THRESHOLDS FOR MEANINGFUL CHANGE FOR THE EQ-5D VAS AND EORTC QLQ-C30 PHYSICAL AND ROLE FUNCTIONING SCALE IN GASTROINTESTINAL-RELATED CANCERS

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Abstract: PG137

Background

- Gastrointestinal stromal tumor (GIST) is a rare form of cancer that starts in interstitial cells of Cajal within the wall of the gastrointestinal (GI) tract[1]
- An estimated 4,000 – 6,000 GIST cases are diagnosed each year in the US and are most commonly diagnosed in people over the age of 50[2,3]
- The main types of treatment for patients with GIST include surgery and targeted therapy[4,5]
- Primary mutations in receptor tyrosine kinase (KIT) or platelet derived growth factor receptor alpha (PDGFRA) occur in >85% of patients with GIST[6]
- In May 2020, the US FDA approved ripretinib for the treatment of adult patients with advanced GIST who have received prior treatment with 3 or more kinase inhibitors, including imatinib[7]
- There is no approved 4th-line therapy for KIT-driven GIST[8,9], except ripretinib[7]
- Treatment choice should balance the potential benefits of treatment and the risk for toxicity including treatment-related symptoms and treatment-emergent adverse events that can negatively impact daily functioning and well-being in both the short- and long-term[10,11]
- Patient-reported outcomes (PROs) are increasingly considered important endpoints in oncology efficacy trials in addition to traditional progression and survival-related endpoints[12]

Objectives

- PROs must meet several well-accepted measurement properties to be considered label-enabling – one of the most important of which is score interpretation or the threshold for within-person meaningful change (formerly referred to as the minimal clinically important difference [MCID])
- We assessed the evidence base for MCIDs for the EQ-5D visual analogue scale (VAS) and the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) physical functioning (PF) and role functioning (RF) scales for use in GIST efficacy trials
- The EQ-5D VAS was chosen because it is an overall measure of general health
- The PF and RF scales were chosen because they characterize GIST patients' daily functioning

Methods

- A targeted literature review was initially conducted within PubMed for methodologically-sound MCIDs for the VAS and the PF and RF for GI-related cancers (e.g., GIST, colorectal, colon, rectal, stomach, GI, gastric, or intestinal sarcomas or carcinomas)
- The search for MCIDs was subsequently expanded to include all cancers
- No MCIDs were found for VAS or C30 for GI cancers

Results

- No articles were identified that provided MCIDs for the VAS in GI-related cancers
- One article provided an empirically-derived MCID for the VAS based upon cross-sectional anchors[13]
  - These MCID estimates ranged from 7–8 points for anchor-based and 9–11 points for distribution-based estimates
- No articles that reported *de novo*, empirically-derived MCIDs for the PF and RF scales were found in GI-related cancers
- Six studies reported anchor- and/or distribution-based methods for the MCID of the PF and RF scales (Tables 1 and 2)
- Where no MCID exists, heuristics may be helpful; the MCID for health-related quality-of-life is often found to be in the range of 0.2–0.5 times standard deviation of the baseline value, which can be used as an estimate[14,15]

