



Health care resource utilization and associated costs among Lower-Risk myelodysplastic syndrome patients in France - EDELWEISS study

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Objectives

Myelodysplastic syndromes (MDS) are a heterogeneous group of malignant hematologic disorders, characterized by ineffective hematopoiesis causing cytopenias. The management of low-risk MDS (LR-MDS) is based on the correction of cytopenias, particularly chronic anemia (80% of cases).^{1,2}

Until now, Erythropoiesis-stimulating agents (ESAs) are the established first-line treatment to prevent the need for red blood cell (RBC) transfusion and its clinical consequences.²

The real-life epidemiology of LR-MDS patients is not well-known, as it is often underreported in registries. Also, implications of LR-MDS on healthcare resource use and associated costs are not well understood.

The objective of this study was to describe healthcare resource utilization (HCRU) and associated costs among lower-risk MDS patients in France.

Methods

Non-interventional, national, retrospective study using data from the Sample of the National Health Data System (ESND).

The ESND corresponds to a representative sampling at 2/100th of the National Health Data System (SNDS) carried out from a random draw (more than 1.6 million beneficiaries who consumed care between 2006 and 2021). The SNDS contains pseudo-anonymous information on all outpatient, ambulatory, and hospital care reimbursed by health insurance, covering > 98% of the French population.^{3,4}

Adult patients with a diagnosis of MDS, at lower risk and receiving first-line treatment (index date) between 01/01/2018 and 31/12/2022 were included.

Patients were followed until death, end of study period or loss of follow-up. Comorbidities and history were collected over a 5-year retrospective period prior to inclusion.

Patients were split according to their red blood cell transfusion history, in line with IWG 2018 criteria⁵, defining:

- The Non-Transfusion Dependent (NTD) group (no transfusion within the 16 weeks prior to first-line)
 - The Transfusion Dependent (TD) group (transfusion within the 16 weeks prior to first line).
- The TD patients was divided in two sub-groups:
- The High Transfusion Burden (HTB) sub-group (patients transfused 4 times or more)
 - The Low Transfusion Burden (LTB) sub-group (patients transfused 1-3 times).

HCRU and costs were described according to French National Health Insurance (NHI) perspective in euro 2022.

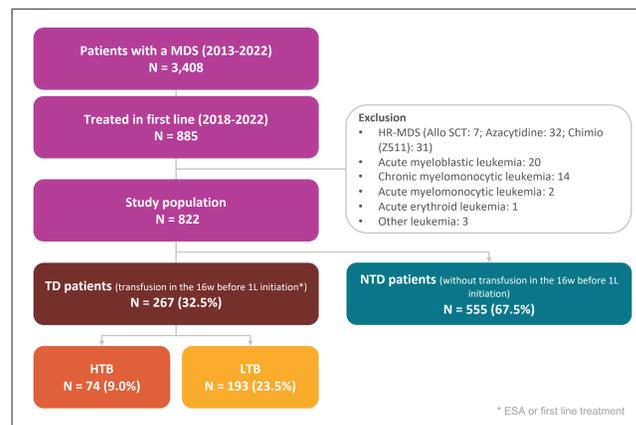
Costs were computed by item and year of follow-up (FU) for incident patients. For prevalent patients, the total cost per patient over the FU was divided by the length of the follow-up of each patient. Total costs were extrapolated by multiplying the calculated cost by 50.

Specific costs of MDS were computed: Hospitalization for MDS, transfusions and drugs of interest (Erythropoietin, Darbepoietin alfa, Luspatercept, Lenalidomide, Azacitidine, GCSF).

Results

A total of 822 patients were included: 555 NTD (67.5%) and 267 TD (32.5%). Among TD group, 74 patients were HTB (27.7%), 193 were LTB (72.3%) (Figure 1).

Figure 1. Flow chart of the study population



Characteristics of LR-MDS patients

The mean age of patients was 80.1 years (±10.1) at inclusion, with no significant difference between NTD and TD groups. TD patients were more often male (55.4% vs. 46.9% NTD; p=0.02) and had more cardiovascular comorbidities (TD: 54.3%, NTD: 44.9%; p=0.01) and chronic renal failure (TD: 34.5%, NTD: 24.1%; p=0.001) (Table 1).

