Real-World Experience of Pediatric Patients With Sickle Cell Disease Treated With Oxbryta®

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Introduction

Background: Oxbryta (voxelotor) is a first-in-class FDA approved therapy that increases hemoglobin (Hb) levels and reduces markers of hemolysis in patients with Sickle Cell Disease (SCD) who are at least 12 years of age.

Objective: To quantify the clinical response to treatment with Oxbryta tablets in a single-center series of pediatric patients and adult patients with SCD.

Methods: Real-world clinical data were collected in 22 pediatric (aged 12 to <21 years) and 54 adult (21 to 70 years) patients with SCD at Prisma Health in Greenville, South Carolina. Data were collected before and after initiation of at least 2 consecutive weeks of Oxbryta treatment.

Results

- Data from twenty-two pediatric (29%) and fifty-four adult (71%) patients treated with Oxbryta were collected
- Demographics: mean age=30.6 years; gender=62% female; HbSS genotype=85%, baseline Hb, 7 to 10.6 g/dL=74%
- Mean duration of Oxbryta treatment: pediatric=8.3 months, adult=8.7 months; all patients=8.6 months
- Most (82%, 14/17) adult patients either reduced or discontinued erythropoietin stimulating agent use from baseline, and transfusion use was discontinued in 1 patient
- Hydroxyurea use was prevalent in most patients at baseline and remained unchanged posttreatment

Results

- 74% of pediatric patients and 86% of adult patients had an Hb response (>1.0 g/dL improvement from baseline)
- Mean post-treatment hemoglobin level increased by 2.0 g/dL from baseline in all patients; an increase of 2.1 g/dL in adult patients and 1.9 g/dL in pediatric patients
- Mean reticulocyte percentage and total bilirubin decreased from baseline by 4.9% (39.9% relative change) and 1.4 mg/dL (32.8% relative change), respectively
- The patient global impression of change (PGI-C) and clinical global impression of change (CGI-C) in most patients were assessed as very much improved or much improved.
- AEs of diarrhea (n=2 adults) and rash (n=1 adult) resolved after dose medication.

Demographics and Baseline Characteristics

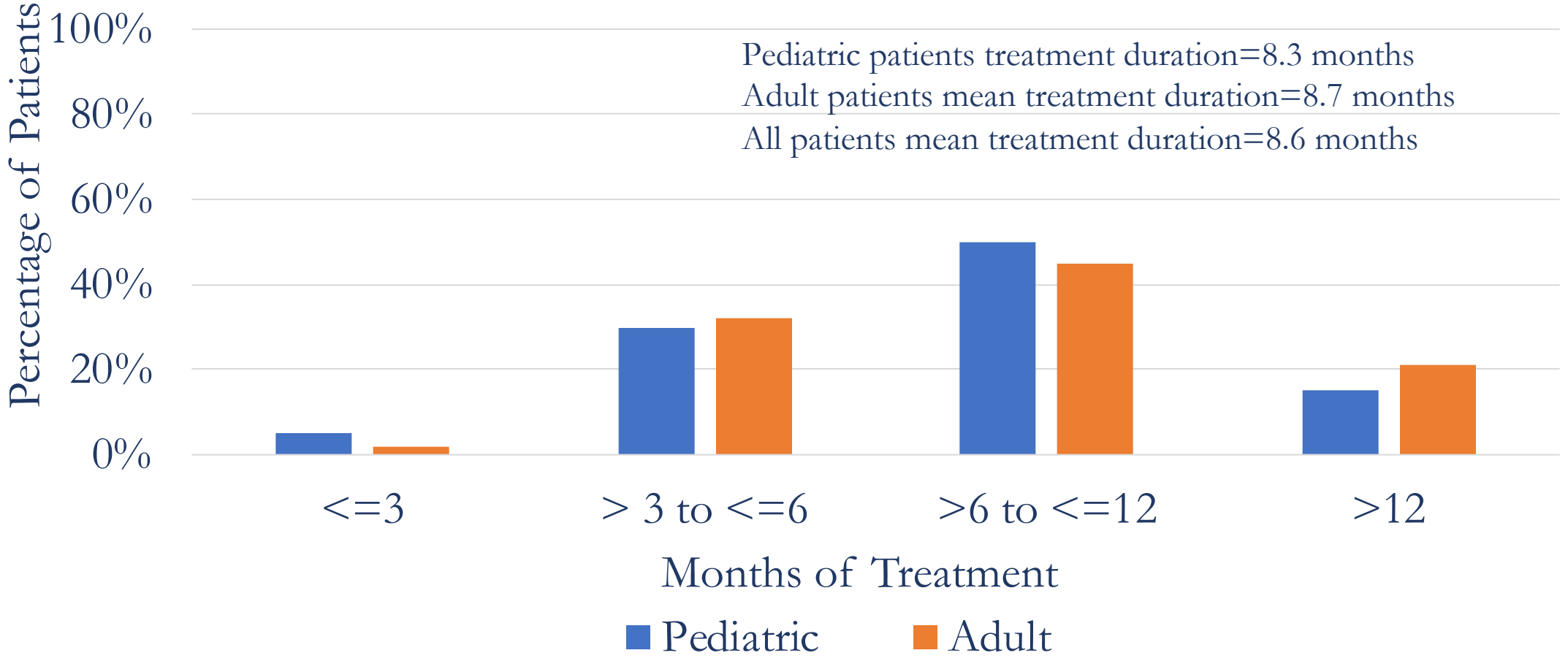
	Pediatrics (< 21 Years) (n = 22)	Adults (≥ 21 Years) (n = 54)	All Patients (n = 76)
Age - n (%)	20 (29%)	54 (71%)	
Mean (SD)	16.0 (2.7)	36.6 (12.5)	30.6 (14.2)
Min, Max	12, 20	21, 70	12, 70
Gender - n (%)			
Male	5 (23%)	24 (44%)	29 (38%)
Female	17 (77%)	30 (56%)	47 (62%)
HbS genotypes - n (%)			
HbSS	19 (86%)	46 (85%)	65 (86%)
HbSC	1 (5%)	5 (9%)	6 (8%)
HBSβ+	0	1 (2%)	1 (1%)
HbSβ0	2 (9%)	2 (4%)	4 (5%)
Mean baseline Hb, g/dL			
<7, n (%)	0	12 (23%)	12 (17%)
7 to 10.5, n (%)	17 (85%)	36 (69%)	53 (74%)
>10.5, n (%)	3 (15%)	4 (8%)	7 (10%)
Missing	2	2	4

