# BURDEN OF DISEASE IN LOW-RISK MYELODYSPLASTIC SYNDROMES IN SPAIN

David Valcárcel,<sup>1</sup> Maria Julia Montoro,<sup>1</sup> Mar Tormo,<sup>2</sup> Joan Bargay,<sup>3</sup> Estela Moreno,<sup>4</sup> Susana Aceituno,<sup>5</sup> Alba Bellmunt,<sup>5</sup> María Soler,<sup>5</sup> Montserrat Rafel,<sup>6</sup> Rocio Villarrubia<sup>6</sup>

<sup>1</sup>Department of Hematology, Vall d'Hebron Institute of Oncology (VHIO), University Hospital Vall d'Hebron, Barcelona, Spain, <sup>2</sup>Department of Hematology, University Hospital Clínico, Instituto de Investigación INCLIVA, Valencia, Spain; <sup>3</sup>Department of Hematology, Hospital Son Llatzer, Palma de Mallorca, Spain; <sup>4</sup>Pharmacy Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; <sup>5</sup>Outcomes'10, Castellón, Spain; <sup>6</sup>Hematology, Bristol Myers Squibb, Madrid, Spain

## INTRODUCTION

- Myelodysplastic syndromes (MDS) are a group of hematological malignancies characterized by cytopenias (primary anaemia) and an increased risk of progression to acute myeloid leukemia (AML)<sup>1</sup>.
- The most common symptoms are usually those related to anaemia, with 50% of patients requiring regular red blood cell transfusions<sup>2</sup>.
- In addition, red blood cell transfusions constitute the main supportive care for patients with MDS after the failure of Erythropoiesis-stimulating agents<sup>2</sup>.
- Red blood cell transfusions provide short-term improvement of symptoms. However, this does not improve health-related quality of life (HRQoL) of patients and results in significant resource consumption<sup>2</sup>.
- The ERASME study included newly diagnosed patients with MDS in Spain. The aim was to assess the impact of transfusion burden on survival and

#### **Cost estimation**

- Pharmacological, follow-up, transfusion and acute complications management costs were included:
- Pharmacological cost: treatment strategies and usage rates based on expert opinion were considered (Table 4). In addition, 22.2% of TD patients were considered to have received chelation therapy. Drug costs were extracted from the official database, BotPlusWeb<sup>9</sup>.

#### Table 4. Treatment strategies for TD and TI patients

Strategies	Drug	TD patient usage	TI patient usage	Resource
Observation	-	11.3%	46.8%	
Support	Erythropoetin	29.3%	29.0%	1
	Darbepoetin	9.3%	11.1%	Experts. 2022
Active treatment	Azacitidine	35.4%	10.8%	
Immunomodulators	Lenalidomide	14.7%	2.3%	
TD: transfusion- dependent; TI:	transfusion- independent	dent	·	

#### Figure 4. Accumulative cost of LR-MDS



• The mean annual cost per patient with TD was estimated at €43,066

comorbidities in patients with low-risk and intermediate-1 MDS<sup>3</sup>.

• The ERASME study concluded that transfusion burden is associated with worse survival and increased comorbidity<sup>3</sup>.

## OBJECTIVES

• The aim was to assess the disease burden in low-risk MDS (LR-MDS) patients from the Spanish National Health System (NHS) perspective. In particular, the impact of the disease and transfusion dependence on HRQoL, survival, resource use and costs were estimated.

## METHODS

#### Model structure

- An incidence-based Markov model was developed in Microsoft Excel. This was done using data from the ERASME study<sup>3</sup> and the opinion of a panel of experts.
- The number of patients was estimated based on MDS epidemiological data (Table 1).
- Four health states were defined: MDS transfusion-dependent (TD), MDS transfusion-independent (TI), AML, and death (**Figure 1**). A cohort of newly diagnosed LR-MDS patients based on the characteristics of the ERASME study<sup>3</sup> entered the model according to transfusion dependence (TD: 21.00%; TI: 79.00%).

