Derivation of Interpretation Thresholds for the Rheumatoid Arthritis Symptoms and Impact Questionnaire (RASIQ) and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Scale

Poster No. POSA378

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Background

- Interpretation thresholds for patient-reported outcome (PRO) scores are of crucial importance, particularly when assessing treatment benefit.
- The Rheumatoid Arthritis Symptoms and Impact Questionnaire (RASIQ) and the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) are two PRO instruments used to assess key concepts reported to be important to patients with rheumatoid arthritis (RA).
  - RASIQ is a novel measure comprised of 16 items across three domains (Joint Pain, Joint Stiffness and Impact); scores from each item are summed and transformed to a metric ranging from 0 (least pain/stiffness/impact) to 100 (most pain/stiffness/impact).
  - The 13-item FACIT-Fatigue questionnaire uses a five-point Likert scale to assess self-reported fatigue and its impact upon daily activities and function over the past seven days; scores are summed and range from 0 (most fatigue) to 52 (least fatigue).

Aim: This post-hoc analysis of data from two Phase 2 otilimab trials in patients with RA aimed to determine the within-patient meaningful improvement (WPMI) thresholds for RASIQ and FACIT-Fatigue among patients with RA.

Methods

- WPMI estimates were based on data from two Phase 2 trials in RA:
  - BAROQUE: NCT02504671 (N=222)
  - RENAISSANCE: NCT02799472 (N=39)
- Primary analyses were based on anchor-based methods, with multiple anchors used (**Table 1**).
- Distribution-based methods and analyses of measurement error and reliable change provided supportive data.
- For each scale, mean change from baseline was calculated across anchor-based categories of change; WPMI was estimated as the mean change to Week 24 for a pre-defined meaningful improvement in each category.
- Receiver operating characteristics (ROC) curve analyses were used to evaluate the sensitivity and specificity of identified thresholds.

Table 1. Anchors used for each of the RASIQ scales and the FACIT-Fatigue scale

Anchor	RASIQ scales			FACIT-Fatigue
	Joint pain	Joint stiffness	Impact	
PGIS: In general, would you say your health is…	✓	✓	✓	✓
PtGA: Considering all the ways your arthritis has affected you, how active do you feel your arthritis is…	✓	✓	✓	✓
PAIN: How much pain are you currently having because of your rheumatoid arthritis?	✓			
BP01: How much bodily pain have you had during the past 4 weeks?	✓			
AN2: I feel tired			✓	
AN1: I feel listless (washed out)			✓	
VT03: How much of the time during the past 4 weeks did you feel worn out?				✓

BP, bodily pain; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; PAIN, Patient's Assessment of Arthritis Pain; PGIS, Patient's Global Impression of Status; PtGA, Patient's Global Assessment of Disease Activity; RASIQ, Rheumatoid Arthritis Symptoms and Impact Questionnaire

Results

RASIQ

- For RASIQ, anchor-based WPMI was determined as a change between –33 and –22 points for the Joint Pain scale, –26 and –23 for the Joint Stiffness scale, and –21 and –17 for the Impact scale (**Table 2**).
- For all three scales, distribution-based results indicated that these ranges were "true" changes well beyond measurement error.
- ROC curve analyses indicated that values of sensitivity and specificity were reasonable at the WPMI estimated by the anchor-based methods.

Table 2. RASIQ mean score change analysis outcomes (baseline–Week 12)

	RASIQ scales											
	Joint Pain				Joint Stiffness				Impact			
Anchor	N	Threshold based on mean change from baseline	95% CI	SRM	N	Threshold based on mean change from baseline	95% CI	SRM	N	Threshold based on mean change from baseline	95% CI	SRM
PGIS*	66	–24.00	[–28.36, –19.65]	–1.34	66	–23.26	[–27.39, –19.13]	–1.31	66	–20.98	[–24.54, –17.43]	–1.35
PtGA†	104	–31.04	[–34.62, –27.47]	–1.70	104	–26.07	[–29.84, –22.31]	–1.44	104	–21.11	[–24.27, –17.94]	–1.35
PAIN‡	97	–32.74	[–36.19, –29.29]	–1.80								
BP01*	71	–21.71	[–25.42, –18.00]	–1.21								
AN2*									70	–17.36	[–20.69, –14.03]	–1.12
AN1*									61	–17.79	[–21.74, –13.84]	–1.14

