

## **PCR166: Supplementary Materials**

**Title:** Tremor Symptoms and Associated Activities of Daily Living Impacts in Essential Tremor: A Qualitative Concept Elicitation and Mapping Study

### **PAS-ET V1.0 – Overview of content**

- Patient reported outcome (PRO) instrument designed for administration in electronic format
- Designed for use in adult populations with essential tremor (ET)
- Developed by Sage Therapeutics in partnership with Acaster Lloyd. Included concepts were based on the content of The Essential tremor Rating Assessment Scale – Activities of Daily Living (TETRAS ADL) subscale<sup>1-3</sup>
- Assesses 10 tremor-related impacts on activities of daily living (ADLs; eating, drinking, hygiene, dressing, pouring, carrying items, writing, using keyboard/smartphone, using keys, working)
- Item stem 1: Respondents rate the importance of improving each ADL on a 5-point Likert scale (1 = 'Not at all important' to 5 = 'Extremely important')
- Item stem 2: Respondents are presented with all ADLs they indicated to be important (i.e., 2 = A little important to 5 = Extremely important) and select which is most important ADL to improve with treatment
- Item stem 3: Respondents rate their current ability to perform each ADL indicated to be important as well as overall ADLs on a numeric response scale (NRS; 0-10 integers; 0 = No problems, 10 = Cannot do) accompanied by illustrative verbal anchors (1-3 = Mild problems, 4-6 = Moderate problems, 7-9 = Severe problems)
- Item stem 4: At baseline administration, respondents are then asked to indicate the smallest improvement in their current score that would be meaningful to them on an NRS (0-10 integers)
- At post-baseline assessments, respondents complete only the items assessing their current ability on each ADL specified as important at baseline, and ADLs overall
- No recall period is specified, but the item 3 stem assesses 'current' ability to perform an ADL

### **MBS-ET V1.0 – Overview of content**

- PRO instrument designed for administration in electronic format
- Designed for use in adult populations with ET
- Developed by Sage Therapeutics. Included concepts were based on the content of the TETRAS<sup>1-3</sup>

- ‘Symptoms’ module: Consists of tremor locations (head, voice, right arm/hand tremor, left arm/hand tremor, right leg/foot tremor, left leg/foot tremor, other)
- ‘ADL’ module: Consists of tremor-related ADL impacts (eating, drinking, hygiene, dressing, pouring, using computer/smartphone, carrying items, writing, working, using keys, other)
- At baseline administration, respondents identify up to three symptoms and three ADLs that they find most bothersome, indicate the one symptom and ADL impact that is most bothersome and indicate the level of bother experienced
- Level of bother is assessed on a numeric response scale (NRS; 0-10 integers; with illustrative verbal anchors: 0 = ‘Doesn’t bother me at all’, 5 = ‘Bothers me sometimes’, 10 = ‘Bothers me all the time’)
- At post-baseline assessments, respondents complete only the items assessing bother on their 1-3 most bothersome symptoms and 1-3 most bothersome ADLs indicated at baseline
- Most items use a recall period of ‘the past 7 days’, apart from item stems 2 & 5 (Most bothersome symptom/ADL) where no recall period was specified.

## Methods

### Institutional Review Board (IRB) approval statement:

- This study was reviewed and approved by the WIRB-Copernicus Group (WCG) IRB on 19th October 2022 (tracking number: 20225601), with subsequent amendments as detailed below:
  - Amendment 1 (3rd November 2022): Study contact information revised
  - Amendment 2 (2nd March 2023)/3 (3rd April 2023)/4 (31<sup>st</sup> May 2023)/5 (12<sup>th</sup> July 2023): Unrelated to current poster

**Table 1. Participant inclusion/exclusion criteria**

Inclusion	Exclusion
<ul style="list-style-type: none"> <li>• Aged 18-80 years</li> <li>• Live in the US</li> <li>• Fluent in spoken and written English</li> <li>• Clinician confirmed diagnosis of essential tremor defined by the following criteria:               <ul style="list-style-type: none"> <li>○ Isolated tremor syndrome consisting</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Onset of tremor was associated with direct or indirect injury or trauma to the nervous system</li> <li>• Previous procedure for the treatment of essential tremor, deep brain stimulation, brain lesioning, or magnetic resonance (MR) guided procedure, e.g., MR-guided focused</li> </ul>

