FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE



CONVEGNO FISiM

Firenze, CSF Montedomini
"Il Fuligno"
23-24 ottobre 2026

Quality of Life in MDS

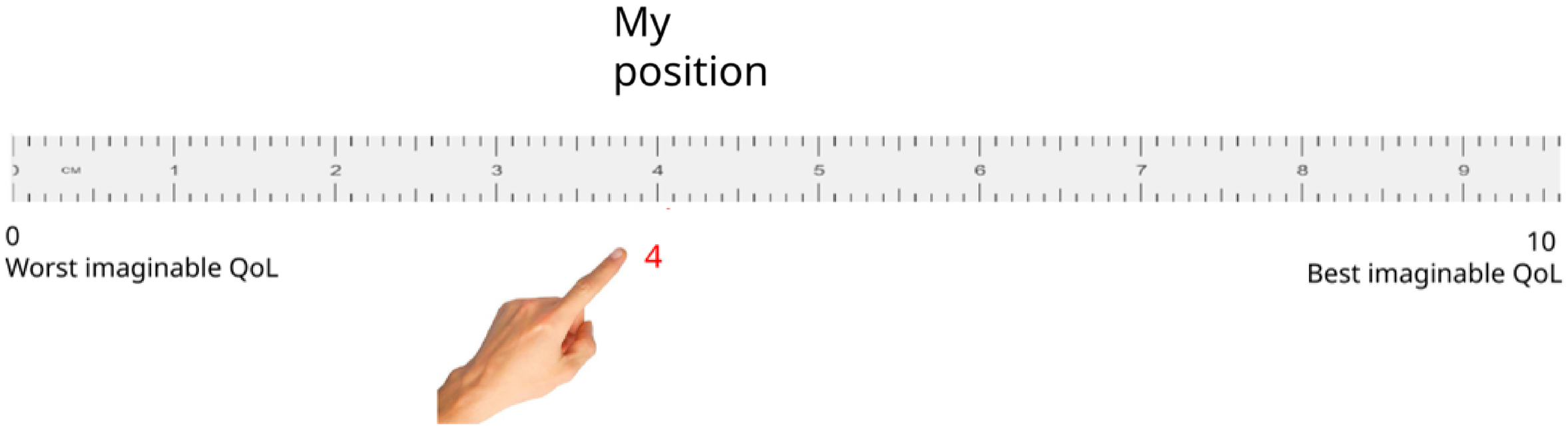
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Disclosures of Esther Natalie Oliva

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Novartis					x		
Halix							x
Servier							x
Daiichi						x	

Quality of life (QoL)

QoL is an individual's perception of his/her position in life in the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards and concerns.
WHO 1994



Patient-reported outcomes (PROs)

Health-related QoL is a complex, multidomain variable[1,2]

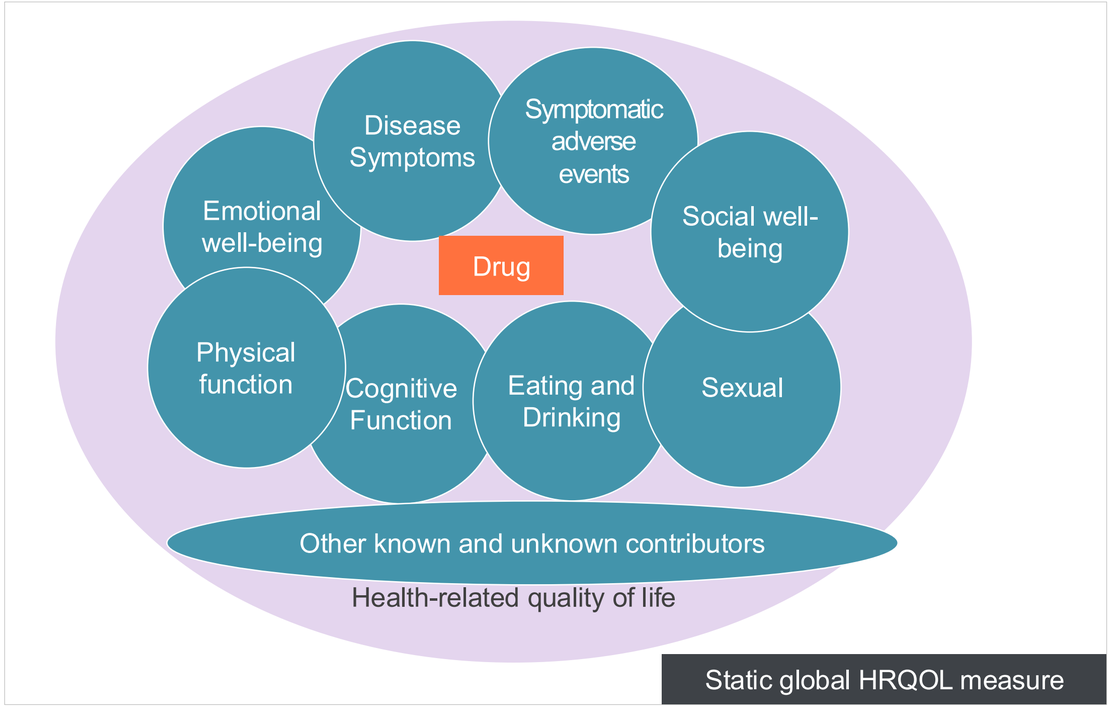
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Symptoms are any subjective evidence of a disease, health condition or treatment-related effect that can be noticed and recognized only by the patient[3,4]

Physicians vary in their ability to elicit PROs[5,6]
Need for instruments

1. Bowling A, et al. BMJ. 1996;312:670–674; 2. Gorodokin GI and Novik AA. Annalsof Oncology. 2005;16(6):991; 3. Trotti A, et al. J Clin Oncol 2007;25(32):5121–127; 4. Spivak J, et al. The Oncologist 2009; 14 (suppl 1):43–56; 5. Passik SD, et al. J Clin Oncol 1998;16(4):1594–1600; 6. Fallowfield L, et al. Br J Cancer 2001;84(8):1011–1015.

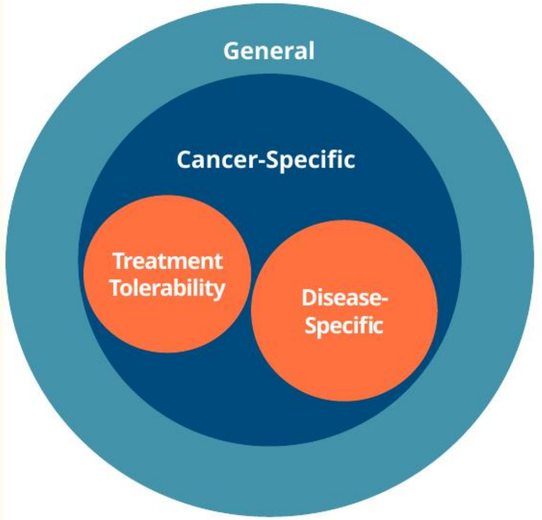
Health-related quality of life (HRQoL)



Adapted from Kluetz et al., Clin Cancer Res. 2016 Apr 1;22(7):1553-8.

Patient-reported outcome instruments for MDS

GENERIC HRQoL INSTRUMENTS	***MYELODYSPLASTIC SYNDROMES***
EuroQol 5 Dimensions (EQ-5D) [59]	Quality of Life in Myelodysplasia Scale (QUALMS) [25]
Short Form 36 Health Survey (SF-36) [60]	Quality of Life E (QOL-E) [24]
CANCER-SPECIFIC HRQoL INSTRUMENTS	***FATIGUE***
EORTC Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) [21]	Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-Fatigue) [61]
Functional Assessment of Cancer Therapy-General (FACT-G) [62]	FACT-Anemia (FACT-An) [63]
	Brief Fatigue Inventory [64]
	Fatigue Symptom Inventory [65]
	Multidimensional Fatigue Inventory [66]
	MENTAL DIMENSION
	Hospital Anxiety and Depression Scale (HADS) [67]
	Memorial Symptom Assessment Scale (MSAS) [68]



Giesinger JM, et al. Clin Pract Epidemiol Ment Health. 2021; 17(1): 307–314

QOL-E domains

- Physical
- Functional
- Social
- Sexual
- Fatigue
- MDS-specific

13) During the last week, did shortness of breath while climbing the stairs disturb you?

Never	Sometimes	Often	Very often

14) What effects of the disease disturb your daily life?

Effect	Not at all	A little bit	Yes, extremely
A. Being dependent on transfusions			
B. Not being able to do house chores			
C. Not being able to travel			
D. Being dependent on the hospital, doctors and/or nurses			
E. Stress and worry because of the disease			
G. Side effects of treatment			

© Oliva E, Dimitrov BD.

