

Comparison of Generic and Condition-Specific Preference Measures to Derive Health Utilities: A Retrospective Analysis of Nivolumab Trials in Solid Tumours

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Disclosures

- Employment and stock ownership with Bristol-Myers Squibb

Background

- For economic evaluation, treatment benefits are most commonly summarized using quality-adjusted life years (QALYs), which combine quantity and quality of survival in a single metric
- The “quality” component is often quantified through use of generic preference-based measures among which the EQ-5D-3L is historically most representative
 - EQ-5D-5L has been developed to provide greater sensitivity, and algorithms have been developed to “map” from the EQ-5D-5L to the EQ-5D-3L and *vice versa*¹
- There is growing interest in using condition-specific preference measures to inform economic evaluations of cancer treatments
 - E.g., European Organization for Research and Treatment of Cancer Quality of Life Utility Measure – Core 10 Dimensions (EORTC QLU-C10D)^{2,3}
 - These measures may provide benefits in terms of reduced need for instrumentation and enhanced sensitivity to treatment effects

¹Hernandez-Alava M, Pudney S. Econometric modelling of multiple self-reports of health states: The switch from EQ-5D-3L to EQ-5D-5L in evaluating drug therapies for rheumatoid arthritis. *J Health Econ*. 2017.

²Norman R et al. Using a discrete choice experiment to value the QLU-C10D: feasibility and sensitivity to presentation format. *Qual Life Res*. 2016;25(3):637-649.

³King MT et al. QLU-C10D: a health state classification system for a multi-attribute utility measure based on the EORTC QLQ-C30. *Qual Life Res*. 2016;25(3):625-636.

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Objectives

To assess the implications of using utility indices based on:

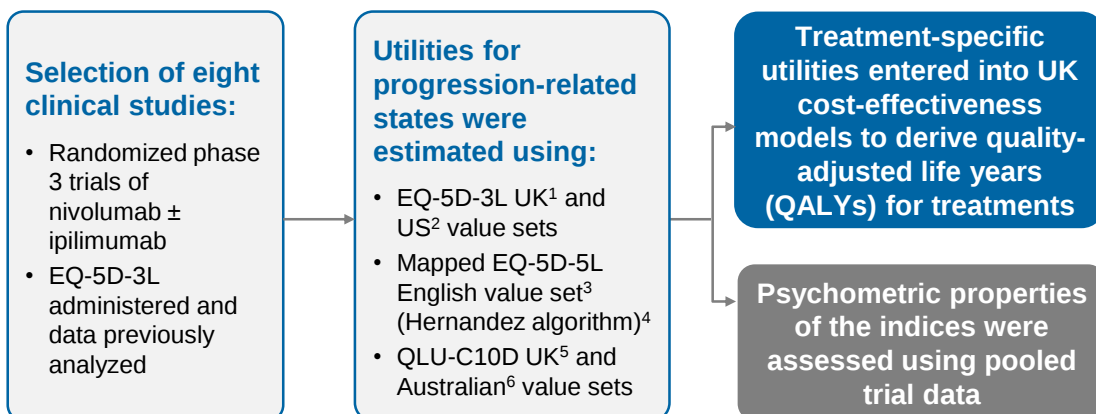
- 3-level EQ-5D (EQ-5D-3L)
- Mapping the EQ-5D-3L to the 5-level EQ-5D (EQ-5D-5L)
- QLU-C10D (UK and Australian)

To compare the psychometric properties of the above indices

- Ability to detect differences between clinically important groups
- Ability to detect improvement and worsening in health over time

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Methods: Overview



¹Dolan P. Modeling valuations for EuroQol health states. *Med Care*. 1997;35(11):1095-1108

²Shaw JW et al. US valuation of the EQ-5D health states: development and testing of the D1 valuation model. *Med Care*. 2005;43(3):203-220.

³Devlin NJ et al. Valuing health-related quality of life: An EQ-5D-5L value set for England. *Health Economics*. 2018;27(1):7-22.

