Cost-utility analysis of darolutamide plus androgen deprivation therapy for patients with high-risk non-metastatic castration-resistant prostate cancer in China

EE168

Jian Ming[1,4], Yuxia Wu[1], Rong Han[2], Xing Xu[2], Reg Waldeck[3], Shanlian Hu[4]

1. Real World Solutions, IQVIA China, Shanghai, China; *2. Medical Affairs, Pharmaceuticals, Bayer Healthcare Company Ltd, Beijing, China*; *3. Bayer Healthcare Pharmaceuticals, 100 Bayer Blvd, Whippany, NJ, USA*; *4. School of Public Health, Fudan University, Shanghai, China*

Corresponding author: Shanlian Hu, MD, MSc, Email: hushanlian@hotmail.com

OBJECTIVES

- To evaluate the long-term cost effectiveness (cost-utility) of darolutamide+androgen deprivation therapy (ADT) compared with apalutamide+ADT and enzalutamide+ADT in the treatment of high-risk non-metastatic castration-resistant prostate cancer (nmCRPC) in China.

METHODS

a) Decision model design

- A three health states partitioned survival model was developed (**Figure 1**).
- The Chinese healthcare system perspective was adopted.
- Clinical outcomes from the ARAMIS, PROSPER and SPARTAN studies were obtained. Other parameters were estimated from published literature, local reference price tables, or physician surveys (**Table 1**).
- The prices of darolutamide, apalutamide and enzalutamide were all assumed to be the same as the initial launch price of darolutamide in China, since their latest prices are commercially confidential, after recent price negotiations.
- Future costs and utilities were discounted at 5% per annum.
- Twelve urologists from 11 different tertiary hospitals were enrolled to finish a questionnaire-based survey verifying data inputs, model structures and closing data gaps.
- One-way sensitivity analysis (OWSA) and probabilistic sensitivity analyses (PSA) were conducted.

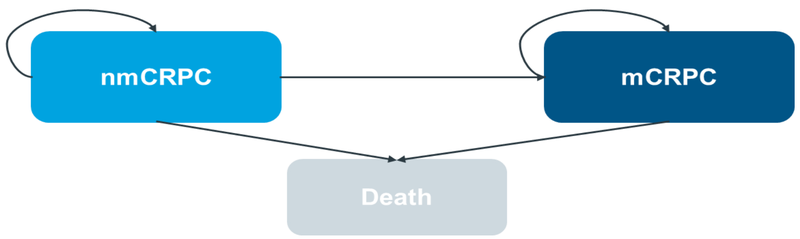

Figure 1: Health-state structure of the partitioned survival model

b) Indirect treatment comparison (ITC)

- In the absence of head-to-head studies, ITC were conducted to capture the comparative effectiveness of darolutamide+ADT vs. apalutamide+ADT and vs. enzalutamide+ADT.
- A systematic review of double-blind, randomized, placebo-controlled trials, including novel androgen receptor inhibitors (ARIs), was conducted in Pubmed, Embase and the Cochrane Library databases from Jan 2018 to Dec 2020.
- Three methods were considered to perform the ITC: the Bucher method, Bayesian network meta-analysis (NMA) and a matching adjusted indirect treatment comparison (MAIC).

Table 1: Key model inputs

Parameter	Base case	Source
Clinical efficacy		
HR-OS darolutamide+ADT vs apalutamide+ADT	0.88	ARAMIS[1], SPARTAN[2]
HR-OS darolutamide+ADT vs enzalutamide+ADT	0.95	ARAMIS[1], PROSPER[3]
HR-MFS darolutamide+ADT vs apalutamide+ADT	1.29	ARAMIS[1], SPARTAN[2]
HR-MFS darolutamide+ADT vs enzalutamide+ADT	1.24	ARAMIS[1], PROSPER[3]
Health utility inputs		
nmCRPC	0.815	ARAMIS trial[1]
mCRPC	0.751	ARAMIS trial[1]
AE Disutility*-darolutamide+ADT	-0.00051	Calculated
AE Disutility*-apalutamide+ADT	-0.00177	Calculated
AE Disutility*-enzalutamide+ADT	-0.00262	Calculated
Drug cost during nmCRPC (CNY) per model cycle		
Darolutamide/apalutamide/enzalutamide	22,026.67	Calculated
Background therapy (ADT) cost-initial cycle	1,614.54	Calculated
Background therapy (ADT) cost-subsequent cycle	1,319.28	Calculated
Subsequent treatment cost during mCRPC (CNY)		
Subsequent drug costs (one-off)	124,659.66	Calculated
Health resources utilization cost (CNY)		
Monitoring cost – nmCRPC per model cycle	1,196.00	Clinical expert interview
Monitoring cost – mCRPC per model cycle	1,394.77	Clinical expert interview
End-of-life cost	13,045.16	Public literature[4]
AE one-off cost- darolutamide+ADT	613.67	Calculated
AE one-off cost- apalutamide+ADT	1,915.75	Calculated
AE one-off cost-enzalutamide+ADT	2,036.22	Calculated