QUALMS: a PROM developed specifically for MDS

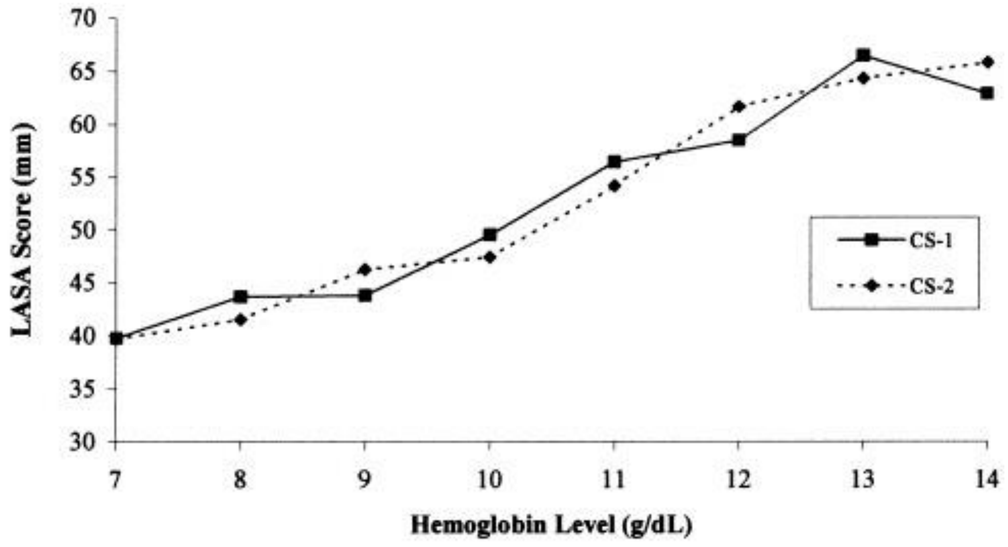
Item	QUALMS item	QUALMS-P	QUALMS-BF	QUALMS-E
Q24	Too tired for prior responsibilities	0.88	−0.02	0.50
Q9	Low energy change schedule	0.83	0.03	0.47
Q23	Weak	0.78	0.09	0.34
Q26	Unable participate in activities	0.78	−0.17	0.35
Q20	Take into account might be fatigued	0.75	0.02	0.47
Q25	Worry about becoming burden	0.73	−0.03	0.51
Q11	Felt hopelessness	0.65	−0.02	0.60
Q33	Change in bowels	0.63	−0.16	0.37
Q8	Shortness of breath	0.62	−0.04	0.38
Q7	Change long-term plans due to health	0.57	−0.27	0.50
Q6	Trouble concentrating	0.57	0.09	0.56
Q10	Life organized around medical	0.56	−0.28	0.42
Q18	Nauseated	0.53	−0.11	0.20
Q13 (R)	Energy for routine tasks	0.52	0.09	0.17
Q22	Family relationships strained	0.48	−0.08	0.47
Q29 (R)	Grateful for tomorrow	0.12	0.66	0.05
Q30 (R)	Get quality information	0.09	0.65	0.22
Q17 (R)	Gratitude when prior took for granted	−0.01	0.57	−0.09
Q31	Bruising	0.32	−0.47	0.37
Q28	Avoid crowds	0.26	−0.38	0.37
Q3	Could not do anything about disease	0.48	0.03	0.67
Q4	Disease unpredictable	0.40	−0.06	0.66
Q32	Lack of concrete answers	0.24	−0.09	0.65
Q1	No clear information	0.33	0.05	0.63
Q14	Afraid of dying	0.32	−0.20	0.62
Q5	Difficulty explaining MDS to others	0.26	0.04	0.61
Q19	Worry progressing/leukemia	0.33	−0.19	0.60
Q27	Anxious about tests or lab results	0.46	−0.16	0.58
Q15	Angry about diagnosis	0.43	−0.10	0.58
Q12	Worried infection	0.33	−0.42	0.58
Q2	Limited emotional support available	0.37	−0.06	0.53
Q16	Worried bleeding	0.21	−0.45	0.48
Q21	Concerned financial burden	0.40	−0.17	0.48

Abel GA, et al. Haematologica. 2016;101(6):781–788. R = reverse-scored item. Item numbering follows the instrument.

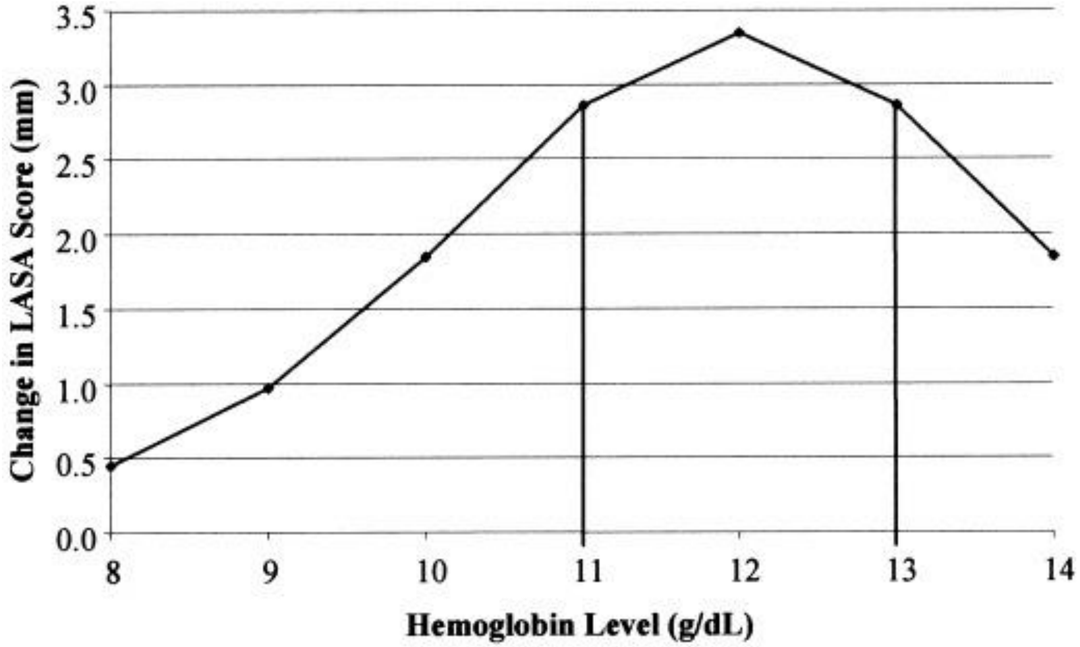
Relationship Between Anemia and QoL

Results from 4382 anemic cancer patients undergoing chemotherapy treated with epoetin alfa

Relationship between Hemoglobin Level and QoL



The Average Effect of a 1g/dL Increase Per Hemoglobin Level



Maximum incremental QoL gain occurred at a hemoglobin level of 12 g/dL (11-13 g/dL)

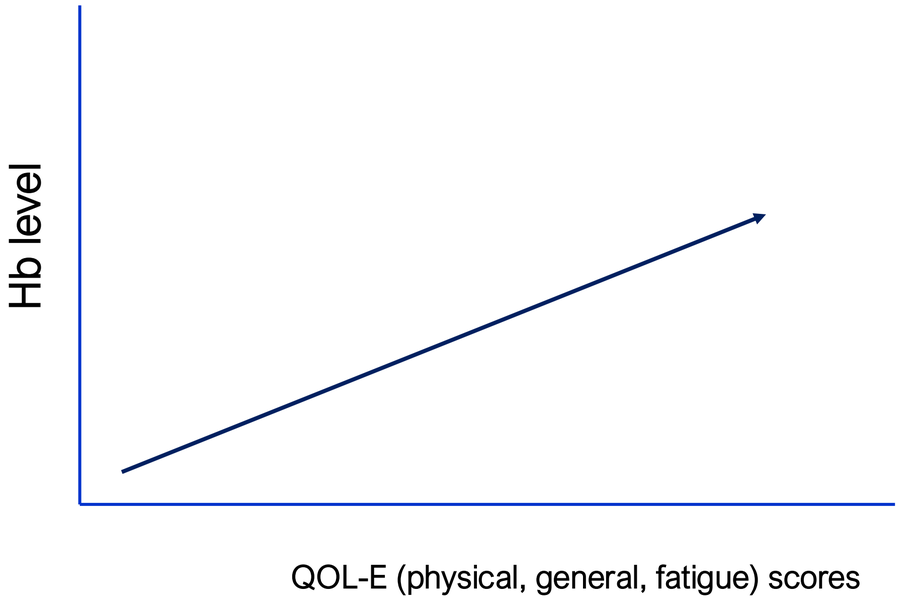
Hb, hemaglobin; QoL, quality of life; LASA, inear analogue scale assessments; QoL-E, myelodysplastic syndrome-specific quality of life scale.

