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Interim Analysis of Phase I/II Trial with  
Trappsol® Cyclo™ Delivered  
Intravenously in NPC Patients

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# Phase I/II Intravenous Trial with Trappsol® Cyclo™ Overview

A Phase I/II Study to Evaluate the Safety and Pharmacokinetics of Intravenous Trappsol® Cyclo™ in Patients with Niemann-Pick Disease type C (NPC1) and the Pharmacodynamic Effects of Treatment upon Markers of Cholesterol Metabolism and Clinical Outcomes (NCT02912793)

- Randomized double blinded, parallel group study with no control to evaluate safety and tolerability of Trappsol® Cyclo™ in 12 subjects aged 2 years and older.
- Three doses studied: 1500 mg/kg, 2000 mg/kg and 2500 mg/kg
- Intravenous infusion over 8-9 hours every two weeks, for a 48-week period
- Fully enrolled in 5 sites in the UK, Sweden and Israel
  - Demographics: Age range 2 years to 39 years; 7 male, 5 female; 11 White, 1 Black or African Caribbean

Unblinded interim analysis completed and reported by Cyclo Therapeutics in May 2020

LPLV expected in early 2021

# Safety and Tolerability

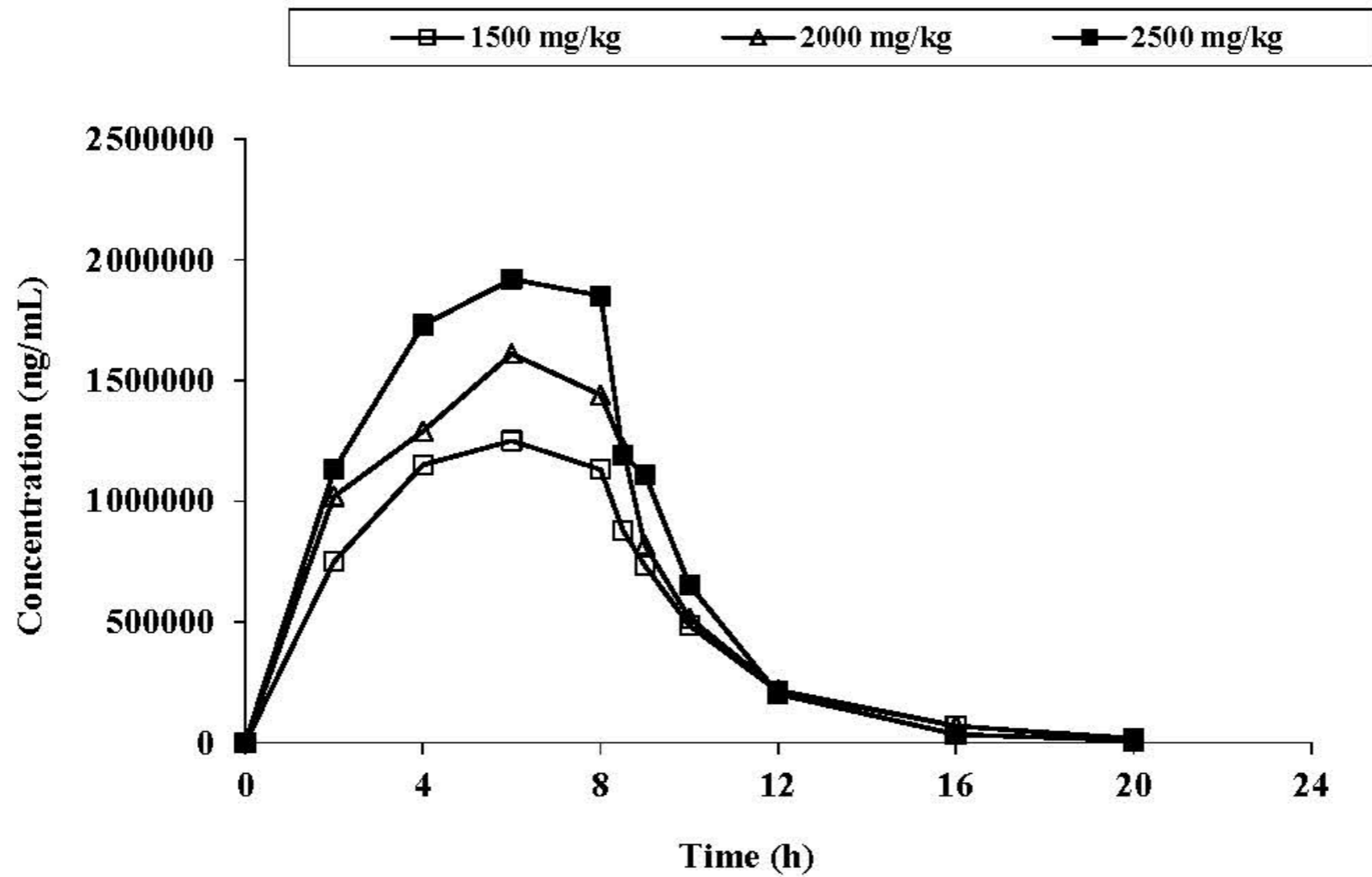
		Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)	Grade 4 (Life-Threatening)
Adverse Event (AE) Profile by CTCAE Toxicity Grading (N = 191)	No. of AE's	155	19	13	2
	No. of Serious AE's (SAE's)	2	1	10	2
	AE's considered Related i.e. Possibly, Probably or Related	24 ↑ bowel movement, fever, ↑ALT, ↑AST, tinnitus, worsened hearing at higher frequencies	4 ↑ bowel movement, ataxia, speech deterioration, ↑ seizures	0	0
	SAE's considered Related	2 Erythema, hand swelling	1 Hearing deterioration	0	0
	AE's / SAE's considered Not Related i.e. Unlikely or Not Related	129 incl. ↓platelets, raised CRP, coughing, vomiting, weight loss, nausea, fall, intermittent absence seizures	14 incl. rash, seizure, cough, vomiting, headache, anaemia	13 anaemia, aspiration pneumonia, backache, hospitalisation for seizures – 7 separate SAE's, CSF fluid leak (required hospitalisation overnight), tonsillitis, influenza	2 Aspiration pneumonia, declining health / unconscious

