EE355

Preprogression Health State Utility Values From the TALAPRO-2 Clinical Trial in Patients With Metastatic Castration-Resistant Prostate Cancer With HRR Mutations

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Objective

The aim of this research was to estimate preprogression health-state utility values (HSUVs) suitable for use in cost-effectiveness analyses in first-line (1L) metastatic castration-resistant prostate cancer (mCRPC) with homologous recombination repair mutations (HRRm).

Conclusions

It is important to understand preprogression impact on quality of life when optimizing patient care and treatment decisions in HRRm mCRPC. Generated HSUVs were numerically higher for TALA + ENZA. HSUVs using the US value set were numerically higher than the UK, but conclusions were consistent across value sets.

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BACKGROUND

- mCRPC represents a lethal transition in the progression of prostate cancer with higher mortality. HRR deficiencies are emerging as a crucial factor in the pathogenesis and progression of mCRPC.[1]
- In a prespecified cohort of patients with HRRm mCRPC, TALAPRO-2, an international phase 3 trial (NCT03395197), compared treatment with talazoparib + enzalutamide (TALA + ENZA) (n = 200) with placebo + enzalutamide (PBO + ENZA) (n = 199). It showed a statistically significant improvement in the primary endpoint of radiographic progression-free survival (rPFS) by blinded independent committee review (hazard ratio = 0.45; 95% confidence interval [95% CI], 0.33-0.61; $P < 0.0001$).[2]
- HSUVs are essential parameters in model-based economic evaluations, and they are typically used to calculate quality-adjusted life-years gained, which are a measure of the overall health benefits of an intervention.
- EQ-5D is a standardized measure of health status developed by the EuroQol Group to provide a simple, generic measure of health for clinical and economic appraisal across all diseases.[3]
  - It is a descriptive system of health-related quality-of-life states consisting of 5 dimensions: Mobility, Self-care, Usual activities, Pain/discomfort, and Anxiety/depression).
  - For the EQ-5D-5L, each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems.
  - A single index value for health states (utility) is calculated from the combination of responses to the 5 dimensions. Value sets are based on a scale anchored at 1 (full health).
- Currently, there are no published data on HSUVs for the mCRPC population with HRRm.

METHODS

DATA

- Patient-level data from TALAPRO-2 for TALA + ENZA (n = 200) or PBO + ENZA (n = 199) in HRRm mCRPC were analyzed.
- In TALAPRO-2, the EQ-5D-5L was administered at baseline, every 4 weeks until week 53 or rPFS, every 8 weeks after week 53 until rPFS when no progression had been documented, or every 12 weeks after progression until study end.

STATISTICAL ANALYSES

- In TALAPRO-2, rPFS based on blinded independent committee review was the primary efficacy endpoint. Health state utilities were estimated based on the time before and after radiographic progression (before and after progression).
- Utility was estimated regardless of and by treatment arm by applying value sets for the United Kingdom (UK)[4] and the United States (US)[5] independently to TALAPRO-2 trial data. For each country, EQ-5D-5L analyses consisted of descriptive statistics on HSUV means and results from mixed-effects models.
- To predict EQ-5D-5L utility by health state, a linear mixed model for repeated measures was used with individual patients as random effects and the following covariates as fixed effects: health state, planned treatment, time of visit (since randomization), baseline age, baseline EQ-5D-5L utility, baseline ECOG performance status, and interaction term between planned treatment and health state (i.e., before and after progression).
- The linear mixed-effect model assumed the missing data mechanism to be missing at random.
- A parsimonious model was selected using backward elimination, where covariates that were not significant were sequentially removed from the model according to their P value [$P < 0.05$]). Health state was forced into the model.
- Descriptive statistics were based on the intent-to-treat population. Statistical models were fit to patients with baseline and at least 1 follow-up EQ-5D-5L value. Only estimates corresponding to the preprogression health state are presented.

