an incidental histologic finding of prostate cancer (stage T1a or T1b). The earliest of death or last available medical record defined the end of study follow-up.

2.3. Patient characteristics & clinical outcomes

Patient demographic and clinical characteristics were assessed at or within 12 months before the study index date, which was defined as the date of LR-MDS diagnosis. Demographic characteristics included patients' country of residence, age at MDS diagnosis, sex and race/ethnicity. The following clinical characteristics at MDS diagnosis were collected: risk status as measured by the IPSS or the IPSS-R, hemoglobin levels, presence of the splicing factor 3b subunit 1 (*SF3B1*) cytogenetic mutation, RS status and serum erythropoietin (EPO) levels. Hemoglobin levels were classified as very low (male: <9 g/dl; female: <8 g/dl), low (male: 9–10.9 g/dl; female: 8–11.9 g/dl), or near normal/normal (male: ≥11 g/dl; female: ≥12 g/dl), and RS status was defined as positive with the presence of ≥15% RS, or ≥5% (but <15%) RS in patients with the *SF3B1* mutation.

Treatment characteristics were assessed during the follow-up period after the study index date, including the number of lines of therapy, all agents received within each line of therapy, regimen start and stop dates, rationale for prescribing each treatment line and reasons for discontinuation of each therapy line. When reporting the rationale for prescribing treatment, physicians were asked to select all reasons that applied among the following options: compliance with national guidelines; compliance with local guidelines; treatment efficacy; patient's overall health; disease characteristics; safety; patient's request; convenience of administration; or other or unknown. Similarly, physicians were asked to select all reasons for treatment discontinuation and were provided the following options: adverse event, patient decision,

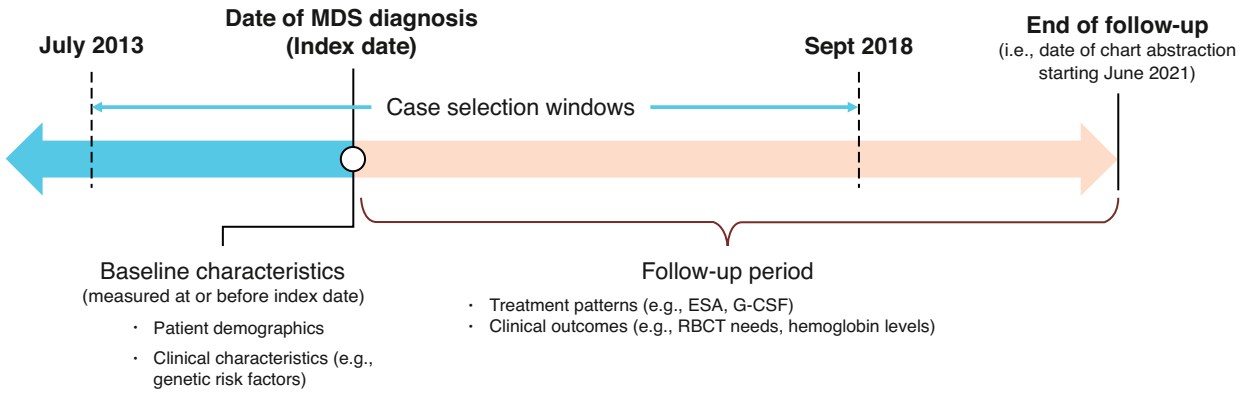

Figure 1. Overview of study design.
ESA: Erythropoiesis-stimulating agent; G-CSF: Granulocyte colony-stimulating factor; MDS: Myelodysplastic syndromes; RBCT: Red blood cell transfusion.

progressive disease, completion of planned course of treatment or lost to follow-up.

All hematologic measures were assessed at the time of initial LR-MDS diagnosis in order to understand the burden of disease at the baseline. Hematologic outcomes during the post-index follow-up period were evaluated for each line of therapy as measured from initiation of the treatment line through discontinuation or, if the treatment was ongoing, through end of follow-up. Hematologic outcomes of interest included: transfusion dependency status, RBCT reduction, hemoglobin levels and serum EPO levels. Transfusion dependence was defined as requiring $\geq$2 RBC units and was measured within the 8-week period [16]. Transfusion independence was defined as requiring $<$2 RBC units and was measured during any 8-week period over the course of a therapy line. Thresholds for hematologic improvement were defined as a decrease of $\geq$50% in the need for RBCT or an increase in hemoglobin level of $\geq$1.5 g/dl or 15 g/l at any point during the therapy line as compared with the corresponding values recorded at the initiation of the therapy line.

2.4. Statistical analysis

Patient demographics, clinical characteristics, treatment patterns and hematologic outcomes were reported descriptively. Aggregated analyses were performed using pooled US/CAN and UK/EU cohorts and for subgroups of patients treated with 1L ESA-containing regimens in each cohort. Additionally, country-specific analyses were performed to further characterize geographic variations in treatment patterns and hematologic outcomes. All analyses were performed in SAS statistical software, version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Patient demographics & clinical characteristics

Medical record data were abstracted for 119 patients with non-del(5q) LR-MDS in USA/CAN and 245 patients in UK/EU. Data were abstracted by 77 physicians in the USA/CAN and 136 physicians in the UK/EU. Participating physicians were primarily hematologist-oncologists (USA/CAN = 83.1%; UK/EU = 50.0%) practicing in academic settings (USA/CAN: 57.1%; UK/EU: 70.6%); detailed physician characteristics are presented in Supplementary Table S1.

The median age of patients was 61.5 years in the USA/CAN and 67.3 years in the UK/EU, and most were male (USA/CAN = 71.4%; UK/EU = 71.4%). Patients who identified as Black, African or African American represented 13.4% of the USA/CAN cohort and 0.8% in the UK/EU, and those who identified as Asian, Native Hawaiian or Other Pacific Islander represented 4.2% (USA/CAN) and 2.0% (UK/EU). The median follow-up time from MDS diagnosis was 50.5 months (USA/CAN) and 67.8 months (UK/EU). Per the IPSS-R, 50.4% (USA/CAN) and 53.5% (UK/EU) of patients were categorized as being at Low risk of MDS at initial diagnosis, whereas a smaller proportion of patients were categorized as being at Very low (USA/CAN: 20.2%; UK/EU: 19.2%) or Intermediate (USA/CAN: 26.1%; UK/EU: 20.8%) risk of MDS. Additionally, 44.5% (USA/CAN) and 43.7% (UK/EU) of patients were TD at initial diagnosis. Demographic and clinical characteristics for the USA/CAN and EU/UK cohorts, including the subgroups of patients treated with ESA-containing regimens in the 1L, are presented in Table 1. Demographic and clinical characteristics by country are reported in Supplementary Table S2.