Duration of Oxbryta Treatment

	Pediatrics (< 21 Years) (n = 22)	Adults (≥ 21 Years) (n = 54)	All Patients (n = 76)
Months			
Mean (SD)	8.3 (3.5)	8.6 (3.7)	8.6 (3.6)
Min, Max	1.5, 14.7	1.7, 15.8	1.5, 15.8
N	20	53	73
Missing	2	1	3

Data cutoff date: 02 April 2021

Mean Duration of Treatment



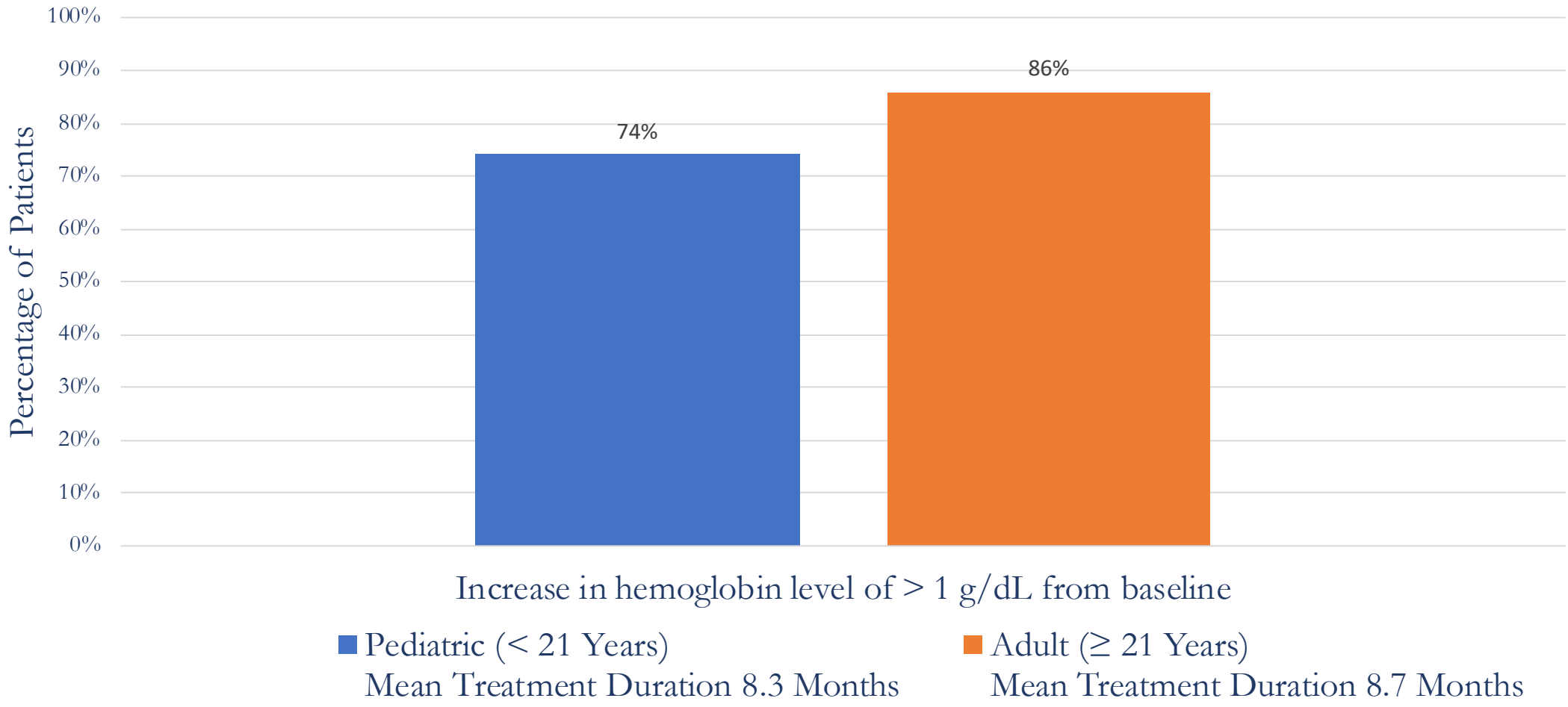
Clinical Response to Oxbryta treatment

	Pediatrics (< 21 Years) Mean (SD), N (n = 22) Mean Treatment Duration 8.3 months	Adults (≥ 21 Years) Mean (SD), N (n = 54) Mean Treatment Duration 8.7 months	All Ages Mean (SD), N (N = 76) Mean Treatment Duration 8.6 months
Hemoglobin (g/dL)			
Pre-VOX	8.6 (1.4), 20	8.2 (1.4), 52	8.3 (1.4), 72
Post-VOX	10.4 (1.2), 18	10.2 (1.5), 44	10.2 (1.5), 62
Change from Baseline	1.9 (1.1), 18	2.1 (1.0), 44	2.0 (1.0), 62
Reticulocytes (%)			
Pre-VOX	10.4 (5.6), 20	12.0 (6.0), 51	11.6 (6.0), 71
Post-VOX	5.4 (3.1), 18	7.0 (4.5), 44	6.5 (4.2), 62
Change from Baseline	-4.8 (3.8), 18	-4.9 (4.0), 44	-4.8 (3.9), 62
Total bilirubin (mg/dL)			
Pre-VOX	3.4 (3.2), 20	3.6 (2.5), 51	3.5 (2.7), 71
Post-VOX	1.7 (1.0), 18	2.1 (1.4), 44	2.0 (1.3), 62
Change from Baseline	-1.8 (3.0), 18	-1.2 (1.6), 44	-1.4 (2.2), 62