⁴Hernandez-Alava M, Pudney S. Econometric modelling of multiple self-reports of health states: The switch from EQ-5D-3L to EQ-5D-5L in evaluating drug therapies for rheumatoid arthritis. *J Health Econ*. 2017.

⁵Norman R et al. U.K. utility weights for the EORTC QLU-C10D. *Health Economics*. 2019. <https://doi.org/10.1002/hec.3950> 5

⁶King MT et al. Australian utility weights for the EORTC QLU-C10D, a multi-attribute utility instrument derived from the cancer-specific quality of life questionnaire, EORTC QLQ-C30. *Pharmacoeconomics*. 2018;36(2):225-238.

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Methods: Phase 3 Trials Included in Analyses

Trial Protocol	Indication	Sample Size (All Randomized Subjects)	Treatment Groups	EQ-5D-3L	EORTC QLQ-C30
CheckMate 017	Previously Treated Advanced or Metastatic Squamous Cell Non-small Cell Lung Cancer	272	nivolumab docetaxel	X	
CheckMate 025	Advanced or Metastatic Clear-Cell Renal Cell Carcinoma Who Have Received Prior Anti-Angiogenic Therapy	821	nivolumab everolimus	X	
CheckMate 037	Advanced (Unresectable or Metastatic) Melanoma Patients Progressing Post Anti-CTLA-4 Therapy	405	nivolumab investigator's choice	X	X
CheckMate 057	Previously Treated Metastatic Non-squamous Non-small Cell Lung Cancer	582	nivolumab docetaxel	X	
CheckMate 066	Previously Untreated Unresectable or Metastatic Melanoma	418	nivolumab dacarbazine	X	X
CheckMate 067	Previously Untreated Unresectable or Metastatic Melanoma	945	nivolumab nivolumab + ipilimumab ipilimumab	X	X
CheckMate 141	Recurrent or Metastatic Platinum-refractory Squamous Cell Carcinoma of the Head and Neck	361	nivolumab investigator's choice	X	X
CheckMate 238	Completely Resected Stage IIIB/C or Stage IV Melanoma with High Risk for Recurrence	906	nivolumab ipilimumab	X	X

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Methods: Psychometric Analyses

Ability to detect differences between clinically important groups

- Known groups defined at baseline based on ECOG performance status (PS), age, EQ-5D-3L VAS, and cancer stage
- Difference in mean utility values at baseline assessed for statistical significance through two-sample t-tests
- Between-group effect size (ES) calculated (Hedges' g: mean score difference divided by pooled weighted standard deviation)

Ability to detect change over time

- Patients categorized into "improved," "stable," and "worsened" groups according to changes in external anchor measures at Week 11-13: tumour response status, EQ-5D-3L VAS, ECOG PS, and EORTC QLQ-C30 Global Health Status
- Paired t-tests evaluated the within-group differences between baseline and Week 11-13
- Within-group ES calculated (standardized response mean [SRM]: mean change divided by standard deviation of the difference)

Note: General rules for interpreting ES or SRM: <0.20 = trivial, 0.20-0.49 = small, 0.50-0.79 = moderate, ≥0.80 = large

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Results: Summary of Incremental QALYs

Study	Indication	QALYs	Mapped EQ-5D-5L English	EQ-5D-3L US	EQ-5D-3L UK	QLU-C10D UK*
CheckMate 037 [BRAF negative]	Melanoma	Incremental QALYs	3.32	3.35	3.16	3.01
CheckMate 066 [BRAF negative]	Melanoma	Incremental QALYs	3.51	3.50	3.38	3.26
CheckMate 067 [BRAF negative]	Melanoma	Incremental QALYs vs. ipilimumab	2.20	2.26	2.10	2.04
CheckMate 067 [BRAF positive]	Melanoma	Incremental QALYs vs. ipilimumab	2.28	2.33	2.17	2.11
CheckMate 017	NSCLC	Incremental QALYs	0.83	0.85	0.75	n/a
CheckMate 057	NSCLC	Incremental QALYs	0.77	0.78	0.71	n/a
CheckMate 025	RCC	Incremental QALYs	0.64	0.65	0.63	n/a
CheckMate 141	SCCHN	Incremental QALYs	0.58	0.56	0.52	0.54

