RELEVANCE OF QUALITY OF LIFE AND PATIENT REPORTED OUTCOMES IN DESIGNING THERAPEUTIC STRATEGIES IN MDS

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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

- **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]

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

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.

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

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 effect on how a patient feels or functions should be meaningful to the patient.
  The treatment effect has a positive impact on an aspect of health affected by the disease that is an alteration in the patient's feeling or functioning. It is an aspect of health that the patient cares about and has a preference that this aspect:
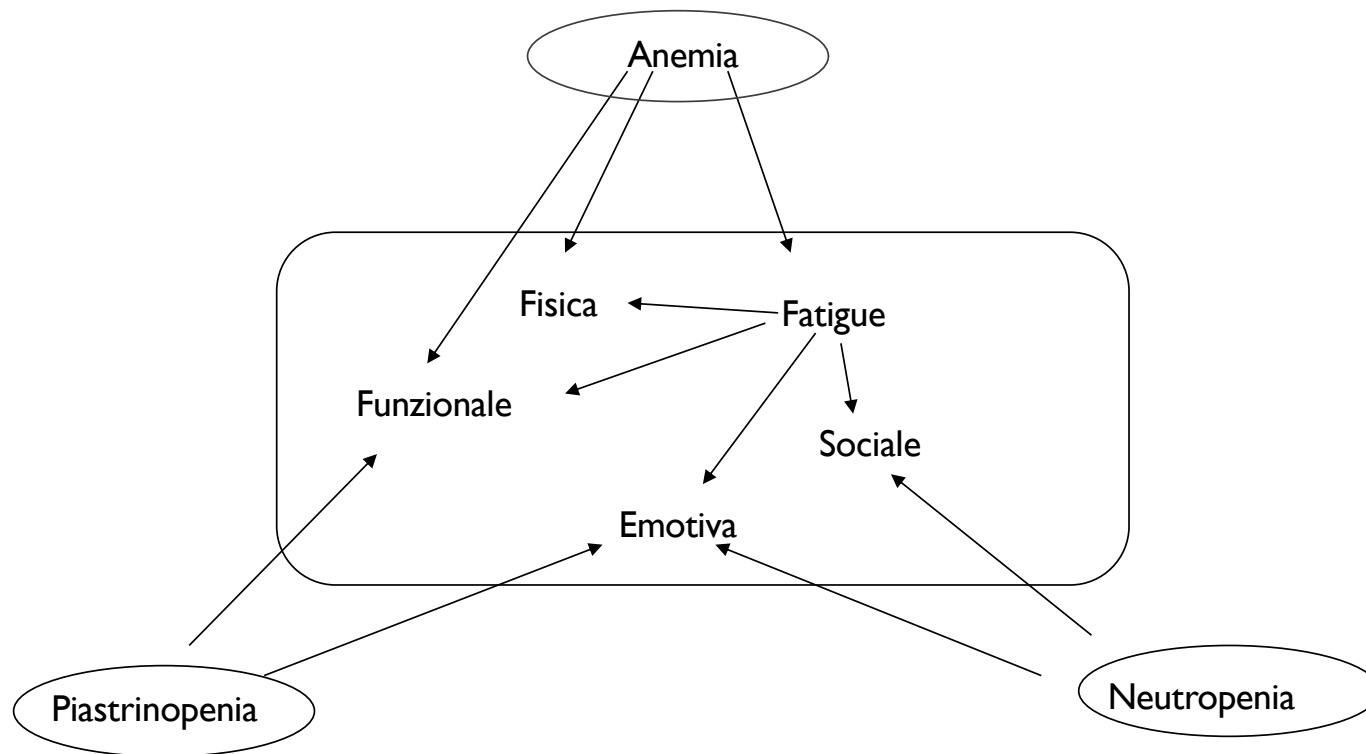
  1. does not become worse (STABLE), or
  2. IMPROVES, or
  3. IS PREVENTED

