ASH 2020 Virtual Congress - Abstract # 365

Improvements in Health-Related Quality of Life for Patients Treated with LentiGlobin for Sickle Cell Disease (bb1111) Gene Therapy

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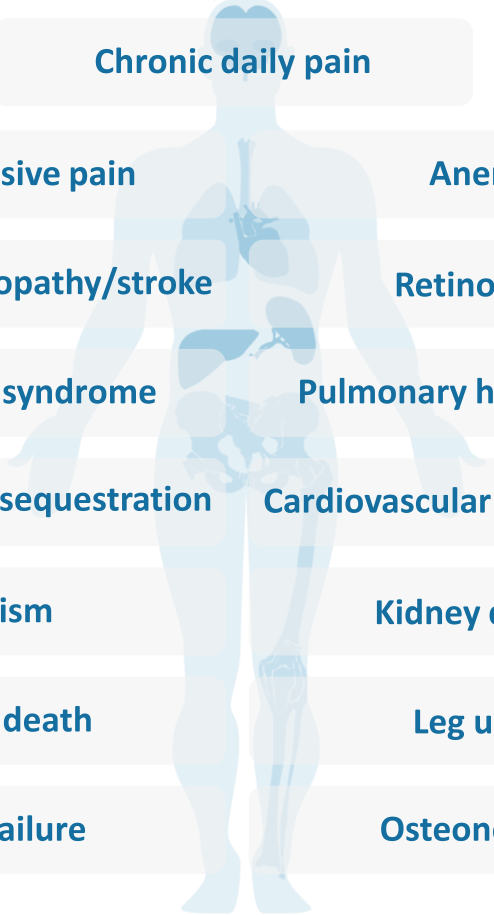
Sickle cell disease is characterized by high morbidity and early mortality, with significant impact on patient quality of life

SCD Complications[1,2]



Chronic daily pain

- **Vaso-occlusive pain**
- **Cerebral vasculopathy/stroke**
- **Acute chest syndrome**
- **Hepato-splenic sequestration**
- **Priapism**
- **Sudden death**
- **Organ failure**
- **Anemia**
- **Retinopathy**
- **Pulmonary hypertension**
- **Cardiovascular complications**
- **Kidney disease**
- **Leg ulcers**
- **Osteonecrosis**

> 50% of patients with SCD die before 45 years of age[1]

Affecting All Aspects of Patient QoL[3,4]

Physical

- Daily activities
- Strength
- Sleep
- Pain
- Fatigue

Mental

- Anxiety
- Depression
- Hopelessness

Socioemotional

- Leisure activities and
- Activities with friends & family

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1. Kanter, et al. Blood Rev. 2013;27(6):279- 287; 2. Hassell K. et al. Am J Prev Med. 2010; 3. Melo, et al. PLoS One. 2018;13:e0208916; 4. Treadwell et al. Clin J Pain. 2014;30(10):902-9144.

Hbs, sickle hemoglobin; RBC, red blood cell; SCD, sickle cell disease; QoL, quality of life.

HGB-206: An open-label, multicenter, Phase 1/2 study of LentiGlobin gene therapy (bb1111) in patients with severe SCD

Group C Enrollment Criteria

- ≥ 12 and ≤ 50 years of age
- $\beta^S\beta^S$, $\beta^S\beta^0$, $\beta^S\beta^+$ genotype
- History of severe VOEs*
- Failure of or intolerance to hydroxyurea

Enrollment completed
(NCT02140554)

Clinical Outcomes

- Weighted average HbA^{T87Q} ≥ 30% of unsupported total Hb for ≥ 6 months post-DP
- Weighted average: unsupported total Hb increase ≥ 3 g/dL vs baseline or total Hb ≥ 10 g/dL for ≥ 6 months post-DP
- Complete resolution of severe VOEs
- Health-related Quality of Life as measured by the Patient Reported Outcomes Measurement Information System 57 item questionnaire (PROMIS-57) (*Secondary endpoint*)

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*Per inclusion criteria, severe VOEs include hospitalization or ER visit ≥ 24 hours or ≥ 2 visits to a day unit or ER over 72 hours, both requiring IV treatment, for the following: acute episodes of pain, acute chest syndrome, acute hepatic sequestration, and acute splenic sequestration. Additionally, priapism events that require visit to medical care facility (without inpatient admission) are sufficient to meet severe VOE criterion.

