Variability and Inconsistency in QoL Assessment in Japanese Oncology HTA: A Review of Public and Manufacturer Analyses

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OBJECTIVE

To understand discrepancies between manufacturer and public analyses regarding QoL assessment in oncology-related Japanese health technology assessment (HTA) evaluations.

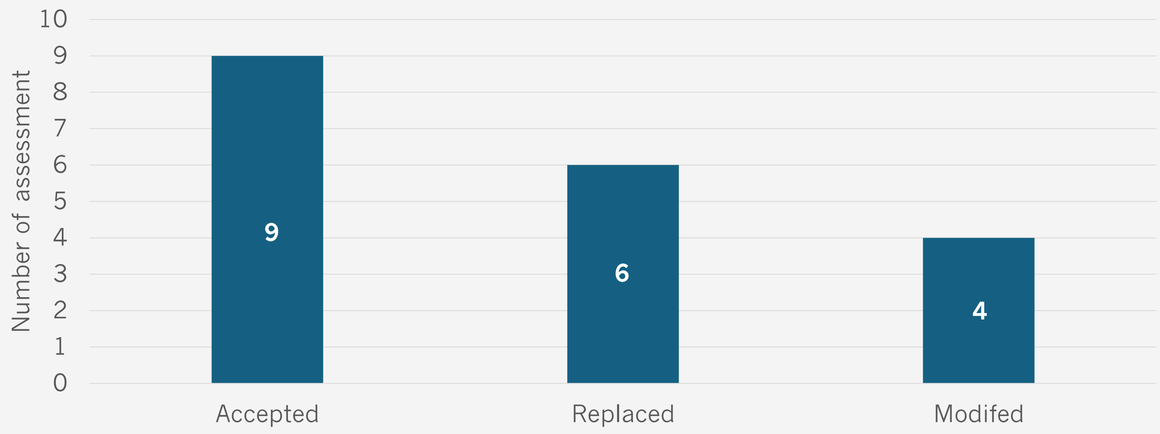
METHODS

Publicly available HTA reports with a "completed" status on the C2H website between April 2019 and May 2026 were reviewed. Differences in QoL assumptions, data sources, and utility estimates between manufacturer-submitted and public analyses were assessed for oncology indications. Minutes from the MHLW Cost-Effectiveness Evaluation Expert Committee (Chuikyo) were also reviewed for additional discussions related to QoL assessment. Public analysis outcomes were classified as Accepted (manufacturer approach retained), Modified (source retained but application revised), or Replaced (alternative utility values adopted) based on whether the manufacturer-submitted QoL data source and its application were retained or changed.

RESULTS

- Among 19 oncology assessments across 13 products, 9 (47.4%) manufacturer-submitted QoL approaches were accepted without major modification, while 6 (31.6%) were replaced and 4 (21.1%) were modified by the public analysis (Figure 1).
- Public analyses showed clear preferences in the selection and application of QoL evidence (Table 1).
  - Directly measured utility data from clinical trials were generally prioritized over mapped or externally derived values
  - Japanese preference-based values or Japan-specific mapping approaches were preferred when relevant data were available
  - Even when data sources were retained, utility assumptions were revised if they were clinically implausible or could favor the treatment.
- Decisions appeared to be influenced by the availability of alternative evidence (Table 1).
  - Manufacturer-submitted QoL inputs were more likely to be retained when no suitable alternative evidence was identified and replaced when alternative evidence was identified and prioritized by the public analysis.
- The selection of "best available evidence" varied when direct utility data were unavailable (Table 1).
  - Approaches included external directly measured utility data, literature-based values, and Japan-specific mapping of internal trial data.
- Treatment-specific utility gains were not accepted when they were unsupported by trial findings or considered likely to overestimate incremental QALYs, as observed for ropeginterferon and sacituzumab govitecan (Table 1).
  - This approach may limit the extent to which treatment-specific improvements observed in PROs are reflected in utility estimates.

Figure 1: Outcome of public analysis of manufacturer-submitted QoL inputs



Note: Different indications or lines of therapy for the same product were counted separately when they were analyzed and evaluated separately

Accepted: Manufacturer-submitted QoL approach largely retained
Modified: Original source retained, but assumptions/application revised
Replaced: Original source rejected and alternative utility values adopted