## Pharmacokinetics:

Single-dose PK show half-life 2 hrs., dose proportional C<sub>max</sub> plasma levels, T<sub>max</sub> 6 hrs.

Trappsol® Cyclo™ crosses the blood-brain-barrier at level of 2% (CSF:plasma ratio) at 8 hrs. after start of IV infusion, and 16% at 12 hrs. suggesting persistence of the drug in the CSF.

**Figure 1** Mean plasma concentrations of HP- $\beta$ -CD following a single intravenous infusion of Trappsol<sup>®</sup> to patients with NPC-1



Peripheral: Trappsol<sup>®</sup> Cyclo<sup>™</sup> affects cholesterol homeostasis

Biochemical results in the Phase I/II study are consistent with those in the Phase I study just shown:

- Blood markers which indicate shutdown of cholesterol synthesis two days following infusions
- Blood markers which indicate increased metabolism of cholesterol, thought to be related to bolus of cholesterol released from lysosomes
- Similar level of effect across dose groups

Central: Tau is reduced in CSF at 24 weeks and 48 weeks in patients who opted for additional lumbar punctures.

# Efficacy – NPC Severity Scoring Tool

4 patients had completed the trial at the time of the Interim Analysis:

3 patients showed improvement of at least 3 points on the NPC Severity Scale (17- domain measurement tool of neurologic features of NPC) at the end of one year.

- Note: Patients not receiving any intervention beyond Standard of Care would be expected to Worsen in total score by 1.5 points over one year.
- Improvements in disease features including gait, ambulation, fine motor, gaze palsy, cognition, incontinence, ability to speak and to swallow, behavioral features of the disease, and ability to control seizures.
- 2 patients improved in some features but worsened in others as part of their overall improvement score