DP, drug product; ER, emergency room; Hb, hemoglobin; IV, intravenous; SCD, sickle cell disease; VOE, vaso-occlusive event.

The Patient-Reported Outcomes Measurement Information System (PROMIS-57), v2.1[1–3]

PROMIS-57 is a 57-question instrument that measures HRQoL across 7 domains and has been validated for use in SCD

Physical Health

- Pain Intensity[a]
- Pain Interference
- Fatigue
- Physical Functioning
- Sleep Disturbance

Mental Health

- Anxiety
- Depression

Socioemotional Health

- Ability to Participate in Social Roles and Activities

Questionnaire Composition (57 Questions)

7 domains 8 questions per domain[a] (56 questions)	Pain numerical rating scale (NRS)[b] (1 question)

Demonstrated psychometric validity in SCD[1-3]

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[a] 7-day recall period for all domains except the “social roles” and “physical functioning” domains, which have no recall period.

[b] Average pain (0-10) over the past 7 days.

1. Esham KS et al. *Blood Adv*. 2020;4(1):19–27; 2. Keller S et al. *Health Qual Life Outcomes*. 2017;15:117; 3. PROMIS Cooperative Group. 2020. PROMIS Adult profile instruments. Available at www.healthmeasures.net/images/PROMIS/manuals/PROMIS_Adult_Profile_Scoring_Manual.pdf. Accessed November 6, 2020. HRQoL; Health-related quality of life; SCD, sickle cell disease.

HGB-206 Group C: Analysis of PROMIS-57 data – methods

- Included in this analysis were HGB-206 Group C adult patients with median age (range) of 25 (19, 36) with PROMIS-57 results available at three timepoints (baseline[*], Month 6, Month 12)[†] who were stratified based on baseline PROMIS-57 scores:
    - Patients with baseline scores **worse** than population norm[‡]
    - Patients with baseline scores **near or better** than population norm[‡]
- The population norm for all domains is 50, with the exception of the NRS which is 2.6.[1]
- Direction of improvement varies by domain, with some domains indicating improvement as scores increase over time (e.g. physical functioning) and for others as scores decline over time (e.g. pain interference)
- Results were analyzed separately by domain as change from baseline to Month 12.
- Summary statistics are presented (mean, SEM).
- Meaningful within-patient change is defined as the threshold of change that is clinically-meaningful for the patient.
    - For PROMIS, this is generally regarded as at least a **2-point change for the pain NRS** and a **5-point change for the other domains**.[2-4]

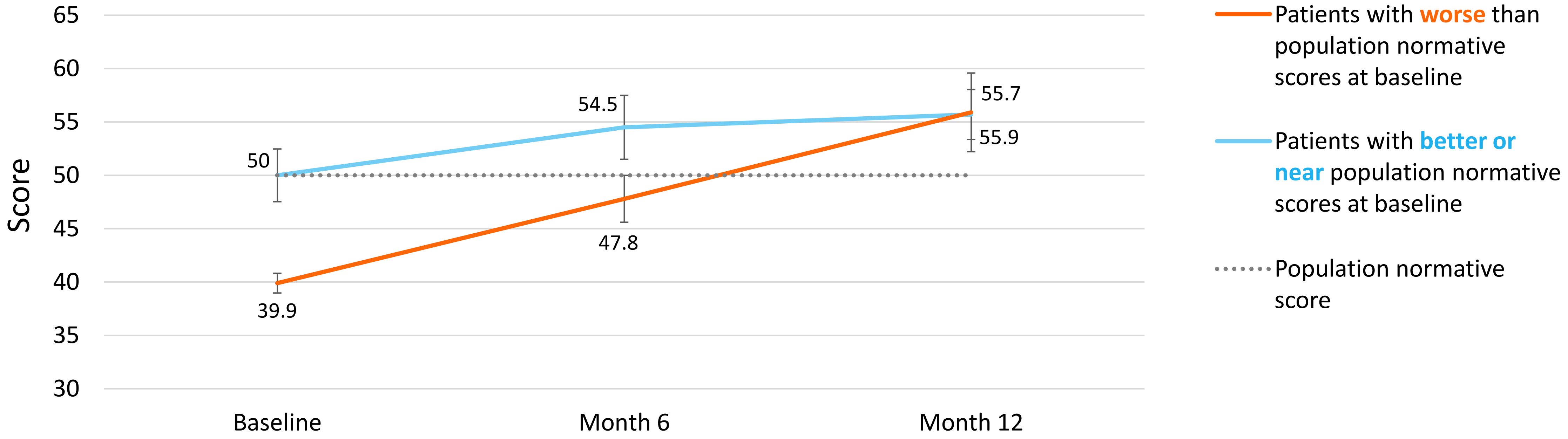
[*] Baseline defined as at screening (up to 90 days before stem cell harvest)
[†] This represents a portion of the HGB-206 Group C patients
[‡] General population normative scores.