Table 1: Comparison of manufacturer and public approaches to QoL assessment

Year	Product / indication	Manufacturer approach	Public analysis	Outcome
2019	Tisagenlecleucel – B-ALL	Literature-based utilities mapped from SF-36 were used because trial QoL data were limited to patients aged ≥15 years and did not cover the entire target population.	Mapped utilities were replaced by directly measured EQ-5D data from the trial because directly measured preference-based data were prioritized over mapped values	Replaced
2019	Tisagenlecleucel – DLBCL	Literature-based utilities mapped from SF-36 were used because EQ-5D was not collected in the trial; the selected source had also been used in US cost-effectiveness models.	The submitted literature values were replaced with values from another literature source because QoL in elderly patients was considered overestimated.	Replaced
2020	Cabozantinib – RCC (1L)	No direct QoL data were available for the target setting; utility values from a later-line trial were used as proxy evidence.	Proxy values were retained as the base case because no direct Japanese first-line data were available, with sensitivity analyses to address uncertainty.	Accepted
2020	Cabozantinib – RCC (≥2L)	Patient-level EQ-5D data from the pivotal trial were used to estimate health-state utilities using Japanese tariff conversion and MMRM methods.	Company values were retained, with scenario analyses conducted because of concerns regarding potential bias and the assumptions underlying the MMRM model.	Accepted
2020	Cabozantinib – HCC	Health-related QoL data directly collected in the pivotal trial were used to estimate utilities.	Company utility values were retained because no major differences were identified between the company and public analyses.	Accepted
2020	Trastuzumab deruxtecan – Breast cancer	Literature-based utilities were selected because a single source provided values across all health states while accounting for the mean age of the target population.	Post-progression utility was revised upward because the submitted values were based on hypothetical valuations from the UK general population and were considered lower than actual Japanese patient experience.	Modified
2020	Trastuzumab deruxtecan – Gastric cancer	EQ-5D-5L data directly collected in the pivotal trial were used; in the absence of comparator QoL data, the comparator was assumed to have the same utility as the treatment group.	Company utility values were retained as a pragmatic approach given the lack of comparator utility data, although the assumption was considered potentially favorable to the product.	Accepted
2021	Polatuzumab vedotin – DLBCL	No QoL data were collected in the pivotal trial; mapped utilities were used based on the precedent of the prior Kymriah assessment in the same target population.	Mapped utilities were replaced with values derived from Yescarta's directly measured EQ-5D data, which were considered more appropriate and conservative.	Replaced
2021	Daratumumab – Multiple myeloma	Literature-based utilities were used because the source had been widely used in multiple myeloma cost-effectiveness analyses; trial utilities were considered to show insufficient differentiation between health states.	Company utility values were retained, although concerns were raised that trial-based utilities showed too little difference between PFS and PD.	Accepted
2021	Daratumumab – AL amyloidosis	EQ-5D-5L data directly collected in the pivotal trial were reanalyzed using Japanese preference weights, with literature values used only for end-stage states lacking trial data.	The utility decrement for end-stage organ failure was revised because the company assumption of universal dialysis and heart failure was considered inconsistent with clinical practice and potentially favorable to the product.	Modified
2021	Selpercatinib – NSCLC	Progression-free utilities were derived by mapping EORTC QLQ-C30 trial data, while post-progression values were obtained from NICE because trial data were insufficient.	The submitted approach was replaced by a Japan-specific mapping algorithm using trial EORTC QLQ-C30 data because the NICE values differed in patient characteristics and mapping methods and were not optimized for Japanese populations.	Replaced
2021	Selpercatinib – Thyroid cancer	No EQ-5D data were available from the pivotal trial; literature-based utilities were used as the only identified QoL evidence and were considered clinically appropriate.	Literature-based values were replaced by EORTC QLQ-C30 data from the manufacturer's trial mapped using a Japan-specific algorithm; vignette-based estimates were considered insufficiently robust.	Replaced
2021	Enfortumab vedotin – Urothelial carcinoma	EQ-5D-5L data directly collected in the pivotal trial were used to estimate utilities.	Trial-derived utility values were accepted without modification.	Accepted
2023	Ropeginterferon – Polycythemia vera	Because no between-group QoL differences were observed in the trial, an independent vignette survey was conducted to capture psychological benefits associated with molecular response.	The incremental psychological utility benefit was rejected and observed trial values were adopted. The vignette survey was considered subjective and insufficiently supported clinically.	Replaced
2023	Epcoritamab – DLBCL	EQ-5D-3L data from the pivotal trial were used to estimate utilities.	The assumption that QoL would recover to the level of the general healthy population after 3 years progression-free was rejected as clinically unrealistic; no subsequent improvement was assumed.	Modified
2024	Capivasertib – Breast cancer	EQ-5D-5L data from the pivotal trial were analyzed using Japanese value sets and MMRM methods.	Company utility values were retained because the use of Japanese value sets and the MMRM approach was considered appropriate.	Accepted
2024	Elranatamab – Multiple myeloma	EQ-5D-5L data from the pivotal single-arm trial were analyzed using Japanese value sets.	Company utility values were retained, although substantial uncertainty and potential bias associated with the unanchored MAIC using observational data were highlighted.	Accepted
2024	Zolbetuximab – Gastric cancer	Health-state utilities were estimated using EQ-5D-5L data directly collected in the pivotal trial.	Utility settings were retained; although other elements of the analysis were modified, no substantive modification to the utility values was made.	Accepted
2024	Sacituzumab govitecan – TNBC	EORTC QLQ-C30 data collected in the pivotal trial were mapped to EQ-5D-3L, generating treatment-specific utility estimates.	Common health-state utilities were applied across treatment arms because utility was considered to depend on health state rather than treatment regimen; treatment-specific values were considered potentially to overestimate incremental QALYs.	Modified

Abbreviations: B-ALL, B-cell acute lymphoblastic leukemia; CAR-T, chimeric antigen receptor T-cell; C2H, Center for Strategic Health Technology Assessment; DLBCL, diffuse large B-cell lymphoma; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; EQ-5D, EuroQol 5-Dimension; HCC, hepatocellular carcinoma; HTA, health technology assessment; MAIC, matching-adjusted indirect comparison; MMRM, mixed model for repeated measures; NICE, National Institute for Health and Care Excellence; NSCLC, non-small cell lung cancer; PFS, progression-free survival; PRO, patient-reported outcome; QALY, quality-adjusted life-year; QoL, quality of life; RCC, renal cell carcinoma; TNBC, triple-negative breast cancer.

DISCUSSION and CONCLUSION

- QoL assessment was relatively predictable when directly measured or Japan-specific evidence was available, but more variable when such evidence was lacking.
- When such evidence is unavailable, manufacturers could reduce uncertainty by predefining and justifying alternative sources based on population relevance, mapping validity, and clinical plausibility.
- Greater clarity on the selection and validation of alternative QoL evidence may improve predictability in evidence-limited settings.

Reference: C2H website https://c2h.niph.go.jp/en/ (Accessed May 2026); MHLW. Pharmaceutical Affairs and Food Sanitation Council, First Committee on Drugs: Meeting Minutes. https://www.mhlw.go.jp/stf/shingi-yakuji_39203.html (Accessed May 2026)