Hemoglobin levels at initial diagnosis were categorized as very low in 47.0% of patients, low in 38.0% of

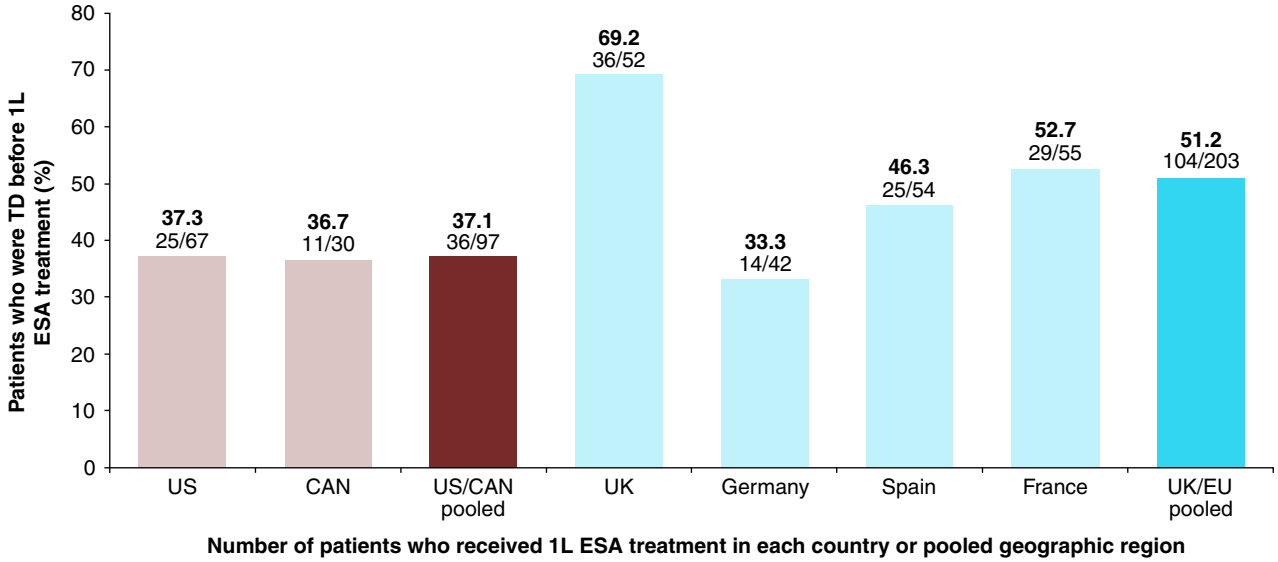

Figure 2. Transfusion dependence before 1L treatment.
Transfusion dependence before 1L treatment among a subgroup of patients with non-del(5q) LR-MDS treated with 1L ESA-containing regimens. Transfusion dependence was defined as a RBCT requirement of ≥2 units and was measured within the 8-week period before treatment initiation. Sample sizes (n) refer to the total sample size in each country or pooled geographic region.
1L: First-line; CAN: Canada; ESA: Erythropoiesis-stimulating agent; LR-MDS: Lower-risk myelodysplastic syndromes; RBCT: Red blood cell transfusion; TD: Transfusion dependent.

patients and near normal or normal in 15.0% of patients in the USA/CAN cohort. In the UK/EU, hemoglobin levels at diagnosis were Very low in 44.9% of patients, low in 41.1% of patients and near normal or normal in 14.0% of patients. Of the 38 patients (31.9%) in the USA/CAN and 92 patients (37.6%) in the UK/EU who were tested for RS status, 13.2% and 27.2% were classified as RS positive, respectively. For the *SF3B1* mutation, 71 patients (59.7%) in the USA/CAN and 123 patients (50.3%) in the UK/EU were tested, and of these patients, 16.9% (USA/CAN) and 15.4% (UK/EU) tested positive. Demographic and clinical characteristics of the subsets of 1L ESA-treated patients were generally consistent with the characteristics of the larger cohorts (Table 1).

3.2. Treatment characteristics

Most patients initiated 1L therapy (USA/CAN: 109 [91.6%]; UK/EU: 225 [91.8%]) with a mean time from MDS diagnosis to initiation of 1L treatment of 10.1 months in the USA/CAN and 9.6 months in the UK/EU. When asked to select all reasons for prescribing 1L treatment, the most frequently reported reasons were compliance with national guidelines (USA/CAN: 52 [47.7%]; UK/EU: 128 [56.9%]), compliance with local guidelines (USA/CAN: 26 [23.9%]; UK/EU: 95 [42.2%]) and treatment efficacy (USA/CAN: 50 [45.9%]; UK/EU: 100 [44.4%]) (Table 2). Supplementary Tables S3 & S4 present the rationale for prescribing treatment by cohort and for the subgroups treated with 1L ESA-containing regimens, respectively.

Most patients were treated with ESA-containing regimens in 1L (USA/CAN: 97 [89.0%]; UK/EU: 203 [90.2%]). The most frequent 1L therapy regimen was ESA monotherapy (USA/CAN: 84 [77.1%]; UK/EU: 174 [77.3%]); G-CSF was combined with ESAs for very few patients across countries (USA/CAN: 4 [3.7%]; UK/EU: 16 [7.1%]) (Table 3). A total of 62 patients (87.3%) in the USA (n = 62) were treated with ESA monotherapy compared with 57.9% of patients in CAN (n = 22). In the UK/EU, the proportions of patients treated with ESA monotherapy were as follows: 73.0% in the UK (n = 46), 71.2% in Germany (n = 37), 87.0% in Spain (n = 47) and 78.6% in France (n = 44). Similarly, the proportion of patients treated with ESA combined with G-CSF in the UK/EU was 7.9% in the UK (n = 5), 3.9% in Germany (n = 2), 5.6% in Spain (n = 3) and 10.7% in France (n = 6) (Supplementary Table S5). Among patients treated with ESA-containing regimens in 1L, the mean time to initiation of treatment was 10.4 months in the USA/CAN and 10.0 months in the UK/EU, and the median duration of therapy was ≥2 years (Table 2).

More than a third of patients initiated a second-line (2L) therapy (USA/CAN: 45 [37.8%]; UK/EU: 89 [36.3%]) (Table 3). Among patients treated with ESA-containing regimens in 2L (12 [26.7%] USA/CAN; 26 [29.2%] UK/EU), most had been treated with ESA in the 1L (USA/CAN: 11 [91.7%]; UK/EU: 22 [84.6%]) (data not shown). In the