- **In their life:**
  the treatment benefit must impact an aspect that occurs in the patient's usual (typical) life.
  A treatment effect is not a treatment benefit if it is relevant only in the medical clinic and has no defined relationship to any usual activity the patient does (or would want to do) in their life outside of the clinical trial setting
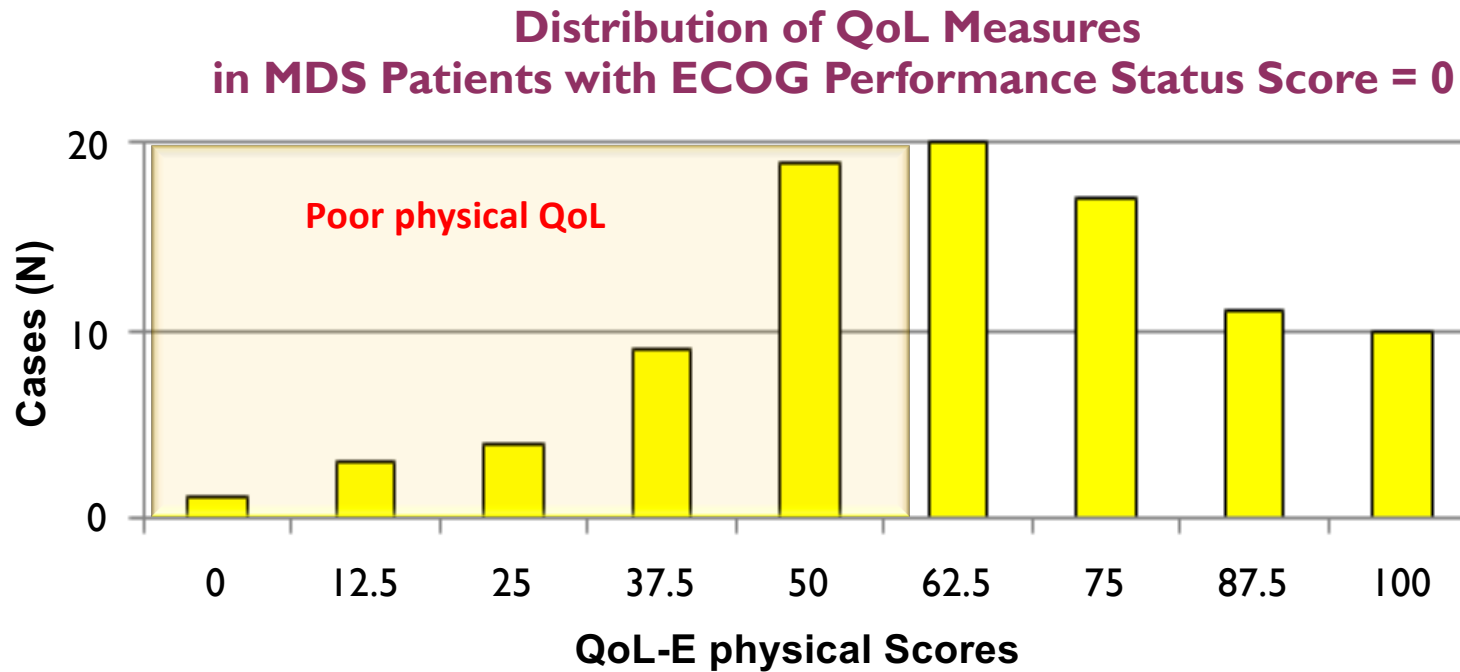
Walton MK, et al. Value Health. 2015;18(6):741–752.

Clinical features of MDS are non-specific and mainly related to cytopenia

Clinical features	Patients (%)	Consequences
Anemia	90	Fatigue Poor QoL Destabilization of underlying cardiovascular disease
Neutropenia, neutrophil dysfunction	33	Infection
Thrombocytopenia, platelet dysfunction	33	Bleeding

MDS, myelodysplastic syndrome; QoL, quality of life.

Adès L, et al. Lancet. 2014;383:2239-52. Goldberg SL, et al. J Clin Oncol. 2010;28:2847-52.

IMPACT of MDS cytopenias on the various dimensions of QoL

Aloe Spiriti MA, Oliva EN, Elsevier 2007.

Discordance Between Patients' and Physicians' Perception of Health

Distribution of QoL Measures
in MDS Patients with ECOG Performance Status Score = 0

Poor physical QoL

Cases (N)

QoL-E physical Scores

QoL-E: higher scores represent better QoL
Physicians overestimate patient perceptions of physical well-being

