Optimal Categorization of High Side-Effect Bother Based on Functional Assessment of Cancer Therapy GP5 (FACT-GP5) Item Among Patients with MCL Enrolled in BRUIN-MCL-321

Angély Loubert [1], Kristin Creel [1], Naleen Raj Bhandari [2], Richard Sizelove [2], Antoine Regnault [1], Lisa M. Hess [2], Amy S. Ruppert [2], Rodrigo Ito [2], Nalin Payakachat [2]

[1] Modus Outcomes, Lyon, France
[2] Eli Lilly and Company, Indianapolis, USA

Scan the QR code for a list of all Lilly content presented at the congress. Other company and product names are trademarks of their respective owners.

OBJECTIVE

- To confirm the FACT-GP5 rating of 3 or 4 points as the optimal categorization of high SE bother among patients with MCL in BRUIN-MCL-321.

CONCLUSIONS

- The primary categorization of high SE bother defined as rating of 3-4 on FACT-GP5, was the most discriminated definition. Therefore, it's the most appropriate categorization for use in BRUIN-MCL-321 tolerability endpoint.

- This finding is consistent with those previously obtained in different cancer populations[2], which reinforces the strength and generalizability of this categorization.

Abbreviations:

FACT-GP5 = Functional Assessment of Cancer Therapy, item GP5; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 items; GHS/QoL = Global health status/quality of life; IQR = interquartile range; MCL = Mantle cell lymphoma; MTC = medullary thyroid cancer; SE = side effect

BACKGROUND

- Functional Assessment of Cancer Therapy-General (FACT) item GP5 is a commonly used patient-reported outcome (PRO) measure of overall side-effect (SE) bother of cancer therapy, recommended as a core concept to be assessed in cancer clinical trials by the US FDA[1].

- The categorization of a FACT-GP5 score of 3 or 4 as high SE bother was previously established in participants with medullary thyroid cancer (MTC), along with sufficient psychometric properties of the FACT-GP5[2].

- BRUIN-MCL-321 is a phase 3, global, randomized open-label trial comparing pirtobrutinib to investigator's choice of covalent BTK inhibitor (ibrutinib, acalabrutinib, or zanubrutinib) in previously treated Mantle Cell Lymphoma (MCL)[3].