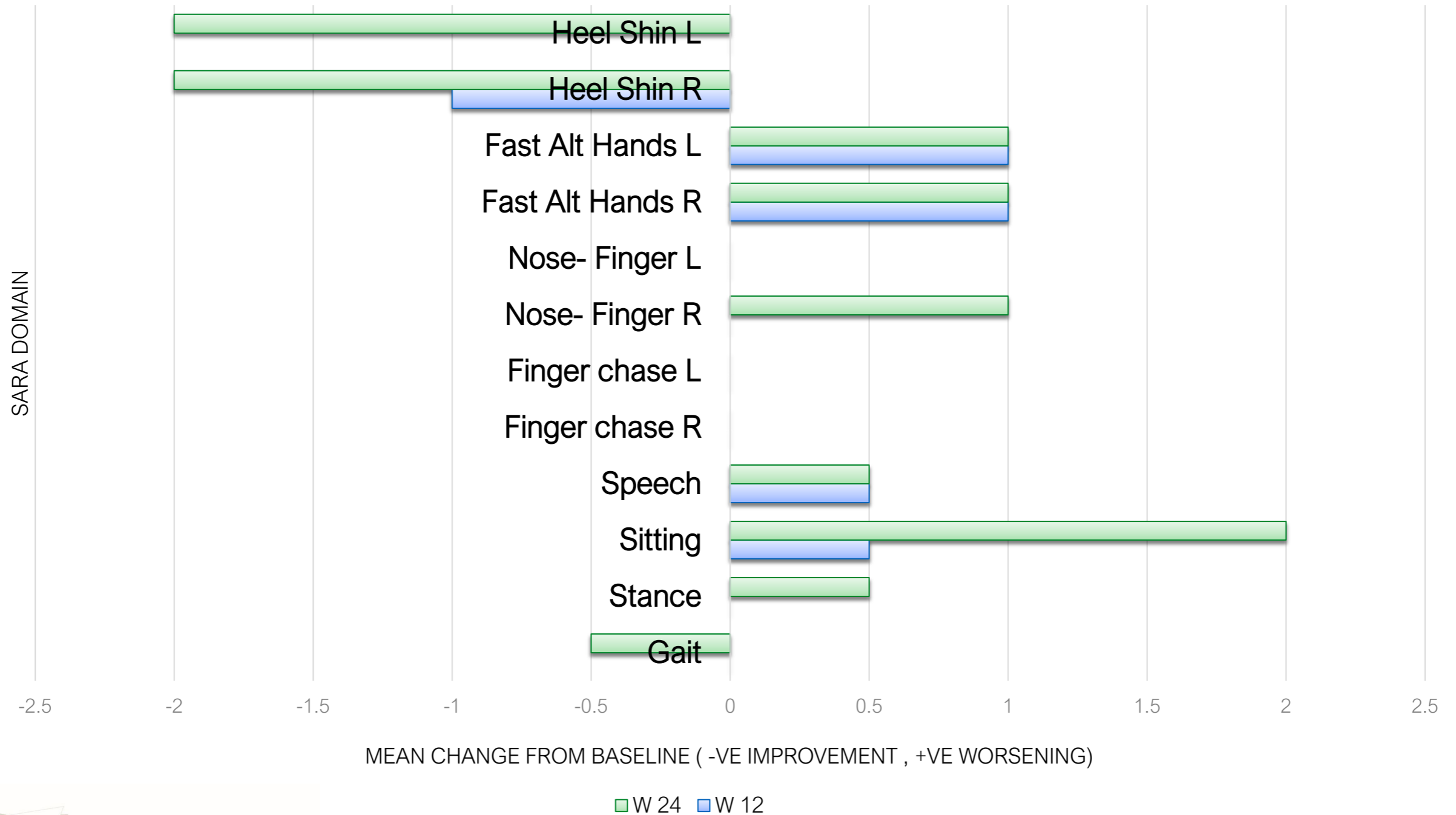
The one patient who worsened overall in total score also showed features of improvement

Not possible to correlate improvement in score to a specific dose group given interim nature of analysis.