Discordance Between Patients' and Physicians' Perception of Health

LOW-RISK MDS
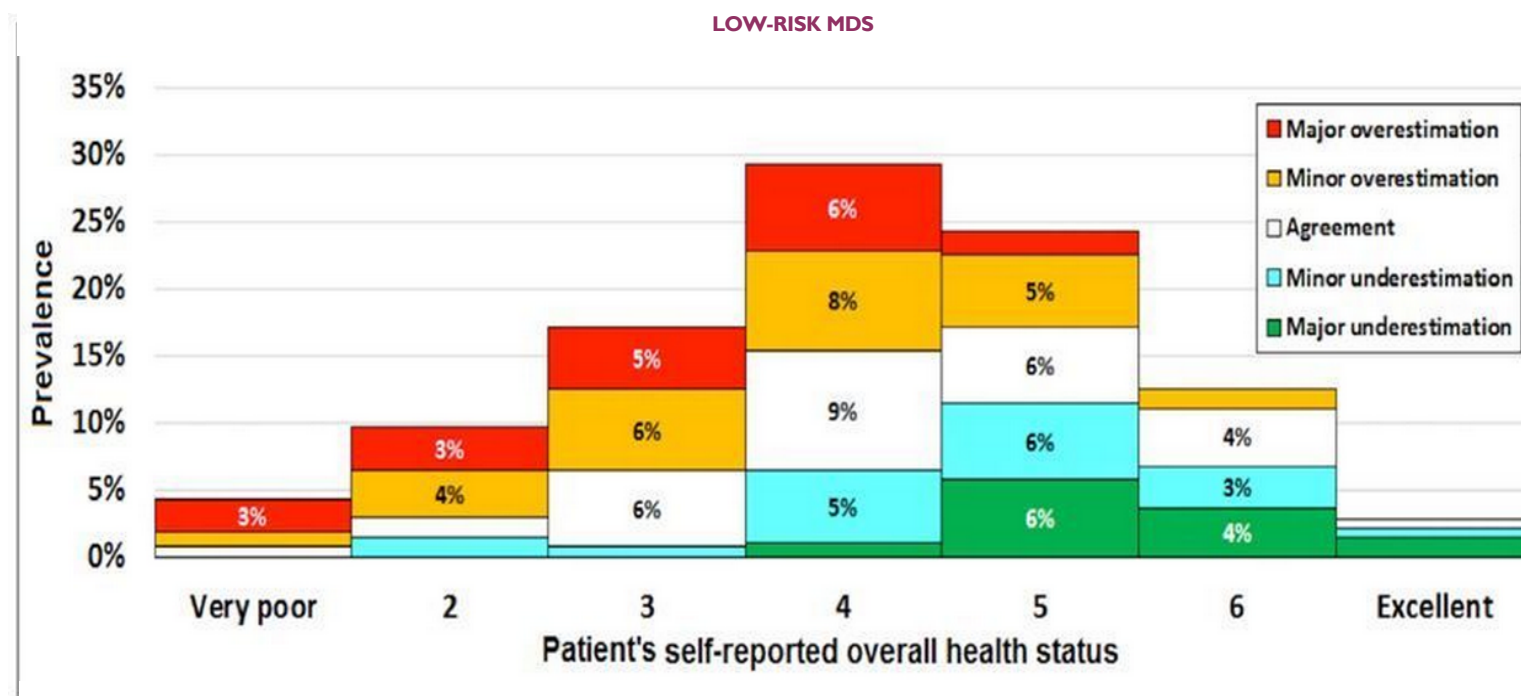
Physicians tend to:
- overestimate patients' health status when it is poor
- underestimate it when it is good

MDS, Myelodysplastic syndrome.

Caocci et al. Abstract: S147 oral presentation, EHA 2015.

QoL Instruments in MDS

Most Frequently Used

Generic Instruments

- EORTC QLQ-C30, FACT-An

MDS-specific Instrument

- QOL-E

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.

QoL-E

QoL-E is an HRQoL instrument developed specifically for MDS

- Contains 29 items to address 2 general health questions, 6 domains, and 3 summary scales with scores between 0-100

  - Higher scores represent better quality of life

HRQoL, health related quality of Life; MDS, myelodysplastic syndrome; QoL, quality of life; QoL-E, MDS-specific QoL scale.; QoL-F, QoL-fatigue; QoL-FIS, QoL-physical well-being; QoL-FUN, QoL- functional well-being; QoL-G, QoL-general; QoL-SEX, QoL-sexual well-being; QoL-SOC, QoL-social and family life; QoL-SPEC, QoL-MDS-specific symptoms; TOI, treatment outcome index.

Table 2. Overview of Scales and Items of the QoL-E

QoL-E Scales	Number of Items	Item Range	Item Numbers (Version 3)
QoL-FIS	4	1–3	3a-d
QoL-FUN	3	1–2 1–4	4a-b 5
QoL-SOC	4	1–3 1–2	6a-c 7
QoL-SEX	2	1–4 1–3	8 14f
QoL-FAT	7	1–4	9, 10, 11a-d, 12
QoL-SPEC	7	1–4 1–3	13 14a-e, 14g
Summary Scales			
QoL-GEN	20	--	sum of all domains, except for QoL-SPEC
ALL	27	--	sum of QoL-GEN and QoL-SPEC
TOI	14	--	sum of QoL-FIS, QoL-FUN, and QoL-SPEC

© Oliva E, Dimitrov BD

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

QoL-E – MDS Specific Domain

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			
F	The effect on your sex life			
G	Side effects of treatment			

Sex Domain Item (→ row F)

MDS, myelodysplastic syndrome; QoL-E, MDS-specific quality of life scale.

Quality of Life in MDS: the QUALMS Subscales

3-factor principal components analysis rotated structure matrix loadings and component correlation matrix used to derive the QUALMS subscales.*

QUALMS Items		Component 1: "QUALMS-P"	2: "QUALMS-BF"	3: "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

*Question numbering reflects the placement of the question in the QUALMS instrument. In bold and italics: items that were used in the calculation of the subscale scores. R: reverse-scored items.

QUALMS-P, Physical Burden ; QUALMS-BF, Benefit Finding" QUALMS-E, Emotional Burden

Abel GA, et al. Haematologica. 2016;101(6):781–788.

Hematological Malignancies HM-PRO INSTRUMENT

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).