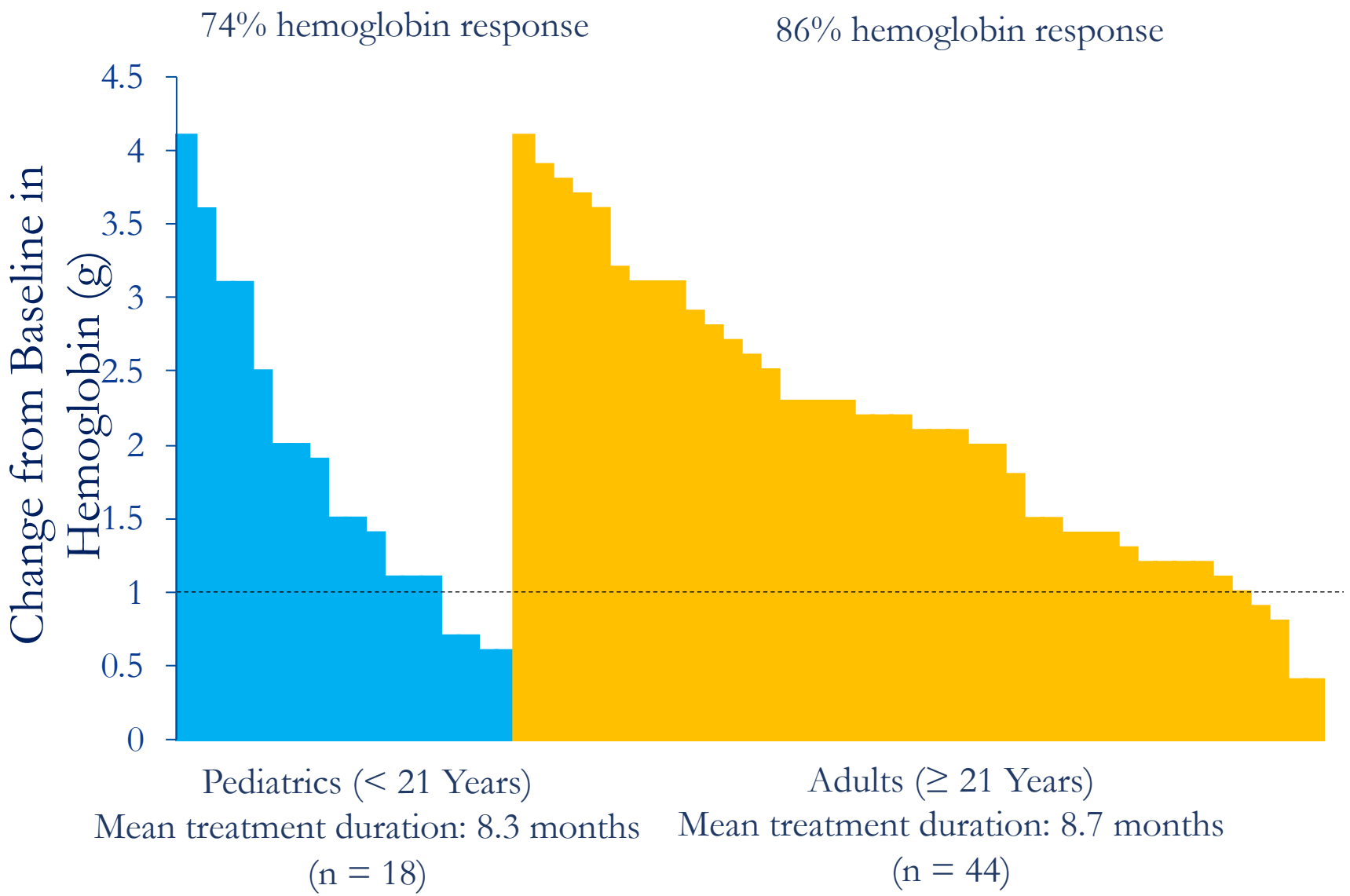
Change from Baseline in Hemoglobin and Markers of Hemolysis

Variable	Pediatrics (< 21 Years) Mean Treatment Duration 8.3 months		Adults (≥ 21 Years) Mean Treatment Duration 8.7 months		All Patients Mean Treatment Duration 8.6 months	
	No	Change from Baseline Mean (95% CI)	No	Change from Baseline Mean (95% CI)	No	Change from Baseline Mean (95% CI)
Absolute change in hemoglobin level (g/dL)	18	1.9 (1.4, 2.4)	44	2.1 (1.8, 2.4)	66	2.0 (1.8, 2.3)
Relative change in hemoglobin level (%)	18	24.2 (17.0, 31.3)	44	26.9 (22.9, 31)	66	26.1 (22.6, 29.7)
Relative change in reticulocyte level (%)	18	-40.3 (-52.7, -27.8)	44	-39.8 (-46.6, -33.0)	66	-39.9 (-45.9, -33.9)
Relative change in total bilirubin level (%)	18	-35.5 (-50.6, -20.3)	44	-31.7 (-43.6, -19.8)	66	-32.8 (-43.6, -19.8)

