EE429

Cost-Effectiveness and Budget Impact Analyses of Enzalutamide for the Treatment of Non-Metastatic Castration-Resistant Prostate Cancer in Mexico

Ruiz B[1*], Polanco A[1], Saturnino LTM[2#], Flores B[3], Gutiérrez M[3]

[1]Astellas Farma Mexico, Mexico City, Mexico; [2]Astellas, São Paulo, Brazil; [3]Pharmamanagement, Mexico City, Mexico; *Presenting author; #Currently affiliated with Vertex Pharmaceuticals, London, United Kingdom

Objective

- **To estimate the cost-effectiveness and budget impact of enzalutamide treatment in patients with high-risk non-metastatic castration-resistant prostate cancer (nmCRPC) from the Mexican health care system's perspective.**

Conclusions

- **Enzalutamide is a cost-effective treatment option for patients with high-risk nmCRPC, increasing the life-years gained (LYG) by 0.04 with a dominant incremental cost-effectiveness ratio (ICER) over a 5-year time horizon as compared with apalutamide.**
- **With potential budget savings, enzalutamide can help optimize the institutional resources within the Mexican health care system.**

Conflicts of Interest: Bárbara Ruiz and Ana Polanco are full-time employees of Astellas; Luciana Tarbes Saturnino was a full-time employee of Astellas when the model was created. Barbara Flores and Mayra Gutiérrez are employees of Pharma Management, who adapted the model as per the Mexican real-world data.

Acknowledgements: This study was funded by Astellas Pharma Inc. and Pfizer Inc., the co-developers of enzalutamide. Medical writing and editorial assistance were provided by Shruti Patil (MPharm), Jay Patel (PharmD), and Laura Huber (BA) from IQVIA, funded by the study sponsors.

Funding: This study was funded by Astellas Pharma Inc. and Pfizer Inc., the co-developers of enzalutamide.

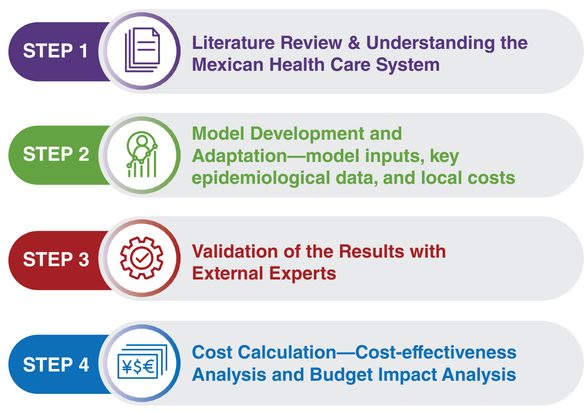
Background

- In Mexico, prostate cancer is the most common cancer in men. It is the leading cause of cancer-related mortality in men, accounting for 7457 deaths and 26,742 incident cases in 2020 alone, thus posing a considerable burden on the Mexican health care system.[1]
- The Mexican health care system includes multiple institutions, such as the Mexican Institute of Social Security (IMSS, Instituto Mexicano del Seguro Social), Institute of Health for Wellbeing (INSABI, Instituto de Salud para el Bienestar), Institute of Safety and Social Services for the Federal Workers (ISSSTE, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado), Health Services of the National Oil Company (PEMEX, Petróleos Mexicanos), Health Services for the Ministry of National Defense (SEDENA, Secretaría de la Defensa Nacional), and Health Services for the Ministry of Navy (SEMAR, Secretaría de Marina), which jointly cover the health care requirement of almost 72% of the total population.[2]
- nmCRPC refers to patients diagnosed with prostate cancer, with elevated prostate-specific antigen (PSA) and serum testosterone at castration levels <50 ng/dL, despite treatment with androgen deprivation therapy (ADT) and no signs of distant metastasis on conventional imaging studies.[3] High-risk nmCRPC is defined as a PSA doubling time of ≤10 months.
- Since 2018, novel hormonal therapies (NHTs) have demonstrated in several clinical trials that treating men with nmCRPC improves survival by delaying metastatic disease.[4]
- The combination of apalutamide and ADT is currently the only NHT-reimbursed treatment option for patients with high-risk nmCRPC in Mexico, as seen in the National Compendium of Medicines and Health Supplies.[5]
- Phase 3 clinical trials have shown that enzalutamide (another NHT) in combination with ADT demonstrates an improvement in median metastatic-free survival of 36.6 months vs 14.7 months when compared with ADT + placebo (P<0.001)[6] and a median overall survival of 67.0 months vs 56.3 months, respectively (P=0.001),[7] in patients with nmCRPC.
- This evolution in the treatment landscape has potentially provided a future alternative treatment option (enzalutamide + ADT) for patients with nmCRPC.

