Transfusion burden in patients with Lower-Risk Myelodysplastic Syndromes in France since 2020: The MYOSOTYS Study

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Context and Objectives

- Myelodysplastic Syndromes (MDS) are a heterogeneous group of clonal hematopoietic stem-cell malignancies defined by ineffective hematopoiesis in the bone marrow, resulting in peripheral blood cytopenias[1].
- In patients with Lower-Risk (LR) MDS, treatment mainly aims to correct cytopenias, particularly chronic anemia[2]. Majority of patients require regular Red Blood Cell Transfusions (RBCTs) which are associated with iron overload leading to possible disruption of organ function. RBCT dependency causes a decrease in quality of life, thus warranting the use of other therapeutic options.
- First-line treatment aimed at reducing the need for transfusions and relies on erythropoiesis-stimulating agents (ESAs), but their effectiveness remains limited and decreases over time.[3]
- Luspatercept -an agent promoting erythroid maturation- was first authorized in the EU as a second-line therapeutic option in 2020 for a subset of LR-MDS with ring sideroblasts. A first-line broader authorization extension was received in 2024[4].
- In France, luspatercept was reimbursed only as a second-line treatment at the time of this analysis.
- **This analysis presents the management of adults with LR-MDS in France between 2020 and 2024, with a focus on luspatercept use under current French availability conditions.**

Methods

A. Study Design

- This is a retrospective longitudinal observational study based on claims data from the French National Health Data System (SNDS), including patients with LR-MDS who initiated an anemia treatment between 1st January 2020 and 31st December 2024.
- SNDS cover all outpatients and in-patients care reimbursed by the French National Health Insurance (NHI).

B. Study population (Figure 1 and Table 1)

- Adult patients with a diagnosis of MDS (ICD-10 code recorded as a principal, related, or associated diagnosis) who initiated first-line treatment for anemia (i.e., ESA, lenalidomide or luspatercept) between 1st January 2020 and 31st December 2024 were included.
  - Patients with HR-MDS, defined as a history of allogenic stem cell transplantation (ICD10 codes and CCAM procedures), and/or dispensation of treatment reserved to HR-MDS, and/or Chemotherapy for HR-MDS, and/or a prior or concurrent diagnosis of another hematological malignancies, were excluded.
- Two study populations were defined: the Incident population and the luspatercept population.
- **Incident population:** all newly treated patients with LR-MDS during the period 2020-2024. The index date was defined as the date of the first MDS treatment dispensation.
  - Incident patients were categorized according to their RBCT dependency status, based on 2018 IWG transfusion criteria[5]:
    - **Non-Transfusion Dependent (NTD) group:** no transfusion within the 16 weeks prior to index date
    - **Transfusion Dependent (TD) group:** at least one transfusion within the 16 weeks prior to index date.
    - TD patients were further classified into:
      - High Transfusion Burden (HTB) group: patients receiving >3 transfusions
      - Low Transfusion Burden (LTB) sub-group: patients receiving 1 to 3 transfusion
- **Luspatercept population:** all incident LR-MDS patients who received luspatercept at any time during their treatment course. The luspatercept index date was defined as the date of the first luspatercept dispensation.
  - luspatercept population was categorized according to their transfusion response. Response to luspatercept at 24 weeks was assessed using the following adapted 2018 IWG transfusion criteria[5]:

Transfusion burden before initiation (nb. of RBCTs during the 16 weeks preceding index date)	**Non-transfusion-dependent** 0 RBCT	**Low transfusion burden** 1-3 RBCTs	**High transfusion burden** >3 RBCTs
Transfusion responders *criterion assessed in the 24 weeks after initiation*	< 2 RBCTs over 24 weeks	At least one transfusion-free interval of ≥ 8 weeks	> 50% reduction in the number of RBCTs vs. the 16 weeks before initiation
Transfusion non-responders	Patients who do not meet the above criteria during the 24 weeks following luspatercept initiation		

- During the study observation period, luspatercept was approved and reimbursed only in second-line treatment in France.

C. Variables and outcomes of interest

- Patients were followed until death, end of follow-up, or loss to follow-up.
- Comorbidities were assessed over the five years preceding the index date.
- Treatment sequence was defined as the successive line of treatment of interest (ESA, lenalidomide, luspatercept, azacitidine) in eligible population with at least 4 months of follow-up.
- Treatment sequences for each patient were computed based on treatments coverages period, treatments discontinuations, and switches.
- Treatment discontinuation was defined as at least 2 consecutives drug coverage periods without drug dispensation after the expected end of drug coverage period of the last dispensation.
- A new treatment line was initiated when:
  - A patient switches to a different active substance, regardless of pharmacological class; or
  - A patient adds another active substance (expected to be rare).
- Number of RBC transfusion during the 24-weeks and 48-weeks periods before and after luspatercept initiation, and associated cost.