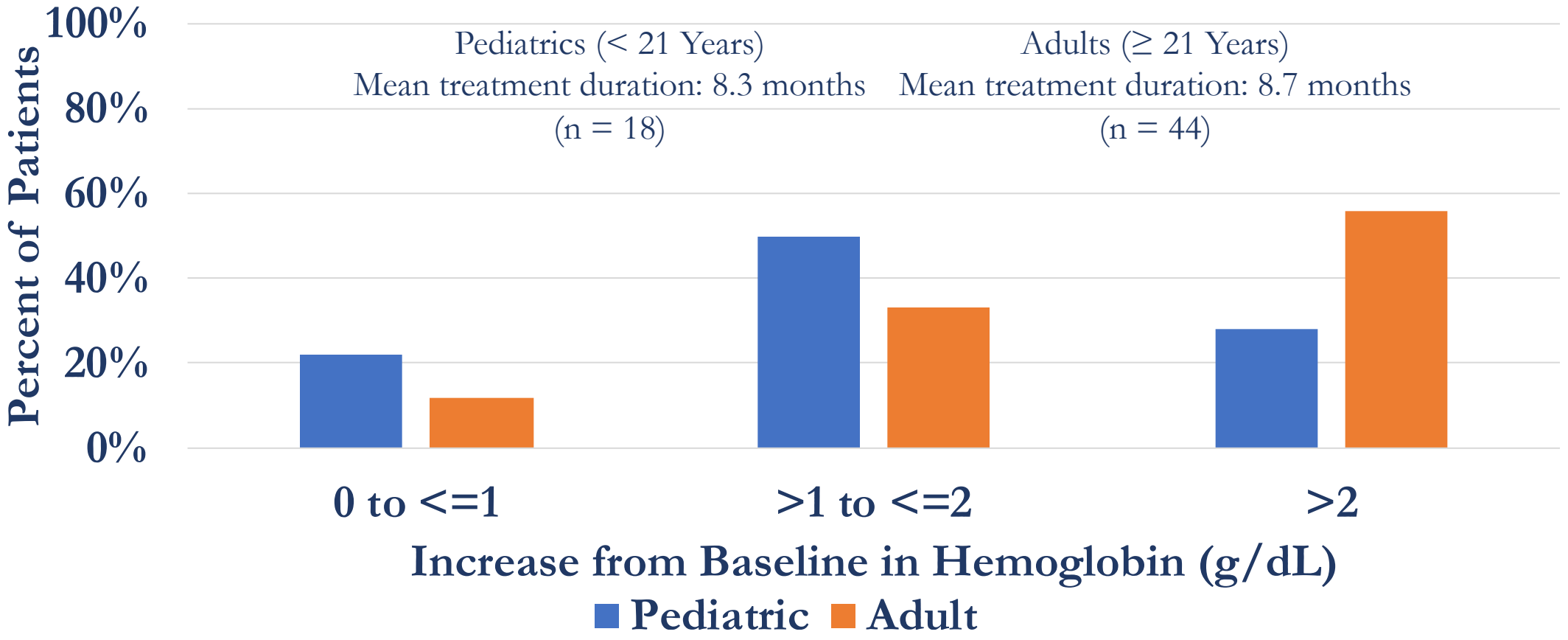
Clinical Response to Oxbryta treatment



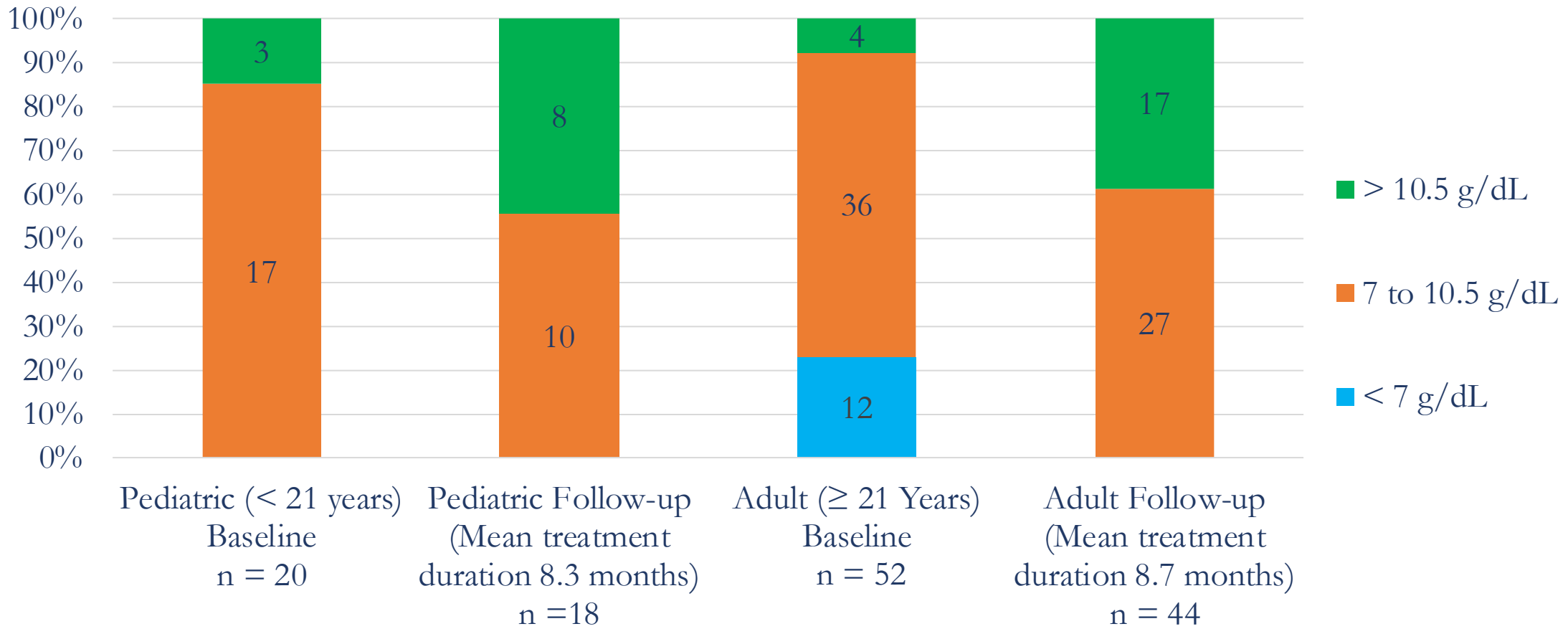
Waterfall Plot Per-Patient Hemoglobin Change



