Come valutare la qualità di vita in MDS:
problemi e possibili soluzioni

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Patient-Reported Outcomes (PROs)

Indicators for assessing impacts of disease and treatment, and symptoms

Include Quality of Life (QoL) + symptoms obtained directly from patients

- **Health-related QoL** is a complex, multidomain variable construct that represents the patient's overall perception of the impact of an illness and its treatment[1,2]

- A **symptom** is 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

PRO measure (PROM):

A measurement based on a report that comes directly from the patient about the status of the patient's health condition without interpretation of the patient's response by a clinician or anyone else

Useful to evaluate the impact of disease and of treatment in all stages of the patient's journey through disease.

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.

PROs, patient-reported outcomes; QoL, quality of life.

Common themes in MDS

Focus group of 70 patients.
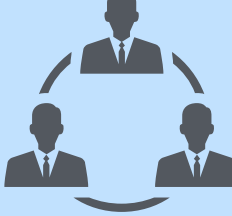
Physical wellbeing

• Symptoms related to anemia	24%
• Symptoms related to treatment	21%

Functional wellbeing

• Decreased ability to function	37%
• Fatigue	39%
• Work associated with administering therapy	24%
• Work associated with interpreting and managing symptoms, side effects, and complications	29%
• Work associated with office visits	32%

Social wellbeing

Activity restrictions	16%
Time associated with office visits	32%
Relinquishing roles	13%
Planning for future	18%

Emotional wellbeing

Shock at diagnosis	10%
Anger and frustration	16%
Depression	25%
Anxiety and fear	29%
Uncertainty	42%

Spiritual wellbeing

Renewed appreciation for life	8%
Renewed appreciation for relationships	10%
Enhanced faith and beliefs	13%

MDS, myelodysplastic syndromes.
Thomas ML. J Support Oncol. 2012;10:37–44.

Core set of PROs for MDS

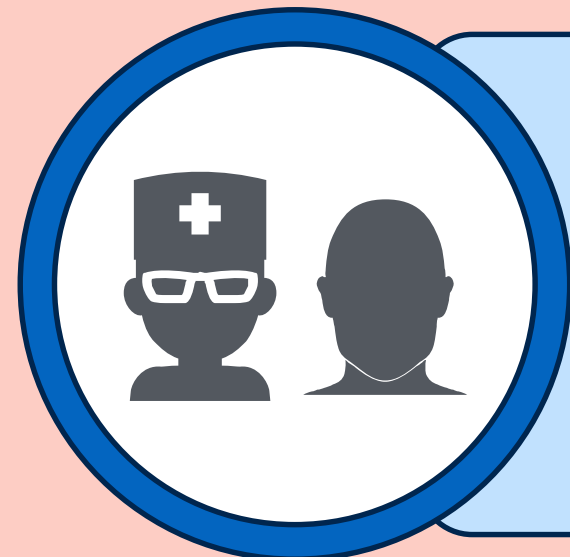**EUMDS Delphi Study in patients and hematologists**

1. Identification of 40 candidate PROs for MDS based on a systematic literature search

2. Evaluation in two-round Delphi survey by:
   – Patients with MDS (40 & 38 participants)
   – MDS experts (38 & 32 participants)
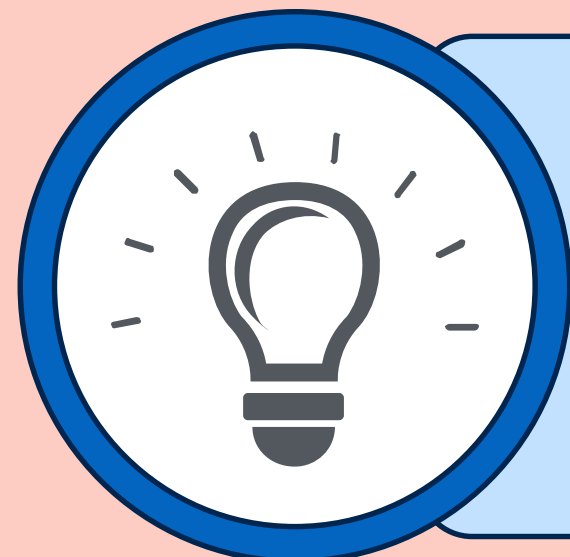
3. Final consensus on three core PROs by patients and experts:
   – General QoL
   – Transfusion-dependency burden
   – Ability to work/activities of daily living

Ranking of outcomes based on Delphi survey

Core PROs defined by patients and experts:

- General QoL

- Transfusion-dependency burden

- Ability to work/activities of daily living

EUMDS, European MDS Registry; MDS, myelodysplastic syndromes; PRO, patient-reported outcome; QoL, quality of life.
Stojkov I, et al. Blood Adv. 2022:6:1–12.

Proportion of moderate/severe problems in MDS compared with the general European population

HRQOL by EQ-5D questionnaire (utility score) at initial diagnosis in 1690 consecutive IPSS-Low/Int-1 MDS patients from the European LeukemiaNet Registry.

MDS   European age- and sex-matched standard population

Percent of male patients having moderate/severe problems
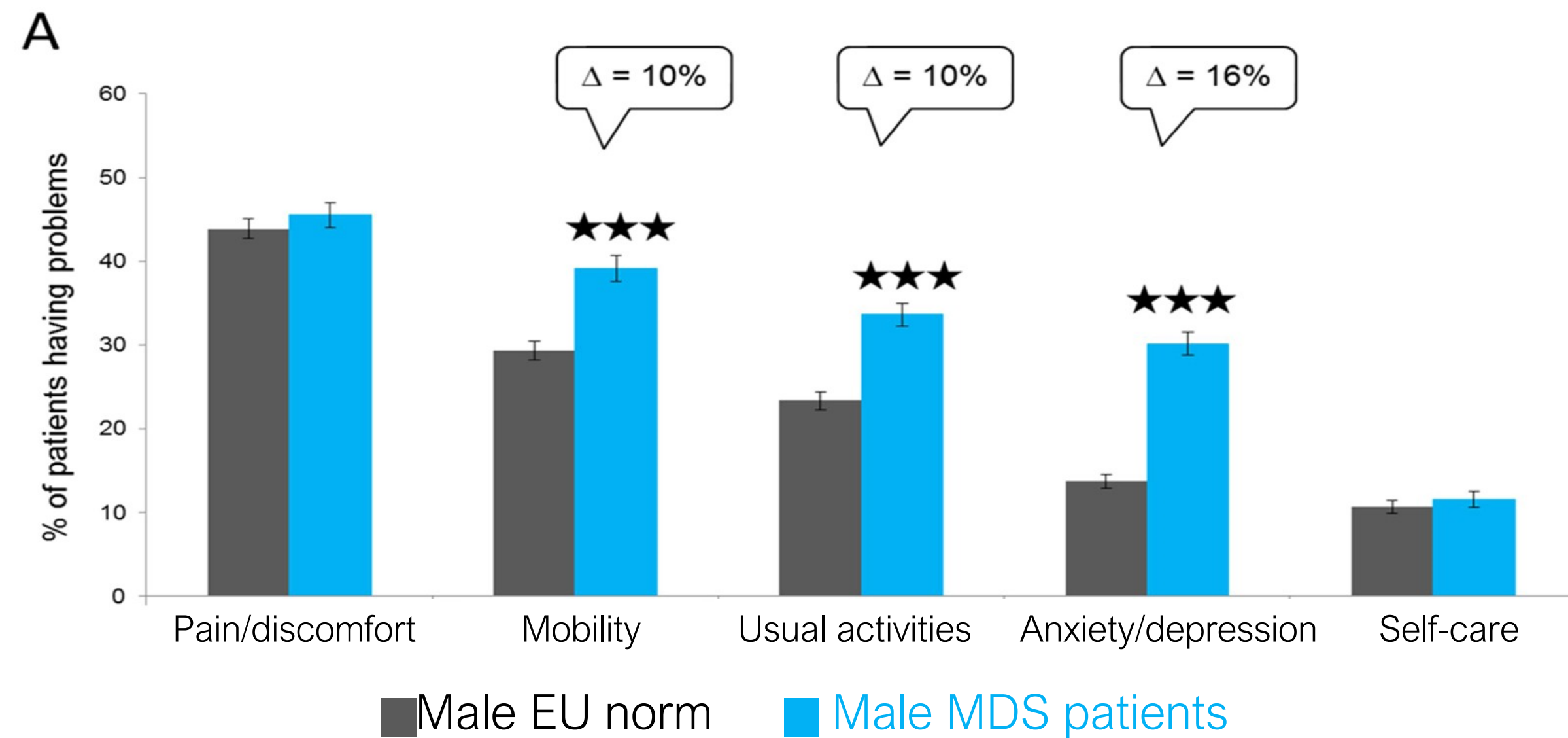
Percent of female patients having moderate/severe problems
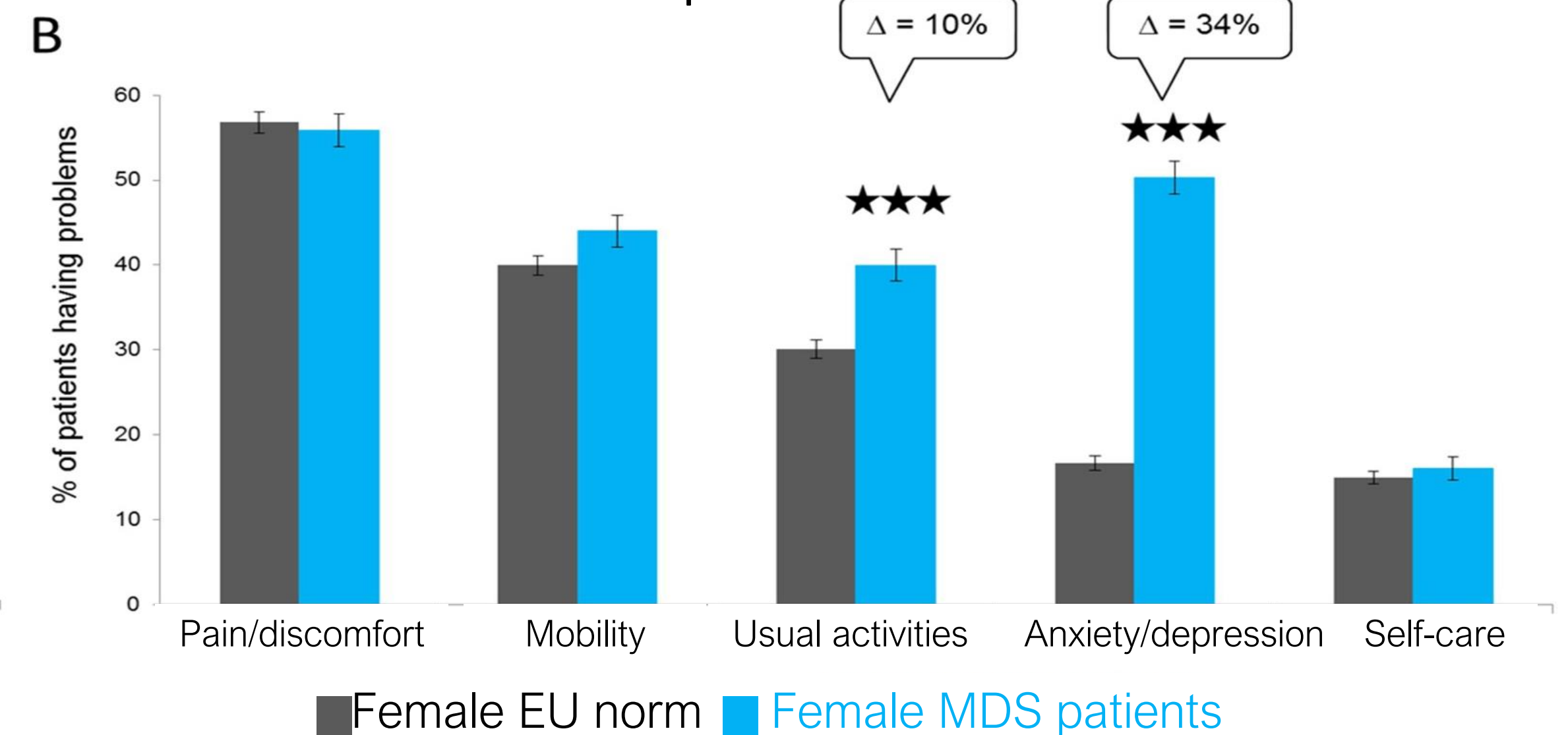
Standard errors indicated as lines. Differences (Δ, delta) of patients with MDS from sex-matched reference group shown when significant (***p < 0.001; **p < 0.01; *p < 0.05; as assessed by Wilcoxon signed rank tests). EU, European Union; MDS, myelodysplastic syndromes.
Stauder R, et al. Leukemia. 2018;32:1380–92. License available at: http://creativecommons.org/licenses/by/4.0/.