Data as of 20 August 2020

1. PROMIS Cooperative Group. 2020. PROMIS Reference Populations. Available at https://www.healthmeasures.net/score-and-interpret/interpret-scores/promis/reference-populations. Accessed November 17, 2020; 2. Norman GR et al. *Med Care*. 2003;41:582-592; 3. Yost KJ et al. *J Clin Epidemiol*. 2011;64:507-516; 4. FDA. 2020. Incorporating clinical outcome assessments into endpoints for regulatory decision-making. Available at: https://www.fda.gov/media/132505/download. Accessed November 16, 2020. PROMIS, Patient Reported Outcomes Measurement Information System; NRS, numeric rating scale; SEM, standard error of mean.

PROMIS-57: Physical function

↑ Direction of improvement (improved physical function)



Sample Size (**worse**/**better or near** at baseline)

Baseline	Month 6	Month 12
n=4/5	4/5	4/5

All patients reported improvement, with 6/9 patients across both groups reporting a clinically-meaningful* improvement at Month 12

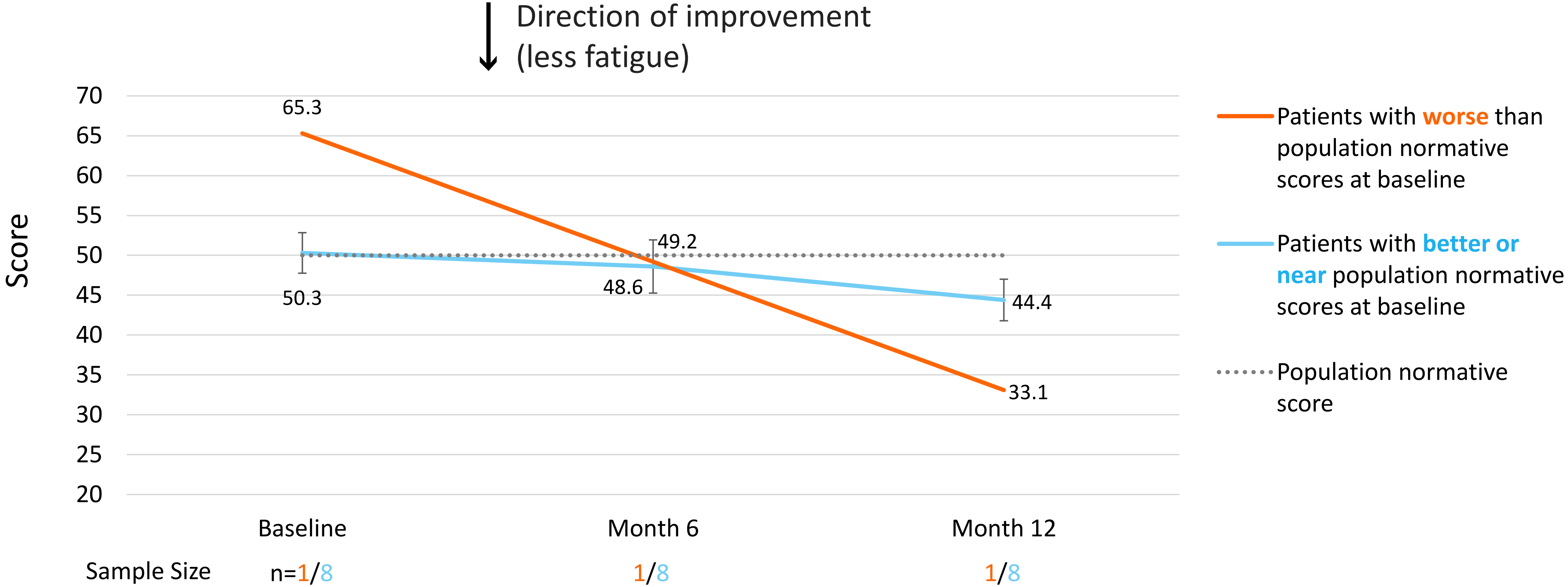
*Defined as the threshold of change that is clinically-meaningful for the patient. For the PROMIS, this is generally regarded as at least a 2-point change for the pain NRS and a 5-point change for the other domains.[1-3]

1. Norman GR et al. *Med Care*. 2003;41:582-592; 2. Yost KJ et al. *J Clin Epidemiol*. 2011;64:507-516; 3. FDA. 2020. Incorporating clinical outcome assessments into endpoints for regulatory decision-making.