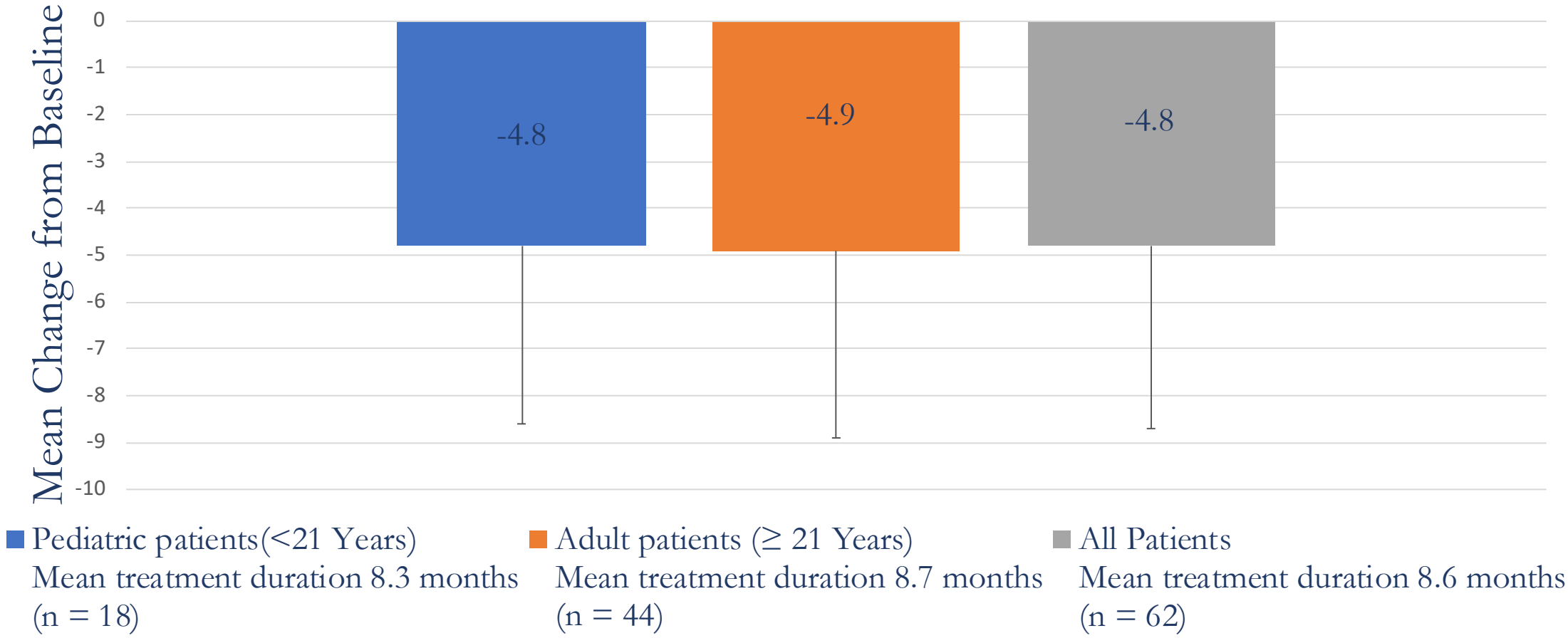
Clinical Response to Oxbryta Treatment
Hemoglobin g/dL