Discordance between patients' and physicians' perception of health

Distribution of QoL measures in patients with MDS and ECOG PS Score = 0
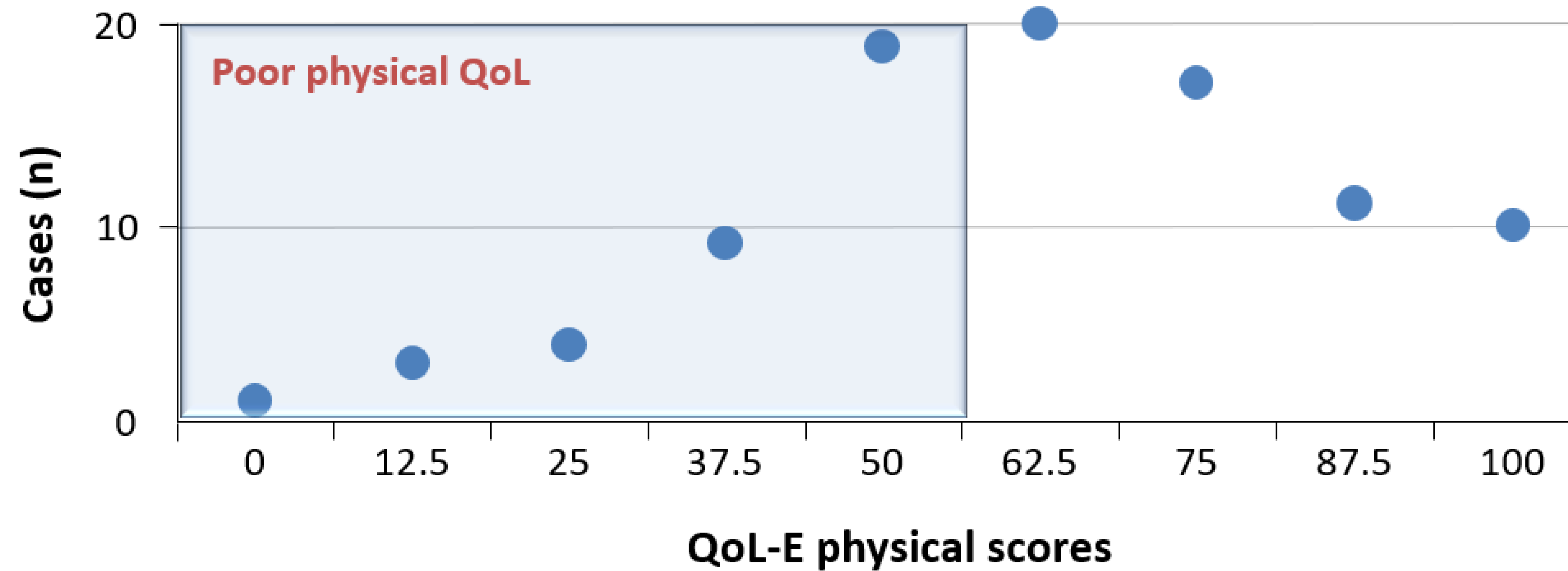
ECOG PS, Eastern Cooperative Oncology Group performance status; MDS, myelodysplastic syndromes; QoL, quality of life; QoL-E, MDS-specific QoL scale.
Oliva EN, et al. Am J Blood Res. 2012;2:136–47.

Factors affecting PRO assessment

- **The specificity and validation of the PROM**

- **The instrument** Length of questionnaire, interview, or task; difficulty of questionnaire or task (e.g., physical performance or cognitive testing); formatting, font size too small to read easily; new instructions for each item; requirement that patients consult records to complete responses

- **Privacy of the setting in which the PROM is completed** (e.g., for patients to complete questionnaires containing sensitive information)

- **Inadequate time to administer or complete questionnaires**, interviews, or tasks

- **Perception by patients that the interviewer wants or expects a particular response**

- **Need for physical help in responding for self-report** (e.g., turning pages, holding a pen, assistance with a telephone, or electronic device)

PROM, patient-reported outcomemeasure.

PROMs in geriatric care

- The goal of geriatric care is to maintain quality of life and functionality

  - PROMs may be more effective in measuring the value healthcare creates in geriatric patients.

- Health states of elderly persons are complex, as older individuals often present different combinations of chronic multi-morbidity and functional limitations.

The Older Persons and Informal Caregivers Minimum Data Set, TOPICS-MDS

- In 2008, the Dutch Care for the Elderly Programme was commissioned by the Ministry of Health, Welfare and Sport with the guiding principles of improving care, quality of life, and self-management among the elderly

- The TOPICS-MDS was developed to evaluate the quality of multidimensional geriatric care, to uniform collection of outcome measures.[1]

  - This has been further reduced to the 22-item TOPICS-SF[2]

- Research from the authors have shown that the "older olds" preferred functional independence while the "younger olds" preferred less morbidity.

- Therefore, age impacts patients' expectations, preferences and outcomes

1. Hofman CS, et al. PLoS One. 2017 Mar 15;12(3);
2. 2. Santoso AMM, et al. Value Health 2018 Oct;21(10):1198-1204.

Measuring PROs in Hematological Malignancies

- Some instruments may not be appropriate

Table 1. QoL instruments that can be used with leukemia patients

Generic QoL instrument
Examples: SF–36, EuroQoL–5D
Cancer-specific QoL instrument
Examples: EORTC QLQ–C30, FACT–G, Life Ingredient Profile
Disease-specific QoL instrument
Examples: FACT–Leu, EORTC QLQ–CLL16
Treatment-specific QoL instrument
Examples: FACT–BMT, FACT–BRM

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire; EORTC QLQ-CLL16, EORTC QLQ chronic lymphocytic leukemia 16; FACT, functional assessment of cancer therapy; FACT-BMT, FACT-bone marrow transplant; FACT-BRM, FACT-biological response modifier; FACT-G, FACT-general; FACT-Leu, FACT-leukemia; PROs, patient-reported outcomes; QoL, quality of life; SF-36, short form 36 item.

Measuring fatigue

Table 6. Fatigue assessment instruments used in patients with hematological malignancies

Title	Abbreviation	Authors, years	Translations
Piper Fatigue Scale	PFS	Piper BF, et al, 1989	8 languages
Multidimensional Fatigue Inventory	MFI	Smets EM, et al, 1995	11 languages
Functional Assessment of Chronic Illness Therapy-Fatigue	FACIT-F	Cella D, 1997	52 languages
Functional Assessment of Cancer Therapy- Anemia	FACT-An	Cella D, 1997	38 languages
Fatigue Symptom Inventory	FSI	Hann DM, et al, 1998	5 languages
Schwartz Cancer Fatigue Scale	SCFS	Schwartz A, 1998; Schwartz A, et al, 1999	5 languages
Brief Fatigue Inventory	BFI	Mendoza TR, et al, 1999	30 languages
Cancer Fatigue Scale	CFS	Okuyama T, et al, 2000	5 languages
EORTC-Fatigue Module	EORTC QLQ-FA13	EORTC Quality of Life Group	Currently in phase IV evaluation

https://ehaweb.org/assets/Uploads/EHA-Guideline-libro.pdf .

Measuring distress and symptoms

Table 7. Instruments to assess psychological distress used in patients with hematological disorders

Title	Abbreviation	Authors, years	Translations
Profile of Mood States	POMS	McNair DM, et al, 1971	21 languages
Hospital Anxiety and Depression Scale	HAD	Zigmond AS, Snaith RP, 1983	79 languages
Psychological Distress Inventory	PDI	Morasso G, Costantini M, 1996	2 languages
Brief Symptom Inventory	BSI	Derogatis LR, et al, 1983	3 languages

EORTC QLQ-C30

- Questionnaire developed to assess the QoL of cancer patients

- It has been translated into and validated in over 100 languages, and is used in more than 5,000 studies worldwide each year

- Contains 30 items to address 15 HRQoL domains with scores between 0–100
  - Higher score on the Global Health Status/QoL and Functional Scales represent better QoL
  - Higher score on symptom scales represent worse QoL

EORTC QLQ-C30 scales	Number of items	Item range	Item numbers (Version 3)
Global Health Status/QoL	2	1–7	29, 30
Functional scales			
Physical functioning	5	1–4	1–5
Role functioning	2	1–4	6, 7
Emotional functioning	4	1–4	21–24
Cognitive functioning	2	1–4	20, 25
Social functioning	2	1–4	26, 27
Symptom scales			
Fatigue	3	1–4	10, 12, 18
Nausea and vomiting	2	1–4	14, 15
Pain	2	1–4	9, 19
Dyspnea	1	1–4	8
Insomnia	1	1–4	11
Appetite loss	1	1–4	13
Constipation	1	1–4	16
Diarrhea	1	1–4	17
Financial difficulties	1	1–4	28

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire; HRQoL, health related quality of life, QoL, quality of life.

Fayers PM, et al. EORTC. 2001;1–73.

FACT-F (fatigue)

- A commonly used scale to measure QoL and fatigue of patients with cancer undergoing chemotherapy

- Consists of the 28-item FACT-G questionnaire as a base plus 13 additional items related to fatigue

  - tiredness, weakness and difficulty conducting everyday activities due to fatigue in the past 7 days.
    Higher scores reflect less fatigue.

Items of the FACT-F

1. I feel fatigued
2. I feel weak all over
3. I feel listless ("washed out")
4. I feel tired
5. I have trouble starting things because I am tired
6. I have trouble finishing things because I am tired
7. I have energy
8. I am able to do my usual activities
9. I need to sleep during the day
10. I am too tired to eat
11. I need help doing my usual activities
12. I am frustrated by being too tired to do the things I want to do
13. I have to limit my social activity because I am tired

FACT-F, functional assessment of chronic illness therapy-fatigue.

Yellen SB, et al. J Pain Symptom Manage. 1997;13(2):63–74.

Hematological malignancy and MDS-specific PRO measures

MDS-specific

QUALMS[a]

- QUALMS-P (physical burden) (14 items: tiredness, effect of low energy on schedule, weakness, inability to participate in activities, fatigue, worry about becoming a burden, hopelessness, bowel changes, shortness of breath, change in long-term plans, concentration issues, effect of health-care on life, nausea, lack of energy)
- QUALMS-BF (benefit finding) (3 items: grateful for tomorrow, quality information, gratitude when used to take for granted)
- QUALMS-E (emotional burden) (11 items: could not do anything about disease, unpredictability, no concrete answers, no clear information, fear of death, difficulty explaining MDS to others, progression worries, test result worries, anger, infection worries, limited emotional support)
- **Other** (5 items: family relationships strained, bruising, crowd avoidance, bleeding worry, financial worry)

QoL-E[b]

- General perception of wellbeing (2 items: currently, compared to 1 month ago)
- QoL-FIS (physical wellbeing) (4 items: heavy activities, climbing stairs, lowering self, self-care)
- QoL-FUN (functional wellbeing) (3 items: got little done, fatigue when working, napping)
- QoL-SOC (social/family wellbeing) (4 items: interference with life, oppressed by disease, burden to family, effect on retaining job)
- QoL-SEX (sexual wellbeing) (2 items: effect on sex life, sexual excitement)
- QoL-FAT (fatigue) (7 items: effect on chores, how much fatigue, headaches, palpitations, disturbance of self-care difficulty, effect of being bed-ridden, sleep quantity)
- QoL-MDSS (MDS-specific) (7 items: shortness of breath climbing stairs, transfusion dependence, ability to do chores, ability to travel, dependency on healthcare, stress/worry, treatment side effects)

Hematological malignancy

HM-PRO[c]

- Impact
- Physical behavior (7 items)
- Social behavior (3 items)
- Emotional behavior (11 items)
- Eating and drinking habits (3 items)
- Signs and symptoms (18 items)

HM-PRO for Hematological Malignancies

Developed within the EHA SWG on Quality of Life and Symptoms
Consists of 2 scales to evaluate PROs in hematological malignancies (HMs):

Part A (impact) measures the impact of HM and its treatment on a patient's HRQoL
24 items in four domains rated on a 3-point Likert scale (0=not at all to 2=a lot), and 'not applicable' as a separate response option. :

      physical behaviour (7)
      social well-being (3)
      emotional behaviour (11)
      eating and drinking habits (3)

Part B (signs and symptoms, SS) captures the severity of different disease symptoms and treatment side effects.
18 items in a single domain, with 3-point severity Likert scale (0=not at all to 2= severe).