Methods

- A cost-effectiveness analysis (CEA) and budget impact analysis (BIA) were performed to compare apalutamide with enzalutamide, both in combination with ADT, for the treatment of patients with high-risk nmCRPC from the Mexican health care system's perspective (Figure 1).

Figure 1: Study methodology



- The estimates of the target population were calculated based on the total number of adult (≥18 years) males in Mexico[8] and patient segmentation (incidence of prostate cancer [35.5/100,000],[9] percentage of patients with CRPC [17.8%],[10] non-metastatic status [30%],[11] high-risk status [60%],[12] and insurance status within the Mexican health care system [71.77%][2]).
- The costs were extracted from the published databases of the Mexican health care system (IMSS, PEMEX, INSABI, ISSSTE, SEDENA, SEMAR). These extracted costs along with the model inputs and assumptions were employed for the data analysis (Table 1).

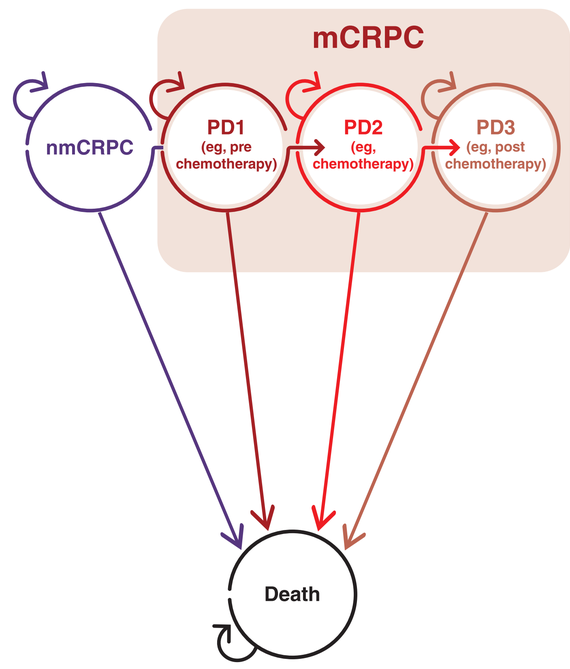
Table 1: Model inputs and key elements

Element	Input/source
Analytical tool	Microsoft® Excel
Time horizon	5 years
Eligible patient population	Population with high-risk nmCRPC in the Mexican public health care system (IMSS, PEMEX, INSABI, ISSSTE, SEDENA, SEMAR)
Comparison	Apalutamide vs enzalutamide
Market share	Anticipated uptake of enzalutamide was considered to increase from 10% in Year 1, to 30% in Year 2, and 50% in Year 3, Year 4, and Year 5
Currency	USD (conversion rate: 1 USD = 20.55 MxP)[13]
Discounting	At 5% rate
Cost inputs	
Cost of treatments	Cost of active treatments: enzalutamide (projected cost) and apalutamide (currently reimbursed cost – ISSSTE) Cost of treatments to progression (ISSSTE) Cost of ADT (ISSSTE) Cost of concomitant treatments (ISSSTE)
Cost of monitoring	Cost of patient monitoring + office/inpatient visits obtained from IMSS
Cost of adverse events	Cost of adverse events from GRDs obtained from the IMSS

GRD, Diagnosis Related Group; MxP, Mexican peso; USD, United States dollar.

- The CEA was performed using a Markov model. Besides emulating the disease progression, the model split the mCRPC health state into three separate mutually exclusive health states (Figure 2), in order to capture the gradual decline in quality of life and expected current/future treatment options. The cost-effectiveness was measured as LYG over a 5-year time horizon with 5% discounting.

Figure 2: Simplified schema of the 3-health state Markov model



PD1, progressed disease 1 health state; PD2, progressed disease 2 health state; PD3, progressed disease 3 health state.

- The BIA estimated the differences in total cost between the current reimbursed scenario (apalutamide + ADT) and the future scenario (inclusion of enzalutamide + ADT) over a 5-year time horizon with 5% discounting.

Results

TARGET POPULATION

- The estimated target population included in the analyses over a 5-year time horizon ranged from 353 to 370 patients (Table 2).

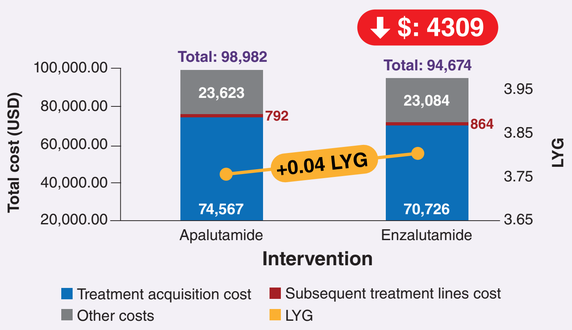
Table 2. Target population (entering point Year 2023)