Abbreviation: AE: Adverse event; CNY: Chinese yuan; Exchange rate: 1 USD =6.7871 CNY

RESULTS

a) ITC results

- Three pivotal trials[1-3] that met the selection criteria were identified evaluating a total of 4,117 patients. The two comparators were connected through a common comparator placebo + ADT (**Figure 2**).
- The Bucher method suggests that there is a decrease in the unadjusted hazard of death by any cause of 12% for patients treated with darolutamide+ADT compared with patients treated with apalutamide+ADT.
- When compared to enzalutamide+ADT, the decrease in hazard of death by any cause is 5% for patients treated with darolutamide+ADT.
- All the ITC methods gave similar results, given that the evidence network only includes three trials (one for each treatment) connected by a common comparator.
- The Bucher method was employed in the base-case analysis owing to its simplicity.

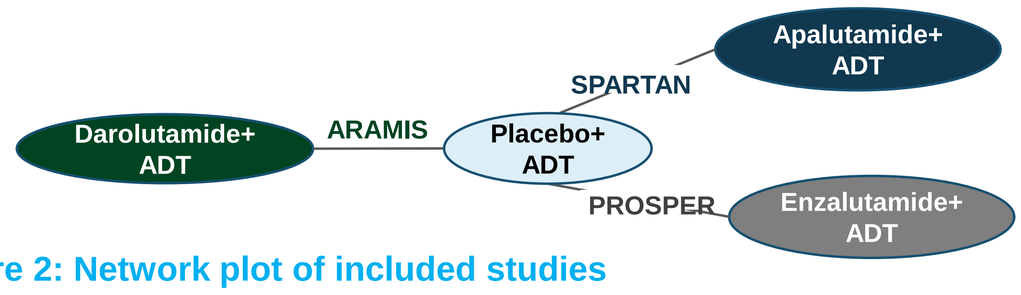

Figure 2: Network plot of included studies

b) Cost-effectiveness results

- In a 20-year lifetime horizon, darolutamide+ADT had better health outcomes and lower total costs compared with both apalutamide+ADT and enzalutamide+ADT (**Table 2**).
- The incremental QALY gains with darolutamide+ADT were mainly driven by the improved life years during the mCRPC phase (+0.92 LYs vs. apalutamide+ADT and +0.65 LYs vs. enzalutamide+ADT).
- OWSA showed that the net monetary benefit (NMB) was most sensitive to variations in parameters of HR of OS, MFS between apalutamide+ADT /enzalutamide+ADT and darolutamide+ADT, cycle cost of three novel ARIs and utility value during mCRPC (**Figure 3**).
- PSA projected that darolutamide+ADT had a chance of 85.41% and 77.62% to be a cost-effective alternative compared to apalutamide+ADT and enzalutamide+ADT, respectively, under the WTP threshold of triple the 2021 China per capita GDP (242,928 CNY).
- Scenario analysis results suggested that different ITC methods had limited impact on the cost-utility results.

Table 2: Base case model results

Outcomes	Daro+ADT	Apa+ADT	Enza+ADT	Incremental (Daro+ADT vs Apa+ADT)	Incremental (Daro+ADT vs Enza+ADT)
LYs	5.98	5.64	5.82	0.35	0.16
QALYs	4.72	4.50	4.63	0.22	0.09
Cost (CNY)	957,674	1,030,492	1,025,125	-72,818	-67,451
Cost/QALY (CNY)	202,897	228,998	221,409		
ICER				Dominant	Dominant
NMB				127,336	89,582

Abbreviation: daro: darolutamide; apa: apalutamide; enza: enzalutamide; CNY: Chinese yuan; Exchange rate: 1 USD =6.7871 CNY

