GOunder/Desmoid Tumor Research Foundation DEsmoid Symptom/Impact Scale (GODDESS): Psychometric Properties and Clinically Meaningful Thresholds as assessed in the Phase 3 DeFi Randomized Controlled Clinical Trial

Mrinal M. Gounder, MD[1]; Thomas M. Atkinson, PhD[1]; Timothy Bell[2]; Christina Daskalopoulou, PhD[3]; Pip Griffiths, PhD[4]; Moriah Martindale[1]; Allison Lim, PharmD[2]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, United States; [2]SpringWorks Therapeutics, Stamford, CT, United States; [3]IQVIA, Patient-Centered Solutions, Athens, Greece; [4]IQVIA, Patient-Centered Solutions, Paris, France

BACKGROUND

- Desmoid tumors (DT) are locally aggressive tumors of the soft tissues associated with significant symptom and impact burden that can impact patients overall patients' health-related quality of life (HRQoL)
- Treatment of DT requires a multidisciplinary approach to create an overall treatment plan with the goal of improving both clinical indicators, such as progression-free survival and objective response, as well as patient relevant endpoints such as DT- specific symptom burden (e.g., pain) and its impact on patients' lives, functioning with everyday activities, and overall health-related quality of life
- Given the need to capture the patients' symptom and impact burden of DT, the Gounder/DTRF Desmoid Symptom/ Impact Scale (GODDESS) patient reported outcome (PRO) tool was developed

OBJECTIVE

- DeFi study data were used to assess the psychometric measurement properties and clinically meaningful change thresholds (MCT) of GODDESS and to establish GODDESS as a fit-for-purpose PRO tool for the evaluation of symptoms and impacts in patients with DT

METHODS

- Analysis of patient responses to the GODDESS tool was conducted using blinded data from DeFi, a placebo-controlled, Phase 3 study of nirogacestat in adults with DT/ aggressive fibromatosis (NCT03785964)
- Select analyses reported here were conducted to answer the following study questions:
  - Which GODDESS questions can be combined to create a multi-item scale (e.g., the concept of pain)?
  - Are results from GODDESS consistent with other well-known patient reported outcomes tools (e.g., Brief Pain Inventory Short Form [BPI-SF], Patient-Reported Outcomes Measurement Information System Physical Function [PROMIS-PF], and European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 [EORTC QLQ-C30]) when measuring similar concepts?
  - Are results from GODDESS clinically meaningful?

GODDESS TOOL DEVELOPMENT

- The GODDESS tool was developed by Memorial Sloan Kettering Cancer Center (MSKCC) and Desmoid Tumor Research Foundation (DTRF) using best practices and is the first disease-specific PRO instrument for desmoid tumors
- Based on multiple rounds of DT patient interviews, the final version of the GODDESS tool was created, which is a 28- item questionnaire that was developed according to the US Food and Drug Administration guidance on developing PRO tools for a disease-specific PRO instrument (Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims, December 2009)

Step 1
Identify DT-specific questions and develop draft PRO tool[1]

→

Step 2
Test measurement properties and confirm it is "fit-for-purpose"

GODDESS DESMOID TUMOR SYMPTOM SCALE (DTSS)[1]

- GODDESS DTSS consists of 11 questions that assess the severity of key signs and symptoms including:
  - Pain, fatigue, swelling, muscle weakness, difficulty moving (items 1-7);
  - A question referring to tumor location (item 8); and
  - Intra-abdominal specific signs/symptoms (items 9-11) administered only to those reporting intra-abdominal tumor location in item 8
- DTSS items 1-7 and 9-11 are evaluated on an 11-point numeric rating scale (NRS) from 0-10 to measure severity from "none" to "as bad as you can imagine", with a 24-hour recall period; item 8 asks for the specific location of the desmoid tumor
- Higher scores indicate more severe symptom burden

GODDESS DESMOID TUMOR IMPACT SCALE (DTIS)[1]

- GODDESS DTIS consists of 17 items that assess the impact of symptoms on functioning and daily living
- DTIS items are evaluated either on:
  - A 5-point Likert scale ranging from "none of the time" to "all of the time" to measure frequency (items 1-9), or
  - An 11-point NRS from 0-10 to measure severity from "none" to "as bad as you can imagine" (items 10-17), with a 7-day recall period
- Higher scores indicate more severe impact

RESULTS

WHICH GODDESS QUESTIONS CAN BE COMBINED TO CREATE A MULTI-ITEM DOMAIN?

