Psychometric Analysis of the EORTC QLQ-NMIBC24 Using Data from a Global Phase 2 Randomized Trial of Erdafitinib in Participants with NMIBC

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Key Takeaway

Results provide additional support from a global study for the reliability and validity of EORTC QLQ-NMIBC24 multi-item domain scores in people living with NMIBC

Conclusions

- Urinary Symptoms and Future Worries domain scores have high internal consistency. These and the Bloating and Flatulence, Sexual Function, and Male Sexual Problems domains also had fair to good test-retest reliability
- All multi-item domain scores have evidence supportive of fair to good convergent/discriminant validity, known groups validity, and ability to detect change
- Distribution-based meaningful score differences suggest change thresholds of around 10 points for most multi-item domains; further evidence is needed for anchor-based thresholds

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Disclosures

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Introduction

- NMIBC is an early-stage bladder cancer that accounts for ~75% of new bladder cancers at diagnosis[1] and can negatively impact health-related quality of life (HRQoL)[2]
- The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Non-Muscle Invasive Bladder Cancer 24 items (EORTC QLQ-NMIBC24)[3,4] is a disease-specific patient-reported outcome (PRO) instrument widely used in clinical studies to evaluate HRQoL of NMIBC patients
  - Evidence supports the measurement properties of the EORTC QLQ-NMIBC24[4], though it has not been examined psychometrically in an international sample
- We investigated the psychometric properties of the EORTC QLQ-NMIBC24 in adults with NMIBC in a global clinical study

Methods

Data Source and Assessments

- Measurement properties were assessed using data from THOR-2 (NCT04172675), an open-label, multicohort, phase 2 study of erdafitinib in participants with NMIBC and fibroblast growth factor receptor (FGFR) mutations or fusions who recurred after BCG therapy
- Participants completed PROs during the treatment phase
  - **Target measure:** EORTC QLQ-NMIBC24
  - **Reference measures:** EORTC QLQ-C30[5], EQ-5D-5L[6], and Patient Global Impression of Severity (PGIS) and Change (PGIC)
- Data from Screening and the first three 28-day treatment cycles (Cycle 1, 2, 3), pooled across cohorts, were analyzed

Analyses

- **Reliability:** Internal consistency (classical test theory [CTT] analyses) for EORTC QLQ-NMIBC24 Urinary Symptoms and Future Worries domains (acceptable $\alpha \geq 0.70$)[7]. Test-retest (correlations and intraclass correlations [ICCs]) for EORTC QLQ-NMIBC24 multi-item domains (ICC <0.40 = poor; 0.40 to 0.75 = fair to good; 0.75 to 0.90 = good)[8]
- **Dimensionality:** Confirmatory factor analysis for EORTC QLQ-NMIBC24 Urinary Symptoms and Future Worries domains (adequate fit TLI $\geq$ 0.95 and RMSEA < 0.08)[9]
- **Validity:** Convergent and discriminant correlations, known-groups analyses, and sensitivity to change analyses for EORTC QLQ-NMIBC24 multi-item domains utilizing reference measures
- **Meaningful Score Difference (MSD):** Explored using PGIS and PGIC as potential anchors as well as distribution-based methods

Results

Table 1. Sample Characteristics (N = 106)

Variable	Mean (SD)
Age (years)	66.6 (11.1)
Height (cm)	169.3 (8.9)
Variable	**n (%)**
Sex	
Female	28 (26.4%)
Male	78 (73.6%)
Race	
Asian	25 (23.6%)
Black or African American	3 (2.8%)
White	62 (58.5%)
Not Reported	11 (10.4%)
Unknown	5 (4.7%)
Study Cohort	
HR-NMIBC, papillary disease only	73 (68.9%)
HR-NMIBC, CIS with or without papillary	16 (15.1%)
IR-NMIBC	17 (16.0%)

SD = Standard deviation. % = Percent. cm = Centimeter. N = participants enrolled with PRO data at Screening. HR-NMIBC = high-risk non-muscle invasive bladder cancer. CIS = carcinoma in situ. IR-NMIBC = intermediate-risk non-muscle invasive bladder cancer.

Reliability

- CTT analyses show Urinary Symptoms and Future Worries domains have acceptable internal consistency, with α above the pre-specified cutoff (other domains have too few items for formal testing)

Table 2: Internal consistency of Urinary Symptoms and Future Worries domains at Screening (N = 106)

Urinary Symptoms		
Alpha	0.86	
Item	Alpha with item removed	Item-total correlation
Frequent urination during the day	0.83	0.65
Frequent urination at night	0.82	0.75
Hurry to get to toilet	0.82	0.74
Difficulty getting enough sleep	0.82	0.72
Difficulty leaving house	0.84	0.61
Unintentional leakage of urine	0.86	0.42
Pain or burning while urinating	0.86	0.48
Future Worries		
Alpha	0.83	
Item	Alpha with item removed	Item-total correlation
Worry about repeated treatments	0.85	0.48
Worry about future health	0.77	0.68
Worry about exam results	0.76	0.69
Worry about future treatment	0.72	0.77