Table 1. EORTC-QLQ-C30 Physical Functioning MCID Evidence Table

	Disease	Distribution-Based				Anchor-Based		
						Anchor	Improved	Deteriorated
		0.20 SD	0.30/0.33 SD	0.50 SD	SEM			
Zeng[16a]	Cancer patients with bone metastases	5.8, 6.6	8.7, 9.9	14.5, 16.4	3.0, 3.4	Improvement and deterioration were classified as an increase in Karnofsky Performance Status (KPS) of 10 and a decrease in KPS of 10, respectively. Patients who had no change in KPS were deemed to be stable. Changes of magnitude greater than 10 were discarded from analysis.	8.0	4.3
Maringwa[17]	Brain cancer	5.1	8.6	12.9	7.7	Change in WHO performance status (PS). Deterioration (PS worsened by one category), no change (PS stayed the same), and improvement (PS improved by one category).	4.3	-9.8
Maringwa[18]	Lung cancer	5.0		12.0	7.0	Change in WHO performance status. Deterioration (PS worsened by one category), no change (PS stayed the same), and improvement (PS improved by one category).	3.6	-9.7
						Weight change. Weight loss (5−<20% loss), no change (<5% loss or gain of total body weight), and weight gain (5−<20% gain).	1.1	-10.5
Bedard[19]	Advanced cancer	6.5	9.7	16.2	1.7	EORTC QLQ-C30 overall health (QLQ-C30 item 29). Changes of two units were used as the anchors.	10.1	7.2
						EORTC-QLQ-C30 overall QOL (QLQ-C30 item 30). Changes of two units were used as the anchors.	2.1	6.1
Raman[20b]	Bone metastases	4.5, 5.1	6.8, 7.7	11.3, 12.8		A 10-point change in the global health status/quality of life score was used to classify improvement or deterioration. Patients with less than a 10-point change were classified as stable. While the change in ≥10 points is arbitrary and requires validation, previously studies have shown that this represents a mild-moderate change that is clinically significant.	5.2	-15.2
Snyder[21]	Breast and colorectal cancer					Supportive Care Needs Survey-Short Form-34. Score changes categorized as improvement, worsening, or unchanged.	15.2 to 17.3	Findings contrary to hypotheses; not reported herein
Mean		5.5	8.6	13.7	4.6		7.4	-3.9
Median		5.1	8.6	12.9	3.4		5.2	-9.7

[a] Distribution-based estimates at baseline and follow-up
[b] Distribution-based estimates at baseline and month 2
EORTC QLQ-C30, European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire.

Table 2. EORTC-QLQ-C30 Role Functioning MCID Evidence Table

	Disease	Distribution-Based				Anchor-Based		
						Anchor	Improved	Deteriorated
		0.20 SD	0.30/0.33 SD	0.50 SD	SEM			
Zeng[16a]	Cancer patients with bone metastases	7.0, 7.4	10.4, 11.1	17.4, 18.6	3.6, 3.9	Improvement and deterioration were classified as an increase in Karnofsky Performance Status (KPS) of 10 and a decrease in KPS of 10, respectively. Patients who had no change in KPS were deemed to be stable. Changes of magnitude greater than 10 were discarded from analysis.	5.8	10.3
Maringwa[17]	Brain cancer	6.7	11.1	16.7	14.2	Change in WHO performance status (PS). Deterioration (PS worsened by one category), no change (PS stayed the same), and improvement (PS improved by one category).	18.7	-7.9
Maringwa[18]	Lung cancer	6.0		17.0	14.0	Change in WHO performance status. Deterioration (PS worsened by one category), no change (PS stayed the same), and improvement (PS improved by one category).	9.7	-8.9
						Weight change. Weight loss (5−<20% loss), no change (<5% loss or gain of total body weight), and weight gain (5−<20% gain).	3.5	-10.5
Bedard[19]	Advanced cancer	4.6	6.9	11.5	1.2	EORTC-QLQ-C30 overall health (QLQ-C30 item 29). Changes of two units were used as the anchors.	15.8	13.5
						EORTC-QLQ-C30 overall QOL (QLQ-C30 item 30). Changes of two units were used as the anchors.	2.4	10.5
Raman[20b]	Bone metastases	6.2, 6.4	9.3, 9.6	15.6, 16.0		A 10-point change in the global health status/quality of life score was used to classify improvement or deterioration. Patients with less than a 10-point change were classified as stable. While the change in ≥10 points is arbitrary and requires validation, previously studies have shown that this represents a mild-moderate change that is clinically significant.	11.9	-24.2
Snyder[21]	Breast and colorectal cancer					Supportive Care Needs Survey-Short Form-34. Score changes categorized as improvement, worsening, or unchanged.	18.1 to 32.3	Findings contrary to hypotheses; not reported herein
Mean		6.3	9.7	16.1	7.4		13.1	-2.4
Median		6.4	10.0	16.7	3.9		11.9	-7.9

[a] Distribution-based estimates at baseline and follow-up
[b] Distribution-based estimates at baseline and month 2
EORTC QLQ-C30, European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire.

Conclusions

- Even in the most widely-used cancer-specific function scales, the MCID has rarely been established in GI-related cancers
- In the absence of *de novo* results based on well accepted anchor-based methods, one may have to rely on distribution-based results
- Where no MCID exists, heuristics may be helpful; the MCID for health-related quality-of-life is often found to be in the range of 0.2 – 0.5 times standard deviation of the baseline value which can be used as an estimate

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