Results from the analysis suggest that the following domains may be created:

GODDESS DTSS

Total Symptom Score
- Combination of items 1-7 (pain, dull pain, shooting pain, fatigue, swelling, muscle weakness, difficulty moving)

Pain Domain
- Combination of items 1-3 (pain, dull pain, shooting pain)

Extra-abdominal Domain
- Combination of items 5-7 (swelling, muscle weakness, difficulty moving)

Intra-abdominal Domain
- Combination of items 9-11 (abdominal pain, nausea, fullness)

GODDESS DTIS

Physical Functioning Impact
- Combination of items 1, 2, 6, 7, 8 (moving, reaching [frequency], vigorous activity, moderate activity, accomplished less)

Sleep Impact
- Combination of items 3-5 (falling asleep, comfortable in bed, staying asleep)

Emotional Impact
- Combination of items 12-17 (fear tests, fear growth/recurrence, hopelessness, anger, anxiety, frustration)

ARE RESULTS FROM GODDESS CONSISTENT WITH OTHER WELL-KNOWN PRO TOOLS WHEN MEASURING SIMILAR CONCEPTS?

GODDESS DTSS

- Moderate to strong correlations (i.e., a positive relationship between two different tools measuring the same concept) of DTSS and domain scores (i.e., pain, extra-abdominal, intra-abdominal) were observed with similar concepts from other PRO tools

For example
- DTSS Pain Domain and BPI-SF Worst Pain (strong)
- DTSS Pain Domain and EORTC QLQ-C30 Pain subscale (strong)
- DTSS Intra-Abdominal Domain and EORTC QLQ-C30 Nausea & Vomiting subscale (moderate)

GODDESS DTIS

- Moderate to strong correlations of DTIS physical, sleep, and emotional impacts also were observed with similar concepts from other PRO tools

For example
- DTSS Physical Functioning Impact and PROMIS-PF Trouble Doing Regular Work (strong)
- DTSS Sleep Impact and EORTC QLQ-C30 Insomnia subscale (strong)
- DTSS Emotional Impact and EORTC QLQ-C30 Emotional Functioning (moderate)

HOW DO I KNOW WHEN RESULTS FROM GODDESS ARE CLINICALLY MEANINGFUL?

Conservative estimates of between-group clinically meaningful change thresholds

GODDESS DTSS

Total Symptom Score
- A change in mean scores of ≥ 1.0 signifies a clinically meaningful difference between 2 groups

Pain Domain
- ≥ 1.2 points

Extra-abdominal Domain
- ≥ 1.0 points

Intra-abdominal Domain
- Number of persons indicating minimal improvement was too low to allow confident recommendations

GODDESS DTIS

Physical Functioning Impact
- ≥ 0.5 points

Sleep Impact
- ≥ 0.5 points

Emotional Impact
- ≥ 2.0 points

CONCLUSIONS

- The GODDESS tool comprises two scales (DTSS and DTIS), with the following domains:
  - DTSS total symptom score, DTSS pain domain, DTSS intra-abdominal domain, and extra-abdominal domain;
  - DTIS physical functioning impact, DTIS sleep impact, and DTIS emotional impact
- The GODDESS results were consistent with other well-known PRO tools (e.g., BPI-SF, PROMIS-PF, and EORTC QLQ-C30) where expected; this provides confidence that the proposed GODDESS domains measure the concepts they were hypothesized to measure
- Conservative estimates of between-group clinically meaningful change thresholds were identified as 1.00 for the DTSS total symptom score and extra-abdominal domain, and 1.20 points for the DTSS pain domain. For the DTIS, a threshold of 0.50 was estimated for physical functioning and sleep impact, and 2.00 for emotional impact
- Results from this study suggests that the GODDESS is a fit-for-purpose PRO tool to assess DT symptom and impact severity improvement

REFERENCES: 1. Gounder MM, Maddux L, Paty J, Atkinson TM. *Cancer* 2020;126:531-9.

FUNDING: SpringWorks Therapeutics, Stamford, CT, USA, provided funding to IQVIA conduct this study and was involved in reviewing this poster.

DISCLOSURES: Mrinal Gounder: Consulting or Advisory Role - Springworks Therapeutics; Patents, Royalties, Other Intellectual Property - GODDESS PRO Desmoid Tumor (Institutional); Other Relationship - Desmoid Tumor Research Foundation. **Timothy Bell** and **Allison Lim** are employees of SpringWorks Therapeutics and hold equity in SpringWorks Therapeutics.

CONTACT INFORMATION

Timothy Bell, MHA
SpringWorks Therapeutics

Phone: 919-698-3583
Email: Timothy.Bell@springworkstx.com

Presented at 2022 Desmoid Tumor Research Foundation (DTRF) Virtual Weekend • September 23-25, 2022 • Virtual