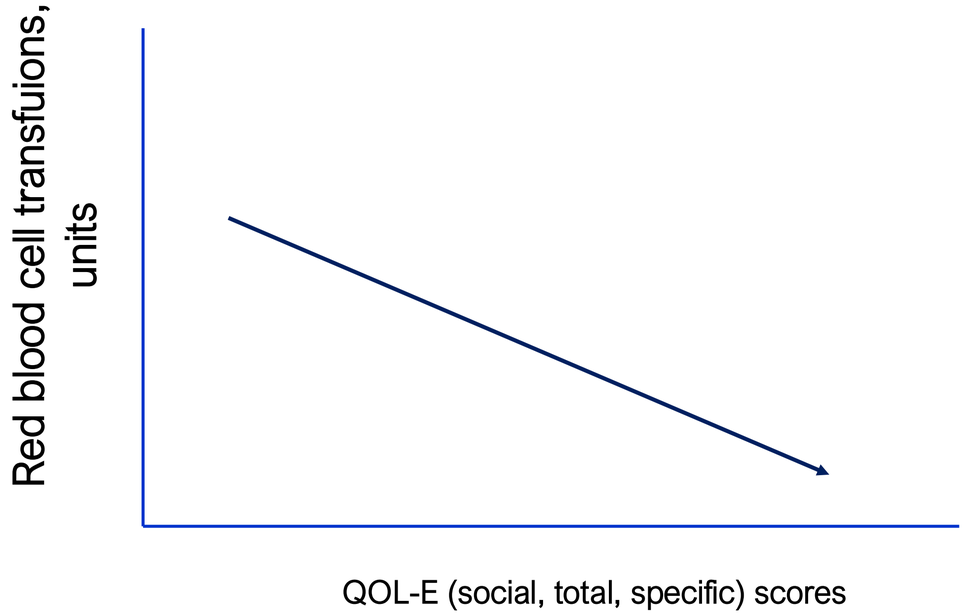
Crawford J, et al. Cancer. 2002; 95:888–895.

Impact of transfusions on HRQoL in Myelodysplastic neoplasms - QOL-E instrument:

Multivariate analysis

Variables
Transfusion requirement
Hb
Age
MDS duration





Oliva EN, et al. J Clin Oncol 2002

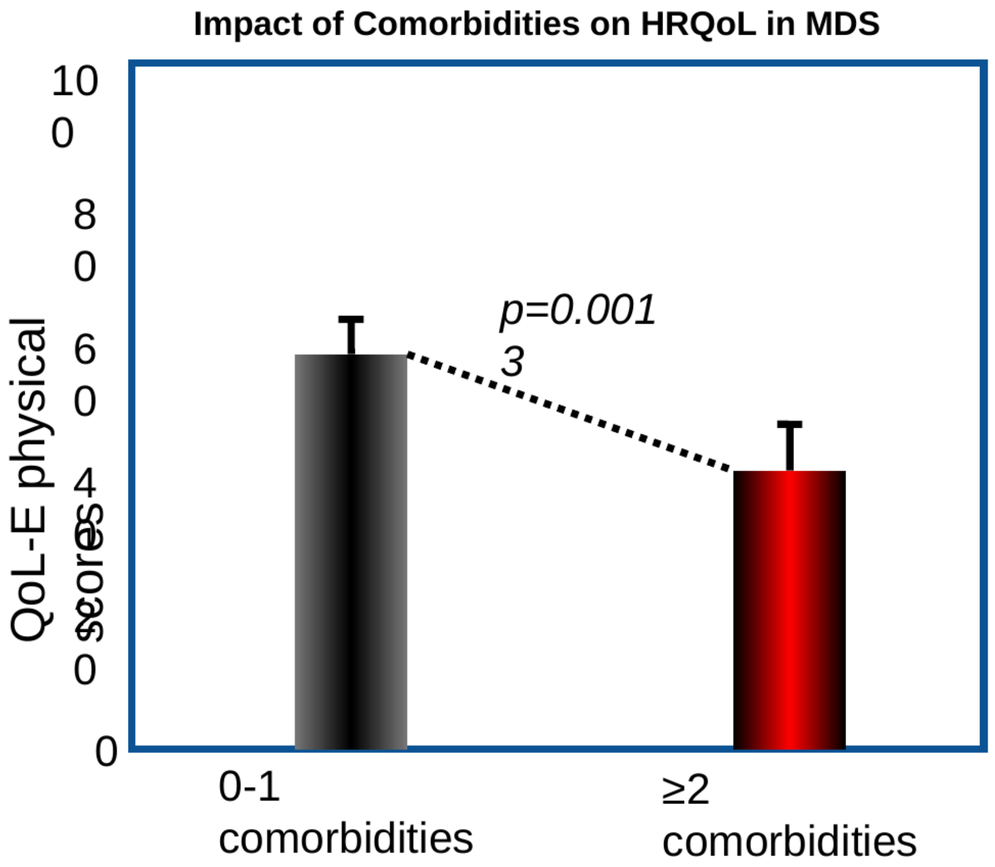
Transfusion dependence and health-related quality of life

Transfusion burden extends well beyond haemoglobin levels

1. **Hospital dependence**
   Repeated visits and dependence on clinical services
2. **Travel restrictions**
   Difficulty planning travel around transfusion schedules
3. **Anticipatory anxiety**
   Concern about the next transfusion and falling haemoglobin
4. **Haemoglobin fluctuations**
   Variable fatigue and physical capacity between visits
5. **Treatment adverse events**
   Possible transfusion-related complications
6. **Everyday functioning**
   Dyspnoea, reduced mobility and difficulty climbing stairs

Oliva EN, et al. J Clin Med. 2022;11:27; Balducci L. Cancer. 2006;106:2087–2094.

Factors predicting QoL in MDS: comorbidities, anaemia and time



QoL-E index*	Factor	Multivariate analysis† Effect (95% CI) ‡	p value
Fatigue			
	Charlson's index (2-5 vs 0-1) §	−8.6 (−12.3, −4.8)	<0.0001
	Hb (1 g/dL) ‖	+1.45 (+0.89, +2.01)	<0.0001
	Transfusions (yes vs no) ¶	−2.6 (−5.4, +0.2)	0.064
	Gender (male vs female)	+3.3 (+0.2, +6.4)	0.038
	Time from baseline (1 month)	−0.11 (−0.25, +0.04)	0.16
MDS specific			
	Charlson's index (2-5 vs 0-1)	−8.8 (−13.5, −4.1)	0.0003
	Hb (1 g/dL)	+1.53 (+0.81, +2.26)	<0.0001
	Transfusions (yes vs no)	−6.8 (−10.2, −3.5)	0.0002
	Time from baseline (1 month)	−0.38 (−0.55, −0.22)	<0.0001

*scaled from 0 (worst possible value) to 100 (best possible value); †variables with p<0.05 are included in the basic model, for other factors the reported p-value tests the addition to this model; ‡mean difference of predicted dependent variable between levels (first - second) of binomial factors or for each 1-unit increase of quantitative factors; §at baseline; ‖ at each visit; ¶ any transfusion within 3 months before the day of visit

CI, confidence interval; Hb, hemoglobin; HRQoL, health related quality of life; MDS, myelodysplastic syndrome; QoL, quality of life; QoL-E, MDS-specific QoLscale.

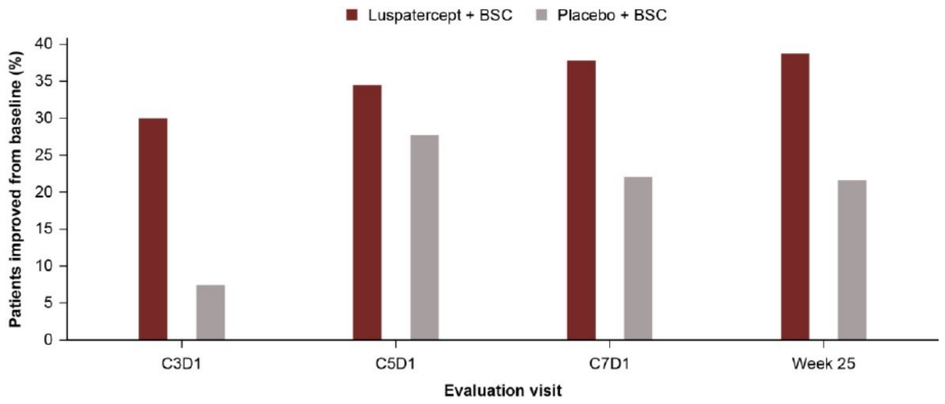
Oliva EN, et al. Am J Blood Res. 2012;2(2):136–47.