PROMIS, Patient Reported Outcomes Measurement Information System

Data as of 20 August 2020

PROMIS-57: Fatigue



Sample Size
(**worse**/**better or near** at baseline)

Baseline	Month 6	Month 12
n=1/8	1/8	1/8

Regardless of group, 8/9 patients improved at Month 12, with 5/9 patients reporting a clinically meaningful improvement*

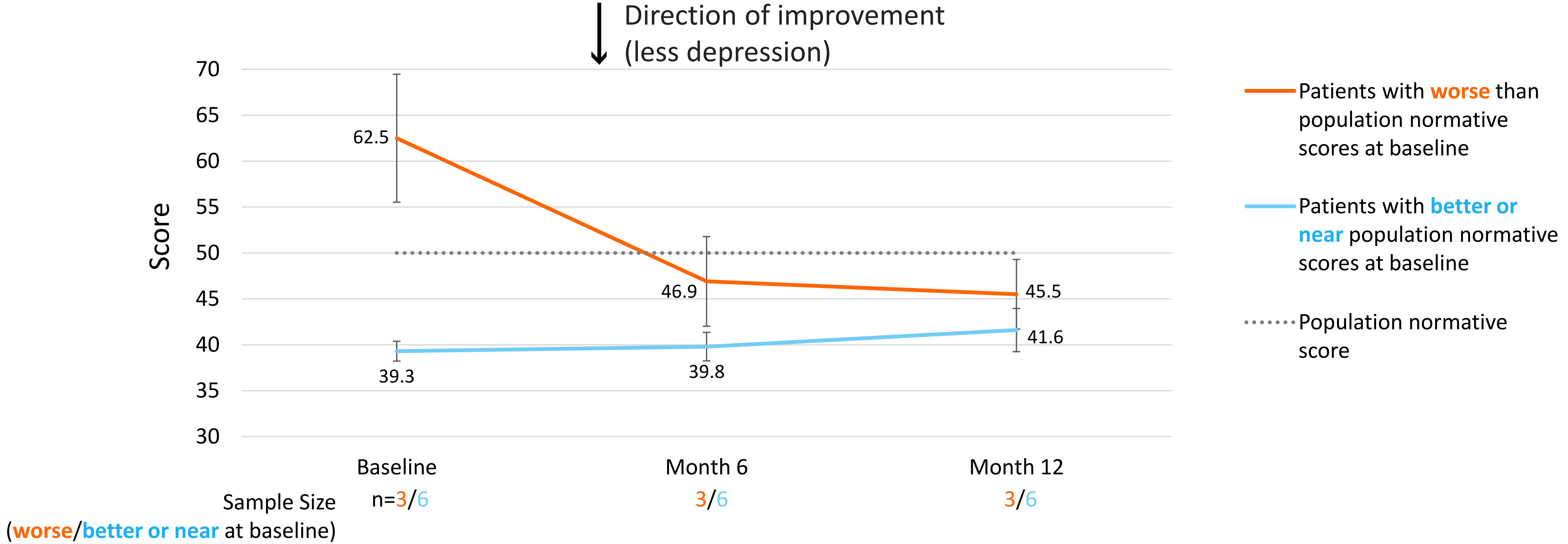
*Defined as the threshold of change that is clinically-meaningful for the patient. For the PROMIS, this is generally regarded as at least a 2-point change for the pain NRS and a 5-point change for the other domains.[1-3]

1. Norman GR et al. *Med Care*. 2003;41:582-592; 2. Yost KJ et al. *J Clin Epidemiol*. 2011;64:507-516; 3. FDA. 2020. Incorporating clinical outcome assessments into endpoints for regulatory decision-making.

