

SING: A Novel Tool for Dietary Management and Monitoring in Clinical Trials of Pegtibatase, an Investigational Enzyme Replacement Therapy for Classical Homocystinuria

Elaina Jurecki¹; Sommer Gaughan²; Sandra Van Calcar³; Lauren Dwyer⁴; John Shea⁵; Kassi Swallow⁶

¹Pharmaceutical Consultant, San Ramon, CA, USA; ²Department of Clinical Genetics and Metabolism, University of Colorado, Denver, CO, USA; ³Department of Molecular and Medical Genetics, Oregon Health & Science University, Portland, OR, USA; ⁴Traverse Therapeutics Inc., San Diego, CA, USA; ⁵Former employee, Traverse Therapeutics Inc., San Diego, CA, USA; ⁶Pharmaceutical Consultant, Saco, ME, USA

INTRODUCTION

Classical homocystinuria (HCU) is a rare, metabolic condition characterized by deficiency of cystathionine β -synthase deficiency and accumulation of homocysteine (Hcy) and methionine (Met) in plasma and tissues^{1,2,3}

HCU is associated with risk of severe multisystemic complications including stroke, cognitive impairment, developmental delays, and ocular and skeletal abnormalities^{1,2,4}

Current standard of care (SOC) treatments include a protein-restricted diet and supplementation with Met-free metabolic formula, pyridoxine (vitamin B6), and betaine.^{2,5} These treatments can impact quality of life and can be challenging for patient adherence²

Pegtibatase is an investigational enzyme replacement therapy in development for the treatment of HCU⁵

To determine the efficacy of novel treatments such as pegtibatase in clinical trials, it is crucial for participants to stabilize and maintain their typical diet and medication intake throughout all study periods

Conventionally, HCU dietary monitoring involves a 3-day diet record, completed by the participant, which captures intake over a limited duration. However, this has been reported as time-consuming for participants, and is often inaccurate, partially complete, or not completed at all

To support the pegtibatase Phase 3 clinical trial programs, a need was identified for a simpler, more robust, and accurate diet monitoring tool for use in clinical trials of HCU treatments

METHODS

A panel of five metabolic dietitians with HCU experience was assembled and tasked with developing an improved method of dietary monitoring for HCU. They were focused specifically on addressing the challenges identified with the 3-day diet record including:

- Participant burden associated with recording food intake
- Incomplete/inaccurate or missing records of diet diaries

The goal was to leverage existing dietary intake methods, including food frequency questionnaires (FFQs), to create a new tool to accurately estimate daily intact protein intake (DIPI), yet be simple and efficient to use in the clinical setting. The aims of this tool are to:

- Reduce participant burden by having the dietitian complete the documents
- Obtain more complete and accurate information regarding dietary intake
- Collect dietary data to better assess the impact of diet vs the investigational drug on biochemical data
- Enable review of previous records and track changes to assist with monitoring diet stability and participant education around maintaining stable protein intake

A combined 24-hour recall and FFQ approach has previously shown potential as a methodology for obtaining dietary histories and reducing reporting and recall bias⁶

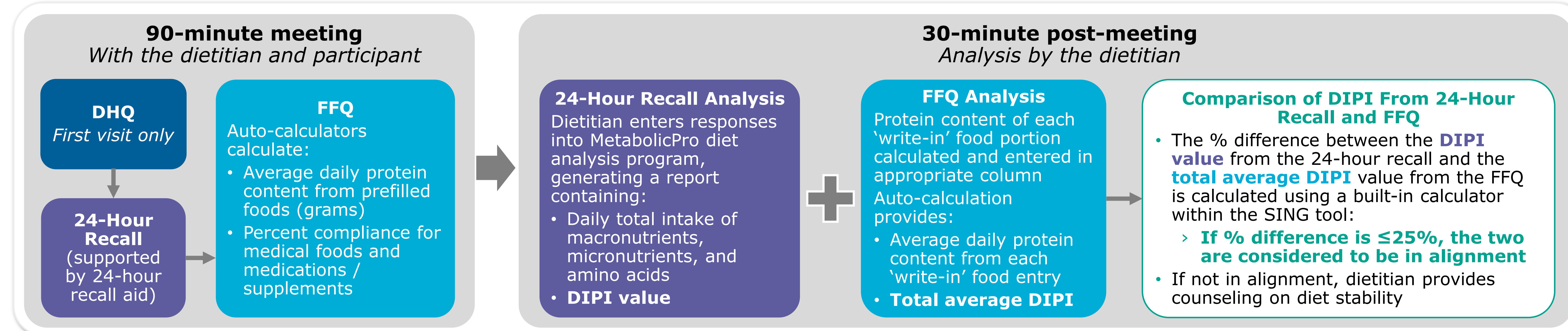
Once developed, the new tool was tested by the dietitian panel to assess accuracy and ease of use