MEDALIST trial: changes in quality of life

Relative mean difference in change in QOL-E domain scores from baseline to Week 25 between luspatercept and placebo[a]

QOL-E domain	Baseline score, mean (SD) (N = 225)	Relative mean difference at Week 25	MCID
Physical well-being	52.87 (21.52)	−5.28	10.69
Functional well-being	53.70 (32.38)	−6.07	16.13
Social and family life	48.41 (37.63)	−8.70	18.76
Sexual well-being	62.42 (36.25)	0.31	18.14
Fatigue	74.98 (14.12)	−5.10	7.14
MDS-specific disturbances	57.04 (23.68)	−2.03	11.90
Treatment outcome index	54.71 (20.65)	−4.71	10.31
General	58.69 (21.06)	−6.30	10.51
All	58.07 (21.09)	−5.10	10.57

Through Week 25, there was no clinically meaningful difference in change from baseline between and within the luspatercept and placebo arms in all QOL-E domains

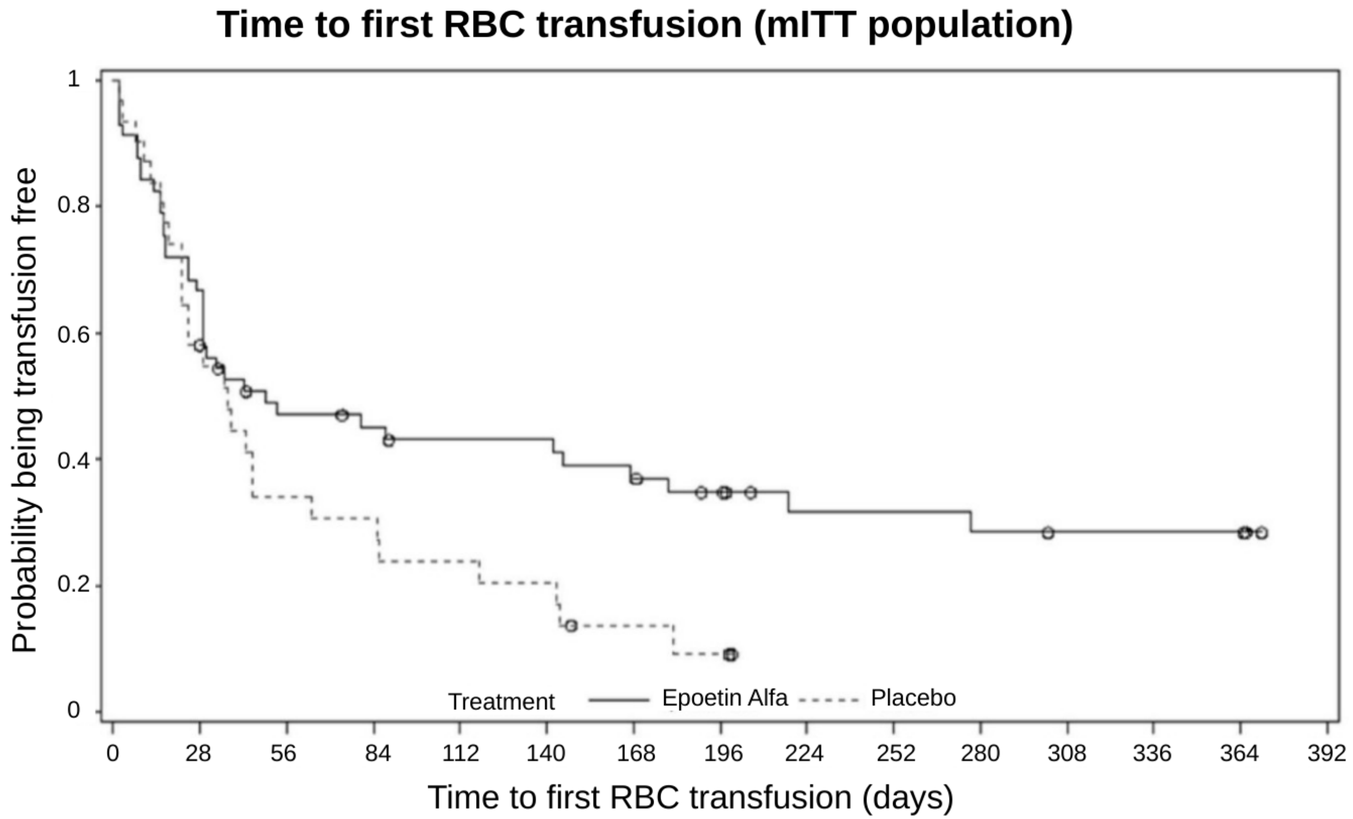


	C3D1		C5D1		C7D1		Week 25	
	Luspatercept	Placebo	Luspatercept	Placebo	Luspatercept	Placebo	Luspatercept	Placebo
N	127	68	122	65	106	59	106	51
Improved, %	30	7	34	28	38	22	39	22
Stable, %	59	74	49	52	47	59	49	57
Worsening 1, %	9	13	15	17	14	17	10	20
Worsening 2, %	2	6	2	3	1	2	2	2

A greater proportion of patients in the luspatercept arm relative to placebo reported improvements in daily life from the impact of transfusion dependence

Oliva et al. J*ournal of clinical medicine*, *11*(1), 27

Epoetin alfa in lower-risk MDS: phase III placebo-controlled study
QoL improvement in responders only



- **Patients with an erythroid response at any time during the first 24 weeks of the study:**
  epoetin alfa versus PBO: 31.8% vs 4.4%; P<0.001

PROs

- There were no significant differences in QoL between the epoetin-α group and the placebo at any time point. QoL at Week 24 was significantly different between the responders in the epoetin-α group and the placebo group (**EQ-5D** index score P = 0.034).

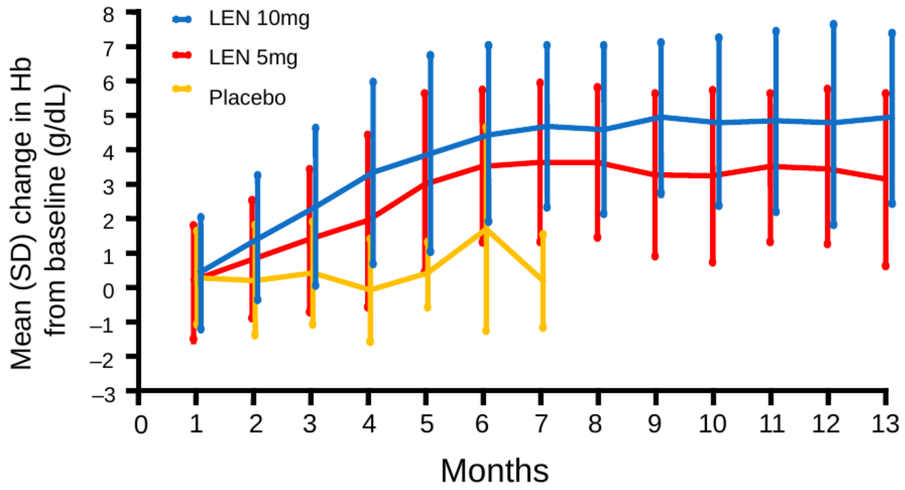
Choice of instrument?
Burden of trial
Hb response?

EQ-5D, EuroQoL 5-dimension scale; Hb, hemoglobin; MDS, myelodysplastic syndrome; mITT, modified intention-to-treat; PBO, placebo; PROs, patient-reported outcomes; QoL, quality of life; RBC, red blood cell.