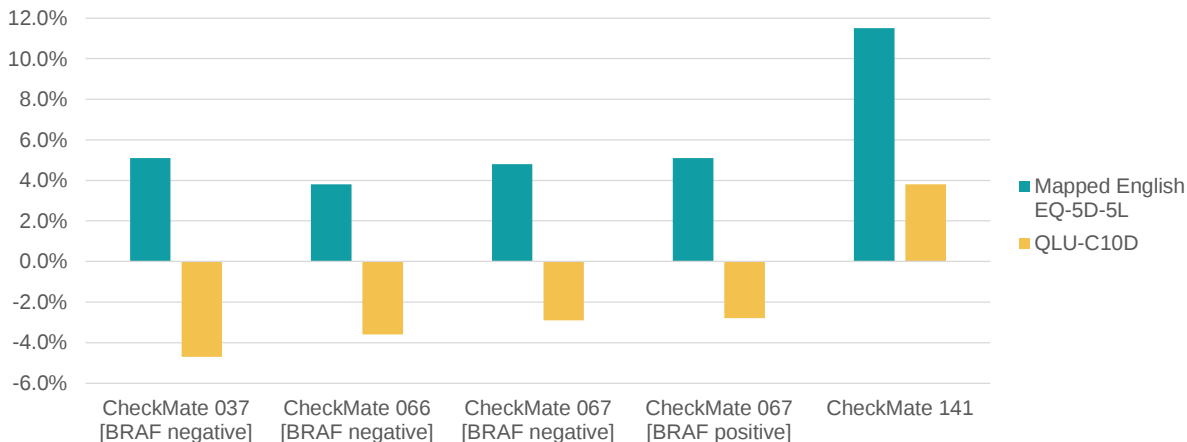
n/a=not applicable

*The EORTC QLQ-C30 was not included in the design and administration for CheckMate 017, 025, and 057

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Incremental QALY Percentage Differences Compared to EQ-5D-3L (UK)

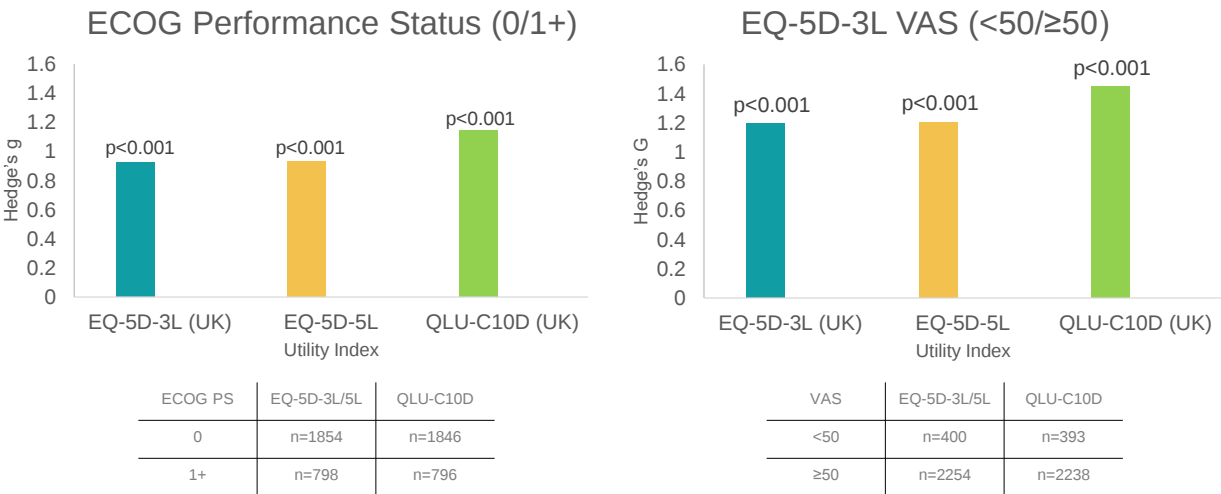
- The mapped EQ-5D-5L English index yielded greater incremental QALYs for nivolumab ± ipilimumab versus comparators than the EQ-5D-3L UK and QLU-C10D UK indices