PROMIS, Patient Reported Outcomes Measurement Information System

Data as of 20 August 2020

PROMIS-57: Depression



All patients with worse than population normative scores at baseline reported clinically meaningful improvement*; most patients (4/6) with scores better/near population normative at baseline remained stable at Month 12

*Defined as the threshold of change that is clinically-meaningful for the patient. For the PROMIS, this is generally regarded as at least a 2-point change for the pain NRS and a 5-point change for the other domains.[1-3]

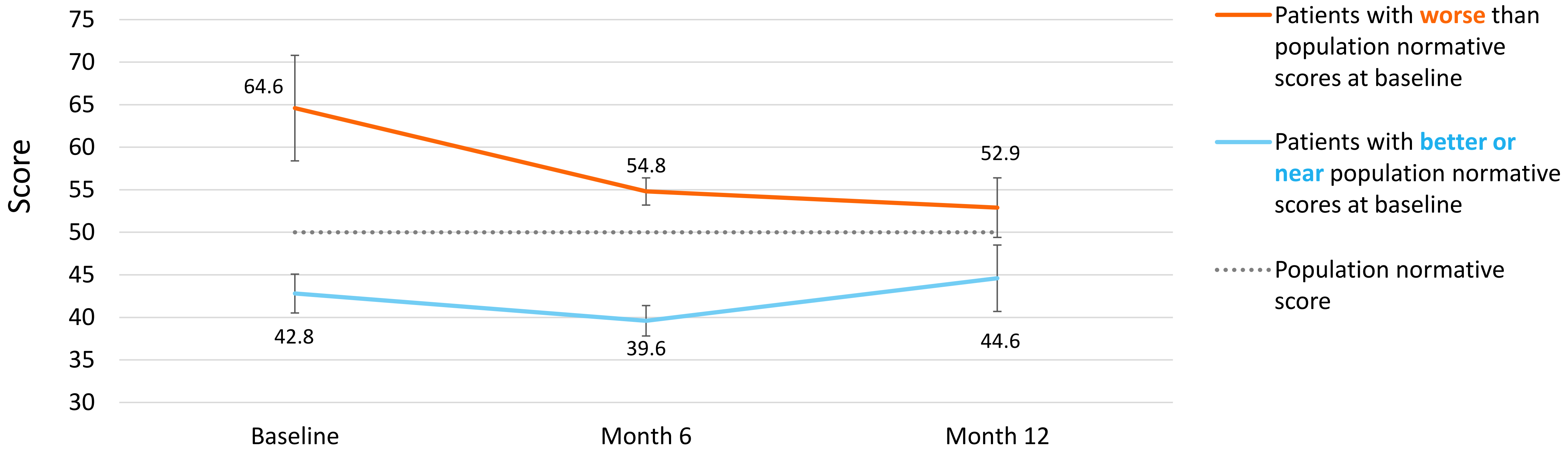
1. Norman GR et al. *Med Care*. 2003;41:582-592; 2. Yost KJ et al. *J Clin Epidemiol*. 2011;64:507-516; 3. FDA. 2020. Incorporating clinical outcome assessments into endpoints for regulatory decision-making.

PROMIS, Patient Reported Outcomes Measurement Information System

Data as of 20 August 2020

PROMIS-57: Anxiety

↓ Direction of improvement (less anxiety)



Sample Size (worse/better or near at baseline)	Baseline	Month 6	Month 12
	n=2/7	2/7	2/7