#### Table 1. Estimation of the number of patients

Description	Data (%)	Number	Resource
Population (Spain, 2022)	-	47.353.590	INE. 2022 <sup>4</sup>
MDS incidence	0.004%	1.894	MDS guideline 2020 <sup>1</sup>
Low Risk MDS	77.00%	1.458	Greenberg et al. 2012 <sup>5</sup>

MDS: Myelodysplastic syndromes

#### Figure 1. Markov health states

 Follow-up cost: tests and medical consultation costs were considered. This cost was estimated based on the frequency of use<sup>10</sup> and unit cost<sup>11</sup>. The cost/cycle was €758.63 for TD patients and €179.83 for TI patients.

- Transfusion cost: transfusion frequency has been based on transfusion regimen (high regimen: 20 transfusions/ 16 weeks; low regimen: 6/ 16 weeks or 2/ 16 weeks). A unit cost of €474.78 per transfusion was considered.
- Complications cost: the cost of acute complications was included based on the incidence of ERASME study<sup>3</sup> and with experts' opinion (Table 5). It was assumed that acute complications require hospitalization, and this cost was extracted from the CMBD (Spanish healthcare database mandatory in public hospitals)<sup>12</sup>.

#### Table 5. Incidence of complications over the 5-year time horizon

Complications	Unit cost <sup>14</sup>	TD patient (%)	TI patient (%)	Resource
Infections	€2,672.38	42.2%	14.5%	
Haematomas/bleeding	€2,232.61	20.0%	6.5%	ERASME study Experts. 2022 <sup>1</sup>
Cardiovascular events	€3,680.73	20.0%	8.9%	

TD: transfusion- dependent; TI: transfusion- independent

#### **Outcome measures**

- Clinical benefit results: survival associated with LR-MDS was estimated. To this end, the life years (LYs) and the quality-adjusted life years (QALYs) gained over the 5-year time horizon were calculated. In addition, these results were extracted for TD patients and TI patients.
- **Cost results:** the cost of the LR-MDS over the 5-year time horizon and annual costs were estimated. In addition, these results were extracted for TD and TI patients.
- Sensitivity analysis: deterministic (DSA) and probabilistic sensitivity analyses (PSA) were performed to assess results robustness. Each parameter was varied individually in its confidence interval (CI95%) or

(Figure 5) compared to €12,558 per patient for TI (Figure 6).

#### Figure 5. Annual cost per patient in TD patients

Total/year	€46,895	€44,133 €	242,633	€41,398	€40,273
€50,000 €40,000 €30,000 €20,000 €10,000	€1,943 €7,958 €9,510 €27,484	€1,993 €7,460 €8,915 €25,765	€2,003 €7,193 €8,595 €24,842	€2,005 €6,974 €8,334 €24,085	€2,008 €6,774 €8,095 €23,396
ŧŪ	Year 1	Year 2	Year 3	Year 4	Year 5
Complic	cations cost	Transfusions cost	Follow	-up cost 🛛 🗖 Pharm	acological cost

## Figure 6. Annual cost per patient in TI patients

Total/year	€13,397	€12,889	€12,508	€12,162	€11,835
€50,000					
€40,000					
€30,000					
€20,000	€303	€332	€361	€390	€420
€10,000	€2,277 €10 818	€2,183 €10,274	€2,112	€2,047 €0,725	€1,985
€0 -	210,010	10,374	£10,030	€9,725	€9,430
	Year 1	Year 2	Year 3	Year 4	Year 5
	Complicatio	ns cost 🛛 🗖 Fo	llow-up cost	Pharmacolog	gical cost

- The pharmacological cost accounts for most of the cost of LR-MDS (TD: 58.3% vs. TI: 80.2%)(Figure 7).
- In TD patients, transfusions accounted for 16.9% of the annual cost (Figure 7).

#### Figure 7. Cost distribution by cost item





## Time horizon, cycle duration and discount rates

- A simulation was carried out over 5-year time horizon and one-month cycles.
- A 3% annual discount rate was used for costs and outcomes<sup>6</sup>.

## **Clinical parameters**

- Transition probabilities were based on ERASME study<sup>3</sup> and a literature review (**Table 2**):
- To MDS TI: data from the ERASME study<sup>3</sup> were used. In particular, the probability of death was modelled based on the overall survival curve in TI patients.
- To MDS TD: the probability of death and progression to AML was modelled based on curves in TD patients collected from ERASME study<sup>3</sup>.