HM-PRO validated in MDS and in elderly patients (N=990)

Age (Years)	Median	66.4
	Mean (SD)	64.3 (± 12.4)
	IQR	57.11–72.6
Time since Diagnosis (Years)	Median	2.08
	Mean (SD)	4.6 (5.2)
	IQR	0.89–6.85

		n	%
Gender	Male	486	53.7
	Female	419	46.3
Ethnic Origin	White	870	96.1
	Asian or Asian British	26	2.9
	Black British or Black British	7	0.8
	Unknown	2	0.02
Disease Type	ALL	29	3.2
	AML	67	7.4
	ANHL	54	6
	CLL	64	7.1
	CML	45	5
	HL	37	4.1
	INHL	41	4.5
	MDS	158	17.5
	MM	296	32.7
	MPN	114	12.6

Stage of Disease	Stable	399	44.1
	Remission	277	30.6
	Progressing	229	25.3
Employment	Employed	252	27.8
	Self-Employed	9	1
	Unemployed	41	4.5
	Homemaker	5	0.6
	Retired	558	61.7
	Student	10	1.1
	Other	6	0.7
	Unknown	24	2.6
Comorbidities	No Other Cases	533	58.9
	Other Comorbidities Cases	319	35.2
	Other Cancer	53	5.9

IQR, Inter-quartile range.

Goswami P, et al. Front Pharmacol. 2020; 11: 1308

Treatment Benefit

A therapy is effective if there is **treatment benefit** presumably caused by use of the therapy

➢favorable effect on a **meaningful aspect** of how a patient feels or functions **in their life,** or on their survival

- **Meaningful aspect:**
  The treatment effect should have a positive impact on an aspect of health affected by the disease that alters the way a patient feels or functions, an aspect of health that the patient cares about and has a preference that this aspect:
  1. does not become worse (STABLE), or
  2. IMPROVES, or
  3. IS PREVENTED

- **In their life:**
  the treatment benefit must impact an aspect that occurs in the patient's usual (typical) life.

Aim of treatment of patients with MDS

Lower risk MDS

Reduce complications related to cytopenias

and maintaining/improving quality of life

- Any drug that also improves survival is desired

Higher risk MDS

Prolong survival
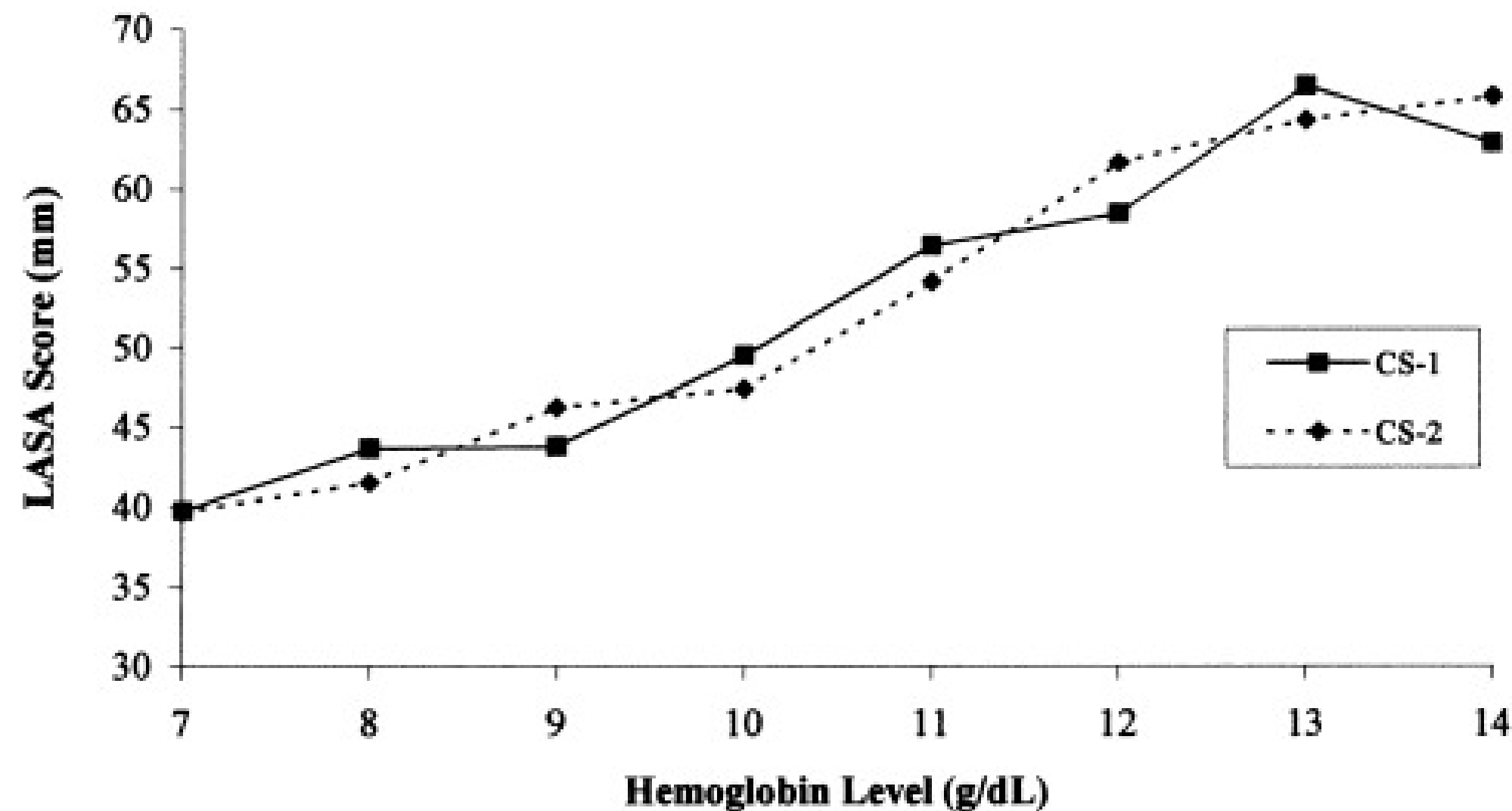
while maintaining/improving quality of life

- Any drug that also improves cytopenias is desired

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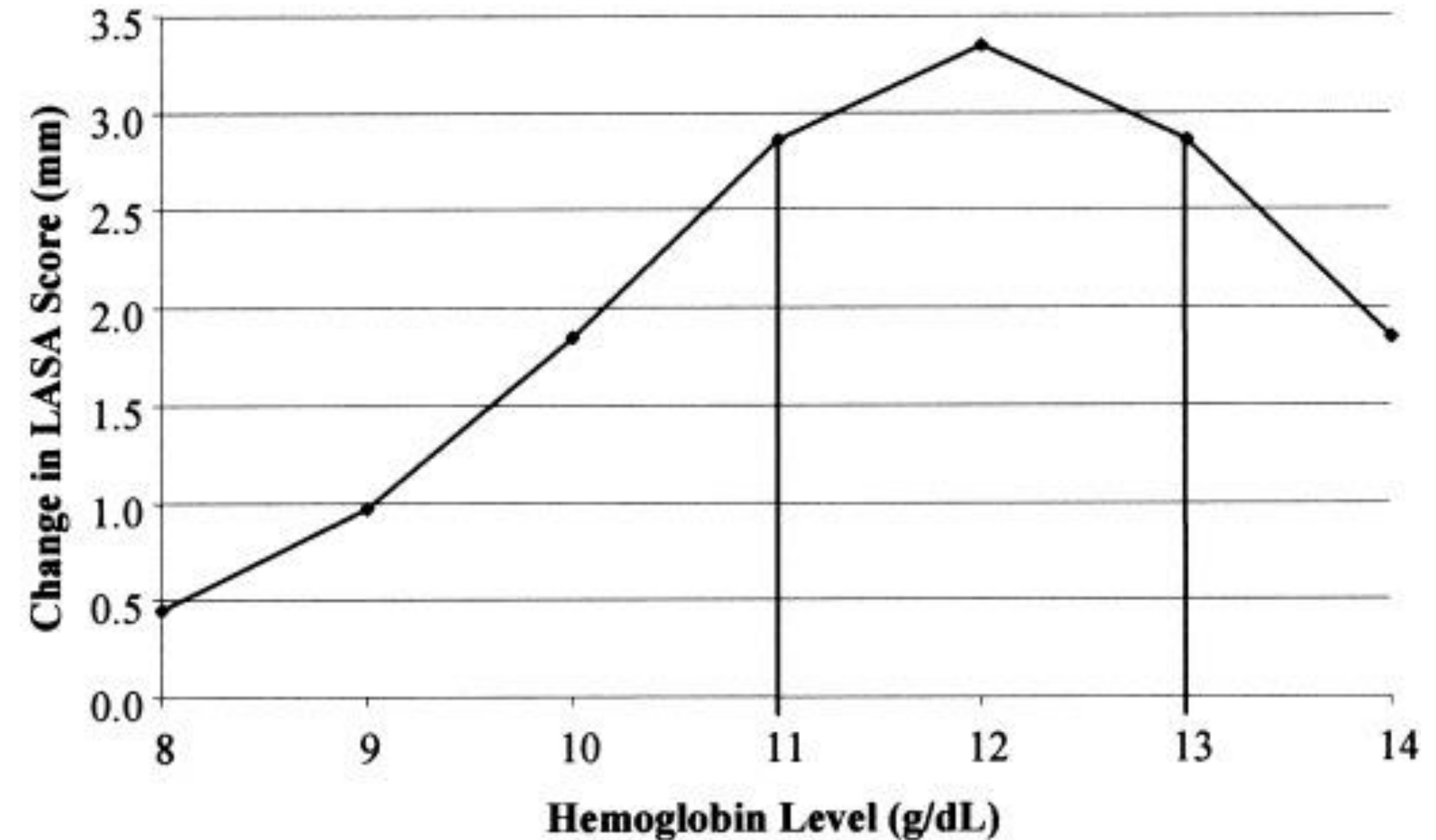
Maximum incremental QoL gain occurred at a hemoglobin level of 12 g/dL (11-13 g/dL)

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.

Transfusion-dependence and QoL

Dependence on hospital and staff[1]

Inability to travel[1]

Fluctuations in Hb[2]
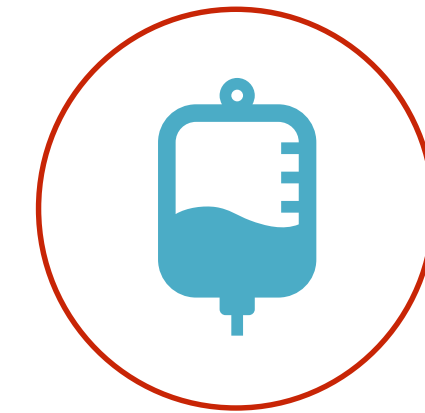
Anxiety to receive transfusion[1]
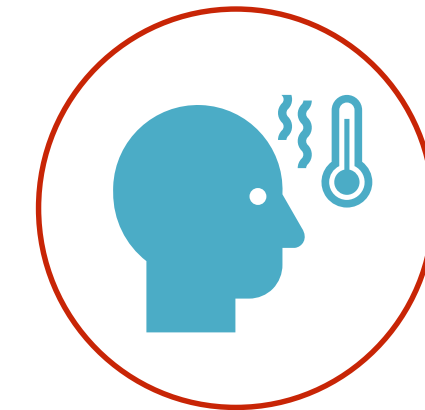
Adverse events[1]
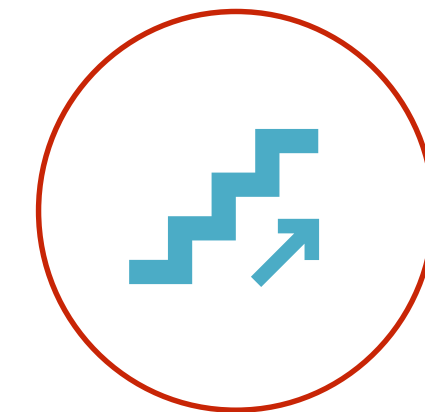
Symptoms (dyspnea, difficulty in climbing stairs)[1]

Hb, hemoglobin; QoL, quality of life.
1. Oliva EN, et al. J Clin Med. 2022;11:27; 2. Balducci L. Cancer. 2006;106:2087-94.