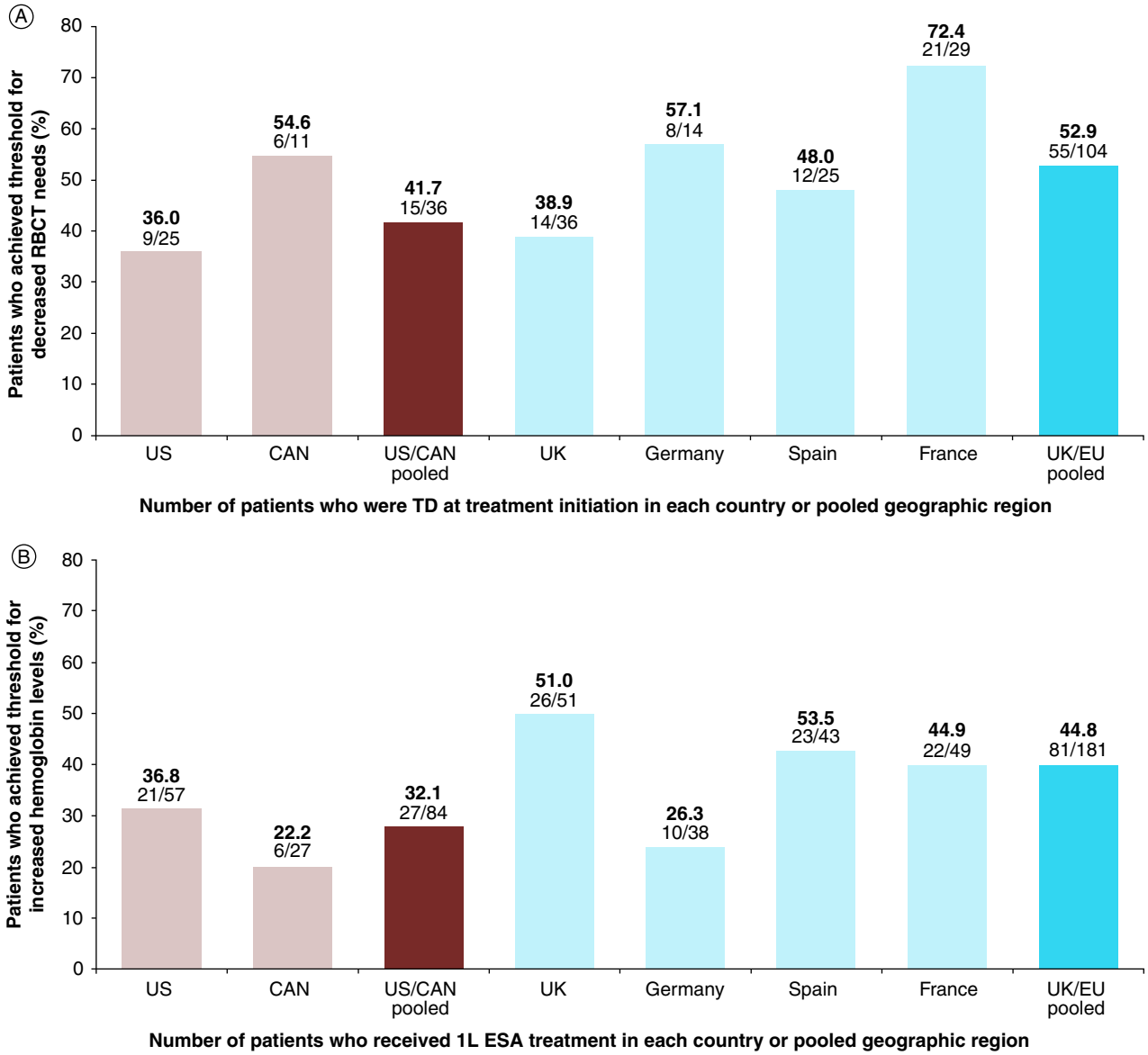

Figure 3. Hematologic improvement achieved during 1L ESA therapy. **(A)** RBCT reduction. Hematologic improvement based on the threshold for RBCT reduction among a subgroup of patients with non-del(5q) LR-MDS treated with 1L ESA-containing regimens. The threshold for hematologic improvement was defined as a decrease of ≥50% in the RBCT need at any point during follow-up compared with diagnosis or treatment initiation. Sample sizes refer to the total sample size in each country or pooled geographic region. **(B)** Increased hemoglobin levels. Hematologic improvement based on the threshold for increased hemoglobin levels among a subgroup of patients with non-del(5q) LR-MDS treated with 1L ESA-containing regimens. The threshold for hematologic improvement was defined as an increase in hemoglobin level of ≥1.5 g/dl or 15 g/l. Sample sizes refer to the total sample size in each country or pooled geographic region. Assessed among patients with known hemoglobin level at treatment initiation.
1L: First-line; CAN: Canada; ESA: Erythropoiesis-stimulating agent; LR-MDS: Lower-risk myelodysplastic syndromes; RBCT: Red blood cell transfusion.

subgroup of patients who reinitiated ESA in 2L, the most frequently reported reasons for discontinuation of 1L ESA were patient decision (42.9%, USA/CAN; 15.1%, UK/EU), completion of planned course of therapy (42.9%, USA/CAN; 30.2%, UK/EU) and progressive disease (25.0%, USA/CAN; 50.9%, UK/EU) (Table 2). The most frequently reported reasons for reinitiating treatment with ESAs in 2L, other than compliance with national and local guidelines, were treatment efficacy (45.2%, USA/CAN; 40.2%, UK/EU), overall health status (33.3%, USA/CAN; 23.2%, UK/EU) and disease characteristics (31.0%, USA/CAN; 30.5%, UK/EU).

3.3. Clinical outcomes in patients treated with ESAs

Clinical outcomes in each cohort were consistent with those in the subgroups of patients treated with ESA-

Table 1. Demographic and clinical characteristics of patients with non-del(5q) LR-MDS.