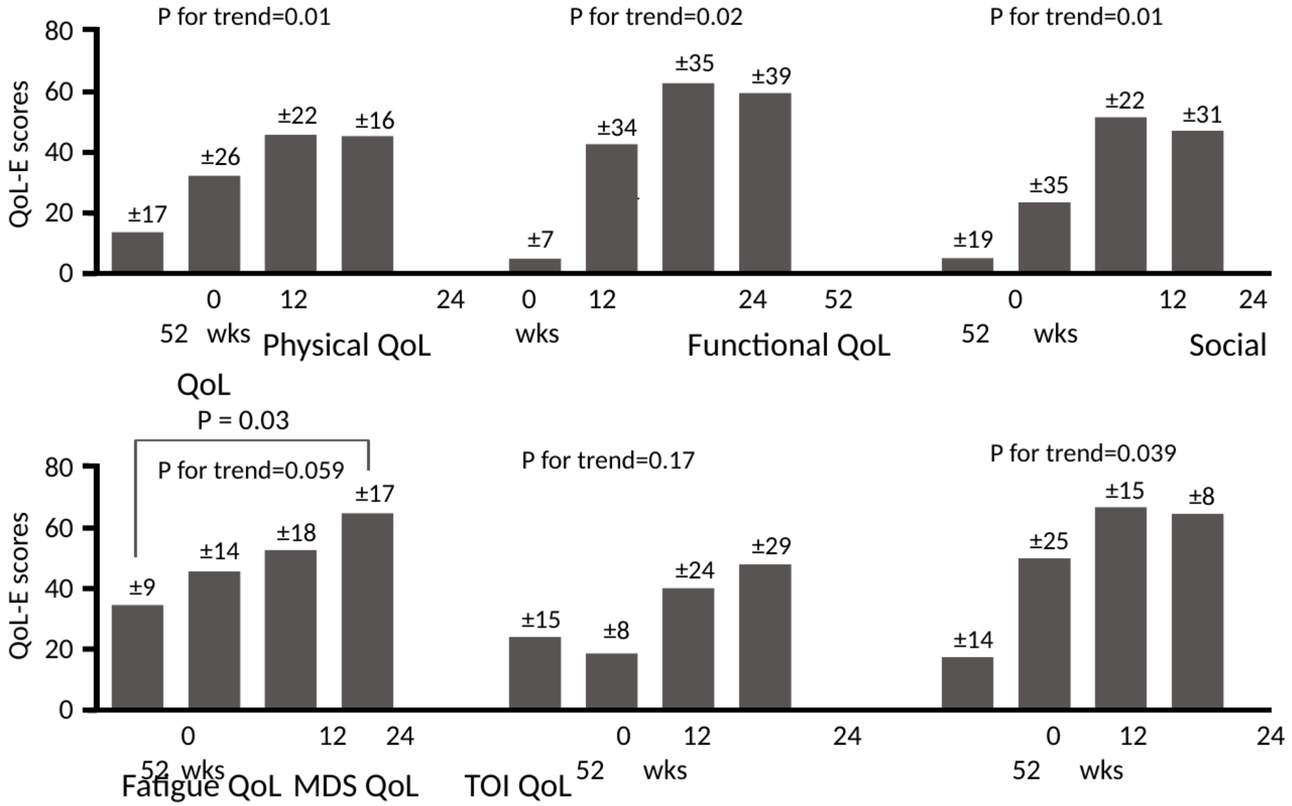
Fenaux P, et al. Leukemia. 2018;32(12):2648–2658.
https://clinicaltrials.gov/ct2/show/NCT01381809

Haemoglobin and HRQoL in del(5q) MDS treated with lenalidomide

Hb Changes in Patients Receiving Lenalidomide: MDS-004[1]



Changes in HRQoL Scores in Anemic MDS with del5q Treated with Lenalidomide in Patients with Poor Baseline QoL[2]



Hb, hemoglobin; HRQoL, health related quality of life; LEN, lenalidomide; MDS, myelodysplastic syndrome; QoL, quality of life; TOI, treatment outcome index.

1. Fenaux P, et al. Blood. 2011;118:3765–3776;
2. Oliva EN, et al. Leuk Lymph. 2013;54(11):2458–65.

Luspatercept response, Hb level and quality of life

COMMANDS post-hoc analysis: HRQoL according to absolute Hb Level (≥ 10 vs < 10 g/dL)[2]

Primary domain	Absolute Hb level (≥ 10 vs. < 10 g/dL)	
	Coefficient (95% CI)	p-value
EORTC QLQ-C30	n = 381 vs 662	
GHS/QoL	5.18 (2.92, 7.44)	< 0.001
Physical functioning	3.93 (1.92, 5.95)	< 0.001
Fatigue	-5.54 (-8.21, -2.87)	< 0.001
Dyspnoea	-4.78 (-8.00, -1.56)	0.004
FACT-An	n = 1011 vs. 1761	
Fatigue subscale	1.29 (0.75, 1.83)	< 0.001
Anemia subscale	1.64 (0.96, 2.33)	< 0.001
Total score	2.99 (1.72, 4.27)	< 0.001

- **Dose escalation resulted in increased Hb** in patients who did not initially reach target Hb or whose Hb did not increase by > 1.5 g/dL[1]
- Achieving **Hb ≥ 10 g/dL** correlated with significant improvements in **anemia-related PROs including QoL, fatigue, physical functioning and dyspnoea**[2,a]

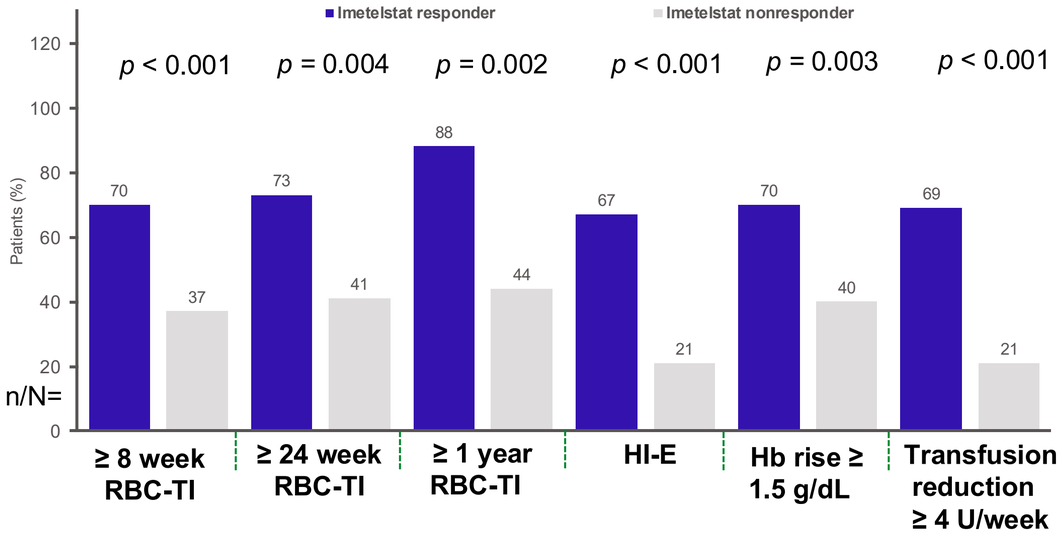
[a] Based on primary domains from the QLQ-C30 questionnaire.

CI, confidence interval; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; FACT-An, Functional Assessment of Cancer Therapy Anemia Questionnaire; GHS, global health status; Hb, hemoglobin; HRQoL, health-related quality of life; ITT, intention to treat; PRO, patient-reported outcome; QoL quality of life.

1. Santini V, et al. ASH 2024; Abstract 1818; 2. Oliva E, et al. EHA 2024; Abstract P774.

IMerge: fatigue, quality of life and anaemia symptoms

FACIT-Fatigue by response status (N = 178)



Change from baseline in QoL and anemia symptoms at C30 (N = 178)

Score	Imetelstat LS mean change from baseline (95% CI) (n = 118)	Placebo LS mean change from baseline (95% CI) (n = 60)	LS mean (95% CI) difference	Nominal *P*- value
QUALMS Total	-0.55 (-2.85, 1.76)	-5.21 (-8.35, -2.07)	4.66 (0.86, 8.46)	0.016
QUALMS Physical burden	-0.41 (-3.18, 2.36)	-6.75 (-10.53, -2.98)	6.34 (1.77,10.91)	0.007
FACT-An Total	-1.6 (-5.00, 1.80)	-9.72 (-14.43, -5.01)	8.12 (2.44,13.81)	0.005
FACT-An Physical well-being	-0.43 (-1.10, 0.24)	-1.16 (-2.08, -0.24)	0.73 (-0.38, 1.84)	0.197

FACT-An, Functional Assessment of Cancer Therapy-Anemia; FACIT, Functional Assessment of Chronic Illness Therapy; Hb, hemoglobin; HI-E, hematologic improvement-erythroid; LS, least squares; QoL, quality of life; QUALMS, Quality of Life in Myelodysplasia Scale; RBC-TI, red blood infusion transfusion independence.

Sekeres MA, et al. ASH 2024; Poster 3210.