- BRUIN-MCL-321 includes a secondary endpoint, the proportion of time on treatment with high SE bother based on a FACT-GP5.
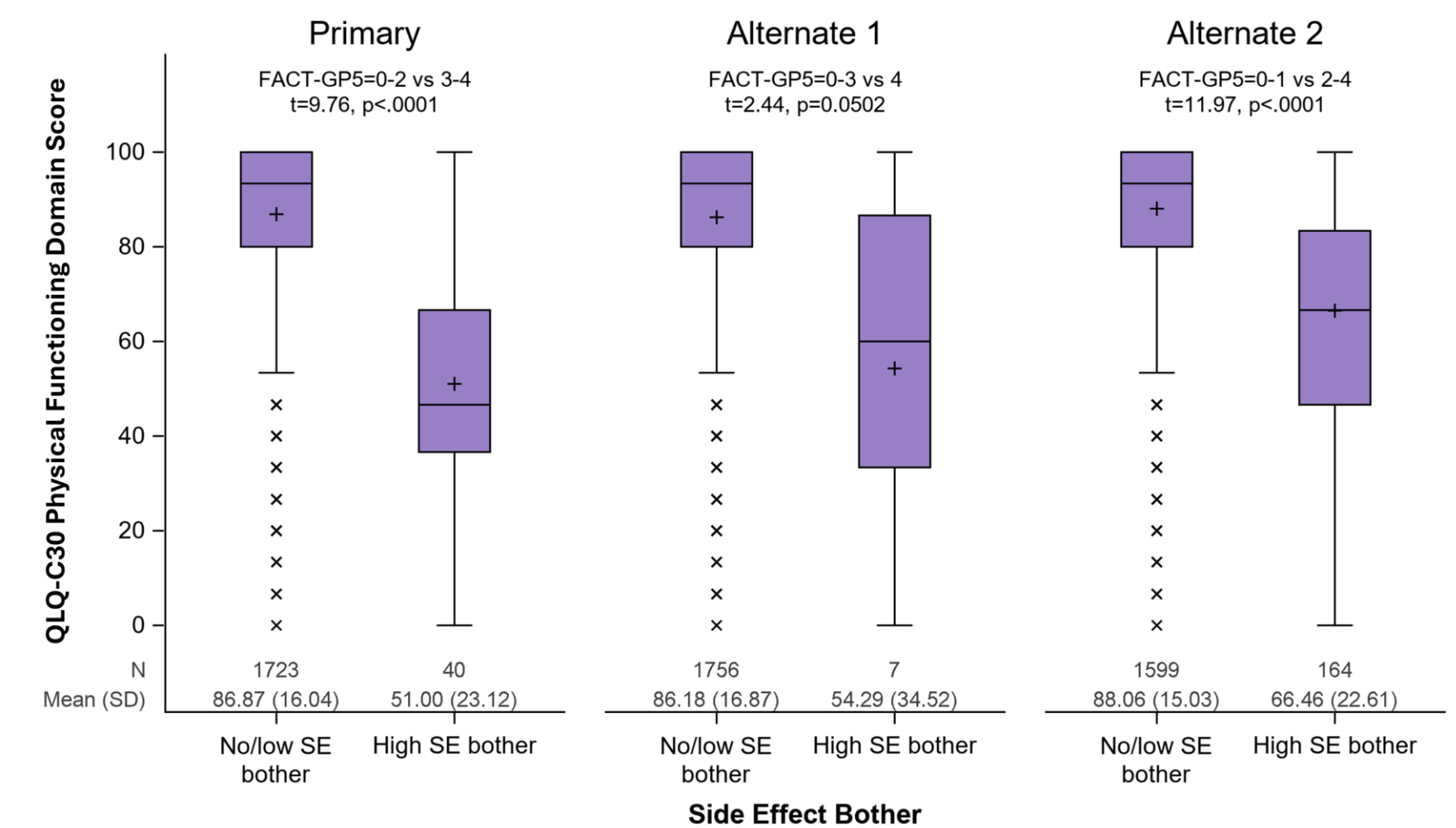
METHODS

- Blinded, pooled data from BRUIN-MCL-321 were used (data cutoff date March 29, 2024, Safety Set; N=523 [out of 549] participants with available PRO data)

- Three categorizations of FACT-GP5 ratings to describe SE bother (high versus no/low) were explored to evaluate the ability of the FACT-GP5 to discriminate Functioning (physical, role, social, emotional, and cognitive) and global health status/quality of life as measured by EORTC QLQ-C30, which are expected to be negatively impacted by SEs

- Distributions of QLQ-C30 functioning and global health status/quality of life (GHS/QoL) scores (higher score=better outcome) were described by high and no/low SE bother for the primary and two alternate categorizations:

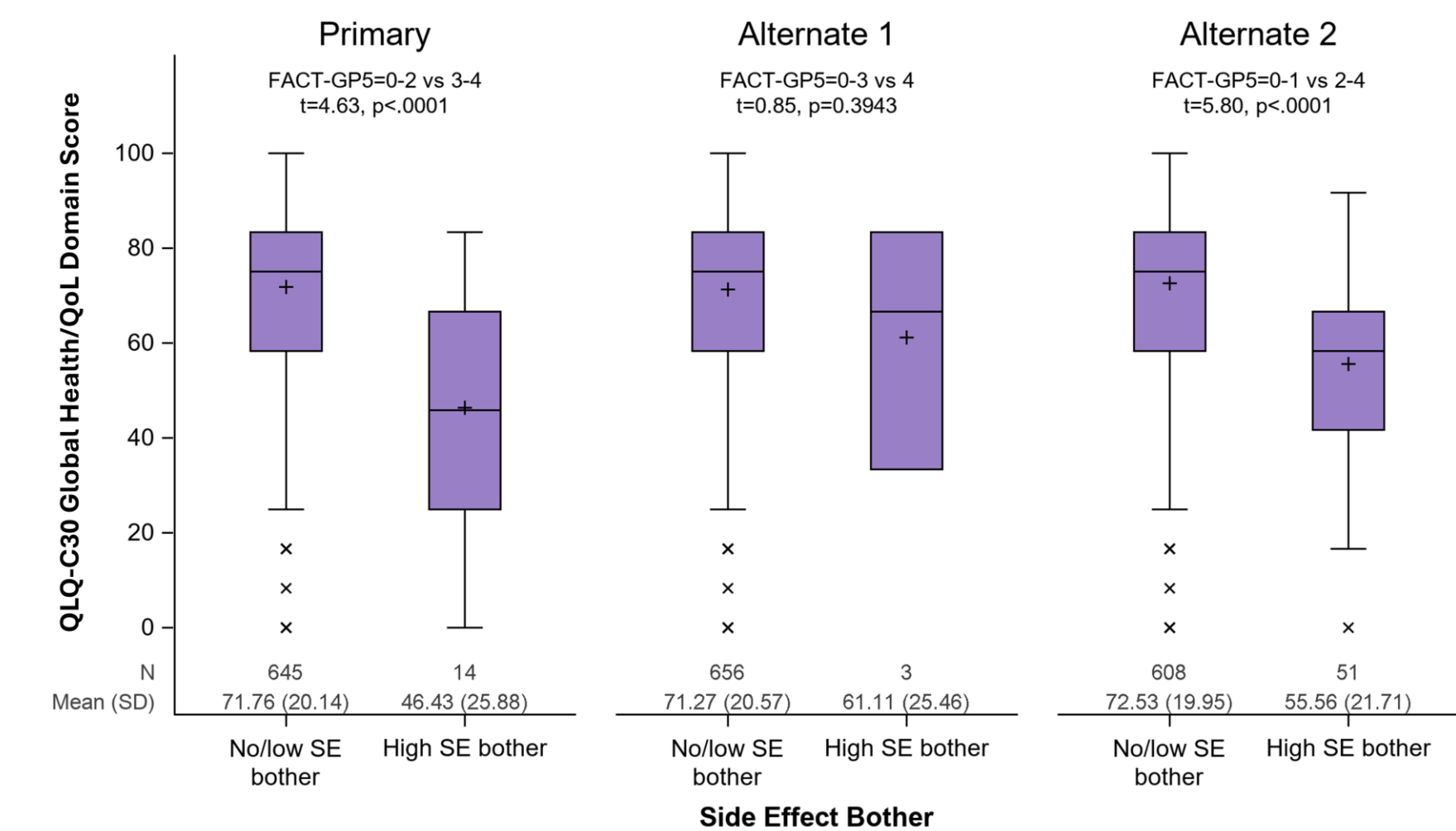|	High SE Bother	No/Low SE Bother
	FACT GP5 Rating	
Primary	3-4	0-2
Alternate 1	4	0-3
Alternate 2	2-4	0-1

References

1. US Federal Drug Administration, Core Patient-Reported Outcomes in Cancer Clinical Trials: Guidance for Industry. 2024.
2. Regnault A., et al. Assessing tolerability with the Functional Assessment of Cancer Therapy item GP5: psychometric evidence from LIBRETTO-531, a phase 3 trial of selpercatinib in medullary thyroid cancer. *Journal of Patient-Reported Outcomes*, 2024 8(1): p 149.
3. Eyre T.A., et al. BRUIN MCL-321: Phase III Study of Pirtobrutinib Versus Investigator Choice of BTK Inhibitor in BTK Inhibitor Naive Mantle Cell Lymphoma. *Future Oncology*, 2022. 18(36): p. 3961-3969.

KEY RESULTS

Note: N=number of assessments

Figure 1: Boxplot of the distribution of the QLQ-C30 Physical Functioning score according to categories of side-effect bother

Note: N=number of assessments

Figure 2: Boxplot of the distribution of the QLQ-C30 GHS/QoL score according to categories of side-effect bother

- The primary definition of High SE bother defined as a FACT-GP5 rating of 3-4 (n=40 assessments) showed best separation from no/low SE bother (n=1723 assessments) for the QLQ-C30 Physical Functioning scale, with non-overlapping inter-quartile ranges (IQRs) (Figure 1)

  - Alternate 1 and Alternate 2 had overlapping IQRs and smaller differences between the mean values

- Role, Social, Emotional, Cognitive and GHS/QoL scores each had overlapping IQRs for all three categorizations (results for GHS/QoL shown in Figure 2)

- Few participants rated SE bother as 4 (n≤7 assessments), limiting interpretation of Alternate 1 that defined high SE bother as a rating of 4