CONCLUSIONS

- ✓ The SING tool is a novel HCU-specific diet assessment tool developed by a panel of dietitians in collaboration with industry partners for pegtibatase Phase 3 clinical trials
- ✓ SING tracks changes made from previous assessments to assist with monitoring diet stability and can provide information for participant education on stable protein intake
- ✓ The SING tool will be further evaluated in upcoming Phase 3 clinical trials of pegtibatase during the DSP and treatment period, and could potentially be used in a clinical setting in the future

RESULTS

Figure 1. The Simplified Ingested Nutrients Guide (SING) Tool



DHQ, Diet Habits Questionnaire; DIPI, dietary intact protein intake; FFQ, food frequency questionnaire; SING, Simplified Ingested Nutrients Guide.

The SING Tool

- The SING tool is a novel HCU-specific diet assessment tool combining a 24-hour recall and HCU-specific elements of an FFQ, developed for use in clinical trials
- The SING tool is designed to be completed by a dietitian within a 90-minute meeting with the study participant plus 30-minute post-meeting analysis (Figure 1, Figure 2)

24-Hour Recall

- During the study visit, the dietitian will collect recall of all food, drink, and medical food consumed in the previous 24 hours, for the most accurate recall
- The dietitian will collect as many details as possible and ask if this represents a typical day of intake; if not, further details will be collected
- A simple, double-sided, 24-hour recall aid is provided to the participant at the first study visit to encourage them to record what they eat, and any medications taken in a format that suits them (eg, photos, notes on their phone, or on the recall aid)
- The aid will not be collected and is for the participant only

FFQ

- During the study visit, the dietitian reviews the FFQ responses with the participant collecting their intake of protein-containing foods and medications/ supplements over the previous week
 - Specific food groups (eg, apples, cucumbers, olive oil, and sugar-sweetened beverages) that do not contain significant amounts of protein are excluded
 - All foods refer to regular/high-protein versions and not specifically modified low-protein counterparts unless specified
 - Foods with >1 gram of protein/serving are included
- Does not capture kilocalorie, macronutrient, micronutrient, or amino acid intake

Figure 2. FFQ Analysis

FFQ portion of SING (Simplified Ingested Nutrients Guide)			Date of visit: MONTH-DAY-YEAR	Participant ID:	Name of dietitian:		
Food	Protein (g) in standard portion	Standard Portion/ Serving size (English, metric units)	Did not consume in the past week.	Amount of standard portion (SP) consumed by participant (1/2 SP, SP, 2x SP, 3x SP, 4x SP - circle or click one?)	Number of times consumed in the past week	Other/ Notes	Average daily protein content of food item in grams
Prefilled Foods							
Fruits							
High protein fruit (e.g. bananas, oranges, orange juice, peaches, pomegranate seeds, raisins)	1.38	1 fruit; 1/2 cup diced or sliced; 8 ounces juice; 1/4 cup dried fruit		1	5		0.99
Vegetables							
Moderate protein vegetables: (e.g. broccoli, brussels sprouts, cauliflower, green beans, kale (cooked))	1.48	1/2 cup		2	4		1.69
High protein vegetables: corn, peas, spinach (cooked)	3.17	1/2 cup		1	2		0.91
Potatoes (white or sweet)	1.12	1/2 cup		2	2		0.64
Write-In Foods							
What type of snack foods have you consumed over the past week? (e.g. snack bars, pretzels, chips, crackers, cookies)	Protein (g) in standard portion	Standard Portion/ Serving size (English, metric units)	Did not consume in the past week.	Amount of standard portion (SP) consumed by participant (1/2 SP, SP, 2x SP, 3x SP, 4x SP - circle or click one?)	Number of times consumed in the past week	Other/ Notes	Average daily protein content of food item in grams
Snyder's pretzel sticks	3	1 oz / 26 sticks		2	5		4.29
Kind bar, chocolate cherry cashew	4	1 bar		1	3		1.71
							0.00

FFQ, food frequency questionnaire.