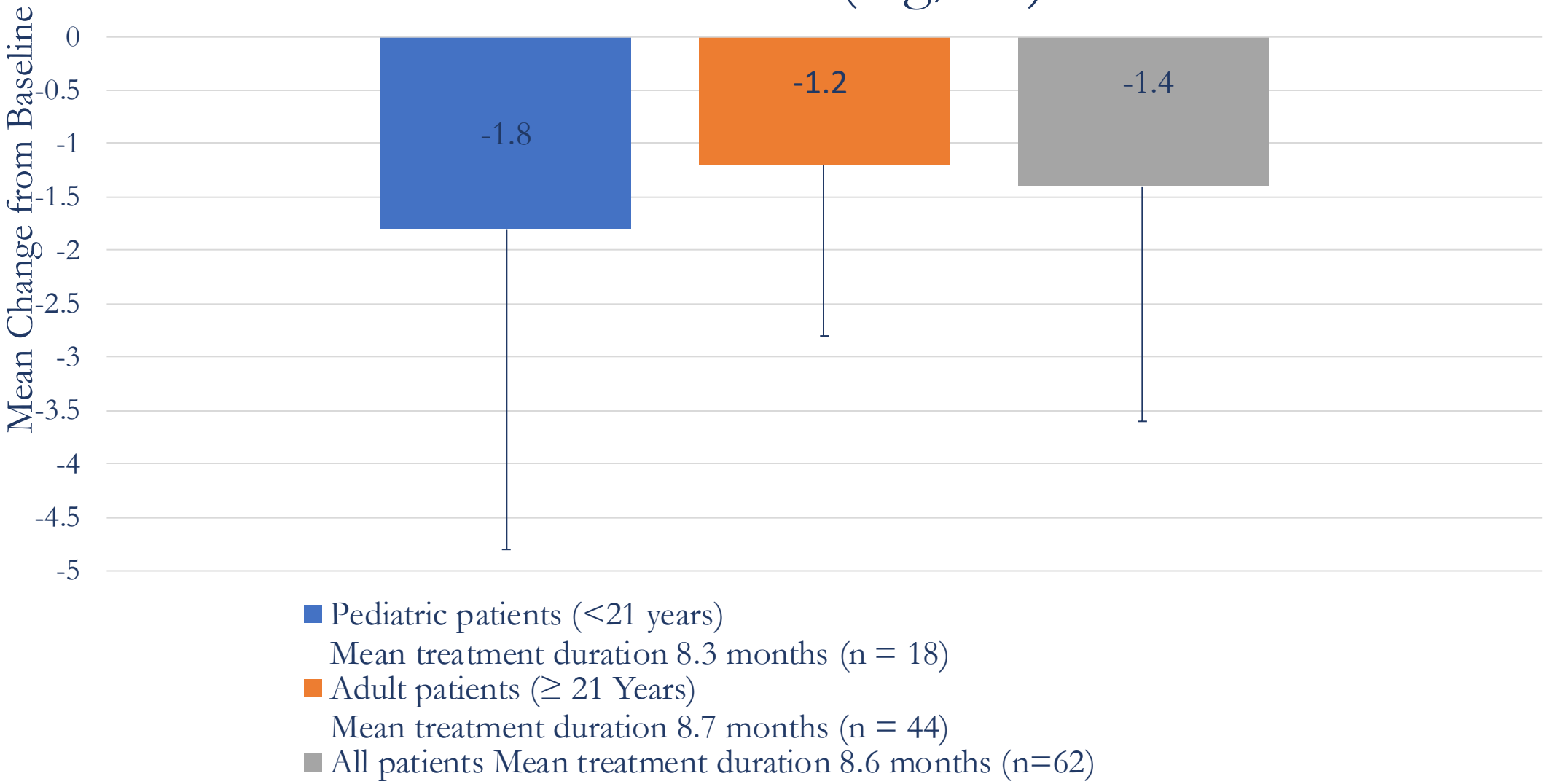
Clinical Response to Oxbryta Treatment by Category Hemoglobin g/dL



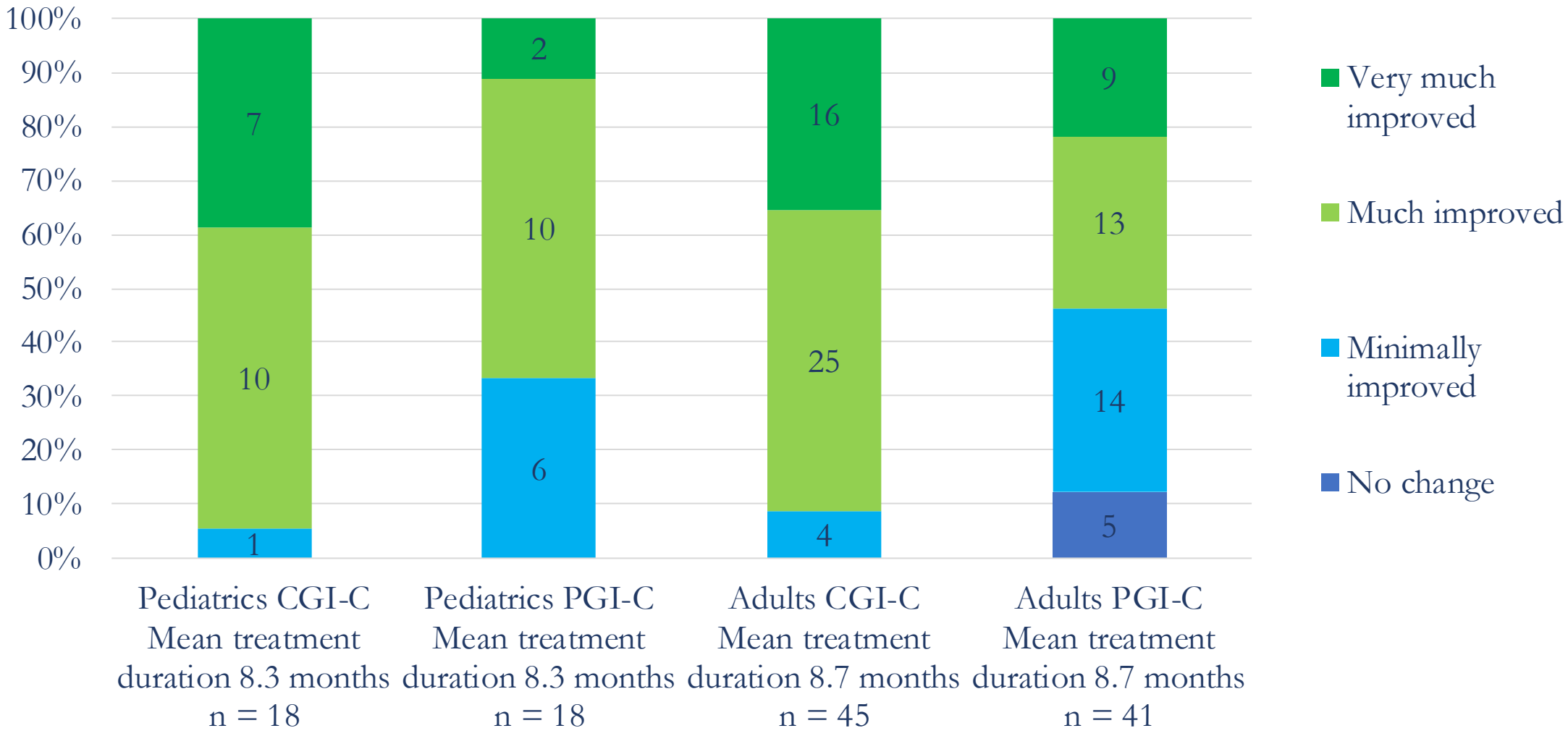
Clinical Response to Oxbryta Treatment
Reticulocytes (%)



