Cost-utility analysis of enzalutamide for patients with chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC) after failure of androgen deprivation therapy (ADT)

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INTRODUCTION

• Metastatic castration-resistant prostate cancer (mCRPC) is the most advanced stage of prostate cancer and, currently, there is no known curative therapy for this indication. Therefore, the goals of treatment for mCRPC are to prolong survival and control symptoms, and improve quality of life.

• The PREVAIL study 1 demonstrated that enzalutamide is a highly effective treatment in chemotherapy-naive patients with mCRPC previously treated with androgen deprivation therapy:
  – significantly reduced the risk of death by 29% compared with placebo (p = 0.001);
  – significantly reduced the risk of radiographic-progression by 81% versus placebo (p = 0.001);
  – significantly delayed the initiation of cytotoxic chemotherapy by 17 months versus placebo (risk reduction of 85%, p = 0.001);
  – significantly increased the proportion of patients with improvements in quality of life measures; a significantly greater proportion of patients in the enzalutamide group than in the placebo group reported clinically meaningful improvements in FACT-P total score (40% versus 23%), EQ-5D utility index (28% versus 16%) and visual analog scale (27% versus 18%); all p < 0.001. 3

• In addition, enzalutamide delayed occurrence of first skeletal-related events in this treatment setting. 4

OBJECTIVE

• The objective of this analysis is to estimate the cost-effectiveness of enzalutamide versus Abiraterone + Prednisone (ABI+P) for patients with chemotherapy-naïve mCRPC, from the perspective of the Canadian Ministries of Health (MoH).

METHODS

• A Markov model was developed to capture time spent by patients in three health states, with modifications to the second state: stable disease, progressive disease (which included post-progression treatment-free, post-progression 1 [second-line treatment], post-progression 2 [third-line treatment] and palliative care), and death (Figure 1).

• Results were reported as incremental costs per additional quality-adjusted life year (QALY) gained over a 10-year period.

• Information on probabilities, utilities and resource utilisation for waitlist waiting, followed by docetaxel and enzalutamide, were derived from the PREVAIL clinical trial, supplemented with literature data, where necessary.

• Estimates of progression-free survival (PFS) and overall survival (OS) for each comparator were obtained by first fitting the parametric survival function to the observed failure time for the reference arm (best supportive care, i.e., placebo arm, from the PREVAIL trial). Five distributions were considered: exponential, Weibull, log-logistic, log-normal and gamma. Evaluating all the criteria for model selection and taking into account the clinical plausibility of the distribution tails, the Weibull distribution was selected as the best fit for each outcome.

• Relative hazard ratios were applied to the survival functions for each of the other comparators. A network meta-analysis (NMA) of available trials was used to obtain the hazard ratios of each comparator (Figure 2).

• Base case analysis focused on direct medical costs from the Canadian MoH perspective.
  – Costs inputs included in the model include costs of treatment with medications, medical resource utilisation (outpatient visits, procedures, laboratory tests, hospitalisations and terminal care costs) and costs for treatment of adverse events and skeletal-related events.

• The improvement in PFS translated into a longer mean duration of PFS (16.4 months) versus placebo (11.3 months) (95% CI: 0.627, 0.652) (Table 2).

• Multivariable cost-effectiveness sensitivity analyses were performed to test the robustness of the results to variations in several parameters at once. The number of simulations to be run was to 1000. The percentage of simulations below the threshold was 60% of iterations for most parameters at once. The model was run in WinBugs 1.4.3.

• The ICER was robust over a wide range of sensitivity analyses. In the probabilistic sensitivity analysis, following 1000 iterations, the mean ICER was $110,036 per QALY gained versus ABI+P, with a 60% of iterations failing below a willingness-to-pay threshold of $100,000 per QALY gained (Figure 3).

RESULTS

• NMA results suggested no difference between enzalutamide and ABI+P for OS, but indicated that enzalutamide is superior to ABI+P for PFS (hazard ratio 0.36; credible interval 0.27, 0.47) (Table 4).

• The improvement in PFS translated into a longer mean duration of stable disease with enzalutamide (38.7 months) than with ABI+P (16.4 months) (Table 4).

• In an analysis, cost-effectiveness refers both to the cost-effectiveness analysis (described by the incremental cost-effectiveness ratio [ICER]), and the cost-utility analysis (described by the incremental cost-utility ratio), similar to convention.

• From the Canadian MoH perspective, enzalutamide had an ICER of $92,690 per QALY gained versus ABI+P, with –40% of iterations failing below a willingness-to-pay threshold of $100,000 per QALY gained (Figure 3).

• The PREVAIL study demonstrated that enzalutamide is a highly effective treatment in chemotherapy-naive patients with mCRPC previously treated with androgen deprivation therapy:
  – significantly reduced the risk of death by 29% compared with placebo (p = 0.001);
  – significantly reduced the risk of radiographic-progression by 81% versus placebo (p = 0.001);
  – significantly delayed the initiation of cytotoxic chemotherapy by 17 months versus placebo (risk reduction of 85%, p = 0.001);

• The ICER was robust over a wide range of sensitivity analyses. In the probabilistic sensitivity analysis, following 1000 iterations, the mean ICER was $110,036 per QALY gained versus ABI+P, with –60% of iterations failing below a willingness-to-pay threshold of $100,000 per QALY gained (Figure 3).

CONCLUSIONS

• NMA results suggest an improved overall benefit/risk profile for enzalutamide over existing therapies.

• The economic evaluation, based on PREVAIL study data and a NMA, indicates that enzalutamide can be considered a cost-effective treatment option compared to ABI+P in patients with chemotherapy-naïve mCRPC after failure of androgen deprivation therapy.

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