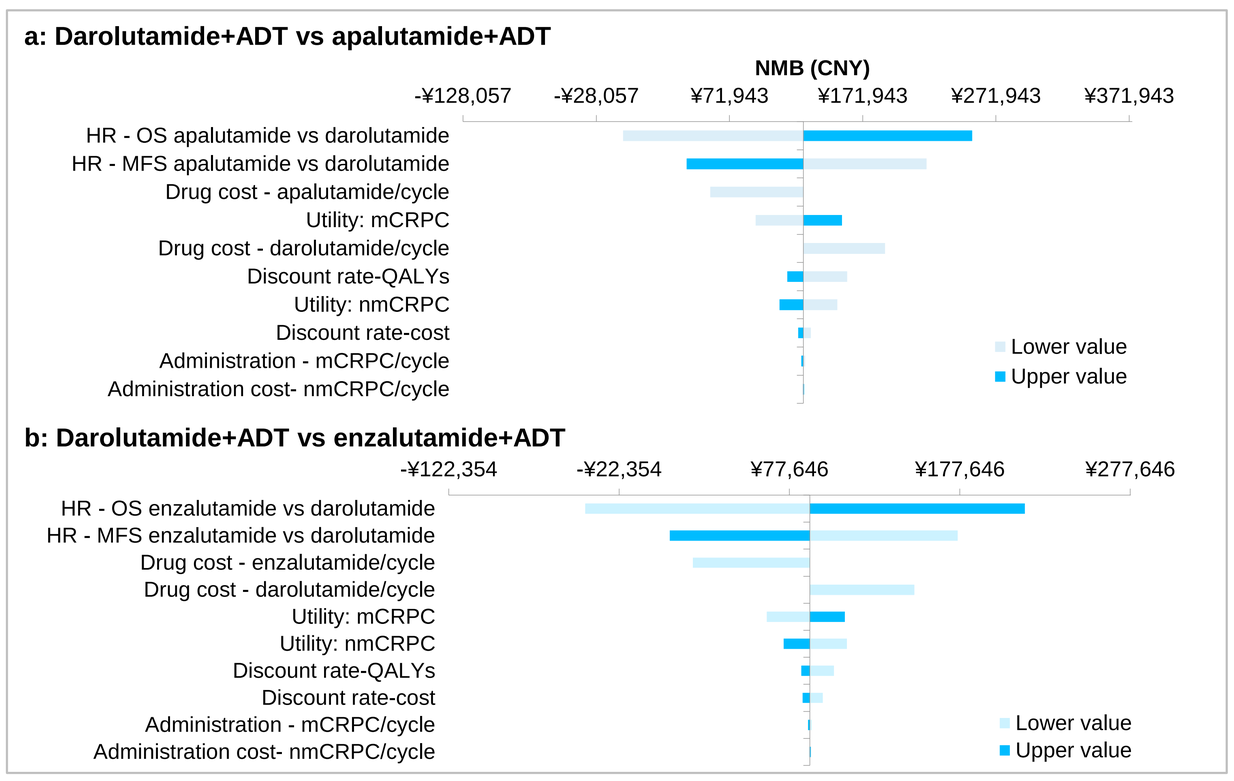

Figure 3: OWSA tornado diagram

CONCLUSION & DISCUSSION

- In comparison with apalutamide+ADT and enzalutamide+ADT, darolutamide+ADT was a **dominant or cost-effective** treatment option for patients with high-risk nmCRPC in China.
- The AE related QALY decrement associated with darolutamide+ADT (-0.00051 QALYs) appears to be less than that associated with apalutamide+ADT (-0.00177 QALYs) and enzalutamide+ADT (-0.00262 QALYs), several ITC studies also found that darolutamide was the best tolerated of all three evaluated agents[5-7].
- Our results may be used as a valuable reference for clinical and reimbursement decision-making in the Chinese healthcare setting.

FUNDING: This study was sponsored by Bayer Healthcare Company Ltd, Beijing, China

DISCLOSURES: The authors declare no competing interests

REFERENCES

1. Fizazi, K.,et al., N Engl J Med 2020, 383 (11), 1040-1049.
2. Smith, M. R., et al. Eur Urol 2021, 79 (1), 150-158
3. Sternberg, C. N.et al., N Engl J Med 2020, 382 (23), 2197-2206.
4. Li, F., et al., Biosci Trends 2018, 12 (1), 87-93
5. Hird, A. E.,et al. Clin Genitourin Cancer 2020, 18 (5), 343-350.
6. Mori, K., et al. Int J Clin Oncol 2020, 25 (11), 1892-1900.
7. Wenzel, M. Prostate Cancer Prostatic Dis 2021