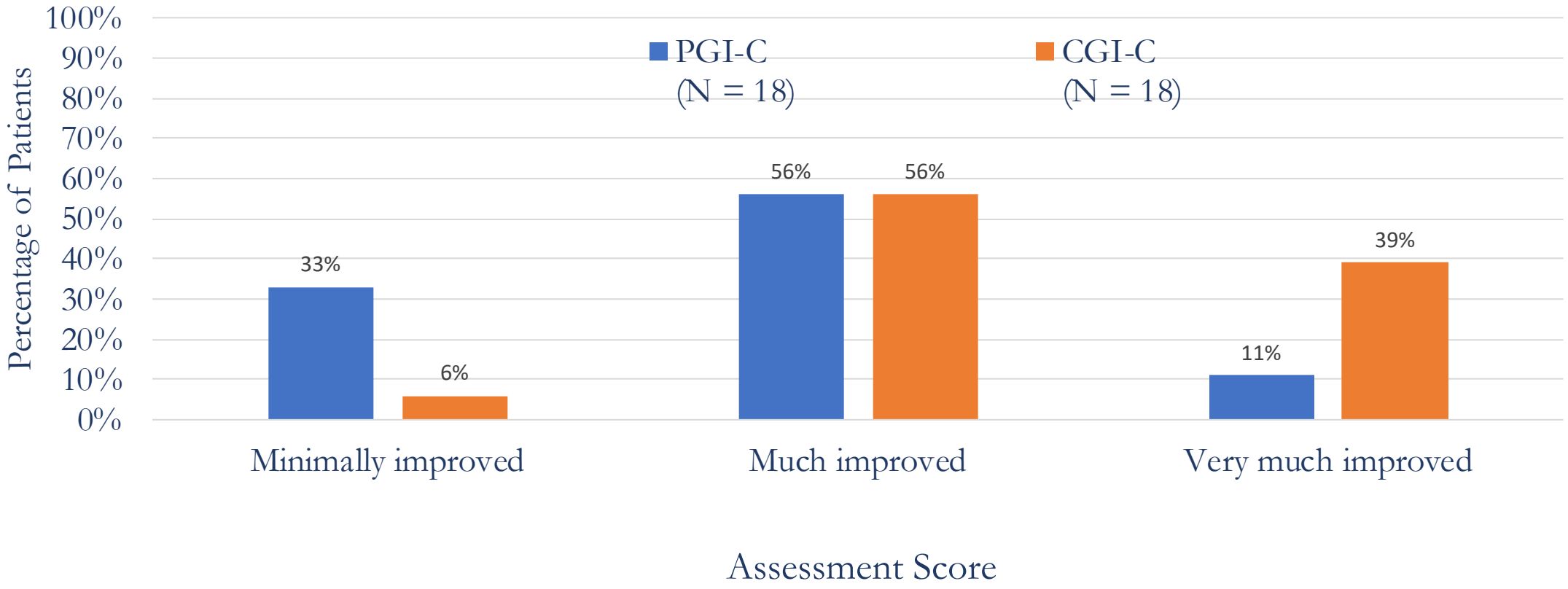
Clinical Response to Oxbryta Treatment
Total Bilirubin (mg/dL)



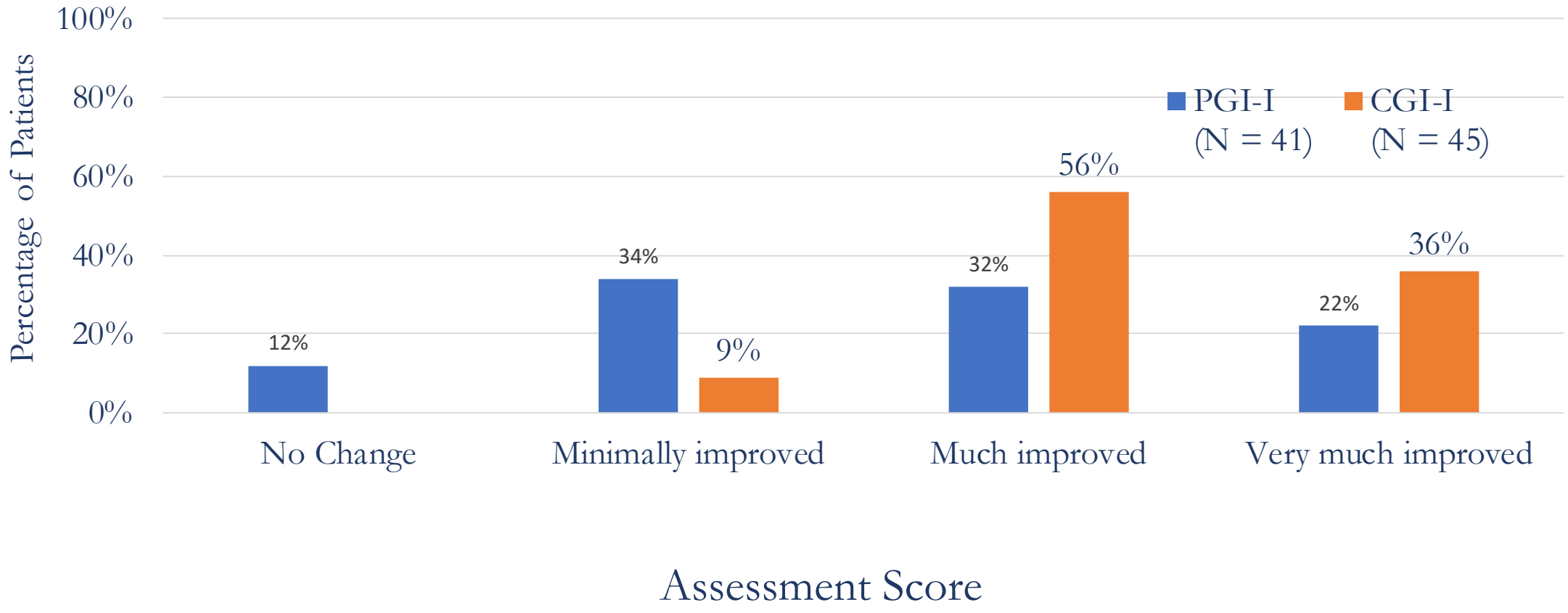
Clinical Improvement as measured by Patient Global Impression of Change (PGI-C) and Clinical Global Impression of Change (CGI-C)