Inclusion	Exclusion
<p>of bilateral upper limb action tremor, with or without tremor in other locations</p> <ul style="list-style-type: none"> <li>○ At least 3 years duration</li> <li>• Had a severity of tremor score of 2 (mild) 3 (moderate) or 4 (severe) on the Clinician Global Impression Scale – Severity of illness (CGI-S)</li> <li>• Had a severity of activities of daily living score of 2 (mild problems), 3 (moderate problems), 4 (severe problems), or 5 (unable to do) on the Patient Global Impression of Severity - Activities of Daily Living (PGI-S ADL) at screening</li> <li>• Absence of other neurological signs, such as dystonia, ataxia, or parkinsonism, isolated focal tremors (e.g., voice, head), task- and position-specific tremors, sudden tremor onset or evidence of stepwise deterioration of tremor</li> <li>• Willing and able to provide consent to take part in a 60-minute audio-recorded interview</li> </ul>	<p>ultrasound</p> <ul style="list-style-type: none"> <li>• Individual had botulinum toxin for treatment of upper limb tremor within 6-months of screening</li> <li>• Historical or clinical evidence of tremor with psychogenic origin</li> <li>• Participant had currently active and medically significant or uncontrolled hepatic, renal, cardiovascular, pulmonary, gastrointestinal, hematological, immunologic and / or metabolic disease</li> <li>• Participant was currently undergoing treatment for oncologic disease at screening or is planned to commence treatment within the next 30-days, excluding skin cancers</li> <li>• Participant had a history of substance or alcohol dependence in the last 6-months</li> <li>• Was enrolled in a clinical trial at the time of recruitment</li> <li>• Previously enrolled in a clinical trial sponsored by Sage Therapeutics</li> </ul>

## Recruitment targets

**Table 2. Recruitment targets for age**

	≤65 years	66-80 years	GRAND TOTAL
Number of participants	7	13	20

**Table 3. Recruitment targets for PGI-S ADL score**

	2 - Mild	3 - Moderate	4 - Severe / 5 - Unable to do	GRAND TOTAL
Number of participants	5	10	5	20

Recruitment targets assumed a total sample of N=20 and were adjusted proportionally to the final sample size.

### Participant ID codes

IDs were allocated in chronological order as participants were consented (starting from P001). IDs contained participants PGI-S ADL score (MLD = 2 / Mild; MOD = 3 / Moderate; SEV = 4 / Severe).

### Interview process

- Interviews lasted approximately 60-minutes. Participants completed a background questionnaire at the start of the interview. The concept elicitation preceded the cognitive debriefing of two PRO instruments. The current poster summarises the concept elicitation findings only.
- Concept elicitation interviews followed a semi-structured interview guide and explored the experience of living with ET, including symptoms and associated impacts on ADLs.

## Results

**Table 4. Sample demographics characteristics from concept elicitation interviews**

Characteristic	Total (N=16)
	<b>Mean (range)</b>
<b>Age (years)</b>	66.13 (48-80) <b>Median</b> 68
	<b>N (%)</b>
<b>Age categories (years)</b>	
≤65 years	5 (31)
66-80 years	11 (69)
<b>Sex</b>	
Male	10 (63)
Female	6 (37)
<b>Transgender</b>	
No	14 (88)
Yes	1 (6)
Prefer not to state	1 (6)
<b>Race</b>	
White	11 (69)
Black or African American	2 (13)
Mixed or multiple ethnic groups	2 (13)
<b>Ethnicity</b>	
Hispanic/Latino	1 (6)
<b>Highest level of education</b>	
College or university degree	7 (44)
Graduate degree	4 (25)
High school diploma	3 (19)
Associates degree	1 (6)
Vocational school or other trade certificate	1 (6)
<b>Employment status<sup>1</sup></b>	

Characteristic	Total (N=16)
Retired	8 (50)
Employed full-time	3 (19)
Self-employed	3 (19)
Employed part-time	3 (19)
Full-time homemaker/caregiver	1 (6)

Note: R1/2/3 = Round 1/2/3; <sup>1</sup>The sum of counts exceeds the total as participants were able to select multiple responses. The sum percentages may be less or greater than 100 as all percentages are rounded to the nearest whole number (0.d.p)

**Table 6. Saturation matrix of concepts from CE interviews**

	P001-MOD	P004-MLD	P002-MOD	P005-SEV	P003-MOD	P007-MLD	P010-MLD	P011-SEV	P006-MLD	P008-MOD	P013-MOD	P012-MOD	P015-SEV	P014-SEV	P016-MLD	P009-MOD
Symptoms																
Upper limb tremor	P	P	S	S	S	S	S	S	S	S	P	P	S	S	S	S
Lower limb tremor	P		P			S				S		P	P	P		
Head tremor	P												P		S	
Voice tremor													P			
Activities of Daily Living																
Fine motor tasks	S	S	S	S	P	S		S	S	S	S		S		S	P
Self-care	S			S			S	S		S			S	S		
Work / housework	P	S					S						S	S		
Cooking			S			S			S	S			S			
Driving			S			S										
Shopping						S										
Drinking	P			S					P		S	S		P		
Eating	P									S	P	S	P	P		S

Note: **Magenta** cells indicate first spontaneous report of a concept. **Grey** cells indicate participant reported no experiencing this symptom / impact, or this concept was not discussed during the concept elicitation portion of the interview; S= concept spontaneously reported by the participant; P= concept discussed when probed by the interviewer