Refinement of the SING Tool

- The tool was refined following initial testing by the dietitian panel to add:
 - A Diet Habits Questionnaire (DHQ) for completion at the first visit only, to aid dietitians when they are unfamiliar with the participant and their dietary and medical history. This was added to help dietitians identify who may need additional counseling to maintain diet stability and to provide the source materials required for electronic data capture
 - A built-in calculator to assist the dietitian in determining the degree of alignment between the 24-hour recall and the FFQ

Next Steps in Optimizing Use of the SING Tool: Incorporating in Upcoming Phase 3 Studies

- The SING tool will be used prior to randomization, during the diet standardization period (DSP) and treatment period of the HARMONY and ENSEMBLE Phase 3 studies
 - HARMONY is a global, Phase 3, multicenter, multinational, randomized, blinded, placebo-controlled trial of SOC plus pegtibatase in participants with HCU
 - ENSEMBLE is a global, Phase 3, multicenter, single-arm, open-label, long-term extension study to assess the long-term safety and efficacy of pegtibatase in participants with HCU receiving SOC
- The DSP is designed to understand and stabilize participant's typical diet, medical food, and medication and supplement intake, to minimize variability during the randomized portion of the studies and enable accurate interpretation of the treatment effect without influence from fluctuations in total Hcy (tHcy) levels from variable protein intake and HCU medications
- The SING tool will be used by study-site dietitians during the DSP and treatment period to:
 - Conduct a 24-hour recall and FFQ
 - Counsel on the importance of stable diet and medication/supplement use
 - Determine participant eligibility for randomization to treatment following the DSP
- A central dietitian will provide training on the SING tool and will also be available for support throughout the studies

Case Study: SING Tool Used With Patient at DSP Visit 1

- The SING tool was used with an adult male patient at an initial DSP visit, with the following results:
 - The DHQ demonstrated that the participant was well versed on their current HCU management
 - 24-hour recall reflected a typical day of intake
 - The FFQ highlighted good compliance with HCU medications
 - The built-in calculator determined alignment between protein content captured by the 24-hour recall and FFQ with a difference of 2.6%
- The post-visit analysis took longer than the expected 30 minutes
- This case highlights the sensitivity of SING for dietary monitoring and shows that more time may be required, and should be set aside, to complete the initial study visit

ABBREVIATIONS

DHQ, Diet Habits Questionnaire; DIPI, dietary intact protein intake; DSP, diet standardization period; FFQ, food frequency questionnaire; HCU, classical homocystinuria; Hcy, homocysteine; Met, methionine; SING, Simplified Ingested Nutrients Guide; SOC, standard of care; tHcy, total Hcy.

DISCLOSURES

EJ, SG, SVC, KS: Consultant, Traverse Therapeutics, Inc. LD: Employee, Traverse Therapeutics, Inc. JS: Former employee, Traverse Therapeutics, Inc.

ACKNOWLEDGMENTS

We would like to thank Hiral Dave, Liz Wilkening, and Sagar Vaidya for their valuable insights. This study was supported by Traverse Therapeutics, Inc. (San Diego, CA, USA). Medical writing assistance was provided by Emmaline Tregembo of LINK Health Group and was funded by Traverse Therapeutics, Inc. We also thank Heather Hartley-Thorne of Sephirus Communications, Inc. for her valuable contributions to data visualization.

REFERENCES

- Mudd SH, et al. *Am J Hum Genet.* 1985;37(1):1-31.
- Morris AA, et al. *J Inher Metab Dis.* 2017;40(1):49-74.
- Weber Hoss GR, et al. *Mol Genet Genomic Med.* 2020;8(6):e1214.
- Sacharow SJ, et al. In: Adam MP, et al., eds. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle 1993-2024 [Updated 2017].
- Bublil EM, Majtan T. *Biochimie.* 2020;173:48-56.
- Looman M, et al. *Public Health Nutr.* 2019;22:2738-2746.

To obtain a PDF of this poster:



Scan the QR code OR visit www.travererepublications.com/GMDI2024/16

Charges may apply.

No personal information is stored.