	Overall		ESA-treated in 1L	
	USA/CAN	UK/EU	USA/CAN	UK/EU
Total patients, n	119	245	97	203
Demographic characteristics				
Age at initial diagnosis of primary MDS, median (Q1, Q3), y	61.5 (53.5, 67.1)	67.3 (61.6, 73.2)	60.7 (54.5, 67.1)	67.8 (61.6, 73.2)
Sex, n (%)				
Male	85 (71.4)	175 (71.4)	72 (74.2)	144 (70.9)
Female	34 (28.6)	70 (28.6)	25 (25.8)	59 (29.1)
Race, n (%)				
White	96 (80.7)	174 (71.0)	79 (81.4)	143 (70.4)
Black/African American (USA only)	14 (11.8)	NA	12 (12.4)	NA
Black/African (UK, CAN, Spain, and Germany)	2 (1.7)	2 (0.8)	1 (1.0)	2 (1.0)
Asian, Native Hawaiian or Other Pacific Islander	5 (4.2)	5 (2.0)	3 (3.1)	2 (1.0)
Unknown	2 (1.7)	1 (0.4)	2 (2.1)	1 (0.5)
Ethnicity,[a] n (%)				
Hispanic	6 (5.0)	NA	4 (4.1)	NA
Not Hispanic	70 (58.8)	NA	61 (62.9)	NA
Unknown	2 (1.7)	NA	2 (2.1)	NA
Clinical characteristics				
Total duration of follow-up,[b] median (Q1, Q3), mo	50.5 (36.1, 74.8)	67.8 (39.1, 79.9)	54.8 (36.2, 77.1)	68.1 (40.9, 80.1)
IPSS-R risk status at MDS diagnosis, n (%)				
Very low	24 (20.2)	47 (19.2)	16 (16.5)	30 (14.8)
Low	60 (50.4)	131 (53.5)	51 (52.6)	116 (57.1)
Intermediate	31 (26.1)	51 (20.8)	27 (27.8)	45 (22.2)
Unknown	4 (3.4)	16 (6.5)	3 (3.1)	12 (5.9)
TD at baseline (i.e., ≥2 units per 8 wk), n (%)	53 (44.5)	107 (43.7)	48 (49.5)	100 (49.3)
Low transfusion burden (2–5 units per 8 wk)	44 (83.0)	82 (76.6)	40 (83.3)	79 (79.0)
High transfusion burden (≥6 units per 8 wk)	9 (17.0)	25 (23.4)	8 (16.7)	21 (21.0)
TI at baseline, n (%)	66 (55.5)	138 (56.3)	49 (50.5)	103 (50.7)
Hemoglobin at MDS diagnosis				
n (%)	100 (84.0)	214 (87.4)	83 (85.6)	177 (87.2)
Very low (male: <9 g/dl; female: <8 g/dl), n (%)	47 (47.0)	96 (44.9)	41 (49.4)	89 (50.3)
Low (male: 9–10.9 g/dl; female: 8–11.9 g/dl), n (%)	38 (38.0)	88 (41.1)	34 (41.0)	72 (40.7)
Near normal/normal (male: ≥11 g/dl; female: ≥12 g/dl), n (%)	15 (15.0)	30 (14.0)	8 (9.6)	16 (9.0)
RS status[c] at MDS diagnosis				
n (%)	38 (31.9)	92 (37.6)	30 (30.9)	81 (39.9)
Positive, n (%)	5 (13.2)	25 (27.2)	5 (16.7)	24 (29.6)
Negative, n (%)	33 (86.8)	67 (72.8)	25 (83.3)	57 (70.4)
SF3B1 mutation at MDS diagnosis, n (%)				
Positive	12 (10.1)	19 (7.8)	11 (11.3)	15 (7.4)
Negative	59 (49.6)	104 (42.5)	47 (48.5)	89 (43.8)
Unknown	48 (40.3)	122 (49.8)	39 (40.2)	99 (48.8)
Serum EPO[d]				
At MDS diagnosis, n (%)	50 (42.0)	105 (42.9)	40 (41.2)	94 (46.3)
IU/l, median (Q1, Q3)	230.0 (160.0, 500.0)	200.0 (100.0, 400.0)	204.5 (140.0, 373.0)	200.0 (100.0, 400.0)
At start of 1L, n/N (%)	30/109 (27.5)	61/225 (27.1)	26/97 (26.8)	56/203 (27.6)
IU/l, median (Q1, Q3)	358.0 (200.0, 550.0)	150.0 (50.0, 350.0)	353.5 (200.0, 500.0)	169.5 (71.3, 367.5)
At start of 2L, n/N (%)	12/45 (26.7)	21/89 (23.6)	12/42 (28.6)	18/82 (22.0)
IU/l, median (Q1, Q3)	205.0 (160.0, 660.0)	50.0 (21.0, 250.0)	205.0 (160.0, 660.0)	34.0 (18.0, 250.0)

[a]Ethnic origin only asked in the USA.
[b]Length of follow-up is the duration of time between the date of initial diagnosis of MDS and death or end of patient record.
[c]RS status defined as positive if ≥15%, or ≥5% but <15% if *SF3B1* mutation is present; otherwise defined as negative.
[d]Includes values reported as IU-based units, g/dl, or mmol/l.
1L: First-line; 2L: Second-line; CAN: Canada; EPO: Erythropoietin; IPSS-R: Revised International Prognostic Scoring System; LR-MDS: Lower-risk myelodysplastic syndromes; Q: Quartile; RS: Ring sideroblasts; *SF3B1*: Splicing factor 3b subunit 1; TD: Transfusion dependent; TI: Transfusion independence; wk: Week; y: Year.

containing regimens in the 1L (Table 4). Because the majority of patients were treated with ESAs in the 1L, the following clinical outcome results focus on this subgroup of patients. Prior to 1L treatment, 37.1% (36/97) of patients treated with 1L ESA-containing regimens were TD in the USA/CAN (USA = 37.3%; CAN = 36.7%); 88.9% of these patients had a low transfusion burden (2–5 RBC units), while 11.1% had a high transfusion burden (≥6 RBC units). In the UK/EU 51.2% of patients were TD (UK = 69.2%; Germany = 33.3%; Spain = 46.3%; France = 52.7%) (Figure 2); 77.9% had a low transfusion burden whereas 22.1% had a high transfusion burden.

Table 2. Treatment characteristics of patients with non-del(5q) LR-MDS.

	Overall				ESA-treated in 1L			
	USA/CAN		UK/EU		USA/CAN		UK/EU	
	1L	2L	1L	2L	1L	2L	1L	2L
Total patients, n	109	45	225	89	97	42	203	82
Rationale for prescribing treatment, n (%)[a]								
In compliance with national guidelines (i.e., NCCN, ESMO)	52 (47.7)	16 (35.6)	128 (56.9)	44 (49.4)	47 (48.5)	16 (38.1)	123 (60.6)	43 (52.4)
In compliance with local guidelines (i.e., institution/hospital guidelines)	26 (23.9)	10 (22.2)	95 (42.2)	34 (38.2)	23 (23.7)	10 (23.8)	91 (44.8)	33 (40.2)
Treatment efficacy (i.e., potential for extending overall survival)	50 (45.9)	19 (42.2)	100 (44.4)	38 (42.7)	43 (44.3)	19 (45.2)	86 (42.4)	33 (40.2)
Patient's overall health (i.e., comorbidities)	24 (22.0)	14 (31.1)	49 (21.8)	24 (27.0)	20 (20.6)	14 (33.3)	34 (16.8)	19 (23.2)
Disease characteristics (i.e., rate of disease progression)	24 (22.0)	14 (31.1)	33 (14.7)	27 (30.3)	19 (19.6)	13 (31.0)	31 (15.3)	25 (30.5)
Safety (i.e., minimize risk of adverse events)	28 (25.7)	10 (22.2)	38 (16.9)	17 (19.1)	25 (25.8)	9 (21.4)	36 (17.7)	14 (17.1)
Patient's request (i.e., patient preference, financial reasons)	7 (6.4)	3 (6.7)	14 (6.2)	7 (7.9)	5 (5.2)	2 (4.8)	10 (4.9)	7 (8.5)
Convenience of administration	12 (11.0)	3 (6.7)	27 (12.0)	7 (7.9)	10 (10.3)	3 (7.1)	27 (13.3)	6 (7.3)
Other or unknown	2 (1.8)	0 (0.0)	6 (2.7)	0 (0.0)	2 (2.1)	0 (0.0)	5 (2.5)	0 (0.0)
Time from MDS diagnosis to initiation of treatment line, mean (SD), mo	10.1 (16.9)	28.0 (18.4)	9.6 (17.5)	32.3 (20.7)	10.4 (17.1)	28.6 (18.2)	10.0 (17.7)	33.3 (20.8)
Median (range), mo	1.3 (0.0–72.2)	26.3 (2.7–68.6)	1.6 (0.0–86.9)	30.4 (1.3–78.4)	1.7 (0.0–72.2)	26.6 (2.7–68.6)	1.9 (0.0–86.9)	30.7 (1.3–78.4)
Proportion of patients who discontinued treatment, n (%)	77 (70.6)	30 (66.7)	155 (68.9)	60 (67.4)	66 (68.0)	28 (66.7)	134 (66.0)	53 (64.6)
Time to treatment discontinuation, Kaplan–Meier estimates, median (95% CI), mo	23.9 (14.5, 36.1)	10 (3.9, 24.1)	28.6 (23.7, 35.0)	12.7 (9.3, 20.7)	25.8 (15.8, 37.9)	10.8 (4.2, 24.1)	31.8 (24.4, 37.8)	12.7 (9.3, 23.9)
Reason for treatment discontinuation, n (%)[a]								
Adverse event	1 (1.3)	2 (6.7)	4 (2.6)	4 (6.7)	1 (1.5)	1 (3.6)	4 (3.0)	4 (7.6)
Patient decision	15 (19.5)	13 (43.3)	25 (16.1)	9 (15.0)	13 (19.7)	12 (42.9)	22 (16.4)	8 (15.1)
Progressive disease	32 (41.6)	7 (23.3)	55 (35.5)	28 (46.7)	30 (45.5)	7 (25.0)	53 (39.6)	27 (50.9)
Completion of planned course of treatment	27 (35.1)	13 (43.3)	46 (29.7)	21 (35.0)	20 (30.3)	12 (42.9)	33 (24.6)	16 (30.2)
Lost to follow-up (only if last line)	2 (2.6)	0 (0.0)	6 (3.9)	2 (3.3)	2 (3.0)	0 (0.0)	3 (2.2)	2 (3.8)
Death (only if last line and if patient is deceased)	4 (5.2)	1 (3.3)	17 (11.0)	3 (5.0)	4 (6.1)	1 (3.6)	16 (11.9)	3 (5.7)
Other or unknown[b]	4 (5.2)	2 (6.7)	13 (8.4)	4 (6.7)	4 (6.1)	2 (7.1)	12 (9.0)	3 (5.7)