QOL-E domains

General wellbeing perception

Physical

Functional

Social

Sexual

Fatigue

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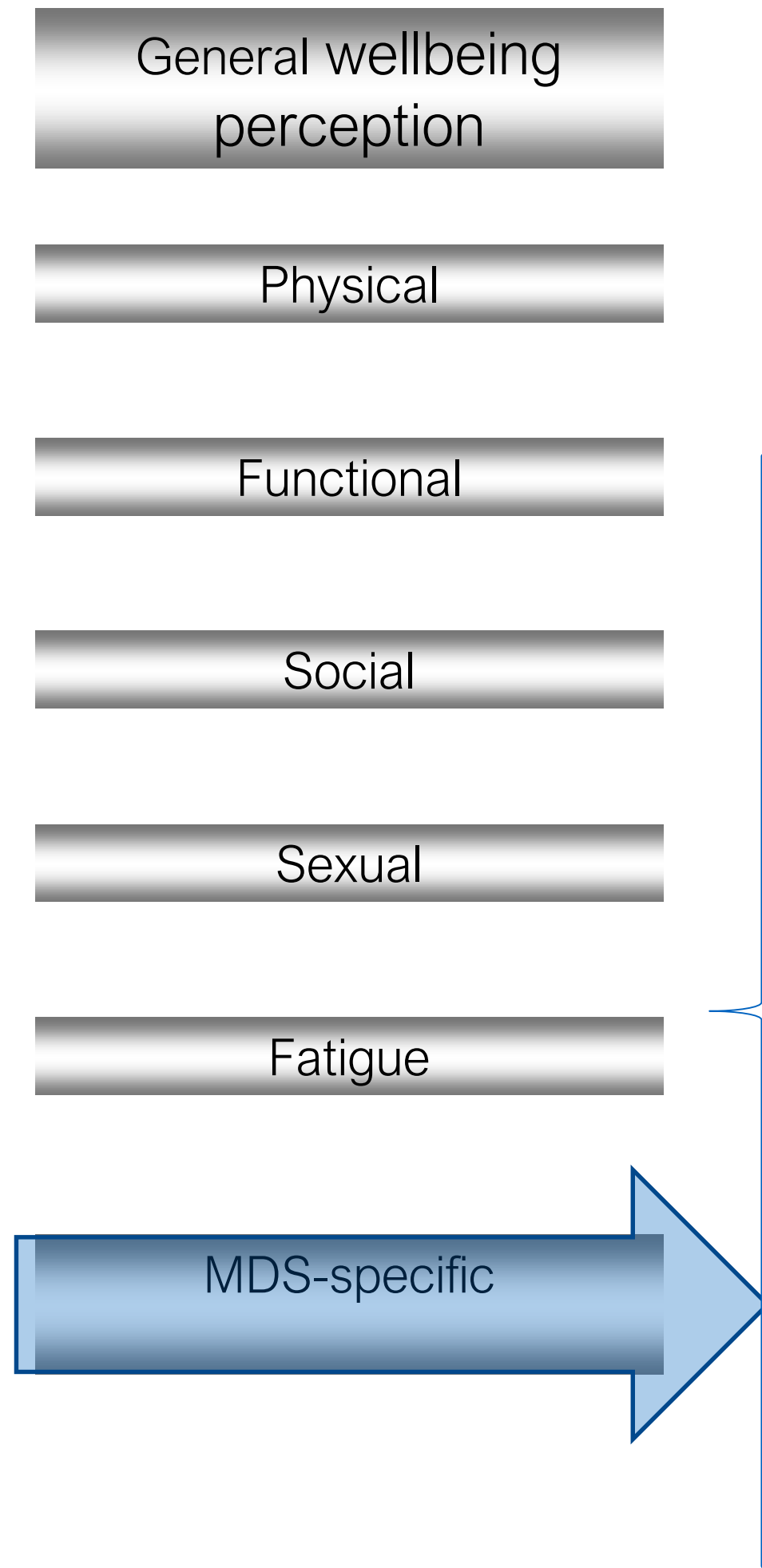
13) During the last week, did shortness of breath while climbing the stairs disturb you?

Never	Sometimes	Often	Very often

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

		No, 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			

[a] © Oliva E, Dimitrov BD.

Impact of transfusions at diagnosis on PROs

Multicenter Italian observational trial
QoL was assessed using the QoL-E instrument (N = 148)
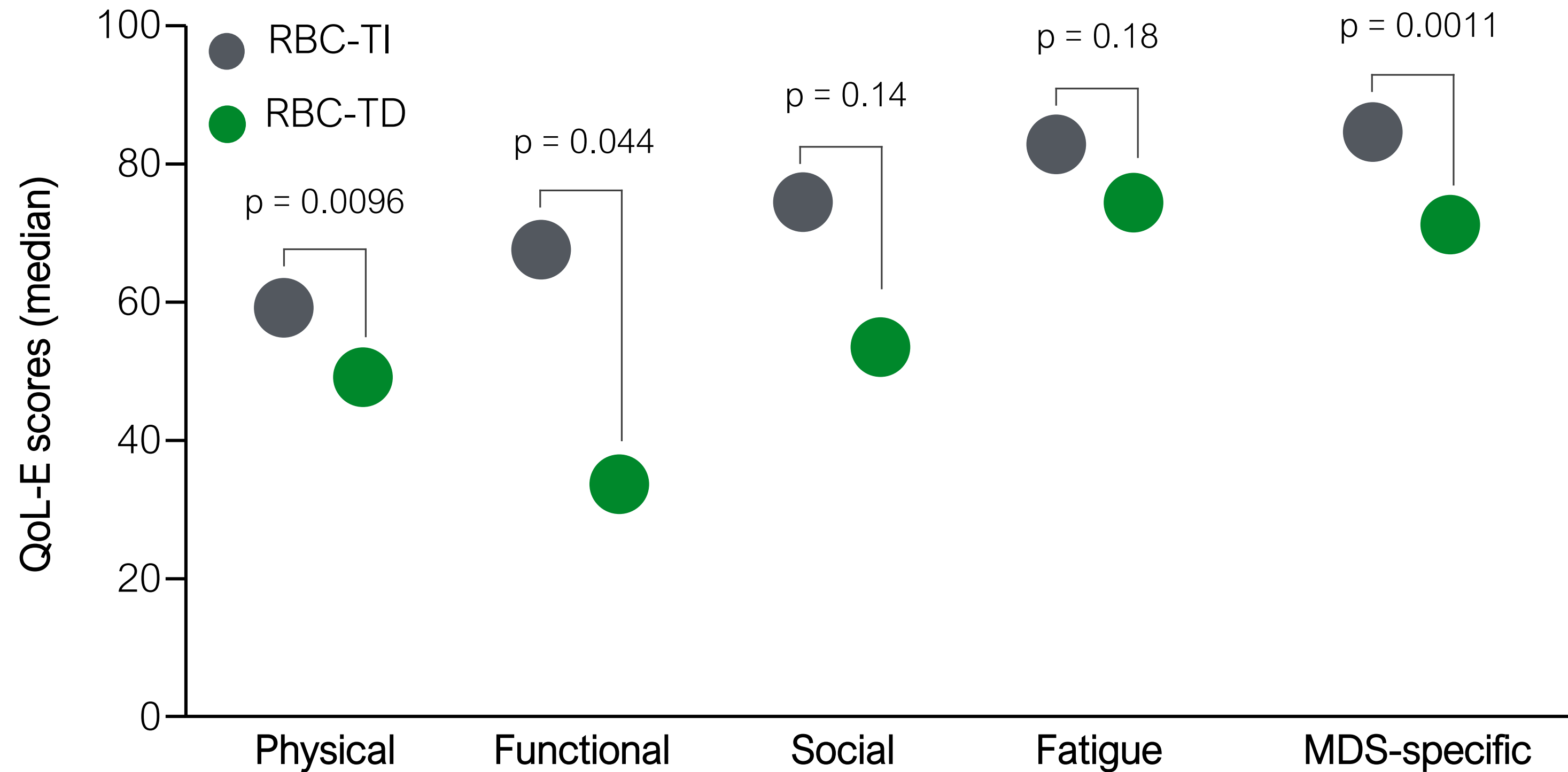
The importance of baseline PRO Scores in determining outcomes

- **Good baseline PRO score**
  Improvement difficult to achieve. The goal during treatment is stability (not deterioration)

- **Poor baseline PRO score**
  Improvement is a desired treatment goal, but when survival is the primary endpoint, stability of HRQoL is accepted

- **In a randomized trial, the comparability of baseline PRO is essential. Sample size, when possible, should be calculated to meet the PRO endpoint.**

COAs, clinical outcome assessments; HRQoL, health-related quality of life;
PRO, patient-reported outcome

Minimal important difference (MID) in PROs

- The smallest difference in the measure (score) that patients perceive as important, either in terms of benefit or harm, and which would lead a care provider to consider changing the patient's management

- Specific to domain scores within a given tool

- It is different from a p-value ("significant difference")

  - In fact, a statistically significant change may be described without that difference reaching minimal importance ("patients' perception of change")

Association of PROMs with clinical outcomes in MDS

Associations between Hb levels, transfusions, and HRQoL

Study	Treatment	Lower/int/higher/ NR risk, n (system)[a]	HRQoL tool(s)	Associations between HRQoL and Hb	Associations between HRQoL and transfusion status
Jansen et al., 2003	Not specified	0/0/0/50 (NA)	MFI, SF-36, EQ-VAS	Correlations with 2/5 MFI and 4/10 SF-36 scales (all p < 0.05); EQ-VAS (p = 0.05)	NR (all patients were TD)
Oliva et al., 2005	Not specified	0/0/0/39 (NA)	QoL-E	Hb < 10.7 g/dL associated with worse functional wellbeing (p = 0.07)	TD patients had significantly lower QoL-E scores for 5/8 domains vs TI
Steensma et al., 2008	Various[b]	0/0/0/359 (NA)	FACT-An[c], BFI	No correlations, validated with adjusted logistic regression models	No correlations
Szende et al., 2009	Not specified	0/0/0/47 (NA)	EQ-5D	NR	Mean EQ-5D score better for TI patients vs "reduced transfusions" and TI vs TD (both p < 0.001)
Oliva et al., 2012	Various[d]	120/0/14/14 (IPSS)	QoL-E, LASA, EQ-5D	Significant associations with: 5/5 QoL-E scales; 3/3 LASA scales; EQ-5D	Transfusions[e] significantly predictive of worse scores for: 4/5 QoL-E scales; 1/3 LASA scales; EQ-5D
Efficace et al., 2015	None[f]	0/0/280/0 (IPSS)	FACIT-F, EORTC QLQ-C30	Lower Hb was independently associated with more severe fatigue (p = 0.026)	TD was associated with more severe fatigue in univariate, but not multivariate, analyses

Associations between Hb levels, transfusions, and HRQoL

Study	Treatment	Lower/int/high/NR risk, n (system)[a]	HRQoL tool(s)	Associations between HRQoL and Hb	Associations between HRQoL and transfusion status
Abel et al., 2016	Various[b]	210/0/40/5 (IPSS); 158/59/33/5 (IPSS-R)	QUALMS	Mean overall scores improved with increasing Hb ($p < 0.001$)	TD patients had a worse mean overall score than TI patients ($p < 0.01$); as did ever vs never transfused patients ($p < 0.01$)
Luskin et al., 2017	Not specified	81/65/105/0 (IPSS-R)	EORTC QLQ-C30	Hb < 10 vs ≥ 10 g/dL significantly correlated with worse fatigue; remained significant in adjusted multivariable model	NR
Ramos et al., 2017	Standard supportive treatment	30/0/0/0 (IPSS)	EORTC QLQ-C30, FACT-An, SF-36	No significant correlations between changes in HRQoL and changes in Hb over 1 year	NR
Stauder et al., 2018	Not specified	1079/341/110/160 (IPSS-R)	EQ-5D, EQ-VAS	Hb ≥ 10 vs < 10 g/dL was associated with improved scores in 5/5 EQ-5D scales, EQ-5D index, and EQ-VAS (all $p < 0.05$)	Patients with vs without transfusions had significantly worse scores in 4/5 EQ-5D scales, EQ-5D index, and EQ-VAS
Efficace et al., 2020	None[c]	506/0/421/0 (IPSS); 381/0/521/0 (IPSS-R)	FACIT-F	NR	TD patients had clinically meaningfully worse fatigue than TI patients (32.4 vs 37.1)

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EQ-5D, 5-item European Quality of Life Five Dimensions; EQ-VAS, European Quality of Live Visual Analog Scale; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; FACT-An, Functional Assessment of Cancer Therapy-Anemia; Hb, hemoglobin; HRQoL, health-related quality of life; IPSS, International Prognostic Scoring System; IPSS-R, Revised IPSS; NR, not reported; QUALMS, Quality of Life in Myelodysplasia Scale; SF-36, 36-item short form; TD, transfusion dependent; TI, transfusion independent.
Oliva EN, et al. Blood Rev. 2021;50:100851.

