Development and Validation of the Ig Patient Experience With Treatment (IgPET), A Novel Patient-reported Measure for Individuals With Primary Immunodeficiency Disease

Dana DiBenedetti,[1] Lori McLeod,[1] Nicole Williams,[1] Theresa Coles,[1] Spiros Tzivelekis,[2] Lisa M. Meckley[2]*

[1]RTI Health Solutions, Research Triangle Park, NC, USA; [2]The Takeda group of companies , Cambridge, MA, USA
*Affiliation at the time of the study

Background

- Primary immunodeficiency disease (PID) describes a group of more than 350 genetic conditions in which the immune system is impaired or absent[1]
  - Individuals with PID are susceptible to repeated and severe infections that may become fatal, resulting in significant morbidity and mortality[2]
- Some patients with PID receive lifelong intravenous or subcutaneous immunoglobulin replacement therapy (IgRT), administered in a home or clinical setting[2]
  - IgRT has been shown to improve survival and health-related quality of life overall; however, aspects of patient experiences may vary depending on the type of IgRT chosen[3,4]
- A better understanding of patient experiences with IgRT may facilitate IgRT individualization and ultimately help optimize satisfaction with IgRT and treatment adherence
- Different self-reported instruments are available to measure various aspects of the patient experience
  - Both the Life Quality Index (LQI),[5] a measure of treatment satisfaction in patients with PID on IgRT, and the Treatment Satisfaction Questionnaire for Medication, 9 questions (TSQM-9),[6] a generic treatment satisfaction instrument, have been used in clinical trials and observational studies of IgRT
- The Ig Patient Experience with Treatment (IgPET) instrument is a novel patient-reported measure of patient experiences with IgRT

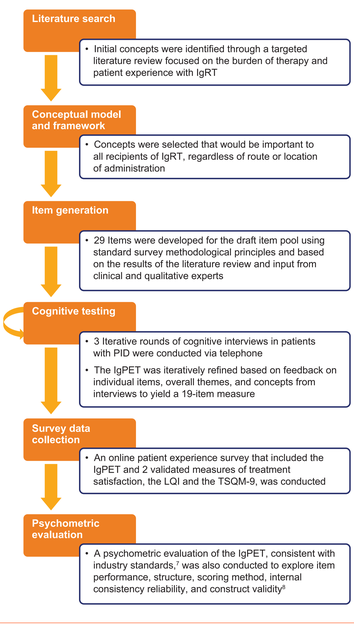
Objective

- To develop and psychometrically evaluate the IgPET instrument and to understand the overall patient experience with IgRT

Methods

- The key steps in the development and evaluation of the IgPET instrument are presented in **Figure 1**
- RTI International's Institutional Review Board approved the cognitive debriefing and online survey study protocols and materials

Figure 1. Key Steps in IgPET Development



IgPET, Ig Patient Experience with Treatment; IgRT, immunoglobulin replacement therapy; LQI, Life Quality Index; TSQM-9, Treatment Satisfaction Questionnaire for Medication 9 questions.

Table 1. Study Design and Eligibility Criteria

	Cognitive Testing	Survey Data Collection
Study type	• 3 Iterative rounds of interviews conducted via telephone	• Noninterventional, cross-sectional, web-based survey
Participant recruitment	• Participants recruited via a patient panel from Rare Patient Voice	• Email invitation sent via Immune Deficiency Foundation to ~7400 members
Eligibility criteria	• Self-reported a PID diagnosis that was given by a physician or other HCP • Self-reported current use of IgRT for PID • ≥16 Years old • Able to read, speak, and understand English	• Self-reported PID and use of IgRT • ≥18 Years old • Could understand and provide consent • Able to complete survey in English
Data collection	• Conducted in April and May 2017 • Concept elicitation focused on patients' experiences with IgRT • Full cognitive debriefing of the IgPET measure	• Conducted over 6 weeks in July and August 2017 • 3 PRO measures (IgPET, LQI, and TSQM-9) were administered **(Table 2)**

HCP; healthcare professional; Ig, immunoglobulin; IgRT, immunoglobulin replacement therapy; LQI, Life Quality Index; PID, primary immunodeficiency disease; PRO, patient-reported outcome; TSQM-9, Treatment Satisfaction Questionnaire for Medication , 9 questions.