USING PRO TOOLS IN CLINICAL TRIALS

Minimal Important Difference (MID)

- 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")

MID, minimal important difference.

Guyatt GH, et al. Mayo Clin Proc. 2002;77(4):371–83.
Jaeschke R, et al. Control Clin Trials. 1989;10(4):407–15.

What Can Determine the Outcome of HRQoL Changes During a Clinical Trial

- Patient expectations

- Efficacy of the investigational drug

- Baseline PRO measures

- Sample size estimation

- Burden of the trial procedures

- Comorbidities

- Training of investigators for the administration of PROs

HRQoL, health related quality of life; PRO, patient-reported outcome.

CORRELATION OF HRQOL WITH CLINICAL OUTCOMES IN MDS

Hb is Correlated with QoL in MDS

R = −0.384
p = 0.006

Relationship Between Hb Level and QoL

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

Relationship between Hemoglobin Level and QoL
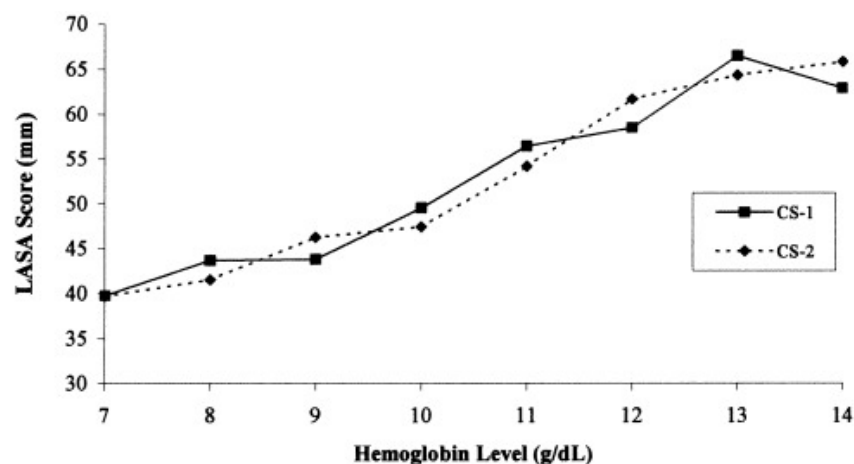
The Average Effect of a 1g/dL Increase Per Hemoglobin Level
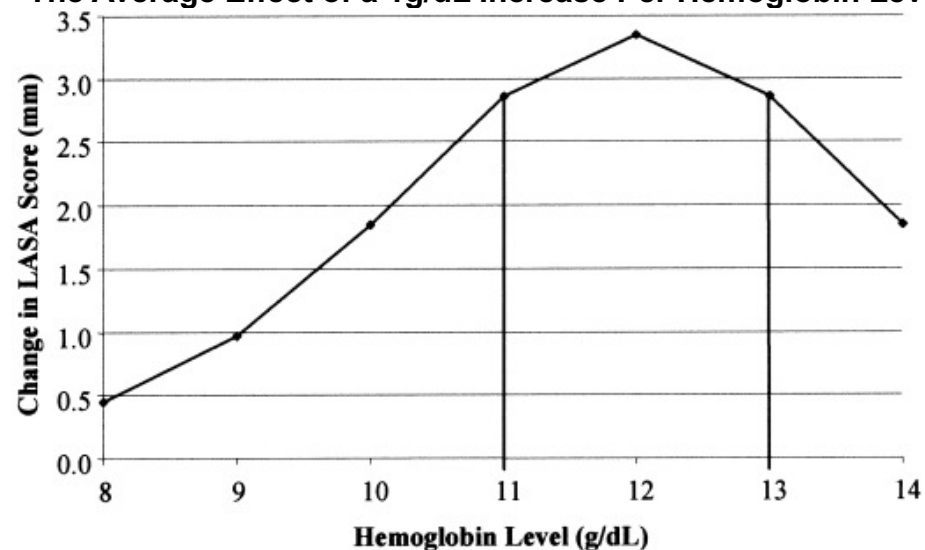
Maximum incremental QoL gain occurred at a hemoglobin level of 12 g/dL (11-13 g/dL)

A Phase III Randomized, Placebo-Controlled Study Assessing the Efficacy and Safety of Epoetin-α in Anemic Patients with Low-Risk MDS