[a]Percentages may not add up to 100 as multiple reasons could be selected for rationale for prescribing treatment and treatment discontinuation.
[b]Other reasons for treatment discontinuation included comorbidity and lack of efficacy.
1L: First-line; 2L: Second-line; CAN: Canada; ESA: Erythropoiesis-stimulating agent; ESMO: European Society for Medical Oncology; LR-MDS: Lower-risk myelodysplastic syndromes; MDS: Myelodysplastic syndromes; mo: Month; NCCN: National Comprehensive Cancer Network; NE: Not estimable; SD: Standard deviation.

Among these patients who were TD before 1L, only a small proportion (2.8% USA/CAN; 14.4% UK/EU) achieved TI during 1L.

The threshold for RBCT reduction (i.e., ≥50% reduction in RBCT) was met by 41.7% of 1L ESA-treated patients who were TD at treatment initiation in the USA/CAN (n = 15/36; mean duration, 23.0 months), with a greater proportion of patients meeting the RBCT reduction threshold in CAN (n = 6/11; 54.6%) compared with the USA (n = 9/25; 36.0%) (Figure 3A). In the UK/EU, 52.9% of 1L ESA-treated patients who were TD at treatment initiation met the threshold for RBCT reduction (n = 55/104; mean duration, 13.0 months) (UK: 14/36 [38.9%]; Germany: 8/14 [57.1%]; Spain: 12/25 [48.0%]; France: 21/29 [72.4%]) (Figure 3A). The mean time to the first record of a ≥50% decrease in RBCT needs was 2.2 months in the USA/CAN and 3.7 months in the UK/EU.

The threshold for hemoglobin improvement (i.e., hemoglobin level increased by ≥1.5 g/dl or 15 g/l) was achieved by 32.1% of 1L ESA-treated patients in the USA/CAN (n = 27/84) (USA: 21/57 [36.8%]; CAN: 6/27 [22.2%]) and 44.8% in the UK/EU (n = 81/181) (UK: 26/51 [51.0%]; Germany: 10/38 [26.3%]; Spain: 23/43 [53.5%]; France: 22/49 [44.9%]) (Figure 3B). The mean time to the first record of hemoglobin increase by ≥1.5 g/dl or 15 g/l was 5.8 months in the USA/CAN and 4.0 months in the UK/EU. Median serum EPO levels generally decreased over time as recorded at the start of each therapy line

Table 3. Treatment utilization patterns of patients with non-del(5q) LR-MDS.

	USA/CAN	UK/EU
Total patients, n	119	245
No systemic lines of therapy, n (%)	10 (8.4)	20 (8.2)
1L, n (%)	109 (91.6)	225 (91.8)
ESA	84 (77.1)	174 (77.3)
ESA + G-CSF	4 (3.7)	16 (7.1)
G-CSF	3 (2.8)	12 (5.3)
Alemtuzumab	2 (1.8)	0 (0.0)
Azacitidine	2 (1.8)	3 (1.3)
Venetoclax + ESA	2 (1.8)	0 (0.0)
Lenalidomide	1 (0.9)	2 (0.9)
Alemtuzumab + azacitidine + ESA + G-CSF	1 (0.9)	0 (0.0)
Alemtuzumab + ESA	1 (0.9)	1 (0.4)
Cyclosporine + azacitidine + luspatercept + ESA + G-CSF	1 (0.9)	0 (0.0)
Cyclosporine	1 (0.9)	1 (0.4)
Cyclosporine + ESA + G-CSF	1 (0.9)	0 (0.0)
Cyclosporine + lenalidomide + luspatercept + ESA + G-CSF	1 (0.9)	0 (0.0)
Decitabine	1 (0.9)	1 (0.4)
Decitabine + ESA + G-CSF	1 (0.9)	0 (0.0)
Lenalidomide + luspatercept + ESA + G-CSF	1 (0.9)	0 (0.0)
Nplate	1 (0.9)	0 (0.0)
Venetoclax	1 (0.9)	1 (0.4)
Lenalidomide + ESA	0 (0.0)	1 (0.4)
Alemtuzumab + azacitidine + luspatercept + ESA + G-CSF	0 (0.0)	0 (0.0)
2L, n (%)	45 (37.8)	89 (36.3)
Azacitidine	9 (20.0)	15 (16.9)
G-CSF	6 (13.3)	28 (31.5)
Lenalidomide	5 (11.1)	4 (4.5)
ESA	4 (8.9)	6 (6.7)
Luspatercept	4 (8.9)	7 (7.9)
Decitabine	3 (6.7)	0 (0.0)
ESA + G-CSF	2 (4.4)	7 (7.9)
Azacitidine + ESA	2 (4.4)	2 (2.3)
Azacitidine + ESA + G-CSF	0 (0.0)	3 (3.4)
Azacitidine + G-CSF	1 (2.2)	0 (0.0)
Alemtuzumab	1 (2.2)	0 (0.0)
Luspatercept + ESA	1 (2.2)	1 (1.1)
Venetoclax	1 (2.2)	1 (1.1)
Alemtuzumab + agent unknown + ESA + G-CSF	1 (2.2)	0 (0.0)
Alemtuzumab + venetoclax + ESA + G-CSF	1 (2.2)	0 (0.0)
Cyclosporine + G-CSF	1 (2.2)	1 (1.1)
Cyclosporine + lenalidomide + G-CSF	1 (2.2)	0 (0.0)
Lenalidomide + agent unknown + SCT + ESA + G-CSF	1 (2.2)	0 (0.0)
SCT	1 (2.2)	1 (1.1)
Cyclosporine + azacitidine + venetoclax + ESA + G-CSF	0 (0.0)	0 (0.0)

1L: First-line; 2L: Second-line; CAN: Canada; ESA: Erythropoiesis-stimulating agent; G-CSF: Granulocyte colony-stimulating factor; LR-MDS: Lower-risk myelodysplastic syndromes; SCT: Stem cell transplant.

