Reflection on Medicines That Have Recently Come off Patent and Have Been Rejected by NICE in the Past 20 Years: A Case Study of Abiraterone for Treating Newly Diagnosed Metastatic Hormone Sensitive Prostate Cancer (mHSPC)

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BACKGROUND

- Patents protect and promote the development of new therapeutic innovations through the exclusive marketing rights provided by the protection guaranteed by patents.
- Patent protection lasts up to 20 years in England and Wales. It may also be extended by an additional five years of protection.
- Since its establishment in 1999, The National Institute for Health and Care Excellence (NICE) has rejected a significant number of medicines. Despite their superior clinical effectiveness, they couldn't attain cost-effectiveness due to their high cost.
- Considering the patent protection period and the time since NICE was founded, there were a limited number of drugs that went off-patent. Nevertheless, these drugs are expected to become more common in the near future.
- Abiraterone is used for treating metastatic hormone-sensitive prostate cancer (mHSPC). The combination of Abiraterone Acetate plus Prednisone (AAP) with the standard androgen deprivation therapy (ADT) showed a better clinical outcome [1].
- In 2021, Abiraterone received a negative recommendation from NICE due to its high cost. However, the cost of Abiraterone was expected to decrease after the expiration of the brand's patent in September 2022, which would lead to the availability of a generic version. This was anticipated to affect cost-effectiveness decisions.

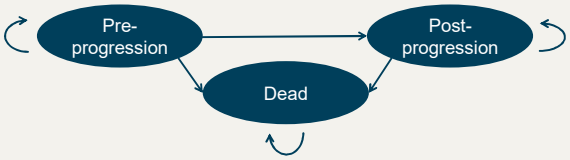
OBJECTIVE

- To assess the cost-effectiveness of Abiraterone using a cost utility analysis (CUA) that provides a potential new price of the generic version of Abiraterone that would make it cost effective.

METHODS

- A partitioned survival model (**Figure 1**) was constructed to compare the cost-effectiveness of AAP + ADT vs. ADT alone over a lifetime horizon from the perspective of the UK National Health Service (NHS).

Figure 1: Patients' Movement in the Model



- The potential price was estimated based on a targeted literature review that was conducted to determine the patterns of price decreases following patent expiration.
- The model population was based on data from LATITUDE, a multinational, randomized, double-blind, placebo-controlled Phase 3 trial [2]. A total of 1199 patients, with 597 in the Abiraterone group and 602 in the comparison group.
- Kaplan-Meier data were reconstructed from published literature [1] using the Graphreader software tool [3].
- Kaplan-Meier data from the LATITUDE trial were used for the first 42 months of overall survival (OS) and the first 40 months of radiographic progression-free survival (rPFS) in both arms of the analysis. Subsequently, parametric distribution methods were employed to extrapolate beyond the trial data.
- Utility values for each health state were obtained from literature [4].
- Cost values were obtained from a healthcare perspective, including expenses for drugs, administration, monitoring, and resources.
- One-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA) were performed.
- Expected Value of Perfect Information (EVPI) was calculated.

RESULTS

I. Base-case analysis

AAP + ADT arm cost £43,822 and gained 4.65 QALYs, while the ADT arm cost £5,328 and gained 3.02 QALYs. This means that the AAP + ADT cost £38,493 more than the ADT arm, with 1.63 incremental QALYs. This results in an ICER of £23,580/QALY, which is considered cost-effective, assuming a WTP threshold of £30,000 per QALY gained (See **Table 1**).

Table 1: Model Base-Case Analysis Result

Arm	Mean Cost	Mean QALYs	ICER (£/QALY)
AAP + ADT	£43,822	4.65	£23,580
ADT	£5,328	3.02	
Incremental difference	£38,493	1.63	

II. OWSA

Figure 2 shows the OWSA tornado diagram, revealing that the most significant impact on the ICER was attributed to changing in the Abiraterone discount rate and the cost of the AAP arm. Changing the AAP pre-progressive state utility values had a moderate effect, while the remaining parameters demonstrated comparatively less influence.

III. PSA

The PSA cost-effectiveness plane and the Base-Case Cost-Effectiveness Acceptability Curve (CEAC) are displayed in **Figure 3** and **Figure 4**, respectively. It is evident that all dots indicate that AAP+ADT is not only more effective but also more expensive. Two thresholds, £20,000 and £30,000 per QALY, are presented on the diagram. AAP + ADT is 86% likely to be considered cost-effective at the £30,000 threshold, but this likelihood decreases to 20% at the £20,000 threshold.

IV. EVPI

The EVPI result, as shown in **Figure 5**, indicates that the monetary value a decision-maker would be willing to pay for perfect information regarding the Abiraterone model at the individual level was £773 per patient at a £20,000/QALY threshold and £661 per patient at a £30,000/QALY threshold.

Figure 2: OWSA Tornado Diagram

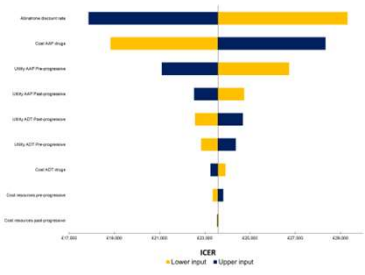


Figure 3: Cost-Effectiveness Plane

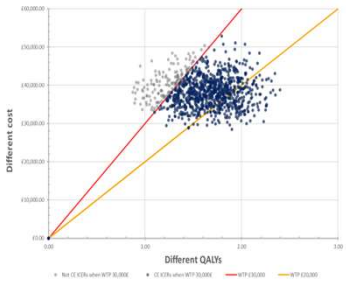


Figure 4: Cost-Effectiveness Acceptability Curve

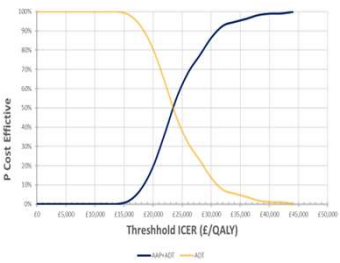
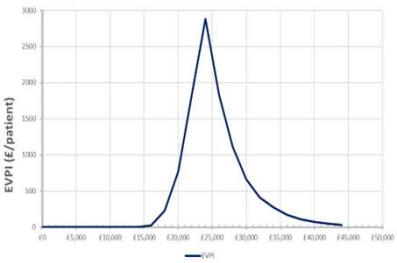


Figure 5: Expected Value of Perfect Information



CONCLUSION

- This analysis highlights a cost-effective treatment opportunity that can enhance management strategies for prostate cancer patients. Notably, the generic Abiraterone was introduced to the market after our analysis, at a price even lower than our estimate, underscoring the significance of exploring these treatment options.

Sources

1. Fizazi, Karim et al. "Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer." The New England journal of medicine vol. doi:10.1056/NEJMoa1704174
2. Kumar G. LATITUDE: A landmark trial for high-risk metastatic castration-sensitive prostate cancer: Final overall survival analysis. Indian J Urol. 2020 Jan-Mar; PMCID: PMC6961436.
3. https://www.graphreader.com/
4. Clarke, Caroline S et al. "Cost-utility analysis of adding abiraterone acetate plus prednisone/prednisolone to long-term hormone therapy in newly diagnosed advanced prostate cancer in England: Lifetime decision model based on STAMPEDE trial data." Jun. 2022, doi:10.1371/journal.pone.0269192