Time to first RBC transfusion (mITT population)
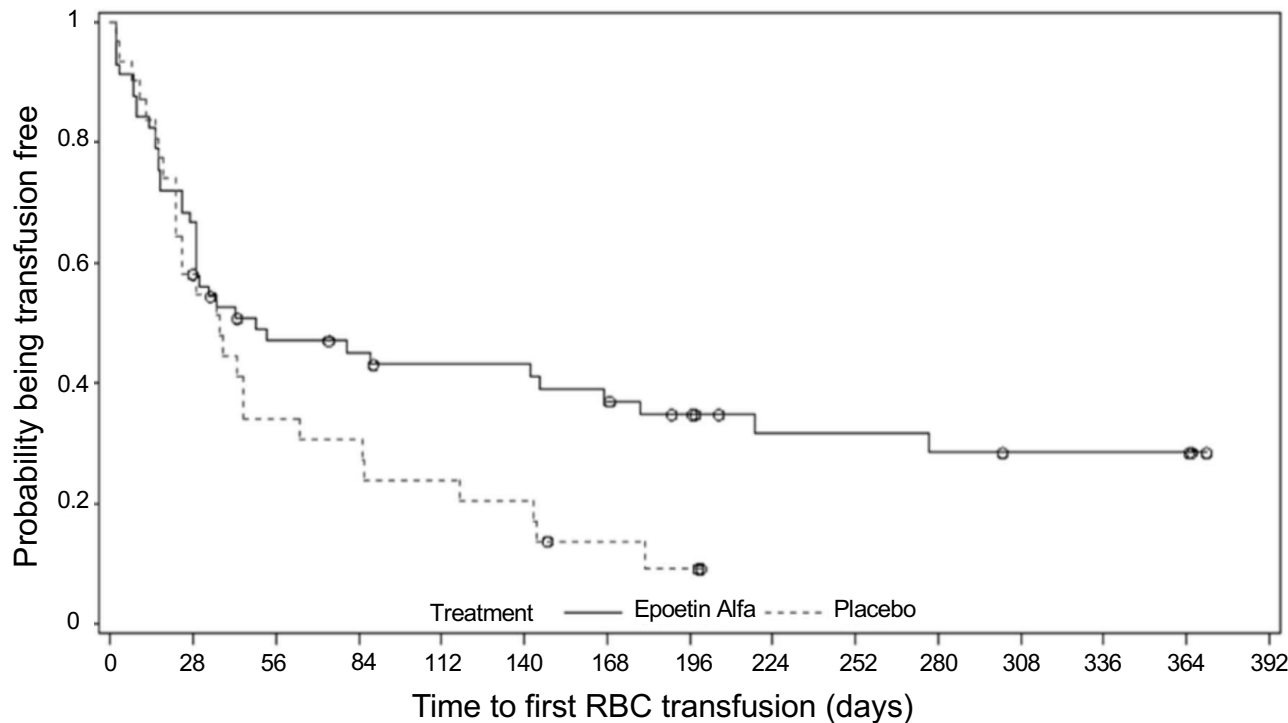
- **Patients with an erythroid response at any time during the first 24 weeks of the study:**
  epoetin alfa versus PBO: 31.8% vs 4.4%; P<0.001

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

The Majority of Interventional Trials in MDS Demonstrate HRQoL Improvements within the Responder Patient Population Only

Overview of literature

Intervention	HRQoL Benefit In Treatment Arm		Baseline Demographics[1]		Study	
	All patients	Treatment responders-only[2]	Median Hb (g/dL)	Median transfusion burden	Details	Ref.
Erythropoietin	❌	✅	9.0	3 units / 4 weeks	Versus placebo; HRQoL instruments: FACT-An, EQ-5D-3L; Hb>12 requires dose adjustment	Fenaux, 2018
	❌	✅	N/A	61% transfusion dependent	Epo +/- GCSF versus supportive care; HRQoL instrument: FACT-G;	Greenburg, 2009
	NR	❌	8.6 (mean)	2 units / 12 weeks	Versus supportive care; HRQoL instrument: FACT-An	Spiriti, 2005
Darbopoietin	❌	❌	9.3	41.8% TD	Versus placebo; HRQoL instrument: FACT-F and EQ-5D	Platzbecker, 2017
		✅	9.2	46% TD	Single arm; HRQoL instrument: FACT-An and SF-36	Kelaidi, 2013
	✅	NR	9.2 (mean)	0-2 units / 4-8 weeks	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	✅*	7.9	2 units / 12 weeks	Single-arm; HRQoL instruments: FACT-An, LASA; Hb>13 requires dose adjustment	Stasi, 2005

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;
GCSF; granulocyte colony-stimulating factor; Hb, hemoglobin; HRQoL, health related quality of Life; LASA, linear
analogue scale assessments; MDS, myelodysplastic syndrome;
N/A, not appliable; NR, no response; SF-36, Short Form 36; TD, transfusion dependant.

[1]All patients low-intermediate MDS; [2]Responder definition may differ between studies; *Versus non-responders

The Majority of Interventional Trials in MDS Demonstrate HRQoL Improvements within the Responder Patient Population Only