Note: Only studies where both the EQ-5D-3L and EORTC QLQ-C30 were administered are shown here

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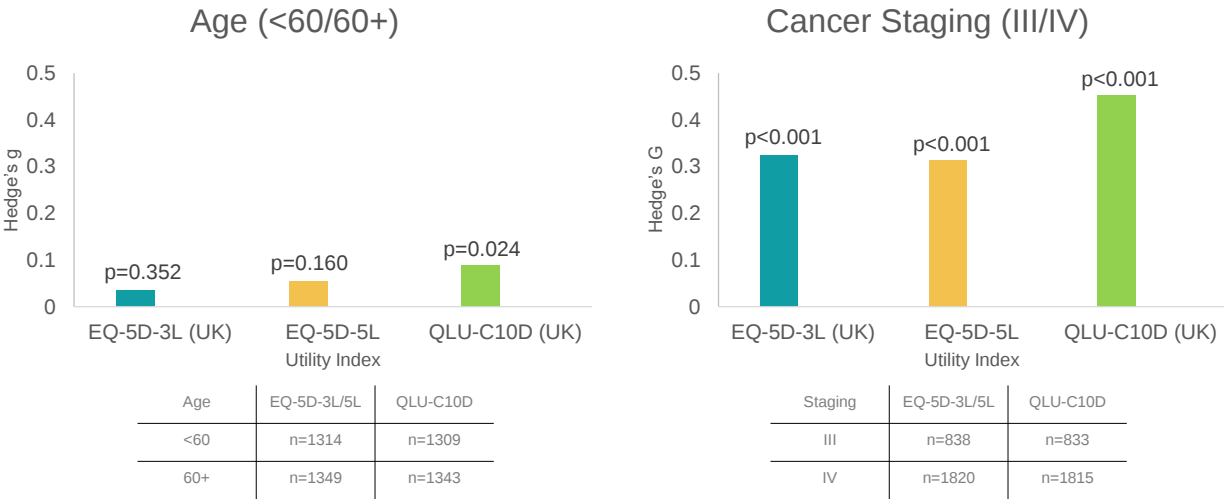
Ability to Detect Differences Between Clinically Important Groups



Two-sample t-test comparing difference in baseline mean scores between groups

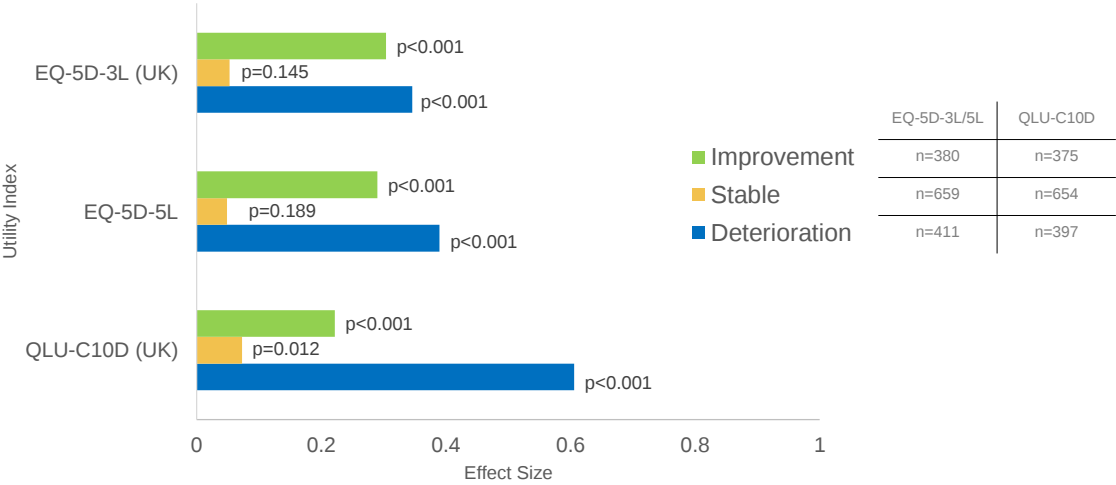
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Ability to Detect Differences Between Clinically Important Groups