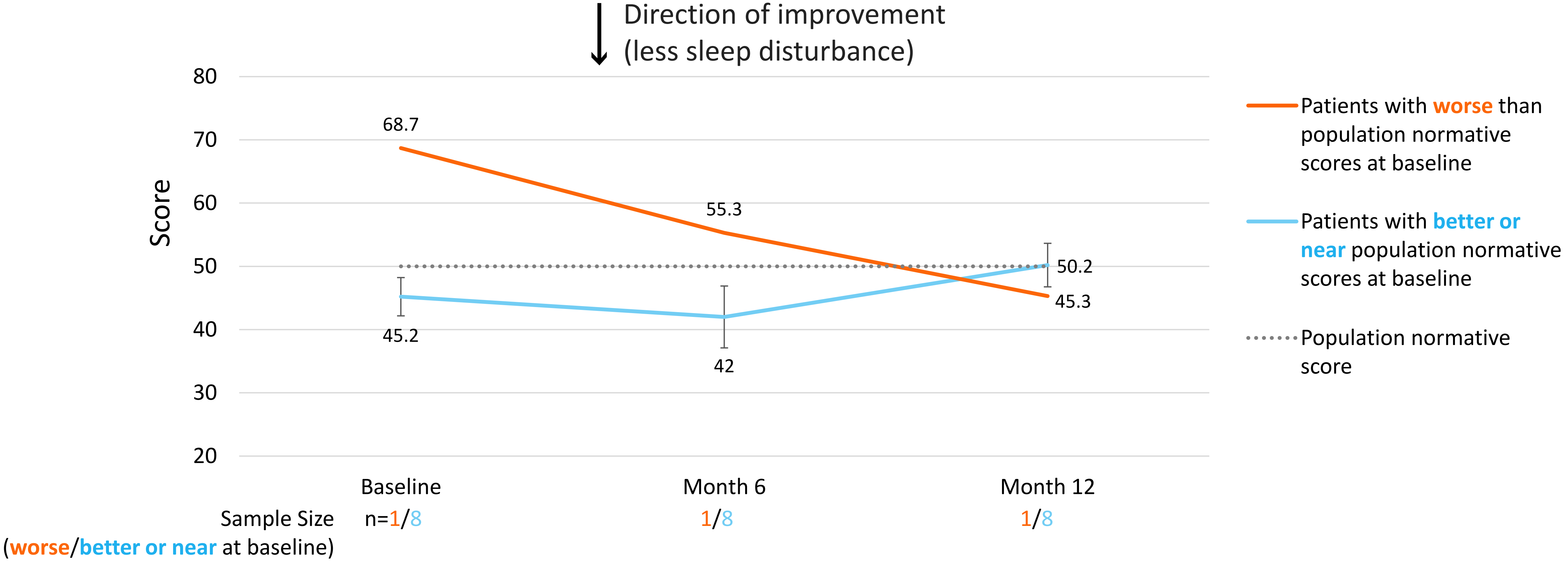
Within the group of patients with scores better/near population normative at baseline, there is patient variation in both directions (improvement and decline)

Data as of 20 August 2020

PROMIS, Patient Reported Outcomes Measurement Information System

For Medical Affairs reactive response to unsolicited requests from HCPs and Payers

PROMIS-57: Sleep disturbance

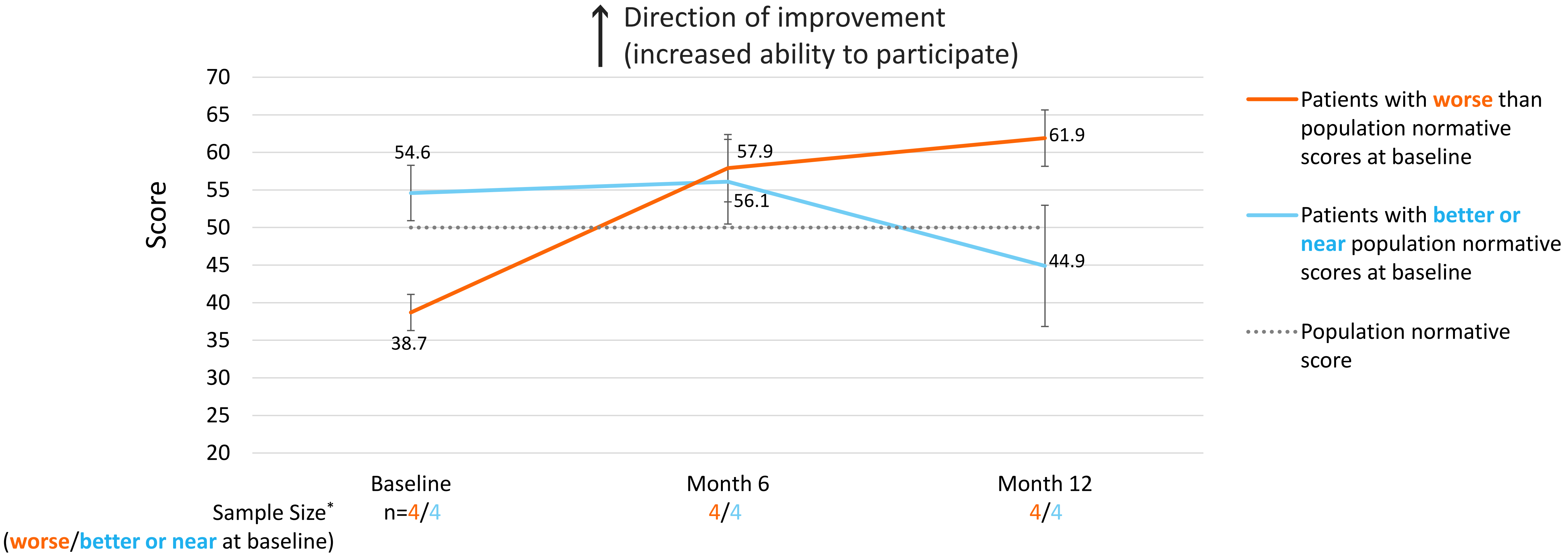


Within the group of patients with better/near population normative scores at baseline, there is patient variation in both directions (improvement and decline)