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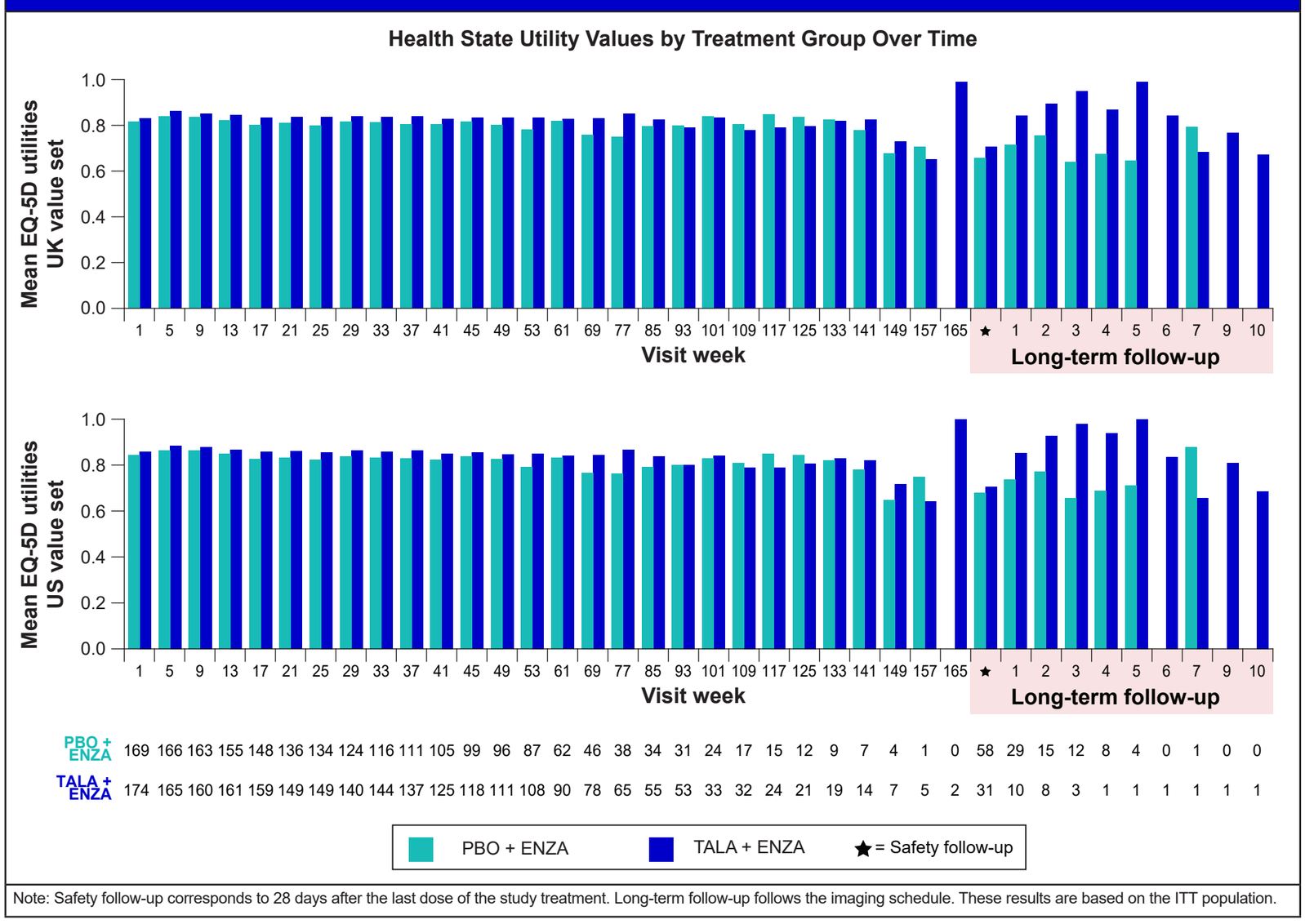
RESULTS

- No differences in patient demographics (e.g., age, ECOG score, baseline pain score, baseline serum prostate-specific antigen, renal impairment, Gleason score, metastatic site, previous treatment with any neoadjuvant hormonal therapy or taxane-based chemotherapy, HRRm status) were identified between treatment arms.
- Descriptive statistics showed that, while the sample was sufficiently large, mean EQ-5D utilities remained relatively stable in both treatment arms until week 49 regardless of and by treatment arm (Figure 1). Variation in this pattern was observed in the remaining visits, with more pronounced differences observed at the safety and long-term follow-up visits, which is likely due to the very small number of observations across the visits.
- Preprogression utility regardless of treatment arm was 0.815 (95% CI, 0.803-0.827) for the UK. Consistent results were found for the US, although utility was slightly higher (Table 1).
- Preprogression HSUVs were numerically higher in the TALA + ENZA arm than PBO + ENZA for both countries.
- The differences in the utilities between TALA + ENZA and PBO + ENZA were not statistically significant in any value set (UK; $P = 0.070$, US; $P = 0.092$).

Figure 1. Mean EQ-5D-5L Utility Values Over Time



Note: Safety follow-up corresponds to 28 days after the last dose of the study treatment. Long-term follow-up follows the imaging schedule. These results are based on the ITT population.

Table 1. Analysis of Utility Score for the Preprogression Health State

	UK value set		US value set	
Treatment	**Mean EQ-5D score (SE)**	**95% CI**	**Mean EQ-5D score (SE)**	**95% CI**
Overall	0.815 (0.006)	(0.803-0.827)	0.835 (0.007)	(0.822-0.848)
TALA + ENZA	0.825 (0.008)	(0.809-0.842)	0.846 (0.009)	(0.828-0.863)
PBO + ENZA	0.803 (0.009)	(0.786-0.821)	0.824 (0.010)	(0.805-0.842)

SE = standard error.

Note: The results presented in this poster are from a model that includes data for both preprogression and post-progression health states; only results for the preprogression health state are shown. Following backward elimination, the covariates that remained significant in the UK analysis were time of visit (since randomization), baseline age, baseline EQ-5D-5L utility, baseline ECOG status, planned treatment, and health state. The same covariates were found to be significant in the US analysis except for planned treatment. These results are based on the patient-reported outcome analysis population (patients with baseline and ≥ 1 follow-up value for EQ-5D-5L).

References: **1.** Stewart MD, et al. Oncologist. 2022 Mar 1;27(3):167-74. **2.** Fizazi K, et al. J Clin Oncol. 2023;41(16_suppl):5004-5004. **3.** EuroQol Research Foundation. 2019. https://euroqol.org/publications/user-guides. **4.** Hernández-Alava M, Pudney S. J Health Econ. 2017;55:139-52. **5.** Pickard AS, et al. Value Health. 2019;22(8):931-41.

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