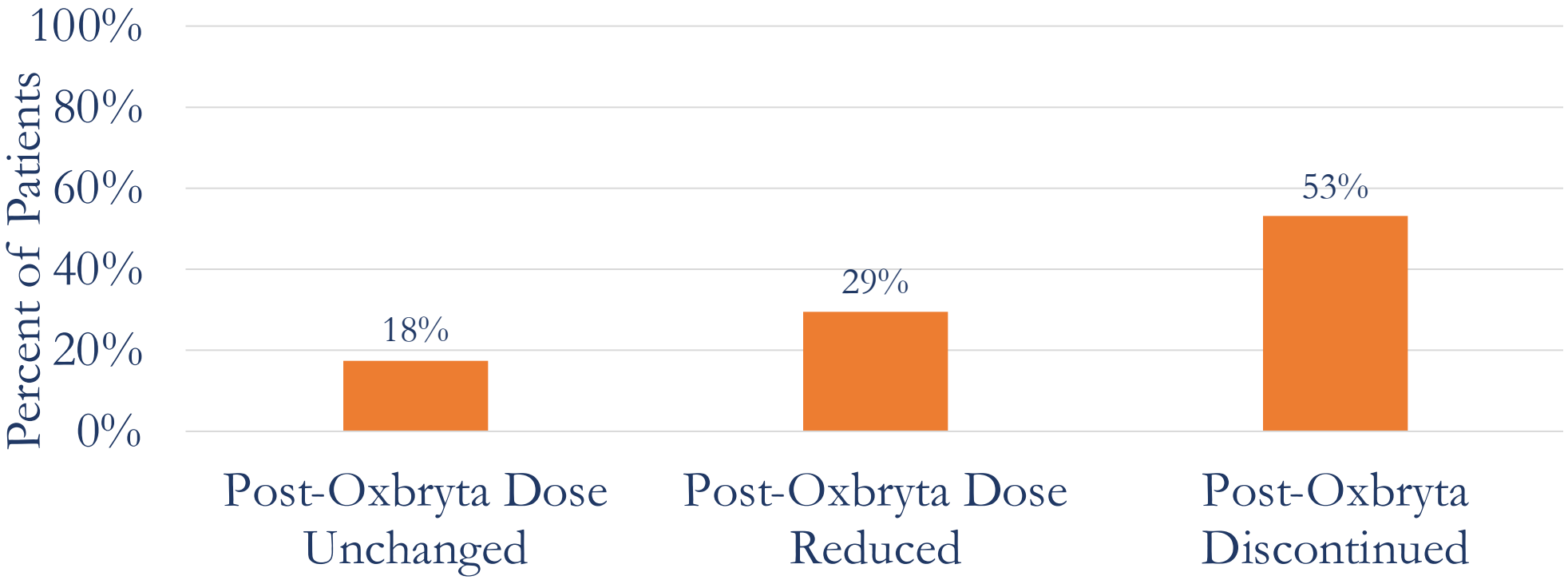
Patient Global Impression of Change (PGI-C) and Clinical Global Impression of Change (CGI-C) Assessments in Pediatric Patients



Patient Global Impression of Change (PGIC) and Clinical Global Impression of Change (CGIC) in Adult Patients



Change in Concomitant Medication use after Oxbryta Treatment in Adults



- 82% of adult patients who received erythropoietin stimulating agents reduced or discontinued use after Oxbryta treatment
- Most patients were treated with hydroxyurea at baseline and demonstrated good results with Oxbryta.
- One adult patient who had regular transfusions pre-Oxybryta and no longer needed transfusions post-Oxbryta.

Adverse Events that Led to Dose Modification

Subject	Reported Adverse Event	Action Taken	Event Resolved
Adult	Diarrhea	Dose reduction to 1000 mg l month Resumption to 1500 mg	Yes
Adult	Diarrhea	Reduced dose to 1000 mg	Yes
Adult	Rash	Reduced dose to 1000 mg, Resumption to 1500 mg with loratidine	Yes

No pediatric patients had adverse events that required dose modification.

Conclusions

- This ongoing study is the first to examine the real-world impact of Oxbryta in a pediatric and adult populations with SCD.
- The effects of Oxbryta on hemoglobin, reticulocyte percentage, and total bilirubin levels were observed and were greater than those reported in the HOPE trial.
- The patient global impression of change (PGI-C) and clinical global impression of change (CGI-C) in most patients were assessed as very much improved or much improved.
- Adverse events were rare, and all resolved after dose medication.
- Further evaluation with a larger population and longer follow-up are needed to confirm these findings.