(USA/CAN: 1L = 353.5 IU/l [n = 26, 26.8%]; 2L = 205.0 IU/l [n = 12, 28.6%]; 3L = 110.0 IU/l [n = 3, 30.0%]; UK/EU: 1 L = 169.5 IU/l [n = 56, 27.6%]; 2L = 34.0 IU/l [n = 18, 22.0%] (Table 1); 3L = 31.5 IU/l [n = 4, 14.3%]) (data not shown).

4. Discussion

This multinational, retrospective study provides valuable insight into the real-world treatment patterns and outcomes of adult patients with non-del(5q) LR-MDS. In both the USA/CAN and the UK/EU, most patients were treated with ESA-containing regimens in the 1L. The mean time to initiation of 1L ESA therapy was 10.4 months in the USA/CAN and 10.0 months in the UK/EU, indicating that patients spent a substantial amount of time without any therapy prior to treatment initiation, despite hemoglobin levels being categorized as very low in approximately half of these patients at MDS diagnosis and treatment initiation. A considerable proportion of patients were TD before initiating 1L ESA therapy, which aligns with previous findings from a US real-world claims analysis of patients with MDS; however, given the limitations of the data, the claims database study was not able to report del(5q) status or IPSS-R risk status distribution [17]. In the present study, the median duration of 1L ESA treatment was 25.8 months in the USA/CAN and 31.8 months in the UK/EU, which suggests a response duration of over 2 years, although only a small fraction of these patients achieved TI, and almost half did not experience clinically meaningful improvements in transfusion burden or hemoglobin levels. Finally, for those who were re-treated with ESAs in 2L, the most common reasons for treatment re-initiation with ESAs were health status, disease characteristics and reported treatment efficacy.

In the overall sample of patients, approximately 90% of patients were treated with ESA-containing regimens in 1L. In contrast with this finding, a real-world study of treatment patterns among US patients with LR-MDS reported that 56% of patients were treated with an ESA [18]. These differences in ESA utilization may be, in part, related to differences in the baseline characteristics of the sample, which included patients with del(5q) LR-MDS [18]. Additionally, in this present study, only 31.9% of patients were tested for RS status and 40.3% of patients had an unknown *SF3B1* mutation status. The most frequent therapy regimen in the USA/CAN and UK/EU was ESA monotherapy; and only a small proportion of patients received ESA combined with G-CSF. The percentage of patients treated with ESA and G-CSF appeared numerically lower in the USA/CAN (3.7%) than in the UK/EU (7.1%). The treatment patterns observed in the USA/CAN and UK/EU cohorts may have differed in some respects due to country- or region-specific guidelines and differences in healthcare delivery models and practices. Indeed, in an observational study of ESA-treated patients with LR-MDS from the European LeukemiaNet MDS registry, Garelius et al. [19] found that ESA use varied widely across 17 European countries. The

Table 4. Hematologic outcomes in patients with non-del(5q) LR-MDS.

	Overall				ESA-treated in 1L			
	USA/CAN		UK/EU		USA/CAN		UK/EU	
	1L	2L	1L	2L	1L	2L	1L	2L
Total patients, n	109	45	225	89	97	42	203	82
TD before treatment initiation (i.e., ≥2 units/8 wk), n (%)	40 (36.6)	20 (44.4)	109 (48.4)	42 (47.2)	36 (37.1)	19 (45.2)	104 (51.2)	41 (50.0)
Low transfusion burden (2–5 units/8 wk), n (%)	35 (87.5)	20 (100)	84 (77.1)	33 (78.6)	32 (88.9)	19 (100)	81 (77.9)	32 (78.1)
High transfusion burden (≥6 units/8 wk), n (%)	5 (12.5)	0 (0.0)	25 (22.9)	9 (21.4)	4 (11.1)	0 (0.0)	23 (22.1)	9 (22.0)
Achieved TI[a], n (%)	1 (2.5)	1 (5.0)	16 (14.7)	2 (4.8)	1 (2.8)	1 (5.3)	15 (14.4)	2 (4.9)
RBCT needs decreased by ≥50% vs treatment initiation[a], n (%)	16 (40.0)	4 (20.0)	56 (51.4)	13 (31.0)	15 (41.7)	4 (21.1)	55 (52.9)	13 (31.7)
Time to first record of ≥50% decrease, mean (SD), mo	2.1 (1.8)	1.3 (1.5)	3.7 (5.7)	1.5 (1.5)	2.2 (1.8)	1.3 (1.5)	3.7 (5.7)	1.5 (1.5)
Duration of maintenance for transfusion needs ≤50%, mean (SD), mo[b]	21.6 (18.0)	10.9 (10.0)	12.8 (17.8)	15.1 (16.1)	23.0 (17.6)	10.9 (10.0)	13.0 (17.9)	15.1 (16.1)
TI before treatment initiation (i.e., <2 units/8 wk), n (%)	69 (63.3)	25 (55.6)	116 (51.6)	47 (52.8)	61 (62.9)	23 (54.8)	99 (48.8)	41 (50.0)
Became TD[b] (i.e., ≥2 units/8 wk)	8 (11.6)	0 (0.0)	17 (14.7)	4 (8.5)	8 (13.1)	0 (0.0)	16 (16.2)	4 (9.8)
Hb at treatment initiation, n (%)	93 (85.3)	38 (84.4)	200 (88.9)	80 (89.9)	84 (86.6)	35 (83.3)	181 (89.1)	73 (89.0)
Very low (male: <9 g/dl; female: <8g/dl)	50 (53.8)	20 (52.6)	88 (44.0)	40 (50.0)	47 (56.1)	19 (54.3)	85 (47.0)	38 (52.1)
Low (male: 9–10.9 g/dl; female: 8–11.9 g/dl)	29 (31.2)	14 (36.8)	87 (43.5)	35 (43.8)	27 (32.1)	12 (34.3)	81 (44.8)	31 (42.5)
Near normal/normal (male: >11 g/dl; female: >12 g/dl)	14 (15.1)	4 (10.5)	25 (12.5)	5 (6.3)	10 (11.9)	4 (11.4)	15 (8.3)	4 (5.5)
Hb improvement[a]								
Hb level increased by ≥1.5 g/dl or 15 g/l, n/N (%)	27/93 (29.0)	10/38 (26.3)	81/200 (40.5)	16/80 (20.0)	27/84 (32.1)	10/35 (28.6)	81/181 (44.8)	16/73 (21.9)
Time to first record of increase by ≥1.5 g/dl or 15 g/l, mean (SD), mo	5.8 (10.0)	6.8 (10.9)	4.0 (4.5)	2.4 (1.6)	5.8 (10.0)	6.8 (10.9)	4.0 (4.5)	2.4 (1.6)

[a]Between the start of current therapy line and the start of next therapy line, if received, or the end of follow-up if no subsequent therapy was received.
[b]Defined based on the RBCT burden recorded at the start of next line of therapy as observed during the available study follow-up.
1L: First-line; 2L: Second-line; CAN: Canada; ESA: Erythropoiesis-stimulating agent; Hb: Hemoglobin; LR-MDS: Lower-risk myelodysplastic syndromes; NE: Not estimable; RBCT: Red blood cell transfusion; SD: Standard deviation; TD: Transfusion dependent; TI: Transfusion independence.

authors attributed these variations, in part, to country-specific differences in financial restrictions placed on ESA use and to differences in transfusion need requirements prior to treatment initiation. Additionally, a retrospective analysis conducted in Europe found that approximately 25% of patients with MDS were treated outside treatment guidelines [20].