## Table 2. Transition probabilities between health states

Transition probabilities	% per cycle (month)	Resource
From MDS TI to		
MDS TD*	0.48%	
AML	0.00%	ERASME study <sup>3</sup>
Death	Overall survival curve-TI	
	population	
From MDS TD to		
AML	Progression curve to LMA	
Death	Overall survival curve-TD	ERASME study <sup>3</sup>
	population	
From AML to		
Death	17.66%	Wahlin et al. 2001 <sup>7</sup>
* In the EDACAAE study a total of 19 20	/ of TL patients received a transfusion is	n 42 months

assuming a  $\pm 15\%$  variation from baseline. For the PSA, 500 Monte Carlo simulations have been carried out, each simulation varies all parameters according to their probability distribution.

# RESULTS

- Based on an incident population, a total of 1,458 patients were analyzed
- The proportion of TD patients increased every year (Figure 2).

#### Figure 2. Annual distribution of patients in health states



- <sup>\*</sup>Survival patients at the end of each year
- For the total population, 5,299 LY and 4,286 QALYs over 5 years were obtained, implying a 27.3% reduction in LYs and a 41.2% reduction in QALYs compared to a healthy population (**Table 6**).
- LR-MDS population accumulated a mean of 4.18 QALYs/patient.

#### Table 6. Clinical benefit results of total population

Outcome measure	Results		
Accumulative LYs over 5 years in LR-MDS population	5,299		
Reduction in LYs vs healthy population*	27.3%		
Accumulative QALYs over 5 years in LR-MDS population	4,286		
Reduction in QALYs vs healthy population*	41.2%		
* Assuming 5 years (7,290 for the total population analyzed) of LYs and OALYs in the healthy population			

- In addition, the DSA and PSA results confirmed the robustness of the results:
- DSA: was observed that the parameters that most influence cost results are the number of patients with LR-MDS and the pharmacological cost.
   Whereas the number of patients with LR-MDS and the utility value of the MDS-TI are the parameters that most influence the QALYs results.
- PSA: to 500 simulations it was found that mean costs and mean QALYs were similar to the results of the analysis (Table 7).

## Table 7. PSA results

Outcome measure	Case base result	PSA result (mean)	CI95% (/	۸in;Max)
Accumulative QALYs over 5 years in LR-MDS population	4,286	4,275	3,135	5,415
Accumulative costs over 5 years in LR-MDS population	€105,582,606	€107,409,438	€83,445,158	€131,373,718
QALYs: Quality-adjusted life years; LR-MDS: Low risk myelodysplastic syndromes; Min: minimum; Max: Maximum				

## **Conclusions**

- The clinical and economic burden associated with LR-MDS is substantial in Spain.
- In patients with transfusion dependence the clinical and economic burden is higher than in transfusion independent patients.

In the ERASME study a total of 18.2% of TI patients received a transfusion in 42 months

• Utility values were associated with each health state. These values were obtained from a systematic literature review (Table 3).

#### Table 3. Utilities values for each heath state

Health state	Utility value*	Resource	
MDS TI	0.56		
MDS TD	0.88	Sugrue. 2018 <sup>8</sup>	
AML	0.57		
*Numerical scale 0 to 1, where 0 is the worst possible state of health (death) and 1 is a state of "perfect health"			

Numerical scale 0 to 1, where 0 is the worst possible state of health (death) and 1 is a state of "perfect health"

TD patients accumulated 2.64 QALYs/patient, while TI patients accumulated 4.15 QALYs/patient over 5 years time horizon (Figure 3).
TD patients accumulated 36.4% fewer QALYs than TI population (Figure 3).

#### Figure 3. Accumulate QALYs based to transfusion dependence



- A cumulative cost of €105,582,606 over the 5-year time horizon was estimated (Figure 4).
- The mean annual cost of LR-MDS was estimated at €21,116,521.

#### References

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#### Disclosure

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Email: saceituno@outcomes10.com

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