Table 1. Patients' characteristics

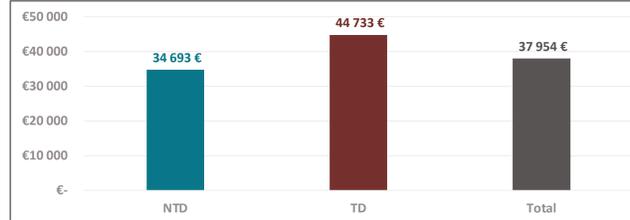
Variables	TD (n=267)	NTD (n=555)	P-value (TD/NTD)	Total (n=822)
Follow-up duration (in year)	Med (Q1; Q3) 1.2 (0.55; 2.67)	2.0 (0.9; 3.8)	<0.0001	1.8 (0.8; 3.3)
Age at inclusion (in year)	Mean (±SD) 80.6 (±11.2)	79.9 (±9.5)	0.1167	80.1 (±10.1)
	Min; Max 40.0; 103.0	40.0; 104.0		40.0; 104.0
	Med(Q1; Q3) 82.0 (74.0; 88.0)	81.0 (74.0; 87.0)		81.5 (74.0; 88.0)
Men	148 (55.4%)	260 (46.9%)	0.0212	408 (49.6%)
Cardiovascular disease	145 (54.3%)	249 (44.9%)	0.0112	394 (47.9%)
COPD	44 (16.5%)	67 (12.1%)	0.0834	111 (13.5%)
Diabetes	67 (25.1%)	119 (21.4%)	0.2412	186 (22.6%)
History of cancer	82 (30.7%)	135 (24.3%)	0.0517	217 (26.4%)
Chronic kidney disease	92 (34.5%)	134 (24.1%)	0.0019	226 (27.5%)
Auto-immune diseases	34 (12.7%)	67 (12.1%)	0.7866	101 (12.3%)
Tobacco dependency ^a	30 (11.2%)	41 (7.4%)	0.0658	71 (8.6%)

^a Consultation with an addiction specialist or withdrawal medications.

Total costs of MDS patient in France

Among the total prevalent treated MDS population, the mean cost per patient per year of follow-up was 37,954€ with an increased cost of 26% in TD patients compared to NTD patients (44,733€ vs 34,693€)(Figure 2).

Figure 2. Mean cost per patient per year



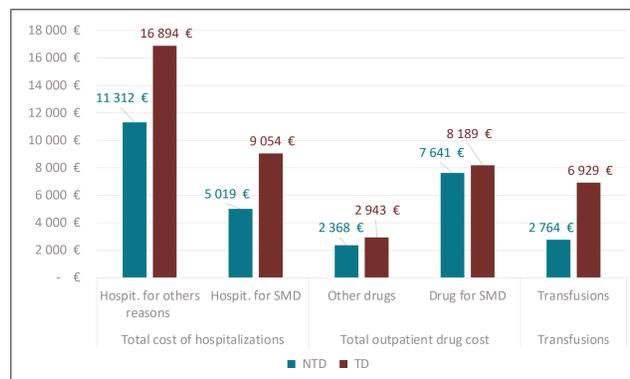
The main difference in costs between TD and NTD populations was due to hospitalizations and transfusions.

TD patients had a significantly higher mean hospitalization cost of 25,947€ per year, with 35% (9,054€) for MDS-related hospitalizations, compared to NTD patients, who had a mean cost of 16,331€ per year, with 30% (5,019€) for MDS-related hospitalizations.

The cost of transfusions was 6,920€ per year for TD patients, which is more than double for NTD patients (2,764€ per year).

Finally, the cost of drugs for the treatment of MDS was comparable between TD and NTD patients, at 8,189€ per year versus 7,641€ per year, respectively. (Figure 3)

Figure 3. Mean cost per item per patient per year

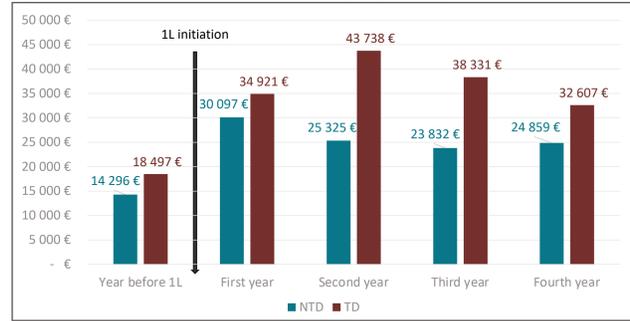


Costs of MDS incident treated patient

Among the 291 incident patients, 73% of them (212) were in the NTD group. The mean cost per patient in the year before treatment initiation was 14,296€ for NTD patient compared to 18,497€ for TD ones.

The average cost of care for TD patients was 15% higher (34,921€ vs 30,097€ for NTD) in the first year of FU. This cost discrepancy escalated to +72% and +61% in Y2 and Y3, respectively (Figure 4).