HT-6184-MDS-001: phase 2 study design

Open-label, Simon's 2-Stage, single-arm, multicenter trial in ESA-refractory, intolerant or ineligible, lower-risk MDS

ELIGIBILITY

- Adults with IPSS-R lower-risk MDS (score ≤ 4.5)
- Symptomatic anemia (Hb < 9 g/dL) OR RBC transfusion-dependent
- ESA-refractory, intolerant or ineligible
- Adequate organ function; ECOG ≤ 2

OFIRNOFLAST (NEK2 inhibitor)

- Ofirnoflast
  2 mg oral, once daily
- Schedule
  5 days on / 2 days off
- Duration
  Up to 32 weeks

ENDPOINTS

PRIMARY

- **Hematologic Improvement (HI) by IWG 2018**

KEY SECONDARY & EXPLORATORY

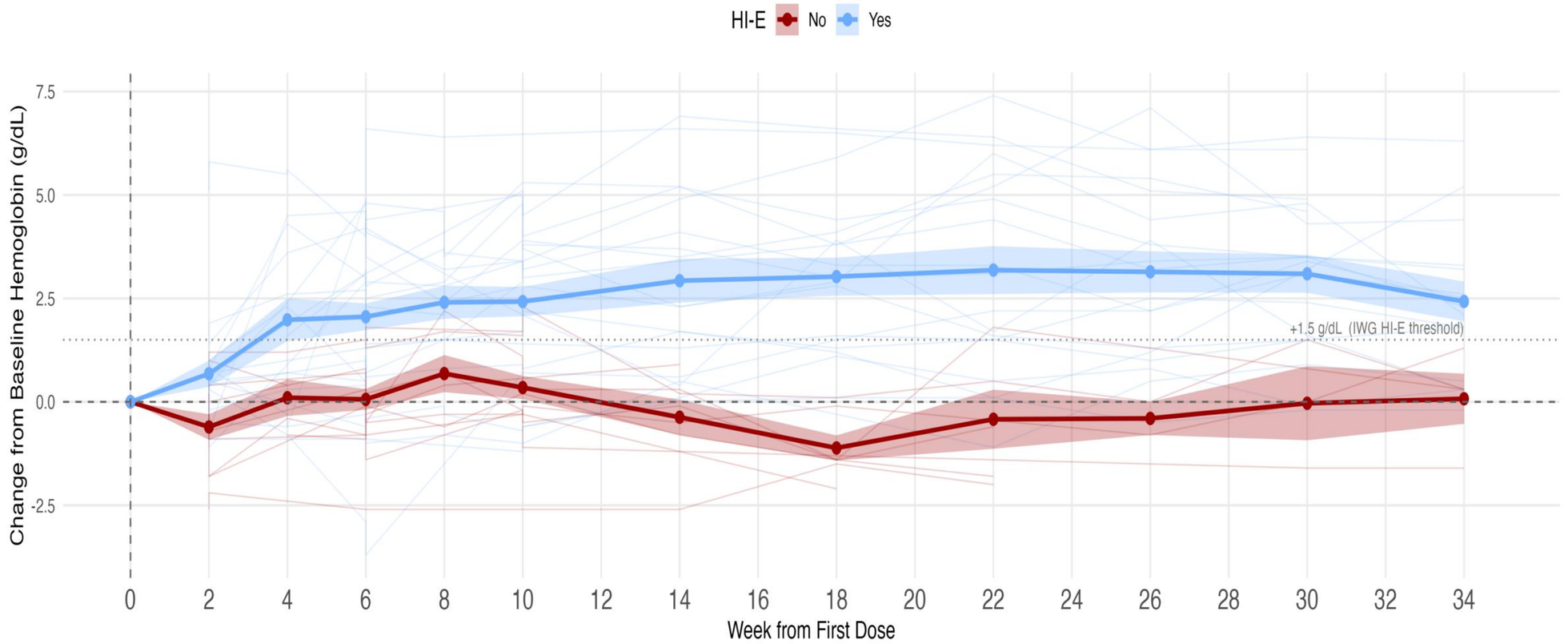
- *Biomarker and molecular* response: change in biomarker and somatic mutation clone size
- *Safety and tolerability*
- *Pharmacokinetics*: trough concentrations
- *Combination therapy response*: rate of HI with ofirnoflast and ESA
- QOL-E

A total of 37 patients were enrolled in the study

Efficacy analyses in following slides are based on the mITT population (N=30)

- 7 subjects excluded from Per-Protocol Population: 6 did not complete 16-week evaluation (3 lost to follow-up, 1 withdrawal of consent, 1 adverse event, 1 death related to disease) · 1 due to eligibility

Mean change in haemoglobin from baseline over time

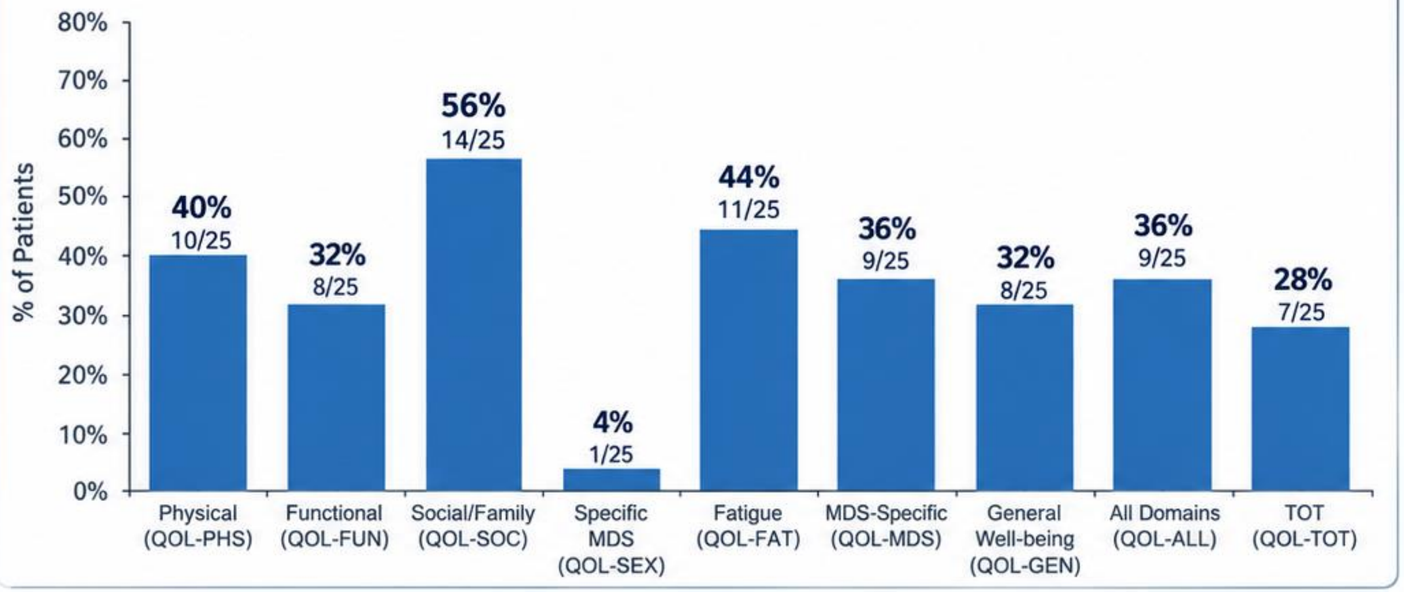


HI-E Response	N =30
Yes	19
No	11

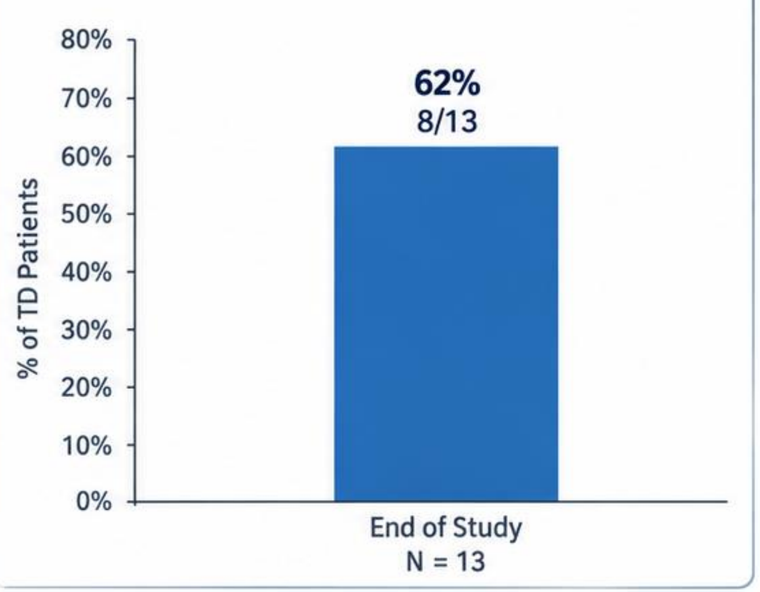
Mean ± SE, stratified by HI-E status. Faint lines represent individual subjects. Hemoglobin values within 7 days of a transfusion were excluded. Baseline defined as the last hemoglobin measurement prior to first dose, set at Week 0. Weeks grouped into 2-week intervals; N reflects the number of participants in that group. Dotted line = +1.5 g/dL increase from baseline

Improvements in patient-reported quality of life on treatment

% OF PATIENTS WHO HAD MINIMAL IMPORTANT CHANGE AT EOS QOL-E SCORES FROM BASELINE



PROPORTION OF TD PATIENTS WHO SHOWED IMPROVEMENT ON PATIENT-REPORTED IMPACT OF TRANSFUSION BURDEN BY QOL-E



Largest improvement: Social/Family well-being (56%); 62% of TD patients improved in perceived transfusion burden.