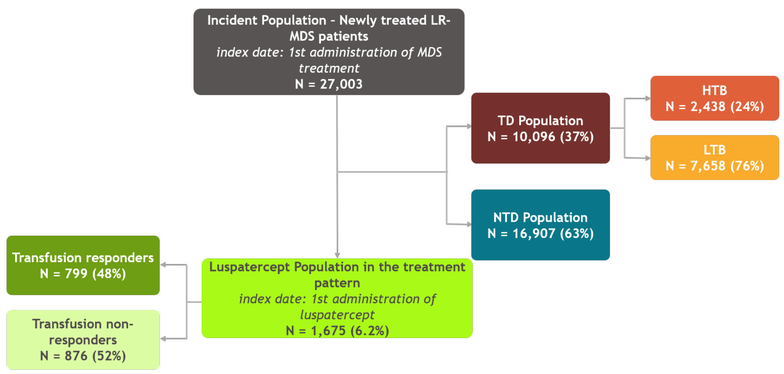
D. Statistical Analysis Method

- Variables were described using appropriate statistics and according to luspatercept transfusion response.
- Treatment sequences were described using Sankey diagrams, with flows showing the switch to different lines of treatment from the inclusion in the eligible population to the end of follow-up (for the 3rd first lines).
- The cumulative incidence of luspatercept discontinuation (persistence) was estimated using cumulative incidence function (CIFs), accounting for death as a competing risk.

Results

- Between 2020 and 2024, a total of 27,003 incident patients initiated a treatment for LR-MDS. Of these, 62.6% were NTD (N=16,907) and 37.4% were TD (N=10,096). Among TD patients, 7,658 (75.9%) had a low transfusion burden (LTB), whereas 2,438 (24.1%) had a high transfusion burden (HTB) (Figure 1).
- Among the 40,921 treated patients with LR-MDS included in the study population, 27,003 were incident patients during the study period.
- Of these, a total of 1,675 patients (6.2% of the incident population) received luspatercept during their treatment course. Following luspatercept initiation, 799 patients (47.7%) achieved a primary transfusion response (Figure 1).
- In the incident population, at index date the mean age was 79.6 years (±10.4), 55.8% of patients were aged ≥80 years and 55.3% were male. The comorbidity burden was high (e.g. 54.0% with cardiovascular disease, 36.2% with a history of cancer, 26.3% with diabetes). The mean Charlson comorbidity index score was 5.9 (±2.9). All these comorbidities were more frequent among TD patients than among NTD patients (Table 1).
- Patients treated with luspatercept were younger than those in the overall incident population (mean age: 77.2±9.2 years; 42.6% aged over 80 years) and had lower comorbidity burden (mean Charlson score 4.5 ±2.2) (Table 1).

Figure 1. Study population flow chart (2020-2024)



HR-MDS, higher-risk myelodysplastic syndromes; HTB, high transfusion burden; LR-MDS, lower-risk myelodysplastic syndromes; LTB, low transfusion burden; NTD, non-transfusion-dependent; TD, transfusion-dependent.

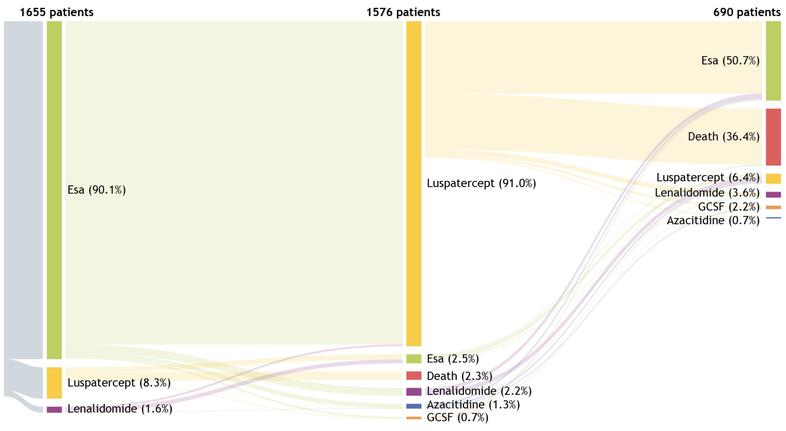
Table 1. Demographic and clinical characteristics of the incident and luspatercept populations