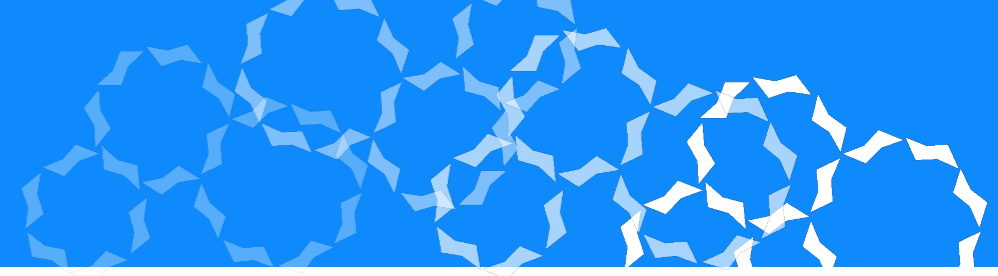


# Efficacy - Scale for Assessment and Rating of Ataxia: (SARA) 1500 mg/kg dose group

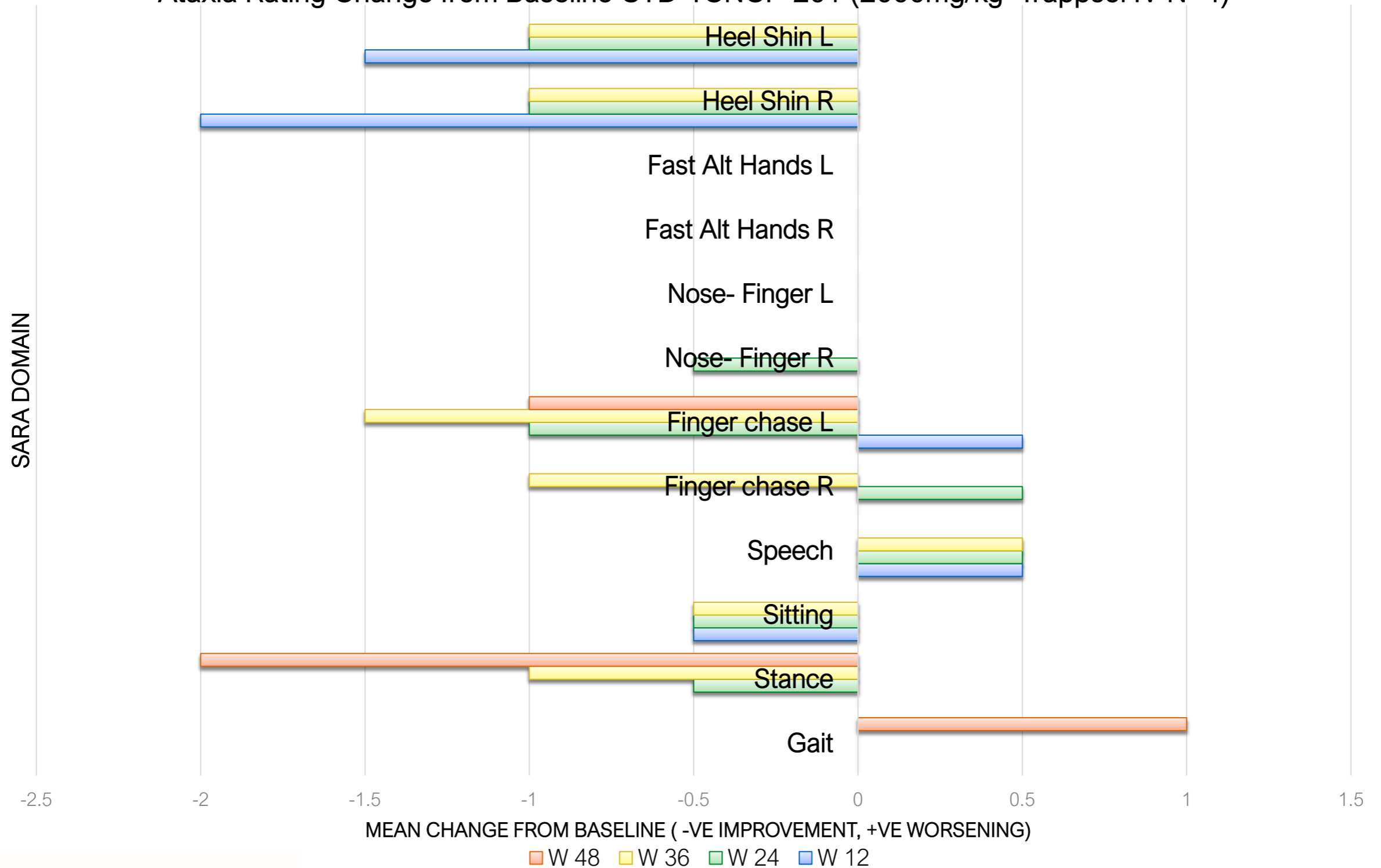
Ataxia Rating Change from Baseline CTD-TCNCP\_201 (1500mg/kg Trappsol IV n=5)