Overview of literature

| Intervention | HRQoL Benefit In Treatment Arm | | Baseline Demographics[1] | | Study | |
	All patients	Treatment responders-only[2]	Median Hb (g/dL)	Median transfusion burden	Details	Ref.
Lenalidomide	❌	-	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 / 4 weeks	Versus placebo; LR non-del (5q), 80% ESA-treated; HRQoL instrument: EORTC QLQ-C30; Hb>14; Large dropouts in Lenalidomide arm	Garcia-Manero, 2019 (MDS-005)
	❌	✅	8.7	3 units / 4 weeks	Versus placebo; LR non-del (5q), 80% ESA-treated; HRQoL instrument: EORTC QLQ-C30; Hb>14; Large dropouts in Lenalidomide arm	Santini, 2018 (MDS-005)
	N/A	✅	8.6	2 units / 8 weeks ; 69% TD at baseline	Single-arm trial; HRQoL instrument: QoL-E, FACT-An	Oliva, 2013 (QOL-ESC REVMDS)
	✅	✅	9.1	6 units / 8 weeks	To hi	Revicki, 2013 (MDS-004)
	✅	✅	8.1	6 units / 8 weeks	Versus placebo; LR del (5q); HRQoL instrument: FACT-An; No Hb cap	Fenaux, 2011 (MDS-004)
Azacitidine	❌	✅	NR	NR	Versus placebo; HRQoL instrument: EORTC (not specific to lower-risk MDS)	Kornblith, 2002 (CALGB 9221)
	❌	✅	9.1	NR	Versus placebo; high risk; HRQoL instrument: EORTC	Silverman, 2002 (CALGB 9221)

[1]All patients low-intermediate MDS; [2]Responder definition may differ between studies; *Versus non-responders

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30;
FACT-An, functional assessment of cancer therapy-anemia; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin;
HR, high risk; HRQoL, health related quality of life; LR, low risk; MDS, myelodysplastic syndrome;
N/A, not applicable; NR, no response; QoL-E, MDS-specific quality of life scale; 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[1]		Study	
			Median Hb (g/dL)	Median transfusion burden	Details of association, if found	Ref.
Lenalidomide	✅	EORTC QLQ-C30	8.7	3 units / 4 weeks	• Low-moderate correlation between Hb and EORTC QLQ-C30 primary domains • Impact of Hb on magnitude of HRQoL change unclear	Santini, 2018 (MDS-005)
Erythropoietin (epoetin alfa) [post-hoc analysis]	✅	LASA, KDQ	9.2	11.2% requiring transfusions during previous 6 months	• Positive and significant relationship between Hb levels and QoL measures from both scales (p<0.05) • The maximal incremental gain in QoL occurred when hb reached 11-12g/dL	Lefebvre, 2006*
Erythropoietin (epoetin alfa)	✅	FACT-An	8.6 (Mean)	2 units / 12 weeks	• 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	11.2% 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 12g/dL (range: 11-13g/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*

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-anemaia; FACT-F, FACT-fatigue;
FACT-G, FACT-general; Hb, hemoglobin; HRQoL, health related quality of life; KDQ, kidney disease questionnaire;
LASA, linear analogue scale assessments; MDS, myelodysplastic syndrome; QoL, quality of life;
TD, transfusion dependant.

Summary of the MDS Literature Reporting Hb vs. HRQoL/Symptoms (2 of 2)

Overview of literature

Intervention	Association between Hb and HRQoL/ Symptoms	HRQoL Instrument(s) Used	Baseline Demographics[1]		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	• Steady 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 / 12 weeks	• ≥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. • >4 g/dL Hb increase required for clinically meaningful improvement on the EQ-5D VAS	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	Not reported	• No correlation found	Steensma, 2008
N/A (Cross-sectional study)	✅	QoL-E	Not reported	44% TD	• Hb < 10.7 g/dL associated with lower functional well-being 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

BFI, brief fatigue inventory; EQ-5D, EuroQoL 5-dimension scale; FACT-An, functional assessment of cancer therapy-anemia; Hb, hemoglobin; HRQoL, health-related quality of life; LASA, linear analogue scale assessments; MDS, myelodysplastic syndrome; MFI, multidimensional fatigue inventory; SF-36, short form 36; QoL-E, MDS-specific quality of life scale; RBCTs, red blood cell transfusions; TD, transfusion dependant; VAS, visual analogue scale.

ABSENCE OF CLINICAL CORRELATION WITH HRQOL

Baseline PRO Scores Determine the Probability of Change: Improvement, Stability, Deterioration

- **Good baseline PRO score**
  Improvement difficult to achieve. The goal during treatment is stability (not deterioration)
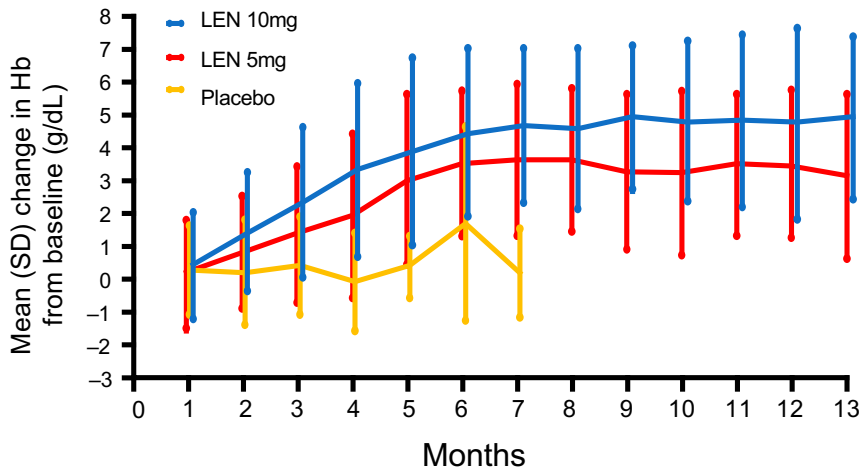
- **Poor baseline PRO score**
  Improvement is a desired treatment goal, but when survival is the primary endpoint, stability of HRQoL is accepted