Patients with MDS followed for PRO changes from diagnosis

Patients:
- N = 148
- Patients with MDS classified as high risk per IPSS were excluded

QoL deteriorates over time in patients with MDS

IPSS, International Prognostic Scoring System; MDS, myelodysplastic syndromes; PRO, patient-reported outcomes; QoL, quality of life.
Oliva EN, et al. Am J Blood Res. 2012;2:136–47.

Factors predicting QoL in MDS: Anemia, comorbidities, and time

QoL-E index[a]	Factor	Multivariate analysis[b]	
		Effect (95% CI)[c]	P value
Physical	Age (1 year)	−0.48 (-0.74, −0.22)	0.0003
	Charlson's index (2−5 vs 0−1)[d]	−14.2 (-20.4, −8.0)	< 0.0001
	Hb (1 g/dL)[e]	+1.69 (+0.71, +2.67)	0.0008
	Transfusions (yes vs no)[f]	−7.2 (−11.7, −2.6)	0.0029
	Time from baseline (1 month)	−0.29 (−0.52, −0.06)	0.014
Functional			
	Charlson's index (2−5 vs 0−1)[d]	−15.5 (−22.9, –8.1)	< 0.0001
	Hb (1 g/dL)[e]	+2.99 (+1.61, +4.36)	< 0.0001
	Transfusions (yes vs no)[f]	−8.3 (−15.1, −1.6)	0.017
Social			
	Charlson's index (2−5 vs 0−1)[d]	−15.6 (−24.3, −6.9)	0.0005
	Hb (1 g/dL)[e]	+2.15 (+0.79, +3.52)	0.0021
	Transfusions (yes vs no)[f]	−6.7 (−12.9, −0.4)	0.037
	Marital status (married vs single)	−9.8 (−18.0, −1.6)	0.019
	Time from baseline (1 month)	−0.42 (−0.76, −0.08)	0.014

[a] Scaled from 0 (worst possible value) to 100 (best possible value); [b] Variables with p<.05 are included in the basic model, for other factors the reported p-value tests the addition to this model; [c] Mean difference of predicted dependent variable between levels (first – second) of binomial factors or for each 1-unit increase of quantitative factors; [d] At baseline; [e] At each visit; [f] Any transfusion within 3 months before the day of visit. CI, confidence interval; Hb, hemoglobin; MDS, myelodysplastic syndromes; PRO, patient-reported outcome; QoL, quality of life; QoL-E, MDS-specific QoL scale.

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

Factors predicting QoL in MDS: Anemia, comorbidities, and time

QoL-E index[a]	Factor	Multivariate analysis[b]	
		Effect (95% CI)[c]	P value
Physical	Age (1 year)	−0.48 (-0.74, −0.22)	0.0003
	Charlson's index (2−5 vs 0−1)[d]	−14.2 (-20.4, −8.0)	< 0.0001
	Hb (1 g/dL)[e]	+1.69 (+0.71, +2.67)	0.0008
	Transfusions (yes vs no)[f]	−7.2 (−11.7, −2.6)	0.0029
	Time from baseline (1 month)	−0.29 (−0.52, −0.06)	0.014
Functional			
	Charlson's index (2−5 vs 0−1)[d]	−15.5 (−22.9, –8.1)	< 0.0001
	Hb (1 g/dL)[e]	+2.99 (+1.61, +4.36)	< 0.0001
	Transfusions (yes vs no)[f]	−8.3 (−15.1, −1.6)	0.017
Social			
	Charlson's index (2−5 vs 0−1)[d]	−15.6 (−24.3, −6.9)	0.0005
	Hb (1 g/dL)[e]	+2.15 (+0.79, +3.52)	0.0021
	Transfusions (yes vs no)[f]	−6.7 (−12.9, −0.4)	0.037
	Marital status (married vs single)	−9.8 (−18.0, −1.6)	0.019
	Time from baseline (1 month)	−0.42 (−0.76, −0.08)	0.014

[a] Scaled from 0 (worst possible value) to 100 (best possible value); [b] Variables with p<.05 are included in the basic model, for other factors the reported p-value tests the addition to this model; [c] Mean difference of predicted dependent variable between levels (first – second) of binomial factors or for each 1-unit increase of quantitative factors; [d] At baseline; [e] At each visit; [f] Any transfusion within 3 months before the day of visit. CI, confidence interval; Hb, hemoglobin; MDS, myelodysplastic syndromes; PRO, patient-reported outcome; QoL, quality of life; QoL-E, MDS-specific QoL scale.
Oliva EN, et al. Am J Blood Res. 2012;2:136–47.

Factors predicting QoL in MDS (EUMDS registry):
Hb and transfusions, comorbidities, and serum ferritin

		Multivariable model EQ-5D index N = 5522; Brier score: 0.20; ROC area: 0.76		**Multivariable model VAS score** N = 5522; Brier score: 0.18; ROC area: 0.80	
		OR	P-value	OR	P-value
Age and sex	60–75 years	1.33	**0.045**	0.96	0.758
	≥75 years	1.84	**0.000**	1.44	**0.015**
	Female sex	1.70	**0.000**	1.22	**0.032**
Clinical variables	SF ≥ 1000 µg/L	1.41	**0.018**	1.37	**0.034**
	TD[a]	1.34	0.127	1.53	**0.037**
	Hb ≤10 g/dL	1.14	0.120	1.34	**0.001**
Treatments	ESA	1.04	0.672	1.13	0.229
	ESA and TD	0.91	0.586	0.72	0.092
Patient-related variables	KPS (per 10 units)	0.62	**0.000**	0.53	**0.000**
	MDS-CI (continuous)	1.11	**0.011**	1.14	**0.002**
	BMI ≥ 30 kg/m^2	1.21	0.068	1.26	**0.033**

[a] At least 1 unit RBC transfusion for a surveillance time of 8 weeks before the HRQoL assessment.

BMI, body mass index; EQ-5D, EuroQoL 5-dimension scale; ESA, erythropoiesis-stimulating agent; EUMDS, European MDS Registry; Hb, hemoglobin; HRQoL, health-related quality of life; KPS, Karnofsky performance status; MDS, myelodysplastic syndromes; MDS-CI, MDS-specific comorbidity indexes; OR, odds ratio; QoL, quality of life; RBC, red blood cell; ROC, receiver operating characteristic curve; SF, serum ferritin; TD, transfusion dependence.

Stojkov I, et al. Blood Adv. 2023:27(12):2772–83.

Association of PROMs with treatment outcomes in MDS

Summary of the MDS literature reporting Hb vs HRQoL/symptoms

Overview of literature

Intervention	Association between Hb and HRQoL/ symptoms	HRQoL instrument(s) used	Baseline demographics[a]		Study	
			Median Hb (g/dL)	Median transfusion burden	Details of association, if found	Ref.
Lenalidomide	✅	EORTC QLQ-C30	–	3 units / 4 weeks	• Low-moderate correlation between Hb and EORTC QLQ-C30 primary domains • Hb level correlated positively with functional scales and negatively with symptom scales	Santini, 2018 (MDS-005)
Erythropoietin (epoetin alfa)	✅	FACT-An	8.6 (Mean)	> 1–2 units / month	• Low-moderate correlation between Hb and FACT-An scale score, fatigue, and non-fatigue subscales • Impact of Hb on magnitude of HRQoL change unclear	Spiriti, 2005
Erythropoietin (epoetin alfa)	✅	LASA	9.9	10.2% requiring transfusions during previous 6 months	• Non-linear and statistically significant positive correlation between Hb levels and LASA scores (r = 0.32 [energy], 0.33 [activity], 0.29 [overall QoL], p < 0.0001) • Hb change found to be a statistically significant determinant of QoL change (p < 0.05), with the greatest incremental QoL gain associated with a 1g/dL increase occuring around 12 g/dL (range: 11–13 g/dL)	Shasha, 2004
Erythropoietin (epoetin beta)	✅	FACT-An, FACT-G, FACT-F	9.2	TD	• Statistically significant correlation between FACT-An scores and Hb values (r = 0.3167, p = 0.001) • A uniform target Hb value associated with optimal QoL could not be identified due to considerable variability between patients	Osterborg, 2002

Direct comparison is not possible as the clinical trials have different backgrounds. [a] All patients low-intermediate MDS. EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30; FACT, Functional assessment of cancer therapy; FACT-An, FACT-anemia; FACT-F, FACT-fatigue; FACT-G, FACT-general; Hb, hemoglobin; HRQoL, health-related quality of life; KDQ, kidney disease questionnaire; LASA, linear analog scale assessments; MDS, myelodysplastic syndromes; QoL, quality of life; TD, transfusion dependent.

Summary of the MDS literature reporting Hb vs HRQoL/symptoms

Overview of literature

Intervention	Association between Hb and HRQoL/ symptoms	HRQoL Instrument(s) Used	Baseline demographics[a]		Study	
			Median Hb (g/dL)	Median transfusion burden	Details of association, if found	Ref.
Darbopoietin alfa	✅	SF-36, FACT-An	9.2	4 units / 8 weeks	• Improvement of all FACT scales among responders compared to non-responders • Improvements in physical functioning and bodily pain domains of SF-36, although scales evaluating mental health were not significantly correlated with erythroid response • Durable rise in Hb level obtained in responders may improve QoL compared to variable Hb levels associated with repeated RBCTs	Kelaidi, 2013
Darbopoietin alfa	✅	FACT-An, LASA	7.9	2 units / 3 months	• ≥ 1 g/dL Hb improvement or ≥50% transfusion burden reduction associated with clinically and statistically meaningful improvement across FACT-An total outcome index, general, anemia, and fatigue scores • No data specific to Hb vs. HRQoL/symptoms	Stasi, 2005
N/A (observational study)	✅	QoL-E, LASA, EQ-5D	10.3 (Mean)	26% TD	• Via multivariate analysis, Hb statistically associated with HRQoL scores.	Oliva, 2012
N/A (observational study)	✅	EQ-5D	Not reported	31% TD	• Patients with Hb > 10 showed a clinically meaningful and statistically significant difference in HRQoL (EQ-5D: 0.77 vs. 0.70; VAS: 0.73 vs 0.66	Stauder, 2018
N/A (cross-sectional study)	❌	FACT-An, BFI	9.8	Median cumulative transfusions, 22 units of packed red cells	• No correlation found	Steensma, 2008
N/A (cross-sectional study)	✅	QoL-E	Not reported	30.7% TD	• Hb < 10.7 g/dL associated with lower functional wellbeing scale	Oliva, 2005
N/A (cross-sectional study)	✅	SF-36, MFI, EuroQoL-5D	9.7	TD	• Positive correlation between Hb level and HRQoL according to SF-36 scores (r = 0.29, p = 0.05); other subscares were not significantly correlated	Jansen, 2003

Direct comparison is not possible as the clinical trials have different backgrounds. [a] All patients low-intermediate MDS. EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30; FACT, Functional assessment of cancer therapy; FACT-An, FACT-anemia; FACT-F, FACT-fatigue; FACT-G, FACT-general; Hb, hemoglobin; HRQoL, health-related quality of life; KDQ, kidney disease questionnaire; LASA, linear analog scale assessments; MDS, myelodysplastic syndromes; QoL, quality of life; QoL-E, MDS-specific QoL scale; TD, transfusion dependent.

QoL improvements within the responder patient population only

| Intervention | HRQoL benefit in treatment arm | | Baseline demographics[a] | | | Study | |
	All patients	Treatment responders only[b]	Median Hb (g/dL)	Median transfusion burden	Details		Ref.
Erythropoietin	✗	✓	9.0	2.4 units / 8 weeks	Versus placebo; HRQoL instruments: FACT-An, EQ-5D-3L; Hb > 12 g/dL requires dose adjustment		Fenaux, 2018
	✗	✓	N/A	61% TD	Epo +/- G-CSF vs supportive care; HRQoL instrument: FACT-G;		Greenberg, 2009
	NR	✓	8.6 (mean)	> 1–2 units / month	HRQoL instrument: FACT-An		Spiriti, 2005
Darbopoietin alfa	✗	✗	9.3	41.8% with ≥ 1 transfusion / 16 weeks	Versus placebo; HRQoL instrument: FACT-F and EQ-5D		Platzbecker, 2017
	NR	✓	9.2	46% TD	Single arm; HRQoL instrument: FACT-An and SF-36		Kelaidi, 2013
	✓	NR	9.2 (mean)	1.08 units / patient-month (mean) TD	Single-arm trial; HRQoL instrument: FACT-F		Villegas, 2011
	✓	✓	9.8 (mean)	12% TD	Single-arm trial; HRQoL instrument: FACT-F and EQ-5D,		Gabrilove, 2008
	NR	✓ [c]	7.9	2 units / 3 months	Single-arm; HRQoL instruments: FACT-An, LASA; Hb > 13 g/dL requires dose adjustment		Stasi, 2005

Overview of literature

[a] All patients low-intermediate MDS; [b] Responder definition may differ between studies; [c] Versus non-responders. FACT, Functional assessment of cancer therapy; FACT-An, FACT-anemia; FACT-G, FACT-general; FACT-F, FACT-fatigue; Epo, erythropoietin; EQ-5D, EuroQoL 5-dimension scale; G-CSF; granulocyte colony-stimulating factor; Hb, hemoglobin; HRQoL, health-related quality of life; LASA, linear analog scale assessments; MDS, myelodysplastic syndromes; N/A, not appliable; NR, no response; SF-36, Short Form 36; TD, transfusion dependent.