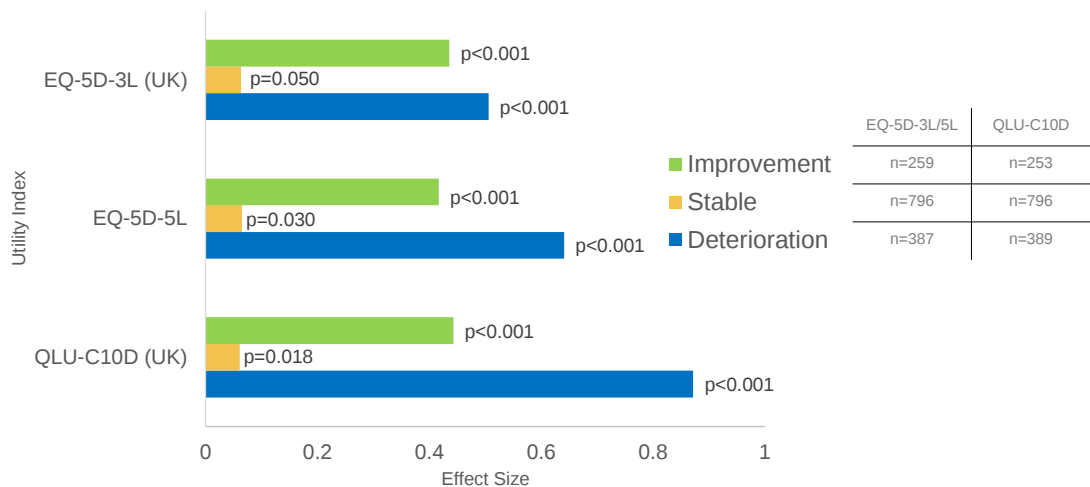
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Ability to Detect Change Over Time: Utility Change by EQ-5D-3L VAS



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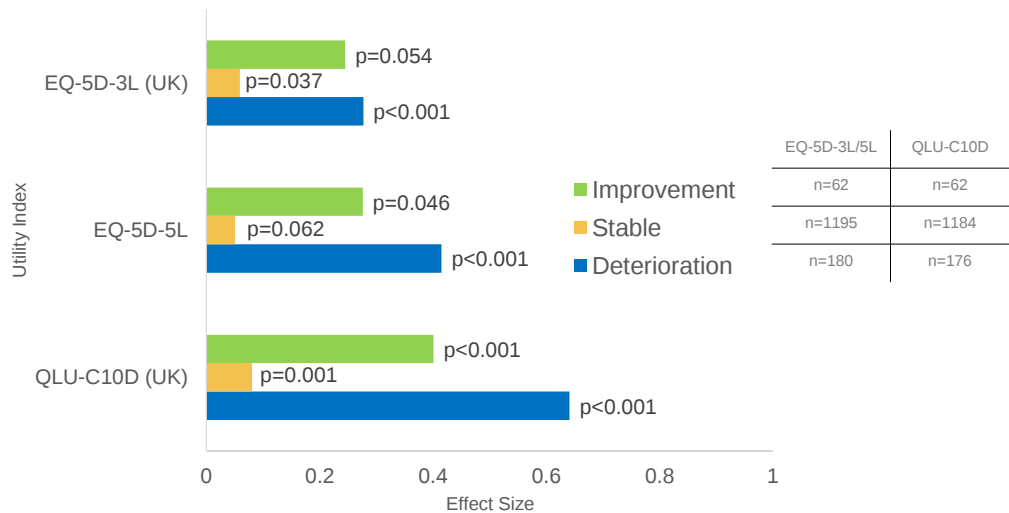
Ability to Detect Change Over Time: Utility Change by EORTC QLQ-C30 Global Health Status



Paired t-test comparing change in mean scores at baseline and post-baseline for each category
EORTC QLQ-C30 Global Health Status does not contribute to the calculation of QLU-C10D
Improvement: ≥10 points increase, stable: <10 points change, and deterioration: ≥10 points decrease