The QOL-E is scored on a scale from 0–100. Better health corresponds to a higher numerical value. A higher % change is an improvement in QOL-E from baseline.
Physical: physical capacity, mobility, self-care, and ability to hustle strenuous activities. **Functional**: well-being; impact of MDS on ability and activity and ability to complete tasks. **Social/family**: well-being; effect of MDS on relationships, social activities, and feelings of burden. **Sexual**: well-being; impact on sex life and sexual excitement. **Fatigue**: severity and impact of fatigue on daily life, chores, and sleep. **Specific MDS**: symptoms and treatment burden including stamina, shortness of breath, transfusion dependence, and treatment side effects. Treatment. **Outcome index**: primary outcome in clinical trials; mean of QOL-ILS, QOL-FUN, and QOL-MDS. **General**: mean of all domains except QOL-MDS. **ALL**: mean of all 8 sub-scales.

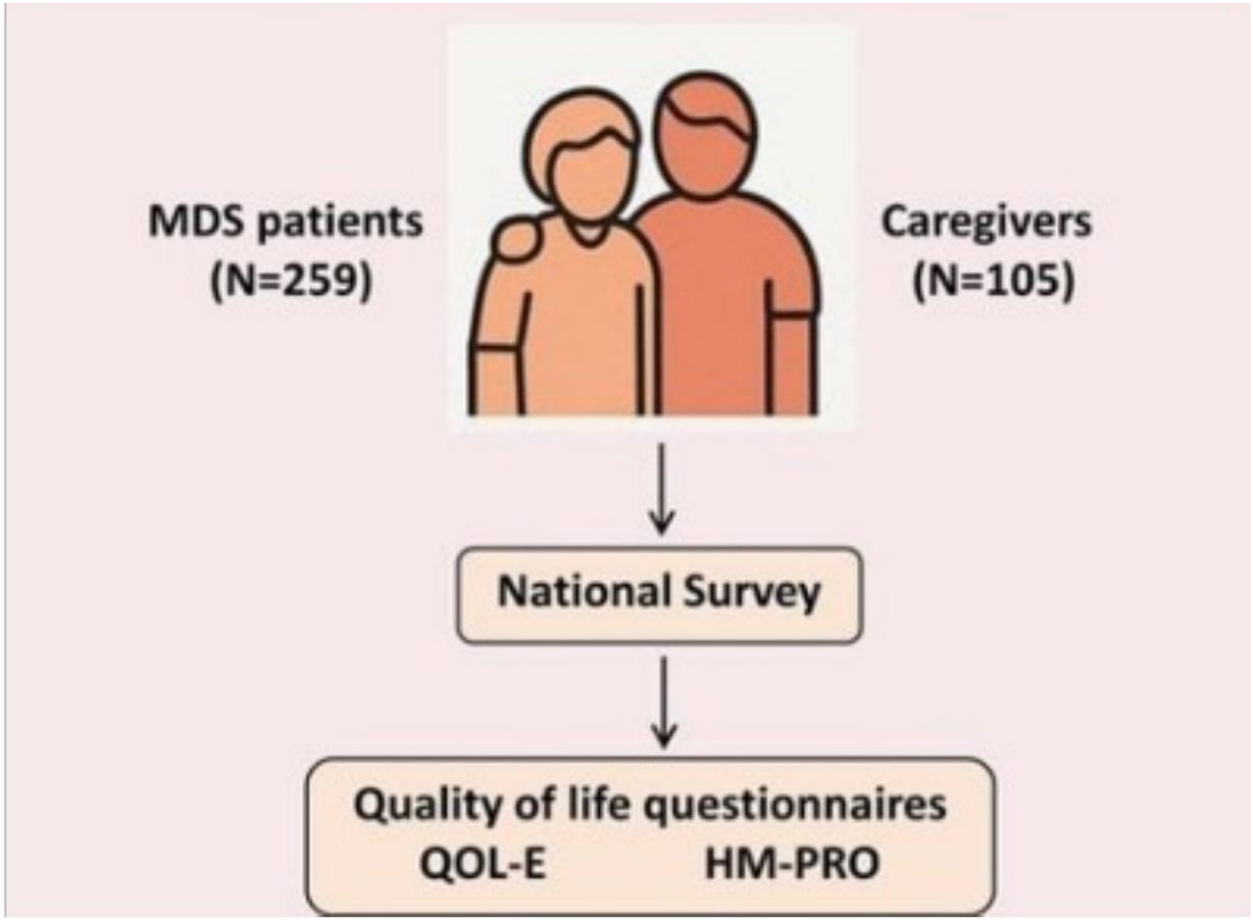
Ofirnahart (P11-0136) | EHA 2025 | Phase 2 Lb-MDS

Platelet response with eltrombopag and QoL (EQoL-MDS):

- For those achieving a platelet response, there were proportionally more cases with stability or clinically meaningful and significant improvement in EORTC QLQ-C30 physical and global scores and QOL-E functional, fatigue, general, total , treatment-outcome index and MDS specific impact scores with respect to non-responders who had a significantly higher proportion of worsening

Oliva EN, et al. Journal of Clinical Oncology, 2023

Italian national survey: patients and caregivers



Crisà E,, et al. *Cancers*. 2025; 17(9):1587.

Italian national survey: patient characteristics and burden

Ongoing treatment	n (%)
Erythropoietin	68 (27.9)
Azacytidine	40 (16.4)
Lenalidomide	14 (5.7)
Hydroxycarbamide	6 (2.5)
Luspatercept	16 (6.6)
Chemotherapy	9 (3.7)
HSCT	5 (2.0)
Eltrombopag	1 (0.4)
Danazol	1 (0.4)
Unknown	11 (4.5)
No treatment	73 (29.9)
Transfusion dependence	
Yes	97 (42.4)
No	132 (57.6)
Missing	30
RBC units/month	
<2	33 (33.0)
2–4	54 (54.0)
>4	13 (13.0)

Difficulty to work, study and to go on holiday, 47%

Anxiety 66%
Worry about treatment 60%
Distress 56%

114 patients (63%) reported that their dependence on hospitals, physicians, or nurses disturbed their everyday life.
Almost half (48%) needed a caregiver to accompany them to the hospital.

For 107 patients (45%), traveling to the hospital was for physical and economic burden and impacted family members and their employment.

Crisà E,, et al. *Cancers*. 2025; 17(9):1587.

Hospital travel, distress and quality of life

Worse PRO scores in 77% of those with distress reaching the hospital and in 20% of those far from the treating centre

Distress was associated with
significantly **worse median HM-PRO scores**

- physical (53.5 vs. 21.4, $p < 0.001$)
- emotional (56.8 vs. 31.8, $p < 0.001$)
- social (66 vs. 50, $p < 0.001$)
- eating and drinking habits ($p < 0.001$)
- Part A (56.0 vs. 26.6, $p < 0.001$)
- Part B symptom score (SS, 20.6 vs. 8.8, $p < 0.001$)

The worst aspect of their treatment journey was waste of time for 37% of patients (N = 86) and hospital disorganization for 20% (N = 46).