In the present study, in both the overall study sample and the subgroup of patients treated with ESAs in the 1L, less than 40% of patients in the USA/CAN were TD before 1L therapy compared with approximately half of patients in the UK/EU. Consistent with this finding, Garelius et al. [19] reported that 54.3% of ESA-treated LR-MDS patients from the European LeukemiaNet MDS registry received transfusions before treatment initiation. In our study, Germany had the lowest percentage of patients who were TD before 1L therapy, and transfusion dependence was highest before 1L therapy in the UK. Among patients treated with ESA-containing regimens in 1L who were TD at baseline, only a small proportion achieved TI; additionally, approximately 40% of these patients in the USA/CAN and over half of patients in the UK/EU achieved the threshold for reduced RBCT needs. The proportion of patients meeting the RBCT reduction threshold was lowest in the USA and highest in France. The proportion of patients meeting the increased hemoglobin level threshold was highest in the UK (50.0%), and less than half of patients treated with ESAs in the 1L achieved the threshold for improved hemoglobin levels in all other countries.

This study has several limitations common to observational studies using data abstracted from medical records. In Europe, the majority of participating physicians were from academic centers and data for the overall study population were collected from a convenience sample and not a random sample due to the shortage of eligible patients, therefore, there is potential for selection bias in this study. These results may not be generalizable to the overall population of patients with LR-MDS in each country/region or of physicians who treat patients with LR-MDS. For the majority of patients, the rationale for prescribing treatment was in compliance with either

national or local guidelines. However, it is likely that treatment guidelines were updated during the case selection window, which spanned over 5 years (1 July 2013 to 30 September 2018), which may have impacted the treatment patterns reported. Additionally, although the electronic case report form included numerous data checks to assess and maximize internal consistency, data were entered by physicians and may therefore have been subject to data entry errors, potentially resulting in inaccuracies in reporting. In order to maintain patient de-identification, responses were not validated against patients' medical records by an independent reviewer external to the study site. However, a key strength of this study was the use of a customized, electronic data collection form that allowed for the abstraction of data in a uniform structure across all sites and geographic locations. Measures that may be subject to a clinician's interpretation and are not typically available in pre-existing coded data sources were also collected as part of this study, contributing to the robustness of the analysis, and adding another dimension of insight to the published literature on this topic.

5. Conclusion

In this real-world study, ESA-containing regimens were the most frequently used treatments for the management of anemia in patients with non-del(5q) LR-MDS. The mean time to initiation of 1L ESA therapy was approximately 10 months in both the USA/CAN and the UK/EU, indicating that patients spent a significant amount of time without any therapy prior to treatment initiation, despite half of patients experiencing severe anemia. A substantial proportion of adults were TD before 1L ESA treatment, and only a small percentage of these adults achieved TI during 1L. These findings highlight an unmet need in anemia management among patients with non-del(5q) LR-MDS and a requirement for new and more effective treatment options.

Article highlights

- Patients with lower-risk myelodysplastic syndromes (LR-MDS) often present with anemia and frequently require red blood cell transfusions (RBCTs). Transfusion dependence is associated with reduced survival and poor quality of life. Therefore, the goal of LR-MDS treatment is to manage anemia and reduce transfusion burden.
- In patients with non-del(5q) LR-MDS, erythropoiesis-stimulating agents (ESAs), with or without granulocyte colony-stimulating factor, are an established treatment for anemia in patients who are ESA-naive. Treatment options are limited for patients who are unresponsive to ESAs. Currently, little is known about the real-world treatment patterns and clinical outcomes of patients with non-del(5q) LR-MDS.
- This retrospective medical record review aimed to describe patient characteristics, treatment patterns and hematologic outcomes among patients with non-del(5q) LR-MDS in the USA, Canada (CAN), UK and EU (France, Germany, Spain).
- Data were abstracted for 119 patients with non-del(5q) LR-MDS in the USA/CAN and 245 patients in the UK/EU.
- Most patients initiated first-line (1L) therapy (USA/CAN: 109 [91.6%]; UK/EU: 225 [91.8%]) with a mean time from MDS diagnosis to initiation of 1L treatment of 10.1 months in the USA/CAN and 9.6 months in the UK/EU.
- The majority of patients received ESAs as 1L therapy (USA/CAN: 97 [89.0%]; UK/EU: 203 [90.2%]) and the median duration of 1L ESA treatment was 25.8 months in the USA/CAN and 31.8 months in the UK/EU.
- Prior to 1L treatment, 36 patients (37.1%) treated with 1L ESA-containing regimens were transfusion dependent (TD) in the USA/CAN, while 104 patients (51.2%) were TD in the UK/EU. Among these patients who were TD before 1L, only a small proportion (2.8% USA/CAN; 14.4% UK/EU) achieved transfusion independence during 1L.
- An RBCT reduction was achieved by 41.7% and 52.9% of 1L ESA-treated patients who were TD at treatment initiation in the USA/CAN and UK/EU, respectively. A hemoglobin improvement was achieved by 32.1% of 1L ESA-treated patients in the USA/CAN and 44.8% in the UK/EU.
- These findings highlight an unmet need in anemia management among patients with non-del(5q) LR-MDS and a requirement for new and more effective treatment options.

Author contributions

A Yucel, RK Goyal, RC Parikh, D Miteva and H Xiao substantially contributed to the conception or design of this research. RK Goyal, RC Parikh, E Esterberg, M Jimenez and M Sluga-O'Callaghan substantially contributed to the acquisition and analysis of data for this work. M Diez-Campelo, A Yucel, RK Goyal, RC Parikh, H Xiao and U Germing substantially contributed to the interpretation of data for this work. A Yucel, RK Goyal and H Xiao substantially contributed to the drafting of the manuscript. All authors critically revised the manuscript for important intellectual content. All authors provided final approval of the version to be published and agree to be accountable for all aspects of the work by ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Competing interests disclosure

RK Goyal, RC Parikh, E Esterberg, M Jimenez and M Sluga-O'Callaghan are full-time employees of RTI Health Solutions, an independent nonprofit research organization that was retained by Bristol Myers Squibb to conduct the research that is the subject of this manuscript. Their compensation is unconnected to the studies on which they work. A Yucel, D Miteva and H

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Ethical conduct of research

This study was reviewed by the RTI International Institutional Review Board (IRB) (Federal-Wide Assurance #3331; Ref # STUDY00021428) and was determined not to involve human subjects. Sites requiring a local IRB were subjected to additional review by country- and site-specific IRBs, as follows: Canada, Advarra IRB (Ref # Pro00048794); UK, National Health Service (NHS); Spain, Comité de Ética de la Investigación con Medicamentos del Área de Salud de Salamanca (Ref # E.O. 21/720); France, Commission Nationale de l'Informatique et des Libertés (CNIL); Germany, Ethikkommission (EK) an der Medizinischen Fakultät der Heinrich-Heine-Universität Düsseldorf (Ref # 2021-1367). Requirements for informed consent from patients were waived because of the use of de-identified/anonymized patient data.

data availability statement

The Bristol Myers Squibb policy on data sharing may be found at https://www.bms.com/researchers-and-partners/independent-research/data-sharing-request-process.html.

