DAROLUTAMIDE AS A LEADING OPTION TO MANAGE PROSTATE CANCER

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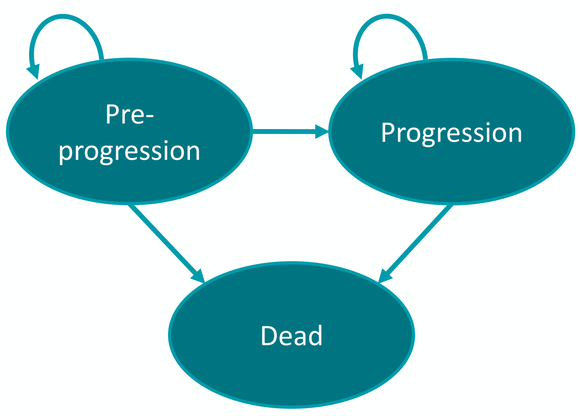
OBJECTIVES

Prostate cancer is a disease with an indolent course, particularly at the earliest stages, and is the most common cause of solid cancers and the fourth most common cause of cancer-related death in men in Portugal [1, 2]. The major clinical burden and need for medical care result in a high economic impact on national healthcare systems (NHS) [3-8]. Darolutamide is a new androgen receptor inhibitor indicated in combination with androgen deprivation therapy (ADT) for non-metastatic castration-resistant prostate cancer (nmCRPC) and in combination with ADT and docetaxel for metastatic hormone-sensitive prostate cancer (mHSPC). The aim of this study is to assess the clinical and economic value of the introduction of darolutamide versus current clinical practice (apalutamide and enzalutamide) in the treatment of nmCRPC and mHSPC in Portugal.

METHODS

A Markov model was developed, using partition survival method and three mutually exclusive health states: pre-progression, progression and death (Figure 1).

Figure 1. Markov model structure



Parametric survival models were fitted to time-to-event from phase 3 studies ARAMIS and ARASENS (NCT02799602), namely log-normal and log-logistic for overall survival (OS) and progression free survival (PFS) in mHSPC patients, respectively, while the Weibull distribution was used for both survival curves in nmCRPC patients.

Unit costs of health resources were collected from Portuguese official databases [9-14] and healthcare resources utilization for Portugal was retrieved from Portuguese experts [15]. The price of darolutamide was provided by Bayer and the price of apalutamide and enzalutamide were derived from a Portuguese official database [9]. Health state utility values (HSUV) were derived from the ARAMIS study for nmCRPC patients. For mHSPC patients, HSUV were retrieved from past submissions to the National Institute for Health and Care Excellence (NICE) and validated by Portuguese experts.

Model cycle duration was 28 days. A 4% annual discount rate was adopted for costs and effects from the Portuguese NHS perspective. A time horizon of 2 years was considered (NHS contract period).

For the sake of comparison, current clinical practice was considered to be an equal distribution of apalutamide, enzalutamide and darolutamide of 33%.

RESULTS

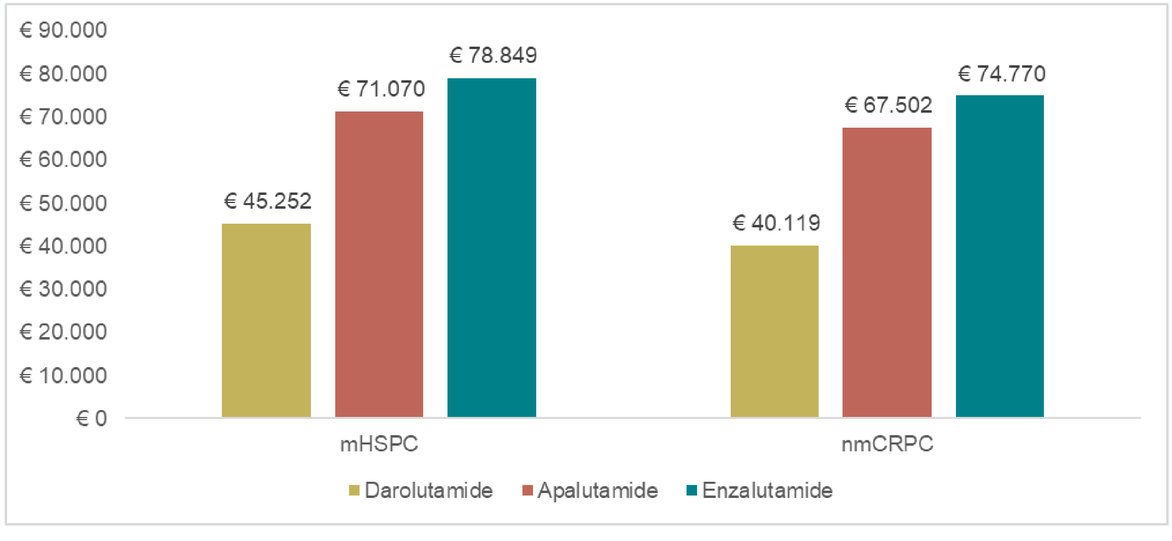
Treatment with darolutamide is associated with an increase in the patients' life expectancy and quality of life (QoL). Table 1 summarizes the life years (LY) and quality adjusted life years (QALY) a patient may gain when treated with darolutamide when compared with being treated with apalutamide or enzalutamide.

Table 1. Survival and QoL indicators over a patients' life-time

Darolutamide vs.	mHSPC		nmCRPC	
	LY Gained	QALY Gained	LY Gained	QALY Gained
Apalutamide	1.34	1.66	0.49	0.25
Enzalutamide	1.44	2.08	0.80	0.48

Results indicate that darolutamida improved outcomes in terms of survival and QoL compared to apalutamide and enzalutamide by prolonging the time to disease progression.

Figure 2. Economic impact of the alternative treatments per patient



The inclusion of darolutamide as a mHSPC first-line treatment option was estimated to reduce the number of outpatient visits by **6** and exams by **21** when compared to apalutamide, and by **10** outpatient visits and **10** exams when compared to enzalutamide in the first two years, per patient. Analogously, the inclusion of darolutamida as a nmCRPC first-line treatment option was estimated to reduce the mean number of outpatient visits and exams by **1**, *versus* the same alternatives in the same time period, per patient.

During the first two years of contract, the Portuguese NHS is estimated to spend 45,252 € per mHSPC patient treated with darolutamide, resulting in a significant cost reduction when compared with the **71,070 € (+57%)** and **78,849 € (+74%)** cost of treatment with apalutamide and enzalutamide, respectively. Similarly, nmCRPC patients incur in costs of around 40,119 € when treated with darolutamide vs. **67,502 € (+68%)** and **74,770 € (+86%)** when treated with apalutamide and enzalutamide respectively (Figure 2).

Considering the improvement in health outcomes and reduction in total costs, the **introduction of darolutamide resulted in a dominant scenario**, relative to the current clinical practice, specially when considering improved survival and quality of life.

= CONCLUSION

The introduction of darolutamide for nmCRPC and mHSPC is associated with increased life expectancy and quality of life, alongside reduced healthcare costs compared to current treatments in Portugal, placing it as an optimal choice for resource allocation within the healthcare system.

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