	Incident population			luspatercept population
Characteristic	**NTD N = 16,907**	**TD N = 10,096**	**Overall N = 27,003**	**N = 1,675**
Age, years - mean (±SD)	79.5 (±10.3)	79.9 (±10.7)	79.6 (±10.4)	77.2 (±9.2)
Age, years - median (Q1; Q3)	81.0 (74.0; 87.0)	82.0 (74.0; 88.0)	81.0 (74.0; 87.0)	78.0 (72.0; 84.0)
Age ≥ 80 years - n (%)	9,320 (55.1)	5,751 (57.0)	15,071 (55.8)	714 (42.6)
Male - n (%)	9,012 (53.3)	5,909 (58.5)	14,921 (55.3)	992 (59.2)
Cardiovascular disease - n (%)	8,421 (49.8)	6,150 (60.9)	14,571 (54.0)	662 (39.5)
Cardiac rhythm or conduction disorders - n (%)	4,079 (24.1)	3,369 (33.4)	7,448 (27.6)	289 (17.3)
Coronary disease - n (%)	3,488 (20.6)	2,507 (24.8)	5,995 (22.2)	281 (16.8)
History of cancer - n (%)	5,731 (33.9)	4,039 (40.0)	9,770 (36.2)	501 (29.9)
Diabetes - n (%)	4,291 (25.4)	2,797 (27.7)	7,088 (26.3)	385 (23.0)
Chronic kidney disease - n (%)	3,539 (20.9)	2,583 (25.6)	6,122 (22.7)	201 (12.0)
Chronic respiratory diseases[a] - n (%)	2,929 (17.3)	2,168 (21.5)	5,097 (18.9)	248 (14.8)
Charlson comorbidity score - mean (±SD)	5.6 (±2.8)	6.3 (±3.1)	5.9 (±2.9)	4.5 (±2.2)

Characteristics assessed at index date (first-line treatment initiation, 2020-2024) for the incident population and at luspatercept initiation for the luspatercept population. Excluding cystic fibrosis. NTD: non-transfusion-dependent; Q1/Q3: first/third quartiles; SD: standard deviation; TD: transfusion-dependent.

- Treatment sequence analysis in patients using luspatercept (Figure 2) showed a highly consistent treatment pathway: ESAs dominate in first line (1,491/1,655; 90.1%), while luspatercept was almost exclusively used in second-line (1,434/1,576; 91.0% of second lines, vs. only 8.3% in first line). Only a limited number of patients progressed to a third line of therapy (n=690) with a mean follow-up of 1.24 (±0.75) years.

Figure 2. Treatment sequences in the luspatercept population (Sankey diagram)



3rd first treatment line since 1st line therapy in patients with at least 4-month of follow-up, N=1,655
Mean follow-up duration in years (all luspatercept population) = 1.24 (±0.75).

- Among patients achieving a transfusion response following luspatercept initiation (N=799), the mean number of RBCT decreased from 5.6 (±7.0) to 2.9 (±5.8) over 24 weeks, and from 9.3 (±12.1) to 5.3 (±9.8) over 48 weeks (Table 2).

Table 2. Description of transfusion burden before and after luspatercept initiation

RBCT burden	Total population (n=1,675)		Responders (n=799)		Non-responders (n=876)	
	Before	**After**	**Before**	**After**	**Before**	**After**
24 weeks						
RBCT, mean (±SD)	6.3 (±6.6)	5.6 (±7.6)	5.6 (±7.0)	2.9 (±5.8)	6.9 (±6.0)	8.1 (±8.1)
RBCT, median (Q1; Q3)	5.0 (1.0;9.0)	3.0 (0.0;8.0)	3.0 (0.0;8.0)	1.0 (0.0;3.0)	6.0 (2.8;10.0)	7.0 (3.0;11.0)
High transfusion intensity (≥6 RBCTs), %	43.7	38.1	36.7	15.1	50.1	59.0
48 weeks						
RBCT, mean (±SD)	10.5 (±11.7)	10.3 (±13.6)	9.3 (±12.1)	5.3 (±9.8)	11.5 (±11.2)	14.8 (±14.9)
RBCT, median (Q1; Q3)	6.0 (2.0;16.0)	5.0 (1.0;15.0)	5.0 (0.0;14.0)	2.0 (0.0;6.0)	8.0 (3.0;17.0)	12.0 (4.0;21.0)
High transfusion intensity (≥6 RBCTs), %	55.2	49.5	47.2	26.0	62.6	70.9

- The proportion of patients with high-intensity transfusion need (≥6 transfusions over 48 weeks) decreased from 47.2% to 26.0% (Figure 3).
- Based on a mean invoiced cost of €1,043.6 per transfusion, this corresponds to estimated transfusion cost savings of €2,818 per patient over 24 weeks and €4,143 over 48 weeks (Table 3).