QoL improvements within the responder patient population only

<div style="writing-mode: vertical">Overview of literature</div>

Intervention	HRQoL benefit In treatment arm		Baseline demographics[a]		Study	
	All patients	Treatment responders-only[b]	Median Hb (g/dL)	Median transfusion burden	Details	Ref.
LEN	✗	-	11.0	57% TD at baseline	Versus azacitidine; HR; HRQoL instrument: EORTC QLQ-C30 (higher risk MDS)	Kenealy, 2019 (ALLG MDS4)
	✗	✓	8.7	3 units / 28 days	Versus placebo; LR non-del(5q), 78.7% ESA-treated; HRQoL instrument: EORTC QLQ-C30; Large dropouts in Lenalidomide arm	Garcia-Manero, 2019 (MDS-005); NCT01029262
	✗	✓	–	3 units / 4 weeks	Versus placebo; LR non-del (5q), ~80% ESA-treated; HRQoL instrument: EORTC QLQ-C30	Santini, 2018 (MDS-005)
	N/A	✓	8.6	2 units / 8 weeks; 69% TD at baseline	Single-arm trial; HRQoL instrument: QoL-E	Oliva, 2013 (QoL-ESC REVMDS)
	✓	✓	9.1	6 units / 8 weeks	–	Revicki, 2013 (MDS-004)
	✓	✓	NR	6 units / 8 weeks	Versus placebo; LR del (5q); HRQoL instrument: FACT-An; No Hb cap	Fenaux, 2011 (MDS-004)
Azacitidine	✓	NR	NR	NR	Versus supportive care; HRQoL instrument: EORTC (not specific to lower-risk MDS)	Kornblith, 2002 (CALGB 9221)
	✓	NR	9.1	NR	Versus supportive care; high risk; HRQoL instrument: EORTC and mental health inventory	Silverman, 2002 (CALGB 9221)

[a] All patients low-intermediate MDS; [b] Responder definition may differ between studies. FACT, Functional assessment of cancer therapy; FACT-An, FACT-anemia; FACT-G, FACT-general; FACT-F, FACT-fatigue; Epo, erythropoietin; EQ-5D, EuroQoL 5-dimension scale; G-CSF; granulocyte colony-stimulating factor; Hb, hemoglobin; HRQoL, health related quality of Life; LASA, linear analog scale assessments; LEN, lenalidomide; LR, low risk; MDS, myelodysplastic syndromes; N/A, not appliable; NR, no response; QoL, quality of life; QoL-E, MDS specific QoL scale; SF-36, Short Form 36; TD, transfusion dependent.

HRQoL changes in MDS del5q patients with poor QOL-E baseline scores treated with lenalidomide

Changes in HRQoL scores in anemic MDS with del5q treated with lenalidomide in patients with poor baseline QoL
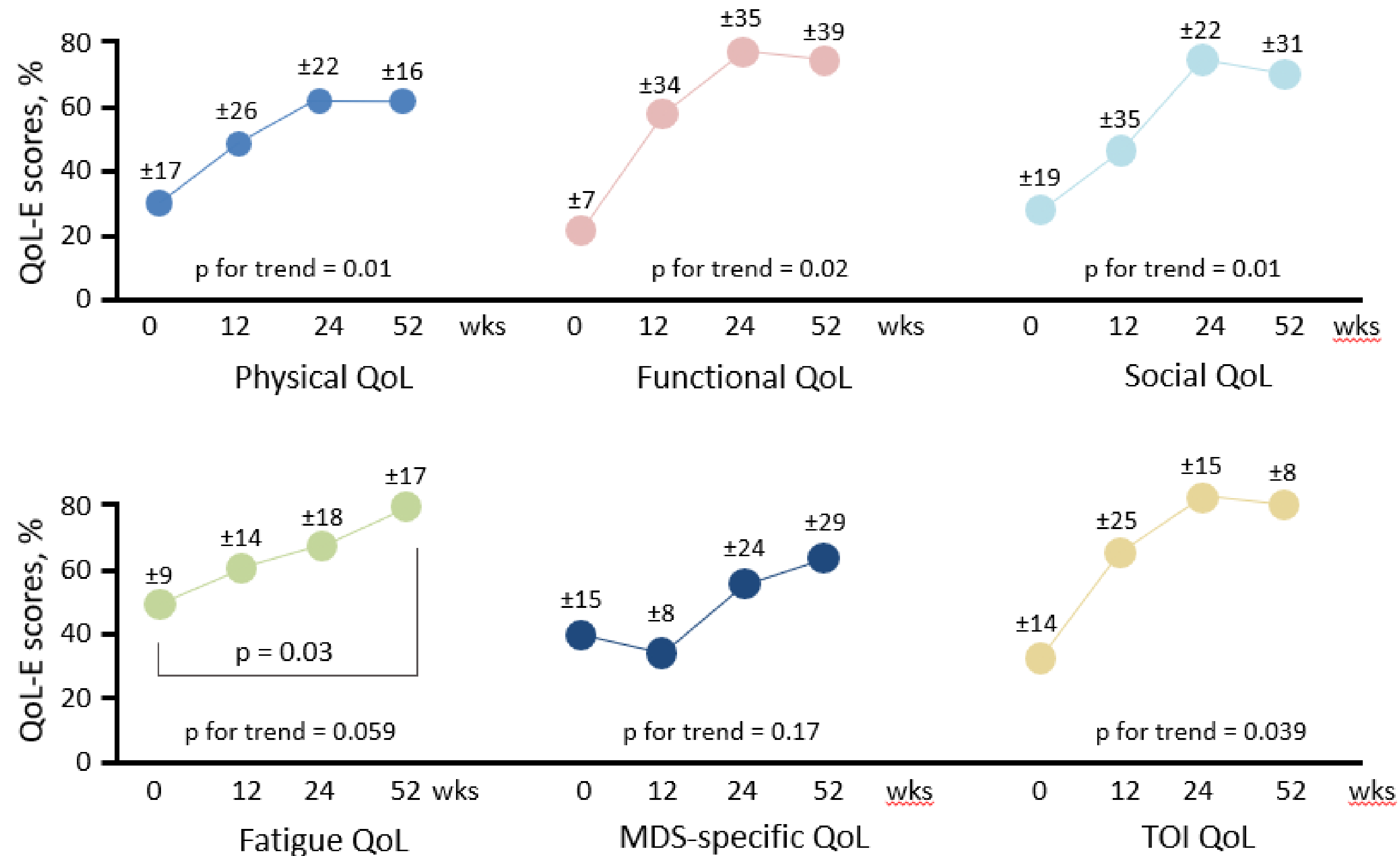
Del5q, deletion 5q; HRQoL, health-related quality of life; LEN, lenalidomide; MDS, myelodysplastic syndromes; QoL, quality of life; QoL-E, MDS-specific QoL scale; TOI, treatment outcome index.
Oliva EN, et al. Leuk Lymph. 2013;54(11):2458–65.

MEDALIST trial. Changes in quality of life in MDS-RS receiving luspatercept vs placebo

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

	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

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

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. *Journal of clinical medicine*, *11*(1), 27

COMMANDS trial exploratory study: Aims and Methods

- To explore the relationship between Hb level (absolute value or change) and QoL in red blood cell (RBC) transfusion-dependent (TD) first-line patients with LR-MDS treated with luspatercept or epoetin alfa

- Patient reported outcome measures (PROMs):
  - EORTC QLQ-C30 global health status (GHS)/QoL, physical functioning, fatigue, dyspnoea
  - FACT-An fatigue subscale, anaemia subscale, total score
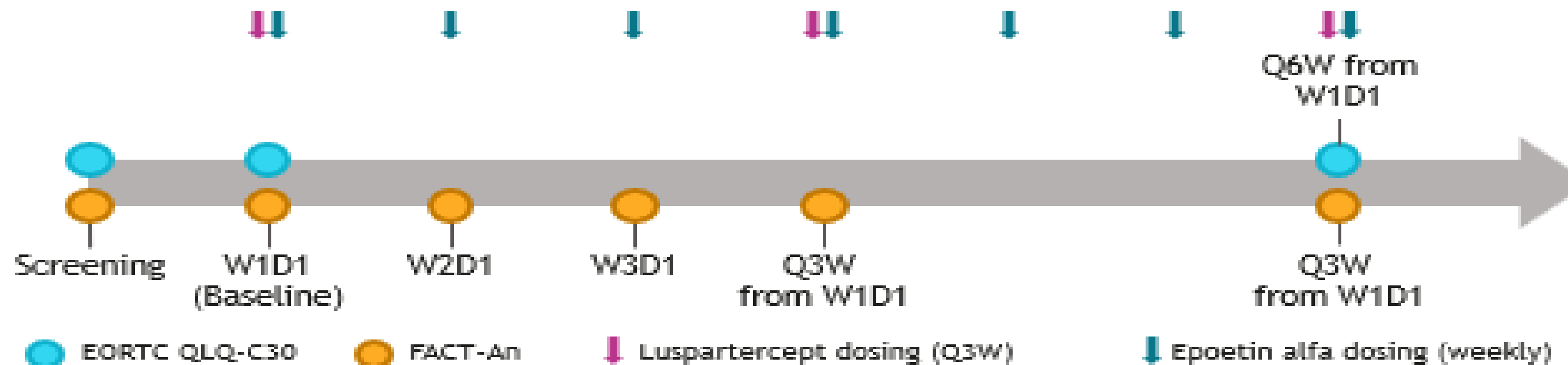 – Higher scores for FACT-An domains and EORTC QLQ-C30 GHS/QoL and physical functioning represents better QoL/functioning, while a higher score for the EORTC QLQ-C30 fatigue and dyspnoea domains represents a worse severity of symptoms

Q6W from
W1D1

Screening | W1D1 (Baseline) | W2D1 | W3D1 | Q3W from W1D1 | Q3W from W1D1

⬤ EORTC QLQ-C30   ⬤ FACT-An   ↓ Luspatercept dosing (Q3W)   ↓ Epoetin alfa dosing (weekly)

PRO assessments administered until treatment discontinuation. Additionally, questionnaires were administered as part of the week 24 and week 48 MDS assessment visits and the end of treatment visit (excluded from current analysis). Abbreviations: D, day; 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; Hb, haemoglobin; MDS, myelodysplastic syndrome; PRO, patient-reported outcome; RBC, red blood cell; Q3W, every 3 weeks; Q6W, every 6 weeks; W, week

Baseline PRO measures

Primary domain	ITT population, mean score (SD)			
	Luspatercept (n = 178)	Epoetin alfa (n = 178)	Overall (n = 356)	
EORTC QLQ-C30	n = 170	n = 169	n = 339	Population norm[a,6]
GHS/QoL	61.6 (18.32)	58.3 (21.08)	60.0 (19.78)	67.0
Physical functioning	69.8 (19.77)	64.0 (22.19)	66.9 (21.17)	81.7
Fatigue	38.9 (23.38)	44.8 (26.31)	41.9 (25.03)	25.1
Dyspnoea	26.3 (27.66)	32.3 (28.74)	29.3 (28.32)	17.3
FACT-An	n = 169	n = 170	n = 339	Population norm[a,7]
Fatigue subscale	34.3 (10.10)	32.1 (11.84)	33.2 (11.04)	42.6
Anaemia subscale	53.2 (13.41)	50.2 (15.18)	51.7 (14.38)	NA
Total score	130.1 (25.38)	123.6 (26.92)	126.8 (26.32)	NA

[a]Age- and sex-adjusted normative data. Abbreviations: 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; ITT, intent-to-treat; NA, not available; PRO, patient-reported outcome; QoL, quality of life.