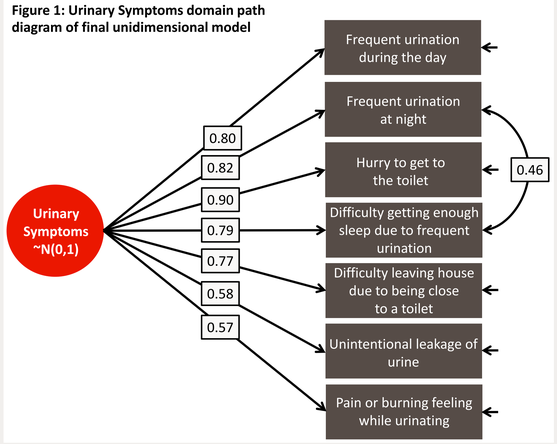
N = Number of participants at Screening with no missing item-level responses

- Test-retest ICCs between Screening and Cycle 1 (baseline) is acceptable for multi-item domain scores and ranged from 0.42 (Bloating and Flatulence) to 0.83 (Sexual Function), except for Malaise (0.19)

Factor Analytic Modeling

- Factor analyses support the unidimensionality for the Urinary Symptoms domain with one pair of correlated item residuals specified in the Figure 1 model (TLI=1.00, RMSEA= 0.04)

Figure 1: Urinary Symptoms domain path diagram of final unidimensional model



- For Future Worries, neither the *a priori* unidimensional model (TLI = 0.63, RMSEA = 0.27) nor a correlated residuals model adequately fit the data (TLI = 0.88, RMSEA = 0.18)

Validity Analyses

- Correlations between EORTC QLQ-NMIBC24 scores and reference variables support convergent/discriminant validity
- Known groups analyses generally reflected that the lower PGIS and EQ-5D-5L severity groups have EORTC QLQ-NMIBC24 scores that indicate less symptoms / better functioning compared to the higher severity groups
- Change score correlations over two different timepoints (Screening to Cycle 2, Screening to Cycle 3) were similar to the cross-sectional correlations, providing evidence in support of the EORTC QLQ-NMIBC24 domain scores' ability to detect change over time

MSD Analyses

- Planned anchors (PGIS and PGIC) were found to be not strongly related to the EORTC QLQ-NMIBC24 domain scores; distribution-based values are reported

Table 4: Distribution-based MSD thresholds for the EORTC QLQ-NMIBC24 domains

Domain	½ SD at Screening	SEM at Screening
Urinary Symptoms	**10.11**	7.65
Future Worries	**10.95**	9.15
Malaise	4.35	**7.85**
Bloating and Flatulence	8.46	**12.50**
*Sexual Function	**12.13**	9.87
Male Sexual Problems	16.27	**20.47**

Underlined/bold values: the largest observed values and the more conservative candidate MSD values.
*Denotes domains that are reverse-coded (higher score indicated greater functioning).
SD = Standard deviation. SEM = Standard error of measurement

- Further research is required to determine patient-centered anchor-based MSD thresholds

Table 3. Convergent/discriminant cross-sectional correlations at Screening for multi-item domains (N=106)

	Urinary Symptoms	Future Worries	Malaise	Bloating & Flatulence	Sexual Function	Male Sexual Problems‡
Reference Variable	**r**	**r**	**r**	**r**	**r**	**r**
Age	0.11	-0.26**	-0.09	-0.05	-0.35**	0.25*
Height	0.00	-0.18	0.05	-0.11	0.18	0.02
EORTC QLQ-C30						
†Physical Functioning	-0.34**	-0.19*	-0.27**	-0.08	0.22*	-0.29*
†Role Functioning	-0.58**	-0.23*	-0.48**	-0.25**	0.08	-0.29*
†Emotional Functioning	-0.32**	-0.58**	-0.28**	-0.36**	-0.01	-0.22
†Cognitive Functioning	-0.33**	-0.17	-0.23*	-0.29**	0.20*	-0.44**
†Social Functioning	-0.47**	-0.42**	-0.48**	-0.34**	0.02	-0.23*
†Global Health Status/QoL	-0.52**	-0.09	-0.37**	-0.12	0.20*	-0.23*
Fatigue	0.47**	0.31**	0.33**	0.19	-0.13	0.30**
Nausea and Vomiting	0.10	0.12	0.20*	0.19	0.17	-0.08
Pain	0.48**	0.09	0.42**	0.14	-0.10	0.28*
EQ-5D-5L						
Mobility	0.28**	0.17	0.11	0.03	-0.14	0.23*
Self-Care	0.03	0.11	0.23*	-0.02	-0.05	0.11
Usual Activities	0.35**	0.22*	0.30**	0.10	-0.04	0.37**
Pain/Discomfort	0.37**	0.07	0.31**	0.19*	0.01	0.21
Anxiety/Depression	0.28**	0.59**	0.23*	0.24*	0.00	0.20
†VAS	-0.33**	-0.32**	-0.38**	-0.11	0.15	-0.28*

*p<.05 (lighter shading), **p<.01 (darker shading).
N = participants enrolled with PRO data at Screening. QoL = quality of life.
†Denotes domains that are reverse-coded (higher score indicates greater functioning).
‡Sample size for Male Sexual Problems = 78.

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