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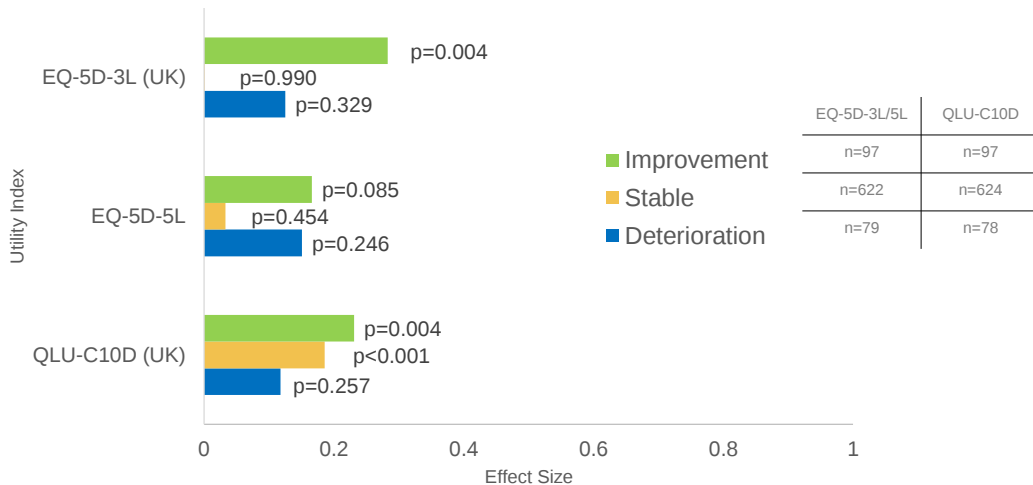
Ability to Detect Change Over Time: Utility Change by ECOG Performance Status



Paired t-test comparing change in mean scores at baseline and post-baseline for each category
Improvement: ≥1 point decrease, stable: no change, and deterioration: ≥1 point increase

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Ability to Detect Change Over Time: Utility Change by Tumour Response Status



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Results: Psychometric properties

- **All indices differentiated groups defined by baseline:**
 - EQ-5D-3L VAS score
 - ECOG performance status
 - Cancer stage
- **All indices detected meaningful change in:**
 - EQ-5D-3L VAS score
 - EORTC QLQ-C30 global health status score
 - ECOG performance status
- **Effect sizes were generally similar in interpretation**
 - QLU-C10D UK index was more sensitive to worsened EQ-5D-3L VAS score, EORTC QLQ-C30 global health status score, and ECOG performance status
 - Mapped EQ-5D-5L English index was less sensitive to improved tumour response

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Conclusions

- On average, the mapped EQ-5D-5L English index and QLU-C10D UK index yielded 6% more and 2% fewer incremental QALYs, respectively, than the EQ-5D-3L UK index
- The lower QALY yields of the QLU-C10D were balanced by slightly greater validity and responsiveness
- Ongoing work seeks to explore determinants of differences in incremental utilities between the QLU-C10D indices and other utility indices
- Specific issues worth exploring for QLU-C10D
 - Aspects of descriptive system particularly relevant to SCCHN
 - Significant, albeit small worsening in index scores among stable subjects
 - Role of nausea and fatigue in determining utilities
- The findings from this study provide insights regarding the performance of the QLU-C10D and suggest potential benefits with use of the measure as a primary means of utility generation to inform economic evaluations of cancer treatments

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Limitations

- QLU-C10D utilities only calculable for trials in which EORTC QLQ-C30 administered
 - Exclusion of both CheckMate 017 and 057 from analyses of psychometric properties
- CheckMate 141 excluded from analyses of responsiveness to change due to differences in PRO administration schedule between trials
- Method of utility generation for CheckMate 141 differed from other trials (i.e., raw means vs. mixed model predictions)
- Characterization of clinical change based on tumour response at Week 11-13 possibly too soon to observe meaningful changes in index scores

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QUESTIONS