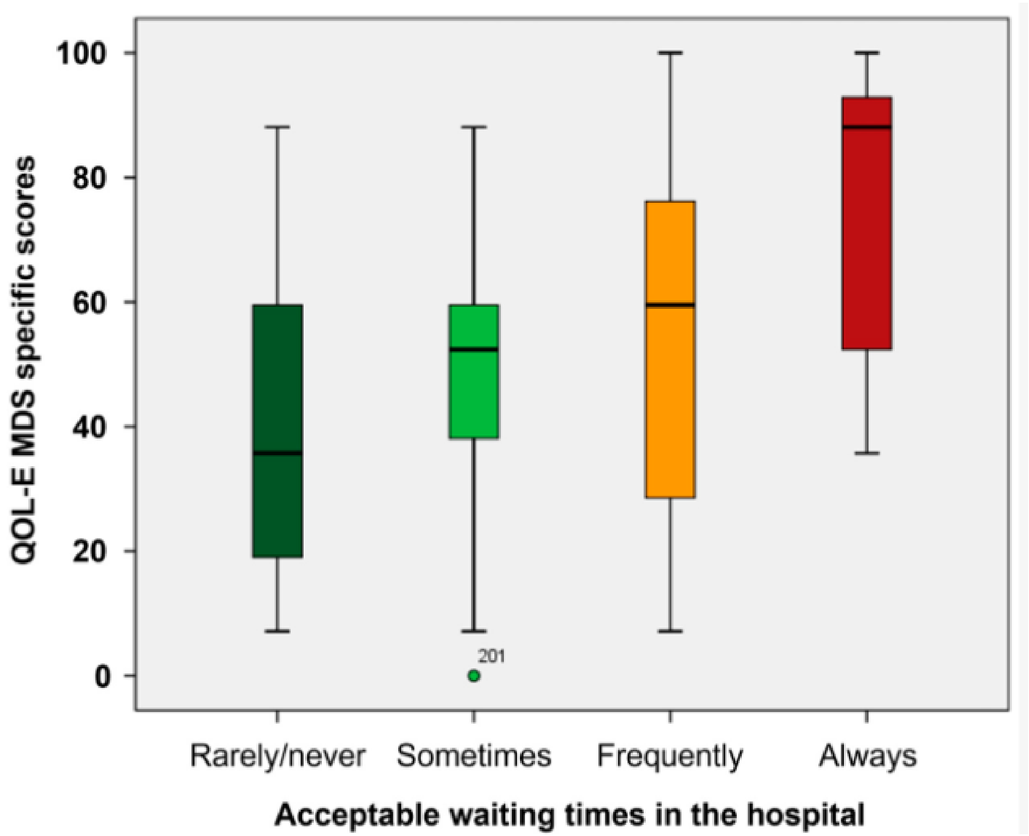
and worse median QOL-E scores

- physical (50.0 vs. 62.5, $p < 0.001$)
- functional (22.2 vs. 88.8, $p < 0.001$)
- social (25.0 vs. 75.0, $p < 0.001$)
- fatigue (64.3 vs. 80.9, $p < 0.001$)
- general (46.7 vs. 72.1, $p = 0.003$)
- MDS specific (44.04 vs. 73.8, $p < 0.001$)
- treatment-outcome index scores (38.2 vs. 69.8, $p < 0.001$)

Telemedicine communication was preferred in 54% particularly if reaching the hospital was reported as being distressful (62% yes vs. 45% no, $p = 0.035$).

Crisà E,, et al. *Cancers*. 2025; 17(9):1587.

Waiting times and QOL-E MDS-specific scores



Waiting times in the hospital were regarded as unacceptable for 87 patients (37%) with worse median scores in

HM-PRO
- EB ($p < 0.001$)
- Part A ($p = 0.020$)
- SS scores ($p = 0.002$)

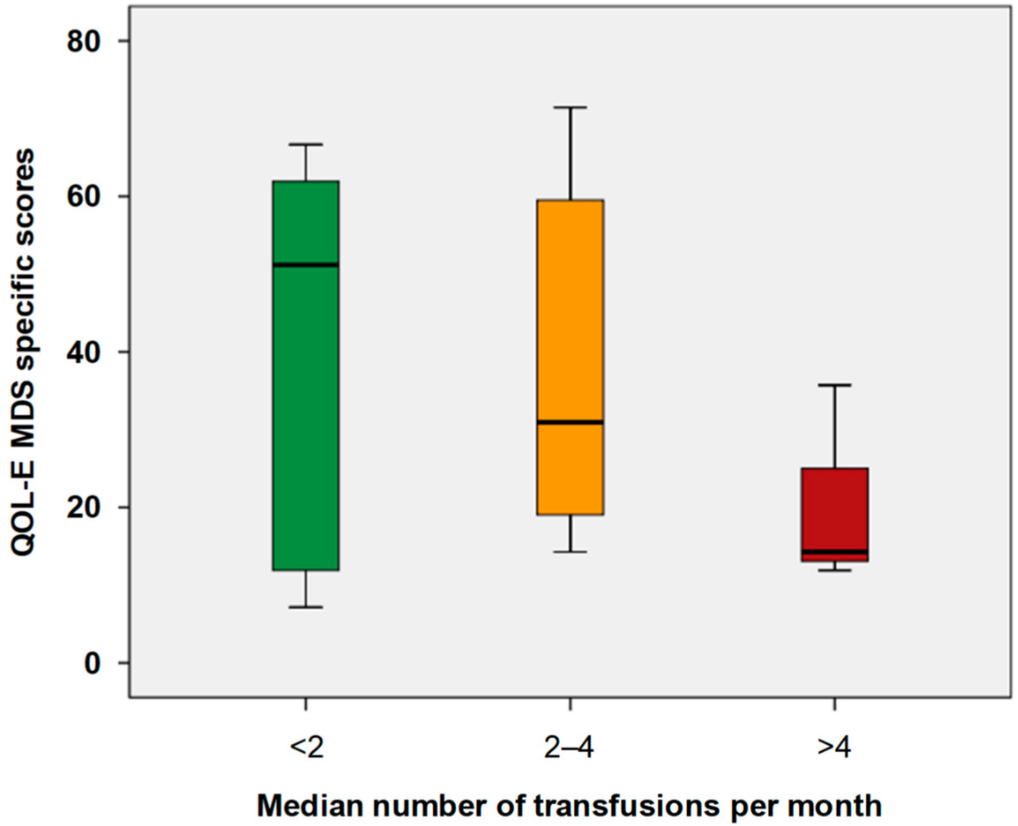
QOL-E
- Fun ($p = 0.004$)
- Fat ($p < 0.001$)
- Ses ($p = 0.018$)
- MDSS ($p = 0.001$)
- Gen ($p = 0.030$)
- TOI ($p = 0.003$)

The worst aspect of their treatment journey was waste of time for 37% of patients (N = 86) and hospital disorganization for 20% (N = 46).

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Transfusion dependence and quality of life

Treatment impacted everyday life negatively for 70% (49/70) of TD patients, compared to 49% (46/94) of TI patients (p = 0.011)
TD patients had significantly worse scores across all domains of QOL-E and HM-PRO.



35 patients felt that they were a **burden for their family**

- TD 61%
- Worse PROs in all domains (p < 0.001)
- MDS impacted their work life 36%
- Needing a caregiver 39%.

Crisà E,, et al. *Cancers*. 2025; 17(9):1587.

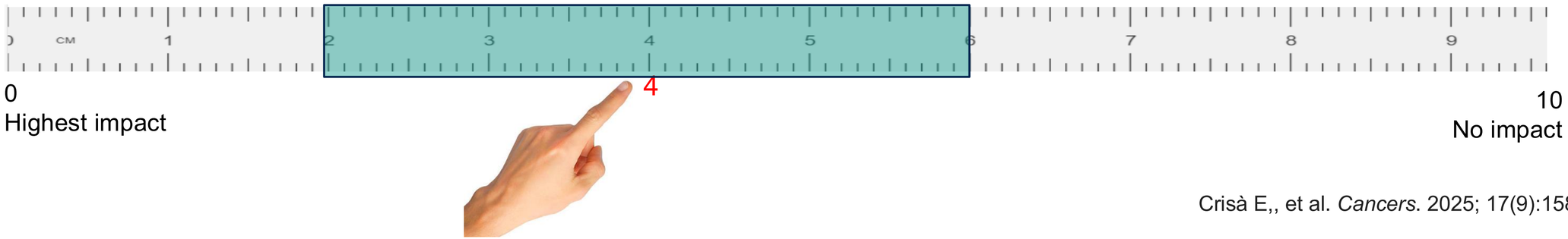
Caregivers and the impact on working life

36% of the patients who responded to the survey had a caregiver.
105 caregivers

- 94% were family members (35% partners and 59% other family components)
- 80% were females
- Median age 56 years (IQ range: 48–64)
- 53% were still employed.

The caregiver's work life was largely affected by their role, leading to a change in type of job (29% of cases), or working hours (30%), or to work discontinuation (14%).

Impact on work-life balance



Crisà E,, et al. *Cancers*. 2025; 17(9):1587.

Conclusions

- In a generally incurable disease with a limited survival rate, quality of life matters.
- Understanding a patient's needs is part of the treatment journey
- Addressing transfusion dependence and improving cytopenias are a major goal
- It is recommended to use disease-specific PROMs to capture what is important to patients
- To improve QoL of patients with MDS, it is the role of healthcare workers to
  - Improve communication
  - Address issues associated with distress
  - Improve organization of outpatient clinics
  - Reduce time in hospital
  - Reduce caregiver stress
  - Evaluate the impact of disease and treatment