Figure 3. RBCT intensity in patients with luspatercept and with transfusion response (N=799)

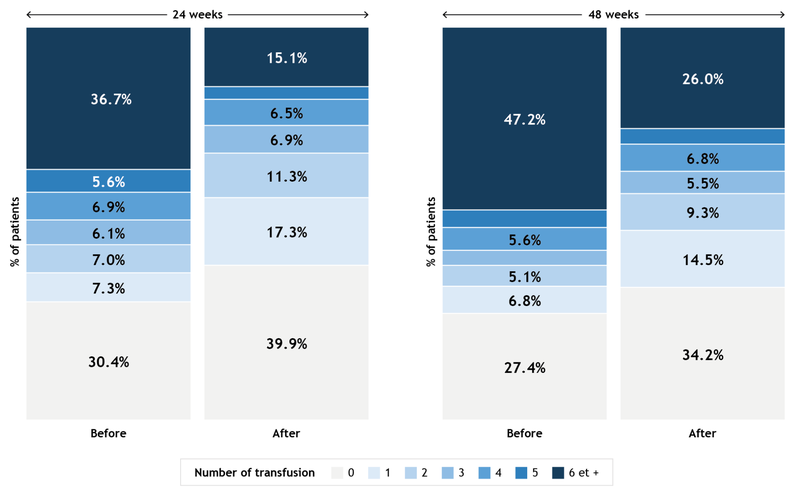


Table 3. Comparison of transfusion cost before and after luspatercept - responders (N=799)

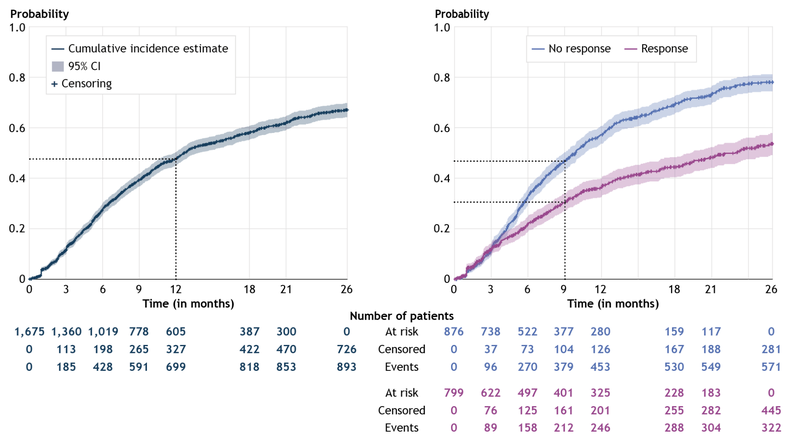
	Mean cost in €2024 (±std)[a]	Estimated savings per patient	RR [CI95%]
Transfusion cost 24 weeks before luspatercept initiation	5,865 (± 7,347)	NA	1
Transfusion cost 24 weeks after luspatercept initiation	3,047 (± 6,001)	**€2,818**	**0.39 [0.35; 0.43]**
Transfusion cost 48 weeks before luspatercept initiation	9,663 (± 12,586)	NA	1
Transfusion cost 48 weeks after luspatercept initiation	5,520 (± 10,258)	**€4,143**	**0.32 [0.28; 0.38]**

[a] Estimated as mean number of RBC transfusions × mean invoiced cost of a hospital stay involving ≥1 transfusion (€1,043.57).

- At 12 months following luspatercept initiation, the probability of remaining on treatment was 52% (95%CI: 50%-55%). This probability was higher among responders (64%; 95%CI: 60%-67%) than among non-responders (43%; 95%CI: 39%-46%).
- The median cumulative exposure duration to luspatercept was 13 months over the entire follow-up (28 months in responders and 10 months in non-responder patients).

Figure 4. Cumulative incidence of luspatercept discontinuation

(Kalbfleisch-Prentice estimate, death as competing risk; N=1,675)



Conclusion

- These results provides a nationwide real-world overview of treated patients with LR-MDS in France based on SNDS data.
- During the time of the study was conducted, luspatercept was used almost exclusively as a second-line treatment, in line with luspatercept approval and French reimbursement conditions.
- Among the 799 responder patients (47.7%), luspatercept reduced the transfusion burden over 48 weeks. The mean number of RBCTs decreased from 9.3 to 5.3, while the proportion of patients with high transfusion burden (≥6 RBCTs) declined from 47.2% to 26.0%.
- Based on an average reimbursed cost €1,043.6 per transfusion, this corresponded to estimated transfusion-related cost saving of €4,143 per patient.
- A subsequent data extraction, planned for 2027, will allow assessment of luspatercept use with extended follow-up and in the context of its more recent reimbursement–as first-line treatment in France.

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- All authors contributed to the work described in this presentation and approved the content of the poster.

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