# SARA 2000 mg/kg dose group

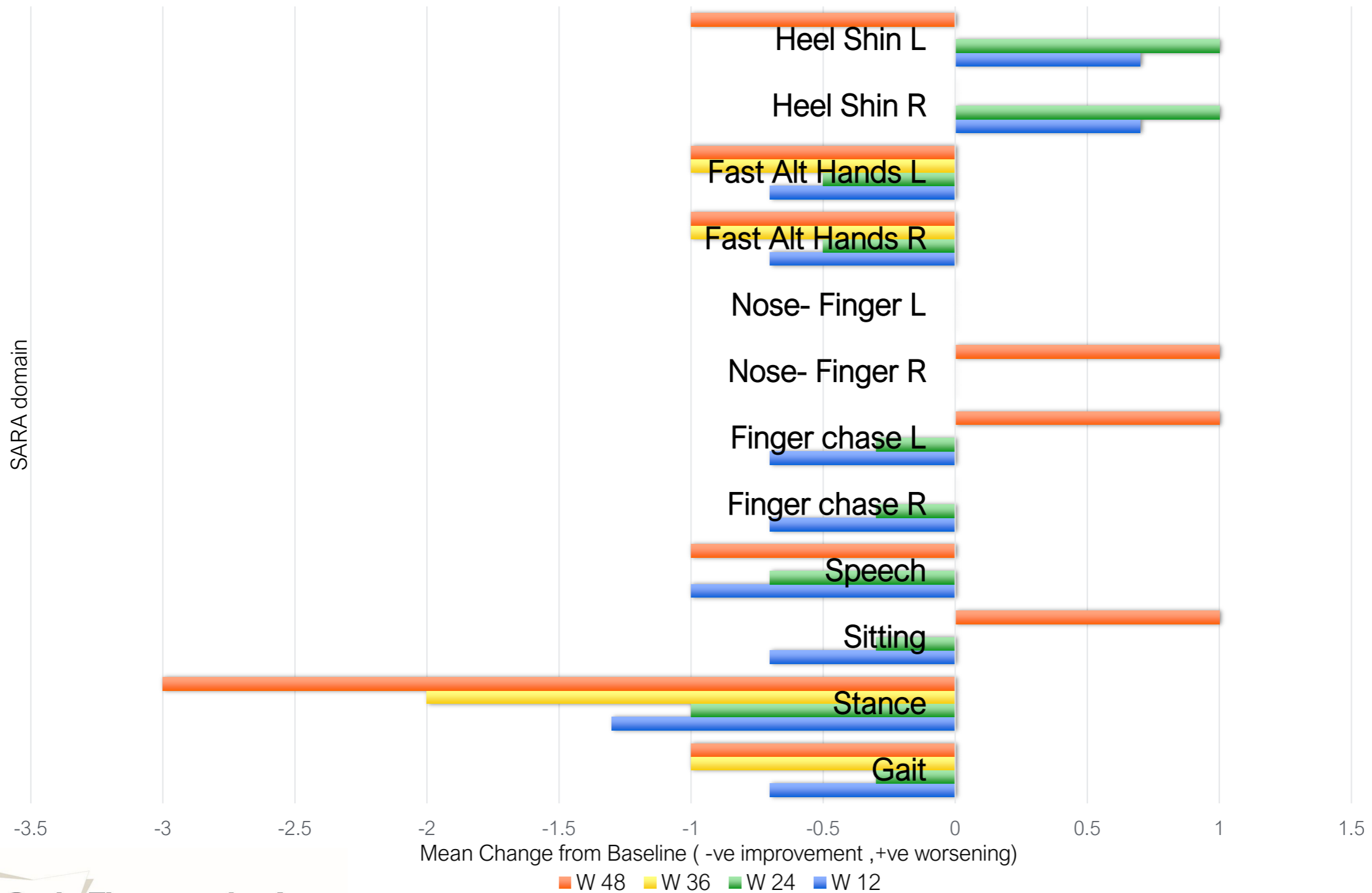


Ataxia Rating Change from Baseline CTD-TCNCP-201 (2000mg/kg Trappsol IV N=4)