Table 2. Measures Included in Patient Experience Surveys

Measure	No. of Items	Content	Recall Period	Response Scale	Score Range, Interpretation
Ig Patient Experience with Treatment Questionnaire (IgPET)	19	3 Subscales: • Convenience • Control • Impacts and Interference 3 stand-alone informative items	Current experiences	5-point ordered response scales: "Strongly agree" to "Strongly disagree" or "Not at all" to "An extreme amount"	1 to 5 Higher scores = better treatment experiences
Life Quality Index (LQI)	15	3 Subscales: • Treatment Interference • Therapy-related Problems • Therapy Settings	Current treatment satisfaction	7-point scale with different anchors per item	0 to 100 Higher scores = greater treatment satisfaction
Treatment Satisfaction Questionnaire for Medication, 9 questions (TSQM-9)	9	3 subscales: • Effectiveness • Convenience • Global Satisfaction	"Over the last 2 to 3 weeks, or since you last used it [Ig medication]"	5- or 7-point anchors	0 to 100 Higher scores = greater treatment satisfaction

Results

Cognitive testing

- Across 3 rounds, a total of 21 interviews were conducted in a mostly female (n=19, 90.5%) and white (n=20, 95.2%) sample, which had a mean age of 42.5 years (range: 17-70 years)
- Generally, interview participants stated that they did not consider their IgRT to be burdensome, therefore the term "burden" was removed from all draft items
- 95% reported at least 1 negative impact of IgRT, with the most commonly reported being side effects (n=11) and impact on social/family activities (n=6)
- IgPET was iteratively refined based on participant feedback, yielding a 19-item measure

Survey data collection

- The online survey was administered to 814 eligible US adults with self-reported PID currently receiving IgRT (of 1086 screened)
- Demographic and clinical characteristics for the 814 patients who met inclusion and exclusion criteria and completed the survey are shown in **Table 3**
- **Figure 2** illustrates the mean IgPET item scores and frequency distribution for each IgPET item based on the survey sample
  - Respondents used the entire range of the IgPET scale from 1 ("strongly agree"/"an extreme amount") to 5 ("strongly disagree"/"not at all") when they considered each item
  - Respondents rated the location of their IgRT and their treatment nurses higher (ie, as better treatment experiences) on average (mean, 4.4 for both items) than any other IgPET items
- 2 Items had a mean score ≤3, indicating neutral to negative responses (**Figure 2**):
  - For the statement, "I am worried about the side effects associated with my Ig treatments," 40% of patients responded with "agree" or "strongly agree" (mean score: 3.0)
  - For the question, "How much do you worry about the costs of your Ig treatment?" 50% of patients responded with "a great deal" or "an extreme amount" (mean score: 2.7)

Psychometric evaluation

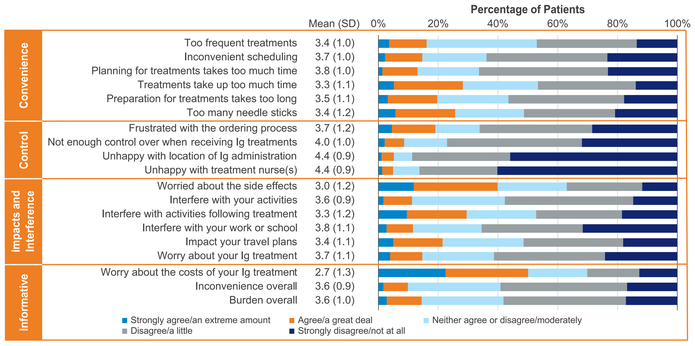
- Results of the psychometric evaluation indicate that the IgPET instrument is an appropriate PRO measure for patients with PID and receiving IgRT[8]
- Factor analysis (exploratory and confirmatory) supported 3 subscales: Control, Convenience, and Impacts and Interference (mean subscale scores shown in **Figure 3**)

Table 3. Patient Demographic and Clinical Characteristics

Patient Characteristic	Frequency	%[a]
Age, years		
18-64	632	77.6
≥65	182	22.4
Sex		
Male	128	15.7
Female	683	83.9
Prefer not to answer	3	0.4
Race/ethnicity[b]		
White	779	95.7
African-American or Black	5	0.6
American Indian	10	1.2
Asian	2	0.2
Mixed race (2 or more races)	17	2.1
Other or prefer not to answer	18	2.2
Current employment status[b]		
Full-time	279	34.3
Part-time	93	11.4
Student	30	3.7
Not employed but looking for employment	19	2.3
Not employed due to disability	176	21.6
Retired	188	23.1
Other or prefer not to answer	51	6.3
Highest level of education		
Less than high school	4	0.5
High school diploma or equivalent (GED)	48	5.9
Some college, associate degree, or technical school	252	31.0
College degree (eg, BA or BS)	264	32.6
Professional or graduate degree (eg, MS, MD, PhD, JD)	236	29.1
Other	7	0.9
Missing	3	0.4
Type of health insurance coverage[b]		
Private insurance or health plan	631	77.5
Medicare	272	33.4
Medicaid	45	5.5
Military-related health care	39	4.8
Other	29	3.6
Not sure	2	0.2
Route of immunoglobulin administration		
Subcutaneous	479	58.8
Intravenous	335	41.2
Location of immunoglobulin administration		
Home	606	74.4
Other (eg, clinic or other medical facility)	208	25.6

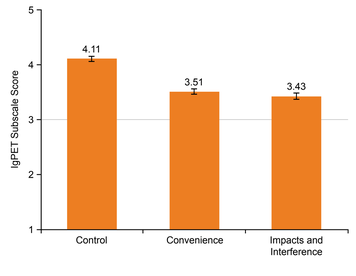
[a]Percentage calculated from valid responses for each item. Missing percentages are calculated from the total.
[b]Patients selected all answers that applied for this prompt, therefore, percentages may total >100%.
BA, bachelor of arts; BS, bachelor of science; GED, general equivalency development; JD, juris doctor; MD, doctor of medicine; MS, master of science; PhD, doctor of philosophy.