Figure 4. Mean total cost of incident MDS per patient per year of follow-up

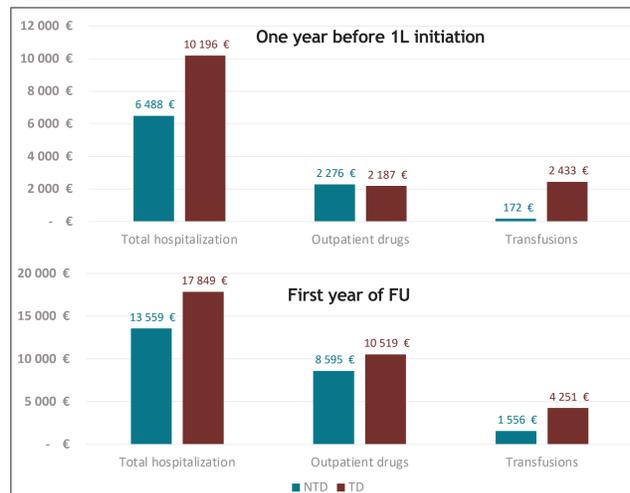


	Before 1L	First year	Second year	Third year	Fourth year
TD	79	79	44	28	15
NTD	212	212	151	102	52

One year before inclusion, TD patients had a mean hospitalization and transfusions cost (10,196€ and 2,433€) higher than NTD patients (6,488€ and 172€). Those two items explain most of the cost discrepancy between the two groups in the year prior to inclusion.

One the first year of FU, the mean cost per patient of hospitalization, treatment and transfusion were all higher in TD patients. More precisely, the mean cost of hospitalization was 32% higher for TD patients (17,849€ vs 13,559€), 22% for outpatient drugs (10,519€ vs 8,595€) and 173% for transfusions (4,251€ vs 1,556€) (Figure 5).

Figure 5. Mean cost per item one year before and after 1L treatment initiation



Transfusions and associated costs

Up to one year after the initiation of treatment, the proportion of patients in the TD group requiring transfusions was twice that of the NTD group, with 36.3% of patients in the TD group still needing transfusions compared to 17.7% in the NTD group. This proportion was 23.6% and 15.0% at two years (Table 2).

Table 2. Percent of patients with RBC transfusions after first treatment initiation over the follow-up

Months	0 to 6	7 to 12	13 to 18	19 to 24	25 to 30
Transfusion Dependent	60.3%	36.3%	29.2%	23.6%	19.1%
Non-Transfusion Dependent	22.7%	17.7%	14.2%	15.0%	13.5%

NB: this percentage of patient is calculated on the total number of patient alive at each month of FU.

The total extrapolated cost of transfusion was 33.2 M€ on the first year of FU and still high during the entire follow up, suggesting an important burden for patients and costs for the healthcare system. (Figure 6).

Also, the mean annual transfusion cost per patient increases every year of follow-up for both TD and NTD patient. During the first year following the 1L initiation, the mean cost was transfusion was respectively 4,247€ vs 1,550€; 4,448€ vs 1,574€ (Y2) and 6,319€ vs 2,842€ (Y3). (Figure 7)

Figure 6. Total extrapolated cost of transfusions by year of follow-up

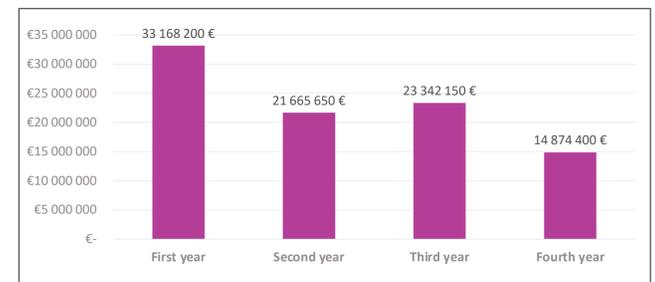


Figure 7. Mean cost of transfusions per patient per year of follow-up



Complications of transfusions and associated costs

Among the 432 patients with at least one RBC transfusion over the follow-up period, 213 (49%) of them experienced at least one complication related to the transfusion (during the transfusion stay or another hospital stay within three weeks after the transfusion stay).

In total, 467 hospital stays for a complication of the transfusion were recorded. Most of the complications were purpura (56.5%) and infections (20.1%) (Table 3).

Table 3. Number of stays among patients who experienced at least one transfusion-related complication (n=213)

Complications	Nb of stay
At least one complication	467
Purpura	264 (56.5%)
Infections	94 (20.1%)
Volume overload	93 (19.9%)
Others (lung damage, Pulmonary injuries...)	62 (13.3%)

The total extrapolated cost of complication was 164,073,900€ with a mean cost per patient of 15,406€ and 7,048€ per stay.

Conclusion

- This study highlights the economic burden of managing LR-MDS patients in France and underscores the increased HCRU and payer costs associated with the transfusion dependency.
- TD patients incurred more hospitalizations, treatments, and transfusions, leading to elevated costs before and after first line treatment initiation.
- The extrapolated total cost of transfusion was 33 M€ on the first year of follow up which suggest an important burden for patients and costs for the healthcare system.
- Transfusion-related complications also impose a significant burden, associated with elevated costs.

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