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References

Papers of special note have been highlighted as: • of interest; •• of considerable interest

1. Zeidan AM, Shallis RM, Wang R, et al. Epidemiology of myelodysplastic syndromes: why characterizing the beast is a prerequisite to taming it. Blood Rev. 2019;34:1–15. doi:10.1016/j.blre.2018.09.001
2. Greenberg PL, Tuechler H, Schanz J, et al. Revised international prognostic scoring system for myelodysplastic syndromes. Blood. 2012;120(12):2454–2465. doi:10.1182/blood-2012-03-420489
3. Almeida A, Fenaux P, List AF, et al. Recent advances in the treatment of lower-risk non-del(5q) myelodysplastic syndromes (MDS). Leuk Res. 2017;52:50–57. doi:10.1016/j.leukres.2016.11.008
•• An overview of the current treatment options for lower-risk non-del(5q) myelodysplastic syndromes (MDS).
4. de Swart L, Smith A, Johnston TW, et al. Validation of the revised international prognostic scoring system (IPSS-R) in patients with lower-risk myelodysplastic syndromes: a report from the prospective European LeukaemiaNet MDS (EUMDS) registry. Br J Haematol. 2015;170(3):372–383. doi:10.1111/bjh.13450
5. Germing U, Lauseker M, Hildebrandt B, et al. Survival, prognostic factors and rates of leukemic transformation in 381 untreated patients with MDS and del(5q): a multicenter study. Leukemia. 2012;26(6):1286–1292. doi:10.1038/leu.2011.391
6. de Swart L, Crouch S, Hoeks M, et al. Impact of red blood cell transfusion dose density on progression-free survival in patients with lower-risk myelodysplastic syndromes. Haematologica. 2020;105(3):632–639. doi:10.3324/haematol.2018.212217
7. Stauder R, Yu G, Koinig KA, et al. Health-related quality of life in lower-risk MDS patients compared with age- and sex-matched reference populations: a European LeukemiaNet study. Leukemia. 2018;32(6):1380–1392. doi:10.1038/s41375-018-0089-x
8. Stojkov I, Conrads-Frank A, Rochau U, et al. Determinants of low health-related quality of life in patients with myelodysplastic syndromes: EUMDS registry study. Blood Adv. 2023;7(12):2772–2783. doi:10.1182/bloodadvances.2022008360
9. Giagounidis AA, Germing U, Aul C. Biological and prognostic significance of chromosome 5q deletions in myeloid malignancies. Clin Cancer Res. 2006;12(1):5–10. doi:10.1158/1078-0432.CCR-05-1437
10. Solé F, Espinet B, Sanz GF, et al. Incidence, characterization and prognostic significance of chromosomal abnormalities in 640 patients with primary myelodysplastic syndromes. Grupo Cooperativo Español de Citogenética Hematológica. Br J Haematol. 2000;108(2):346–356. doi:10.1046/j.1365-2141.2000.01868.x
11. Rose C, Brechignac S, Vassilief D, et al. Does iron chelation therapy improve survival in regularly transfused lower risk MDS patients? A multicenter study by the GFM (Groupe Francophone des Myélodysplasies). Leuk Res. 2010;34(7):864–870. doi:10.1016/j.leukres.2009.12.004
12. Suragani RN, Cadena SM, Cawley SM, et al. Transforming growth factor-β superfamily ligand trap ACE-536 corrects anemia by promoting late-stage erythropoiesis. Nat Med. 2014;20(4):408–414. doi:10.1038/nm.3512

13. Fenaux P, Platzbecker U, Mufti GJ, et al. Luspatercept in patients with lower-risk myelodysplastic syndromes. New Engl J Med. 2020;382(2):140–151. doi:10.1056/NEJMoa1908892
14. Platzbecker U, Della Porta MG, Santini V, et al. Efficacy and safety of luspatercept versus epoetin alfa in erythropoiesis-stimulating agent-naive, transfusion-dependent, lower-risk myelodysplastic syndromes (COMMANDS): interim analysis of a phase 3, open-label, randomised controlled trial. Lancet. 2023;402(10399):373–385. doi:10.1016/S0140-6736(23)00874-7
•• Reports the efficacy and safety of luspatercept versus epoetin alfa for treatment of anemia due to lower-risk MDS (LR-MDS) in the phase 3 COMMANDS trial.
15. Della Porta M, Platzbecker U, Santini V, et al. The COMMANDS trial: a phase 3 study of the efficacy and safety of luspatercept versus epoetin alfa for the treatment of anemia due to IPSS-R Very low-, Low-, or Intermediate-risk MDS in erythropoiesis-stimulating agent-naive patients who require RBC transfusions. Blood. 2020;136(Suppl. 1):1–2.
16. Cheson BD, Greenberg PL, Bennett JM, et al. Clinical application and proposal for modification of the International Working Group (IWG) response criteria in myelodysplasia. Blood. 2006;108(2):419–425. doi:10.1182/blood-2005-10-4149
17. Mukherjee S, Slabaugh SL, Copher R, et al. Real-world treatment patterns and transfusion burden among us patients with newly diagnosed myelodysplastic syndromes (MDS). Blood. 2019;134(Suppl. 1):3499.
•• Describes treatment patterns and transfusion burden in patients with MDS in the USA.
18. Mukherjee S, Zimmerman Savill KM, Gajra A, et al. Real-world erythropoiesis-stimulating agent (ESA) treatment patterns and outcomes among US patients with lower-risk myelodysplastic syndromes (LR-MDS). J Clin Oncol. 2022;40(Suppl. 16):e19065. doi:10.1200/JCO.2022.40.16_suppl.e19065
•• Outlines erythropoiesis-stimulating agent treatment patterns and outcomes among patients in the USA with LR-MDS.
19. Garelius HKG, Johnston WT, Smith AG, et al. Erythropoiesis-stimulating agents significantly delay the onset of a regular transfusion need in nontransfused patients with lower-risk myelodysplastic syndrome. J Intern Med. 2017;281(3):284–299. doi:10.1111/joim.12579
• Reports the clinical outcomes in patients with LR-MDS treated with erythropoiesis-stimulating agents in Europe.
20. Kasprzak A, Nachtkamp K, Kondakci M, et al. Analysis of the impact of adherence to guidelines and expert advice in patients with myelodysplastic syndromes. Ann Hematol. 2021;100(2):455–463. doi:10.1007/s00277-020-04325-7
• Reports on whether adherence to current treatment guidelines improves survival in patients with MDS.