Figure 2. IgPET Mean Scores and Distribution of Responses (n = 814)



Ig, immunoglobulin; IgPET, immunoglobulin Patient Experience with Treatment; SD, standard deviation.

Figure 3. IgPET Subscale Scores (n = 814)



IgPET, immunoglobulin Patient Experience with Treatment.
Bars provide the 95% confidence interval for the mean. IgPET items are scored using 5-point-ordered response scales, with higher scores indicating better treatment experiences. Scores above 3 indicate positive experiences.

- Reliability
  - Cronbach's alphas were within the recommended range (0.70-0.90) for all subscales, indicating that each set of items was strongly related and capable of supporting a unidimensional scoring structure, without being redundant.
- Construct Validity
  - Positive correlations were observed between all IgPET items and the LQI subscales and between IgPET items and the TSQM-9 subscales
  - Almost all hypothesized correlations with TSQM-9 subscales and LQI items were at least moderate in strength.
- Known-groups Validity
  - IgPET mean scores were higher among respondents in the top quartile of the TSQM-9 Global Satisfaction Subscale (indicating higher patient satisfaction) and lower for respondents in the bottom quartile of the TSQM-9 subscale scores (P<0.05 for all IgPET items and subscales)
  - Respondents who had been on IgRT >1 year had higher mean IgPET item-level scores compared with those who had been on Ig therapy ≤1 year (P<0.05 for IgPET Items 3, 4, 5, 8, 11, 13, 16, and 18, and the "Control" and "Impacts and Interference" subscales)

Limitations

- The sample size for the cognitive testing was small, limiting the generalizability of the qualitative results
- Each study sample was comprised primarily of adults; the experiences of children and adolescents undergoing IgRT were not characterized and remain a question for future research
- The study was conducted in the US, and the sample was of limited demographic diversity, which may impact the generalizability of the results

Conclusions

- **The IgPET instrument is a treatment-specific measure of patient experience for PID that was developed using industry best practices and psychometrically evaluated in a robust survey sample size of 814 respondents**
- **Generally, patients reported favorable experiences with their IgRT; however, they identified areas for improvement in treatment satisfaction (eg, cost, side effects)**
- **Future studies may be warranted to evaluate the IgPET instrument in broader patient populations and using longitudinal study designs to inform how it could be used in clinical settings**

References

1. Picard C, et al. *J Clin Immunol*. 2018;38:96-128.
2. American Academy of Allergy, Asthma, and Immunology. Primary immunodeficiency disease. http://www.aaaai.org/conditions-and-treatments/primary-immunodeficiency-disease. Accessed May 10, 2019.
3. Wood P. *Ther Clin Risk Manag*. 2012;8:157-67.
4. Espanol T, et al. *Patient Prefer Adherence*. 2014;8:621-9.
5. Nicolay U, et al. *Qual Life Res*. 2005;14:1683-91.
6. Bharmal M, et al. *Health Qual Life Outcomes*. 2009;7:36.
7. Food and Drug Administration. Guidance for industry. December 2009. http://www.fda.gov/media/77832/download. Accessed May 10, 2019.
8. Coles TM, et al. Poster presented at the International Society for Quality of Life Research 25th Annual Conference; October 24-27, 2018; Dublin, Ireland. Poster number 2058.

Acknowledgments

The authors wish to thank the patients, families, and caregivers. This research was sponsored by Baxalta US Inc, a member of the Takeda group of companies, Cambridge, MA, USA. Oxford PharmaGenesis, Inc., Newtown, PA, USA, assisted with editing, layout, and printing this poster; this support was funded by Baxalta US, Inc., a member of the Takeda group of companies, Cambridge, MA, USA.

Disclosures

D DiBenedetti, L McLeod, and **N Williams** are employees of RTI Health Solutions, and **T Coles** was an employee of RTI Health Solutions at the time of the study. **S Tzivelekis** and **LM Meckley** are employees of the Takeda group of companies, Cambridge, MA, USA.

Presented at: International Society for Pharmacoeconomics and Outcomes Research 2019 Conference, May 18-22, 2019; New Orleans, LA, USA.