*Based on 1-point increase of PGIS anchor on a 5-point Likert scale to define improvement.
†Based on 18-point decrease or more in PtGA as an anchor to define improvement.
‡Based on 20-point decrease or more in PAIN as an anchor to define improvement.
RASIQ score ranges from 0–100 (0=least pain/stiffness/impact, 100=most pain/stiffness/impact).
BP: bodily pain; CI, confidence interval; PAIN, Patient's Assessment of Arthritis Pain; PGIS, Patient's Global Impression of Status; PtGA, Patient's Global Assessment of Disease Activity; RASIQ, Rheumatoid Arthritis Symptoms and Impact Questionnaire; SRM, standardized response mean

FACIT-Fatigue

- For FACIT-fatigue, WPMI estimates ranged from 9.7 to 11.3 points (**Table 3**).
- Compared to WPMI, distribution-based estimates of reliable change were smaller (range 3.2–4.9).
- The cut-point associated with the best sensitivity/specificity balance based on ROC curve analyses was slightly smaller than WPMI estimated by anchor-based mean change methods.

Table 3. FACIT-Fatigue mean score change analysis outcomes (baseline–Week 24)

Anchor	N	Threshold based on mean change from baseline	95% CI	SRM
PGIS*	80	9.73	[8.07, 11.38]	0.99
PtGA†	120	11.27	[9.68, 12.85]	1.15
VT03	74	11.12	[9.36, 12.89]	1.13

*Based on 1-point increase of PGIS anchor on a 5-point Likert scale to define improvement.
†Based on 18-point decrease or more in PtGA as an anchor to define improvement.
FACIT-Fatigue score ranges from 0–52 (0=most fatigue, 52=least fatigue).
CI, confidence interval; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; PGIS, Patient's Global Impression of Status; PtGA, Patient's Global Assessment of Disease Activity; SRM, standardized response mean

Conclusions

- This study derived WPMI thresholds for RASIQ and FACIT-Fatigue using multiple anchors.
- Derivation of WPMI for RASIQ and FACIT-Fatigue will enable broader use of these PROs to better evaluate and interpret treatment benefit in future RA studies.
- Subsequent analyses conducted with data from a naturalistic setting would enable estimation of interpretation thresholds that indicate decline and worsening of symptoms.
- Please see our related poster POSC381 on WPMI thresholds for SF-36 in RA.

Acknowledgements

- Editorial support (in the form of writing assistance, including preparation of the draft poster under the direction and guidance of the authors, collating and incorporating authors' comments for each draft, assembling tables and figures, grammatical editing, and referencing) was provided by Kathryn Wardle, MSc, of Aura, a division of Spirit Medical Communications Group Ltd, and was funded by GlaxoSmithKline.

Disclosures

- This study was funded by GlaxoSmithKline (GSK ID: 212734).
- W-HC and MB are employees and stockholders/shareholders at GlaxoSmithKline. RR-B, XL, MK and JBB are employees of QualityMetric Inc, who received consulting fees for the conduct of the data analysis.
- RR-B and XL contributed substantially to the work, revised, approved and agreed to be accountable for all aspects of the associated abstract and revised this poster critically for important intellectual content; however, were unable to review and approve the final version of this poster. All other authors contributed substantially to the work, revised, approved, agreed to be accountable for all aspects of this poster and agree that RR-B and XL should remain listed as authors.

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Presented at Virtual ISPOR Europe 2021, 30th November–3rd December