Data as of 20 August 2020

PROMIS, Patient Reported Outcomes Measurement Information System

PROMIS-57: Ability to participate in social roles/activities



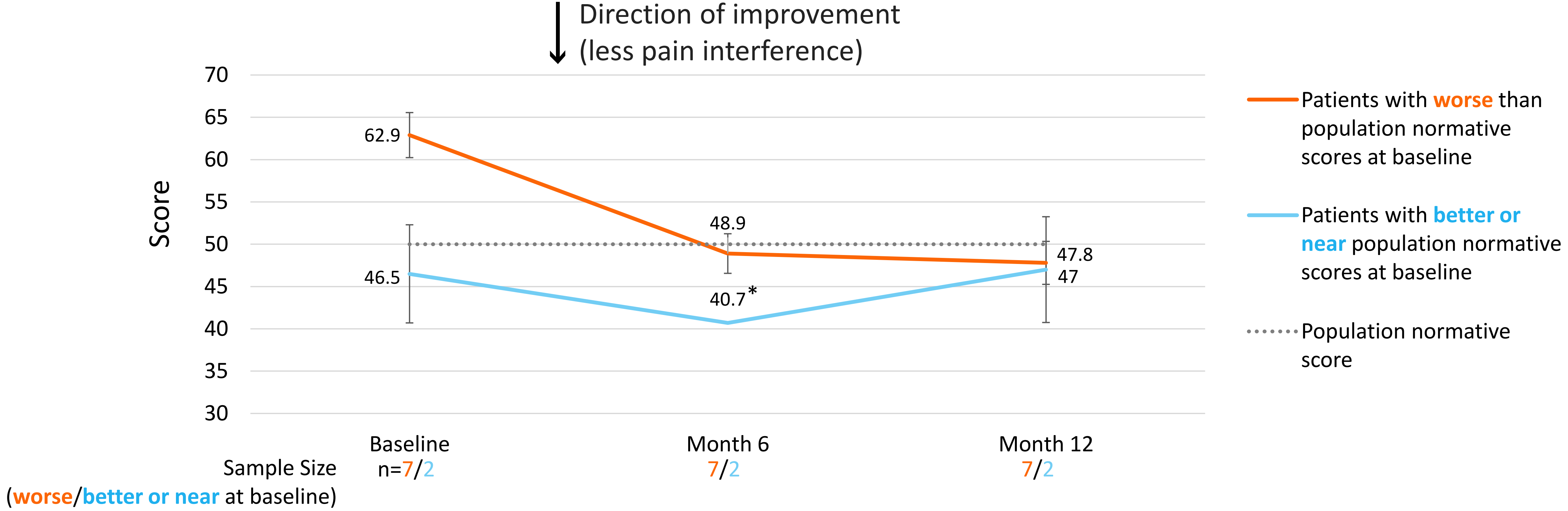
There is variation in both directions (improvement and decline) across both groups

[*] One patient did not have Month 12 data

Data as of 20 August 2020

PROMIS, Patient Reported Outcomes Measurement Information System

PROMIS-57: Pain interference



All patients with worse than population normative scores at baseline improved, with 5 reporting clinically-meaningful improvements† in pain interference at Month 12

*No reported SEM as the 2 patients have the same score.