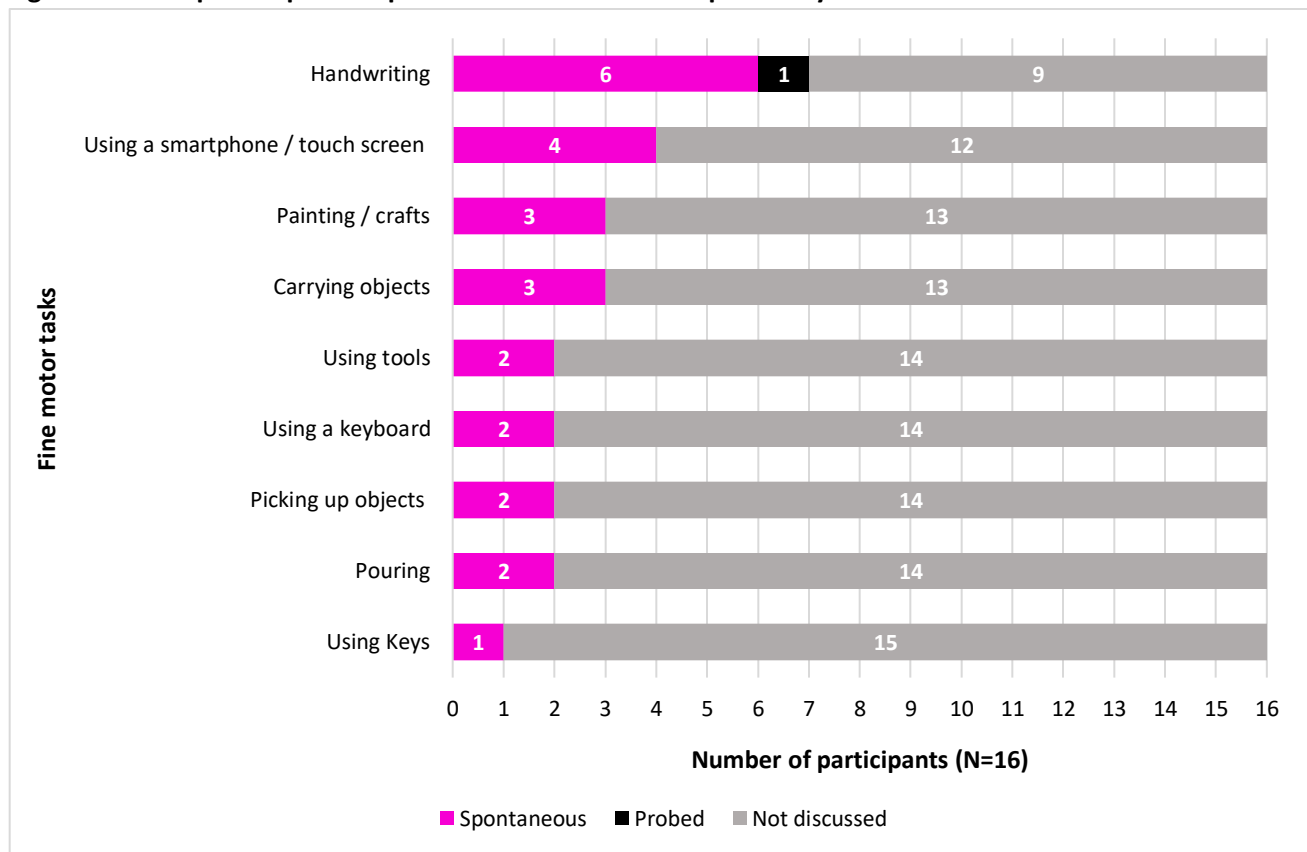
**Table 7. Saturation matrix of specific fine motor tasks from CE interviews**

	P001-MOD	P004-MLD	P002-MOD	P005-SEV	P003-MOD	P007-MLD	P010-MLD	P011-SEV	P006-MLD	P008-MOD	P013-MOD	P012-MOD	P015-SEV	P014-SEV	P016-MLD	P009-MOD
Using a keyboard	S									S						
Handwriting	S				S				S	S	S				S	P
Painting / crafts		S			S				S							
Using a smartphone / touch screen			S	S						S	S					
Carrying objects					S						S					S
Using keys								S								
Pouring								S		S						
Using tools								S		S						
Picking up objects								S					S			

Note: **Magenta** cells indicate first spontaneous report of a concept. **Grey** cells indicate participant reported no experiencing this symptom / impact, or this concept was not discussed during the concept elicitation portion of the interview; S= concept spontaneously reported by the participant; P= concept discussed when probed by the interviewer



**Figure 1. Participant-reported specific fine motor tasks impacted by ET**



## References

### Supplementary materials

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### Poster

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