Oliva EN, et al. Poster EHA 2024

FACT-An item GP5 changes from baseline by visit and treatment group

■ ≥ 2 levels of improvement   ■ 1 level of improvement   ■ No change

■ 1 level of worsening   ■ ≥ 2 levels of worsening

FACT-An Item GP5: "I am bothered by side effects of treatment"

No. of patients	W2D1	W3D1	W4D1	W7D1	W10D1	W13D1	W16D1	W19D1	W22D1	W25D1
Luspatercept	116	113	151	133	118	117	112	108	104	98
Epoetin alfa	130	126	125	119	110	106	116	102	93	82

Oliva EN, et al. ASH 2023 [Abstract #4596]
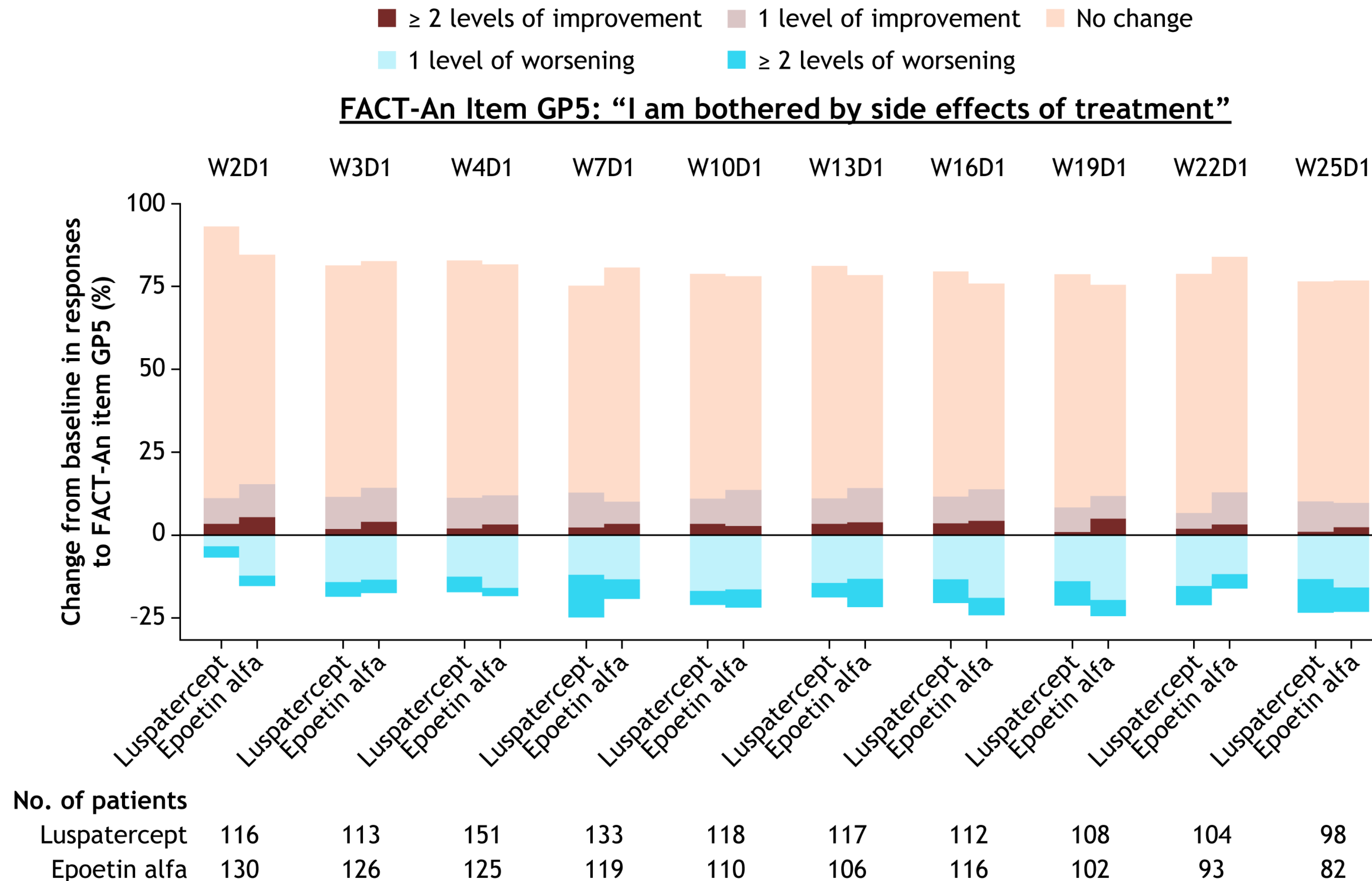
EORTC QLQ-C30 time to sustained improvement through W24

Significantly better times to sustained improvement were observed in the luspatercept treatment arm for 8 EORTC QLQ-C30 domains

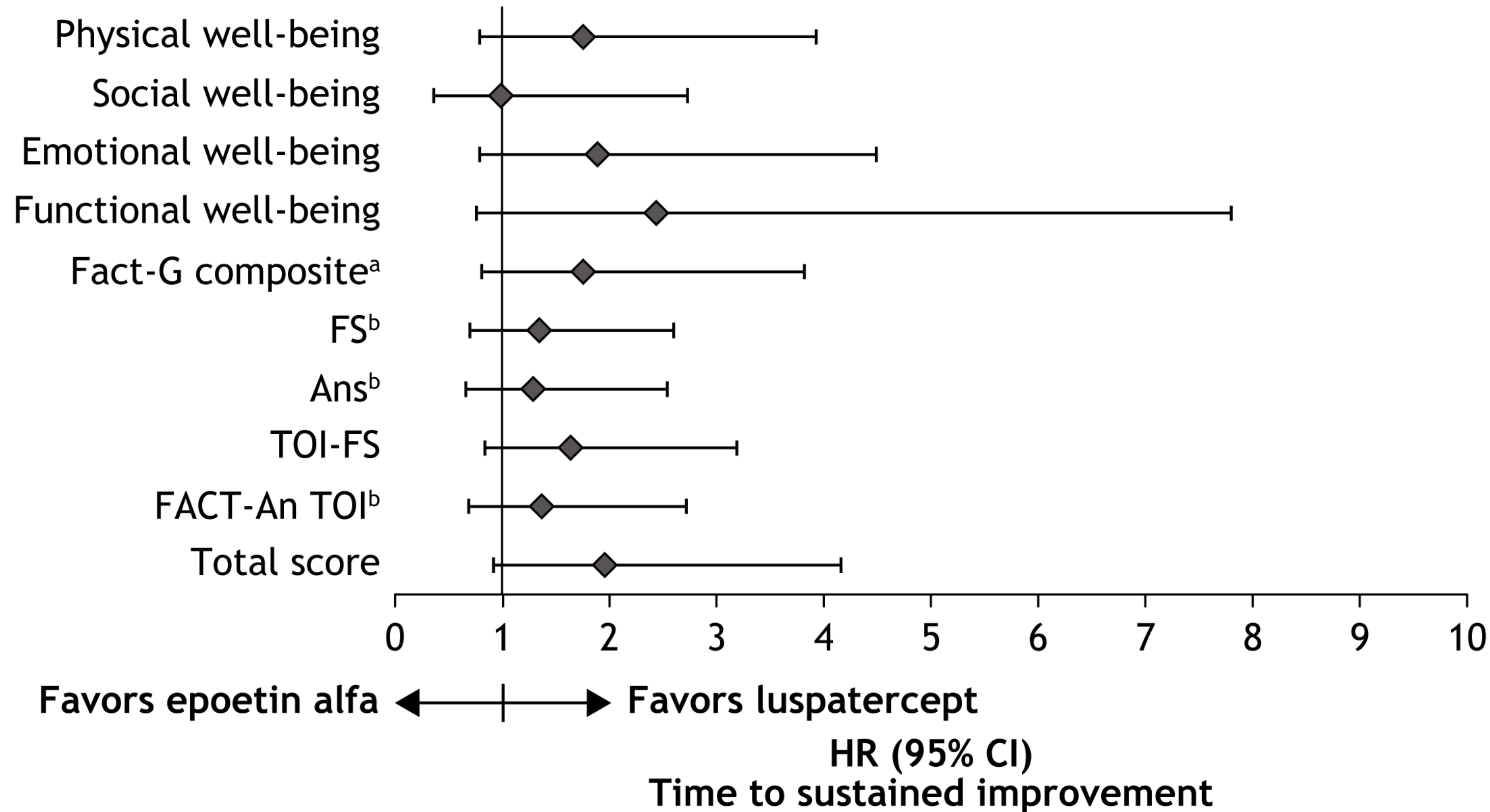| EORTC QLQ-C30 domain	HR (95% CI)	P value[c]
Global health status/QoL	0.73 (0.29–1.85)	0.501
Physical functioning[a]	1.48 (0.66–3.32)	0.339
Role functioning	**2.69 (1.04–6.93)**	**0.034**
Emotional functioning	2.31 (0.93–5.71)	0.066
Cognitive functioning	**4.45 (1.63–12.14)**	**0.002**
Social functioning	1.40 (0.58–3.35)	0.456
Fatigue[a]	1.80 (0.85, 3.78)	0.119
Nausea and vomiting	2.13 (0.32–14.01)	0.424
Pain	**3.95 (1.43–10.97)**	**0.005**
Dyspnea[a]	**3.18 (1.03–9.81)**	**0.035**
Insomnia	**3.02 (0.97–9.42)**	**0.045**
Appetite loss[b]	-	**0.001**
Constipation	**16.43 (2.03–132.99)**	**0.001**
Diarrhea	1.23 (0.16–9.57)	0.840
Financial difficulties	**10.90 (1.36–87.32)**	**0.006**

Favors epoetin alfa ← → Favors luspatercept

Hazard ratio (95% CI)
Time to sustained improvement

Blue markers and bold text indicate nominal *P* < 0.05 from stratified log-rank test. [a]Primary domains of interest; [b]Appetite loss was significantly in favor of luspatercept, but no patients in the epoetin alfa arm experienced sustained improvement; [c]Nominal *P* values were estimated based on stratified log-rank test, whereas HR and 95% CI were estimated using stratified Cox regression; minor discrepancies could occur due to use of different methods for these estimates. HR, hazard ratio.

Firenze, 24-25 ottobre 2024

Oliva EN, et al. ASH 2023 [Abstract #*4596*]

FACT-An time to sustained improvement through W24

No statistically significant differences were observed between groups in the FACT-An-evaluable population

FACT-An domain/subscale	HR (95% CI)	*P* value
Physical well-being	1.76 (0.79–3.93)	0.164
Social well-being	0.99 (0.36–2.73)	0.983
Emotional well-being	1.89 (0.79–4.49)	0.144
Functional well-being	2.44 (0.76–7.80)	0.121
Fact-G composite[a]	1.76 (0.81–3.82)	0.148
FS[b]	1.35 (0.70–2.60)	0.372
Ans[b]	1.29 (0.66–2.54)	0.449
TOI-FS	1.64 (0.84–3.19)	0.142
FACT-An TOI[b]	1.37 (0.69–2.72)	0.366
Total score	1.96 (0.92–4.16)	0.077

Favors epoetin alfa ← | → Favors luspatercept

HR (95% CI)
Time to sustained improvement

[a]FACT-G composite score is a component of FACT-An; [b]Primary domains of interest.