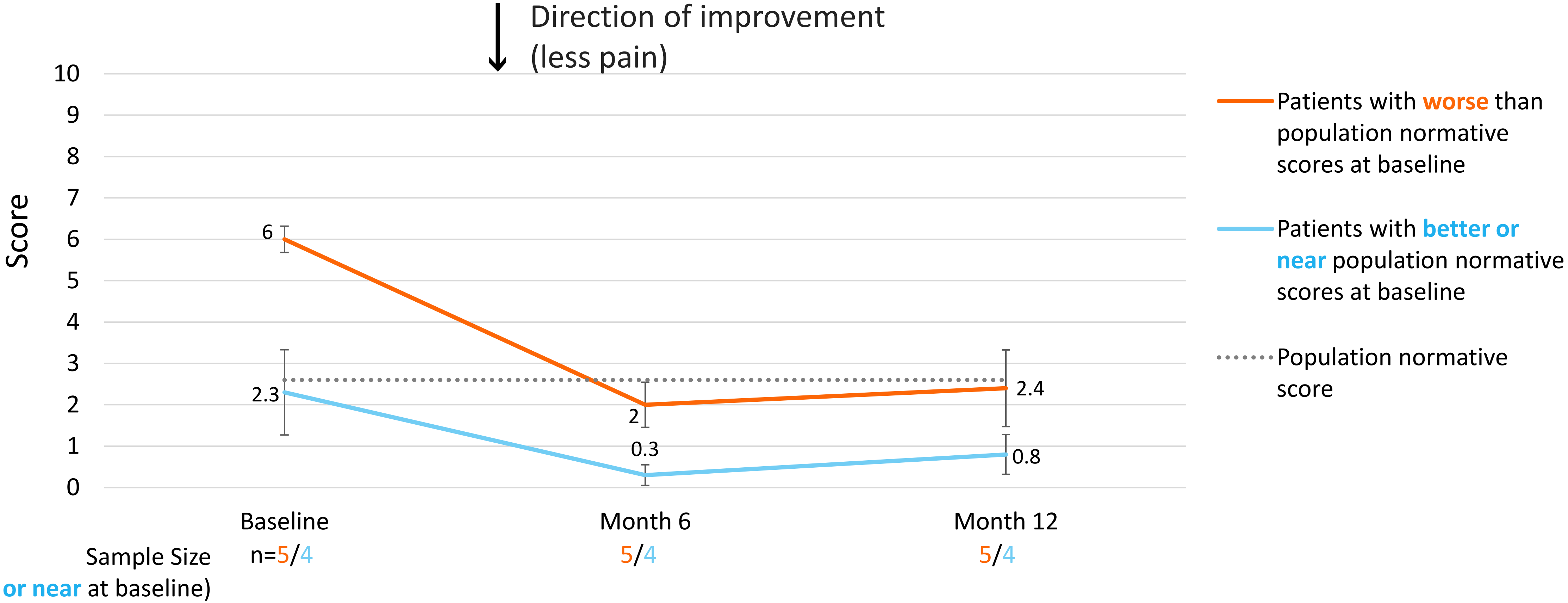
†Defined as the threshold of change that is clinically-meaningful for the patient. For the PROMIS, this is generally regarded as at least a 2-point change for the pain NRS and a 5-point change for the other domains.[1-3]

1. Norman GR et al. *Med Care*. 2003;41:582-592; 2. Yost KJ et al. *J Clin Epidemiol*. 2011;64:507-516; 3. FDA. 2020. Incorporating clinical outcome assessments into endpoints for regulatory decision-making.

PROMIS, Patient Reported Outcomes Measurement Information System; SEM, standard error of the mean

Data as of 20 August 2020

PROMIS-57: Pain intensity NRS



Regardless of group, all patients improved or remained stable at Month 12, with 6/9 patients demonstrating a clinically-meaningful improvement*

*Defined as the threshold of change that is clinically-meaningful for the patient. For the PROMIS, this is generally regarded as at least a 2-point change for the pain NRS and a 5-point change for the other domains.[1-3]

1. Norman GR et al. *Med Care*. 2003;41:582-592; 2. Yost KJ et al. *J Clin Epidemiol*. 2011;64:507-516; 3. FDA. 2020. Incorporating clinical outcome assessments into endpoints for regulatory decision-making.

PROMIS, Patient Reported Outcomes Measurement Information System

Data as of 20 August 2020

HGB-206 Group C PROMIS-57: Summary

- These data represent the first quality of life data reported for an investigational gene therapy in sickle cell disease.
- Sickle cell disease profoundly effects QoL. Outcomes for gene therapy must include long-term measurement of QoL to understand the potential benefit of gene therapy.
- Within the Physical Functioning, Fatigue, Pain Interference and the Pain NRS domains, the majority of patients reported clinically meaningful improvements at Month 12 post-LentiGlobin infusion.
- Sample size at group level and within- and across-group variation currently limits interpretation for the PROMIS-57 domains.
- Continued analysis of QoL outcomes over time following treatment with LentiGlobin for sickle cell disease is recommended.

NRS, numeric rating scale; QoL, quality of life.

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