# SARA 2500 mg/kg dose group

Ataxia Rating Change from Baseline in CTD-TCNCP-201( 2500mg/kg Trappsol IV n=3)



# Efficacy - Patient and Clinician Perspectives / Global Impressions of Change

**Patient, Family and Clinicians' Impressions of Benefit play a key role in regulatory approvals of orphan drugs.**

score	Patient Global Impression of Change (PGIC) Scale
1	No change (or worse)
2	Almost the same, hardly any change at all
3	A little better but no noticeable change
4	Somewhat better but the change has not made any real difference
5	Moderately better and a slight but noticeable change
6	Better and a definite improvement that has made a real and worthwhile difference
7	A great deal better and a considerable improvement that has made all the difference

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# Efficacy - Patient and Clinician Perspectives / Global Impressions of Change

**Patient, Family and Clinicians' Impressions of Benefit play a key role in regulatory approvals of orphan drugs.**

score	Patient Global Impression of Change (PGIC) Scale	Clinical Global Impression – Global Improvement (CGI –I) Scale	score
1	No change (or worse)	Very much worse	7
2	Almost the same, hardly any change at all	Much worse	6
3	A little better but no noticeable change	Minimally worse	5
4	Somewhat better but the change has not made any real difference	No change	4
5	Moderately better and a slight but noticeable change	Minimally improved	3
6	Better and a definite improvement that has made a real and worthwhile difference	Much improved	2
7	A great deal better and a considerable improvement that has made all the difference	Very much improved	1
		Not assessed	0



# Efficacy - Patient and Clinician Perspectives / Global Impressions of Change

**Patient, Family and Clinicians' Impressions of Benefit play a key role in regulatory approvals of orphan drugs.**

score	Patient Global Impression of Change (PGIC) Scale	Week 12	Week 24	Week 36	Clinical Global Impression – Global Improvement (CGI –I) Scale	score
		Scores of 2y subject				
1	No change (or worse)				Very much worse	7
2	Almost the same, hardly any change at all				Much worse	6
3	A little better but no noticeable change				Minimally worse	5
4	Somewhat better but the change has not made any real difference				No change	4
5	Moderately better and a slight but noticeable change				Minimally improved	3
6	Better and a definite improvement that has made a real and worthwhile difference	x			Much improved	2
7	A great deal better and a considerable improvement that has made all the difference		x	x	Very much improved	1
					Not assessed	0



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4	Somewhat better but the change has not made any real difference				No change	4
5	Moderately better and a slight but noticeable change	x			Minimally improved	3
6	Better and a definite improvement that has made a real and worthwhile difference	x	x	x	Much improved	2
7	A great deal better and a considerable improvement that has made all the difference		x	x	Very much improved	1
					Not assessed	0





# Efficacy - Patient and Clinician Perspectives

## Study Population (n=10) as of June 29, 2020

score	Patient Global Impression of Change (PGIC) Scale	Study population		Clinical Global Impression – Global Improvement (CGI –I) Scale	score
1	No change (or worse)	1 (2)		Very much worse	7
2	Almost the same, hardly any change at all			Much worse	6
3	A little better but no noticeable change	2	1	Minimally worse	5
4	Somewhat better but the change has not made any real difference	2	3	No change	4
5	Moderately better and a slight but noticeable change		2	Minimally improved	3
6	Better and a definite improvement that has made a real and worthwhile difference	2	3	Much improved	2
7	A great deal better and a considerable improvement that has made all the difference	1	1	Very much improved	1
				Not assessed	0

# Contact Information

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Thank You!