- **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

Hb and HRQoL Changes in MDS Patients 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]
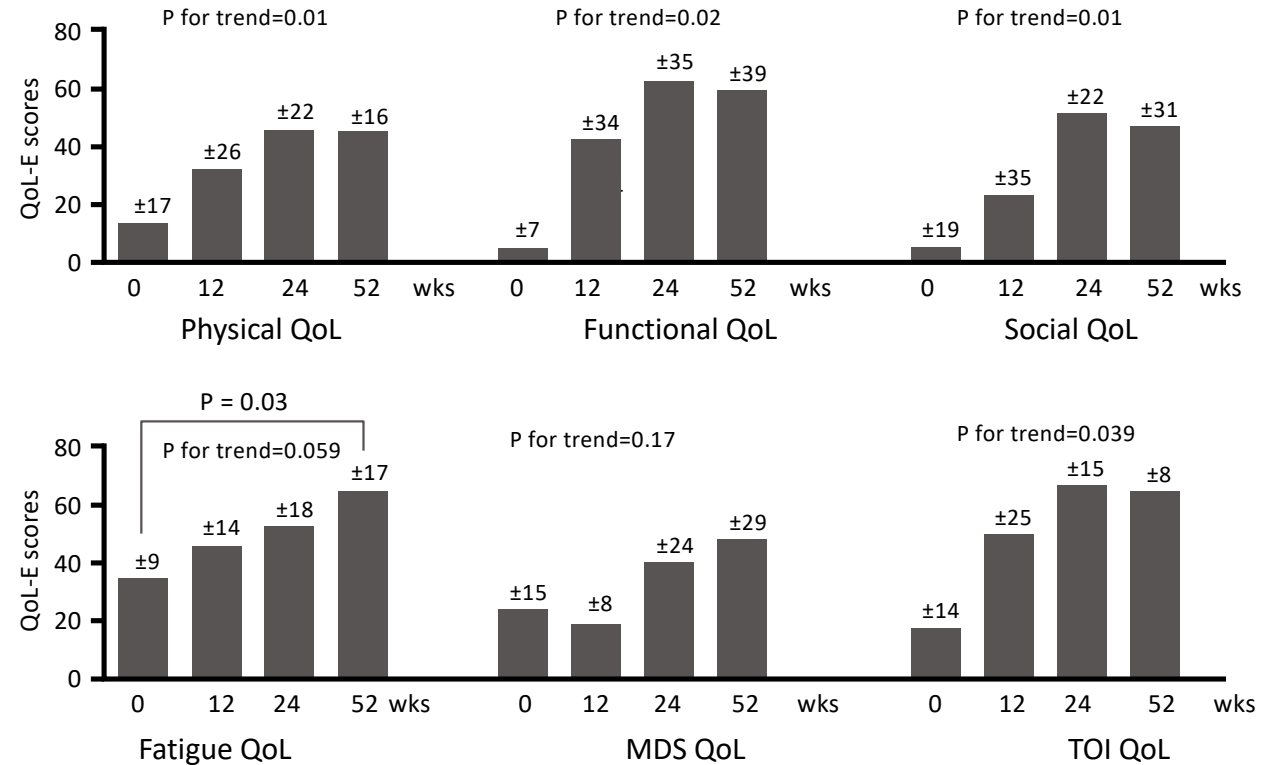

Hb, hemoglobin; HRQoL, health related quality of life; LEN, lenalidomide; MDS, myelodysplastic syndrome; QoL, quality of life; TOI, treatment outcome index.

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

Common Themes in MDS

Common Themes from Focus Group Discussions

| Physical well-being	
Symptoms related to anemia	24%
Symptoms related to treatment	21%
Functional well-being	
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 well-being	
Activity restrictions	16%
Time associated with office visits	32%
Relinquishing roles	13%
Planning for future	18%
Emotional well-being	
Shock at diagnosis	10%
Anger and frustration	16%
Depression	25%
Anxiety and fear	29%
Uncertainty	42%
Spiritual well-being	
Renewed appreciation for life	8%
Renewed appreciation for relationships	10%
Enhanced faith and beliefs	13%
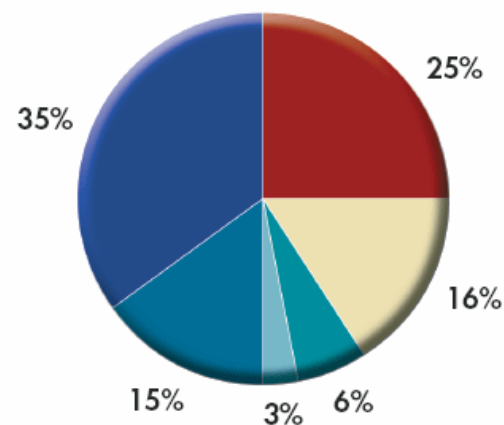
- Normal
- Carry on with normal life, with minor symptoms
- Takes an effort to engage in normal activities
- Cares for self but does no active work
- Requires occasional assistance with personal needs
- Requires considerable assistance