Oliva EN, et al. ASH 2023 [Abstract #4596]
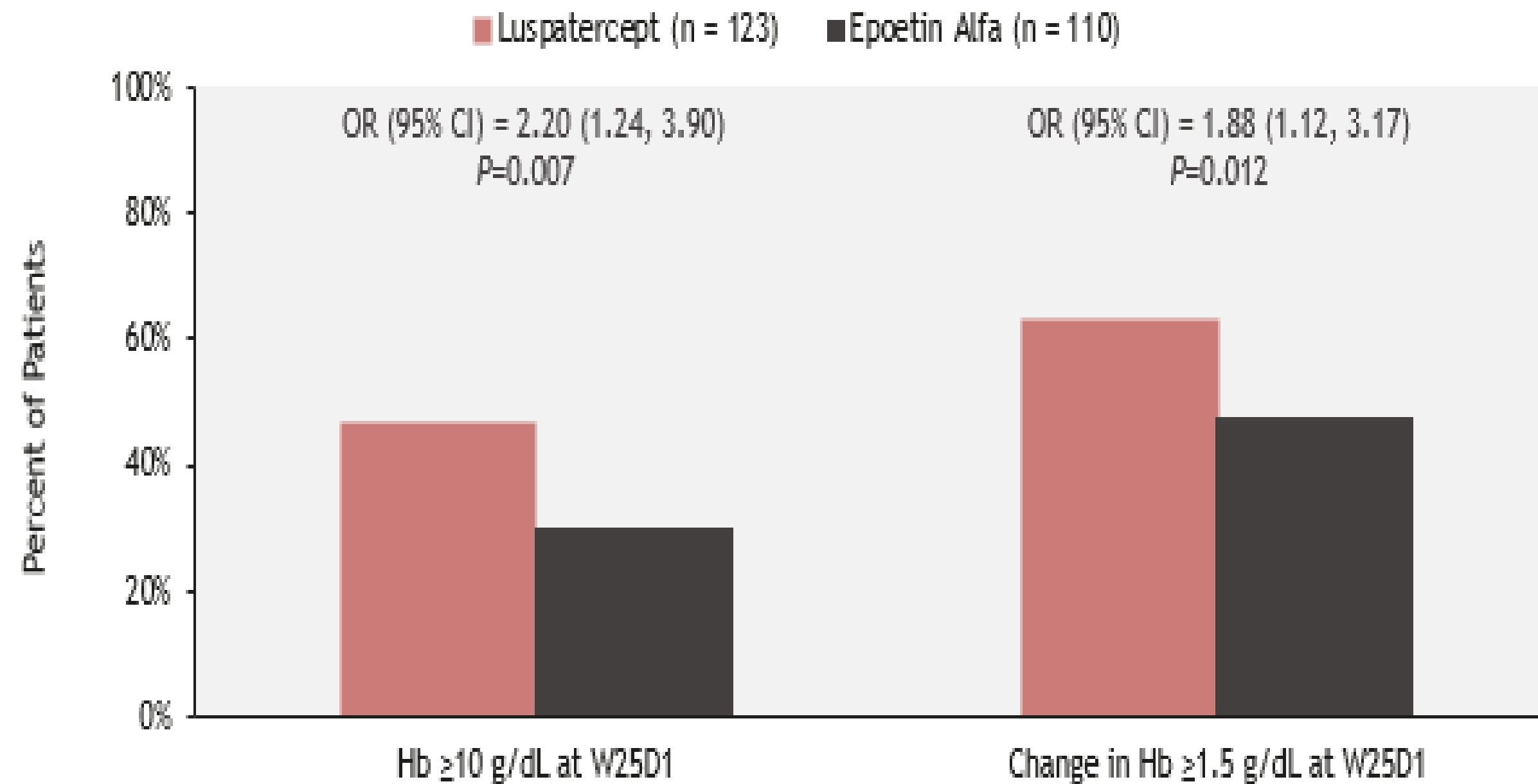
Hb changes and changes in HRQoL

Primary domain	Change from baseline in Hb (continuous)		Change from baseline in Hb (≥1.5 vs <1.5 g/dL)		Absolute Hb Level (≥10 vs <10 g/dL)		CID[a,8,9]
	Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value	
EORTC QLQ-C30	N[b] = 1043		N[b] = 621 vs 422		N[b] = 381 vs 662		
GHS/QoL	2.43 (1.54, 3.31)	<0.001	3.94 (1.87, 6.02)	<0.001	**5.18 (2.92, 7.44)**	<0.001	±4
Physical functioning	2.30 (1.49, 3.10)	<0.001	2.45 (0.62, 4.28)	0.009	3.93 (1.91, 5.95)	<0.001	±5
Fatigue	-3.20 (-4.24, -2.16)	<0.001	-3.70 (-6.13, -1.27)	0.003	**-5.54 (-8.21, -2.87)**	<0.001	±5
Dyspnoea	-3.10 (-4.37, -1.83)	<0.001	**-5.23 (-8.19, -2.28)**	0.001	**-4.78 (-8.00, -1.56)**	0.004	±4
FACT-An	N[b] = 2772		N[b] = 1682 vs 1090		N[b] = 1011 vs 1761		
Fatigue subscale	1.21 (0.97, 1.45)	<0.001	1.42 (0.92, 1.91)	<0.001	1.29 (0.75, 1.83)	<0.001	±3
Anaemia subscale	1.54 (1.23, 1.84)	<0.001	1.76 (1.13, 2.38)	<0.001	1.64 (0.96, 2.33)	<0.001	±4
Total score	2.66 (2.09, 3.23)	<0.001	3.04 (1.88, 4.20)	<0.001	2.99 (1.72, 4.27)	<0.001	±7

Coefficients exceeding the between-group CID threshold are bolded in green. Data across week 37 were considered in the analyses to ensure model convergence. Coefficients can be interpreted as the change from baseline in PRO score per 1 g/dL increase in Hb, or the difference in PRO changes from baseline while a patient was experiencing a concurrent increase of ≥1.5 g/dL vs <1.5 g/dL from baseline in Hb or had a concurrent Hb value of ≥10 g/dL vs <10 g/dL, depending on the model used.
[a]Between-group CID. [b]N is number of observations contributing to each estimate. Abbreviations: CID, clinically important difference; 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, haemoglobin; HRQoL, health-related quality of life; QoL, quality of life.

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Hb levels and fatigue in patients achieving RBC-TI for ≥12 weeks

Legend (left panel): Luspatercept (n = 123), Epoetin Alfa (n = 110)

OR (95% CI) = 2.20 (1.24, 3.90) P=0.007 — Hb ≥10 g/dL at W25D1

OR (95% CI) = 1.88 (1.12, 3.17) P=0.012 — Change in Hb ≥1.5 g/dL at W25D1

Denominator includes ITT patients with non-missing Hb at W25D1. OR (95% CI) and P-value from the Cochran-Mantel-Haenszel test stratified by randomization stratification factors. Abbreviations: CI, confidence interval; Hb, haemoglobin; OR, odds ratio; W25D1, Week 25 Day 1

Legend (right panel): Concurrent Hb <10 g/dL (n = 50), Concurrent Hb ≥10 g/dL (n = 59)
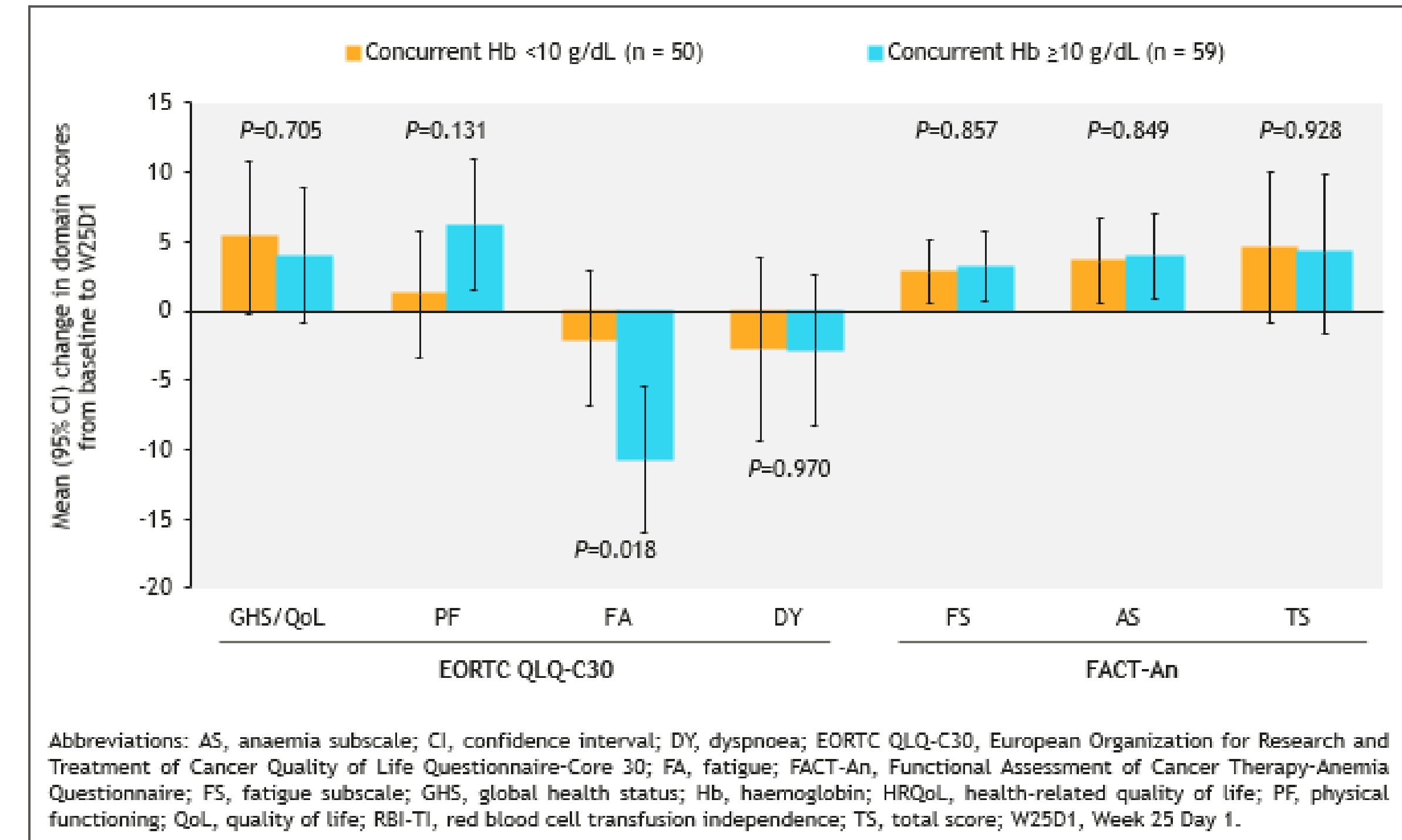
Abbreviations: AS, anaemia subscale; CI, confidence interval; DY, dyspnoea; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; FA, fatigue; FACT-An, Functional Assessment of Cancer Therapy-Anemia Questionnaire; FS, fatigue subscale; GHS, global health status; Hb, haemoglobin; HRQoL, health-related quality of life; PF, physical functioning; QoL, quality of life; RBI-TI, red blood cell transfusion independence; TS, total score; W25D1, Week 25 Day 1.

Hb levels and fatigue in patients achieving RBC-TI for ≥12 weeks

- Our results suggest that reaching the specified thresholds of both absolute Hb level and Hb change from baseline are significant predictors of improvements in anaemia-related PRO changes, with reaching absolute Hb ≥10 g/dL potentially being the strongest predictor

- Achieving a Hb level ≥10 g/dL was associated with meaningful improvement in PROs for all QLQ-C30 primary domains except for physical functioning

- Among those who achieved RBC-TI, concurrent Hb ≥10 g/dL was associated with significantly greater improvement in QLQ-C30 fatigue at W25D1 than Hb <10 g/dL, further demonstrating the importance of this threshold

- More patients receiving luspatercept achieved either threshold (Hb ≥10 g/dL or change in Hb ≥1.5 g/dL) by Week 25 than those receiving epoetin alfa

   –Luspatercept dose escalation resulted in additional patients achieving these thresholds

- These findings may help inform clinicians' decisions on the optimal Hb target for treatment of patients with LR-MDS who have anaemia

The impact of QoL on the decision to pursue SCT for elderly patients with advanced MDS

MDS Transplant-Associated Outcomes (MDS-TAO) prospective observational study:
127 fit patients aged 60–75 years with advanced MDS followed through reduced intensity conditioning allogeneic hematopoietic cell transplants (RIC HCT) vs non-HCT treatment from 2011 to 2014

- The influence of age, gender, cytogenetics, IPSS category, performance status, distance from transplant center and baseline EORTC QLQ-C30 scores on the likelihood of receiving RIC HCT using competing risk regression modelling were examined
- Median follow-up of 16 months among survivors, 44 patients (35%) had undergone RIC HCT
- In multivariable analyses, age (per year; HR, 0.87; 95% CI, 0.81–0.92, $p < 0.001$) and higher IPSS (intermediate-2/high; HR, 2.29; 95% CI, 1.25–4.19, $p = 0.007$) were significantly predictive of receipt of RIC HCT
- **Neither global QoL score nor any QoL subscales scores were predictive**

- **These data suggest that baseline patient-reported QoL has little influence on the decision to undergo RIC HCT for older patients with advanced MDS**

Conclusions

- Shared decisions are based on the knowledge of patients' unmet needs
- Physicians often require validated instruments to retrieve information regarding the impact of disease and treatment on patients' lives
- There are few validated instruments to explore the items and domains of QoL and symptoms in MDS
- MDS-related cytopenias are associated with poor QoL
- Other factors which may impact patients' lives are age, comorbidities and transfusion-dependence
- Treatments which can resolve cytopenias, reduce/abolish transfusion-dependence and increase Hb levels are warranted to improve PROs

Thanks for your endurance.