Figure 1: MDS Patients' Ability to Perform Daily Living Activities: Findings from the MDS Foundation's US and European Patient Forums—A total of 269 MDS patients and caregivers, spouses, or friends participated in the 13 forums for which data were available (128 patients and 102 caregivers participated in 10 forums).

MDS, myelodysplastic syndrome.

Factors Predicting QoL in MDS: Comorbidities, Anemia and Time

Impact of Comorbidities on HRQoL in MDS
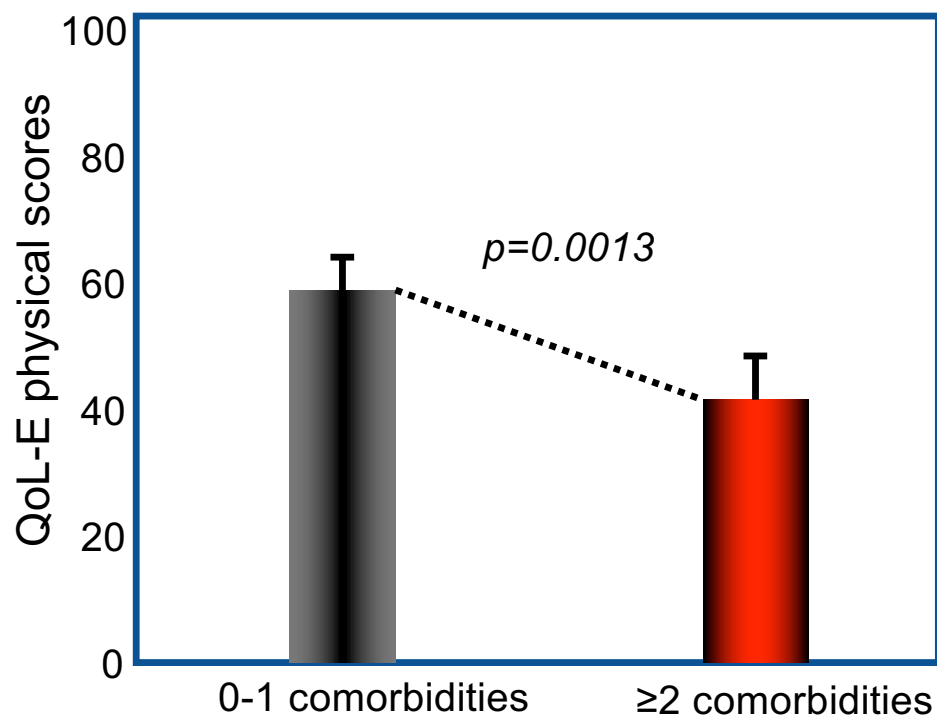
QoL-E index*	Factor	Multivariate analysis† Effect (95% CI) ‡	p value
Fatigue			
	Charlson's index (2-5 vs 0-1) §	−8.6 (−12.3, −4.8)	<0.0001
	Hb (1 g/dL) ‖	+1.45 (+0.89, +2.01)	<0.0001
	Transfusions (yes vs no) ¶	−2.6 (−5.4, +0.2)	0.064
	Gender (male vs female)	+3.3 (+0.2, +6.4)	0.038
	Time from baseline (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.

QoL in Lower risk MDS with severe thrombocytopenia:

Interim analysis of the EQOL-MDS randomized clinical trial

- Baseline QoL is generally poor

QoL-E index	All patients (N = 90)
Physical	50 (25–75)
Function	56 (22–100)
Social	50 (12–75)
Sexual	67 (42–100)
Fatigue	71 (56–86)
MDS-specific	62 (42–81)
General	57 (43–74)
Treatment outcome index	55 (36–74)
All	58 (43–74)

Oliva EN, et al. Lancet Haematol. 2017;4:e127-36.

Factors affecting PRO assessment

- **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.

Summary

- The selection of appropriate instrument/s is fundamental

- Outcome is based on baseline PRO measures: stability or improvement should be a defined outcome in assessing treatment benefit

- Treatments that improve cytopenias are beneficial

- Patients with comorbidities may not perceive the expected treatment benefit

- Training for professionals to guarantee proper administration of PRO tools is recommended

HRQoL, health related quality of life; PROs, patient-reported outcomes.

THANK YOU