Screening criteria (n)	Year 1	Year 2	Year 3	Year 4	Year 5
Male population in Mexico (adults ≥18 years old)[8]	43,268,227	43,803,146	44,328,700	44,843,476	45,348,501
Mexican population with prostate cancer	15,360	15,550	15,737	15,919	16,099
Mexican population with CRPC	2734	2768	2801	2834	2866
Mexican population with nmCRPC	820	830	840	850	860
Mexican population with high-risk nmCRPC	492	498	504	510	516
Mexican population with high-risk nmCRPC in public health institutes	**353**	**358**	**362**	**366**	**370**

COST-EFFECTIVENESS ANALYSIS

- The CEA estimated that compared to apalutamide, treatment with enzalutamide reduced total cost by USD 4309 and the difference in LYG was +0.04 (Figure 3).
- The treatment acquisition cost accounted for a majority of the cost associated with treatment of high-risk nmCRPC (apalutamide: USD 74,567 vs enzalutamide: USD 70,726) (Figure 3).

Figure 3. Total costs and life-years gained with apalutamide and enzalutamide NHTs over a 5-year time horizon



- Thus, the ICER revealed that enzalutamide was the dominant treatment (Table 3).

Table 3. Overall life-years gained with NHTs over a 5-year time horizon

Parameters	Apalutamide	Enzalutamide
LYG	3.76	3.80
LYG difference	-	+0.04
ICER (cost/LYG)	-	Dominant

BUDGET IMPACT ANALYSIS

- A comparison of the current and future scenario in the BIA estimated an average 5-year reduction of cost by USD 119,211 in the future scenario with an average percent impact on the medical budget of –0.00263%.
- The incremental year-wise budget impact of the two scenarios is presented in Table 4.

Table 4. Overall budget impact of NHTs over a 5-year time horizon

Parameters	Year 1	Year 2	Year 3	Year 4	Year 5
Current scenario					
Population with high-risk nmCRPC in public health institutes* treated with apalutamide	353	358	362	366	370
Total cost	**$6,992,782**	**$7,079,233**	**$7,164,170**	**$7,247,366**	**$7,328,985**
Future scenario					
Population with high-risk nmCRPC in public health institutes* treated with apalutamide	318	250	181	183	185
Cost	**$6,293,504**	**$4,955,463**	**$3,582,085**	**$3,623,683**	**$3,664,493**
Population with high-risk nmCRPC in public health institutes* treated with enzalutamide	35	107	181	183	185
Cost	**$668,839**	**$2,031,324**	**$3,426,160**	**$3,465,947**	**$3,504,981**
Total cost	**$6,962,343**	**$6,986,787**	**$7,008,245**	**$7,089,630**	**$7,169,473**
Budget impact analysis					
Difference in budget with current scenario and future scenario (USD)	–$30,439	–$92,446	–$155,925	–$157,735	–$159,512
% Impact on the medical budget	–0.0007%	–0.0020%	–0.0034%	–0.0035%	–0.0035%

*Public Health Institutions include IMSS, INSABI, ISSSTE, PEMEX, SEDENA, and SEMAR.

References

1. International Agency for Research on Cancer. Cancer Today—Mexico. Published March 2021. Accessed September 20, 2022. https://gco.iarc.fr/today/data/factsheets/populations/484-mexico-fact-sheets.pdf
2. INEGI. Derechohabiencia INEGI. Obtenido de Salud y Seguridad Social. Published 2019. Accessed June 1, 2022. https://www.inegi.org.mx/temas/derechohabiencia/
3. NCCN Prostate cancer advanced stage guidelines 2022. Accessed October 3, 2022. https://www.nccn.org/patients/guidelines/content/PDF/prostate-advanced-patient.pdf
4. Smith M, et al. Apalutamide treatment and metastasis-free survival in prostate cancer. *N Engl J Med*. 2018,378:1408-1418.
5. DOF. Edición 2021 del Libro de Medicamentos del Compendio Nacional de Insumos para la Salud. 2021; México: CSG.
6. Hussain M, et al. Enzalutamide in men with nonmetastatic, castration-resistant prostate cancer. *N Engl J Med*. 2018;378:2465-2474.
7. Steinberg CM, et al. Enzalutamide and survival in nonmetastatic, castration-resistant prostate cancer. *N Engl J Med*. 2020;382:2197-2206.
8. CONAPO. Proyección de la población 2010-2050. Accessed June 1, 2022. http://www.conapo.gob.mx/work/models/CONAPO/Resource/1529/2/images/DocumentoMetodologicoProyecciones2010_2050.pdf
9. Gómez-Dantes H, et al. The burden of cancer in Mexico 1997-2013. *Salud Pública de México*. 2016;58(2):118-131.
10. Kirby M, et al. Characterising the castration-resistant prostate cancer population: a systematic review. *Int J Clin Pract*. 2011;65:1180-1192.
11. Nakabayashi M, et al. Clinical predictors of survival in men with castration-resistant prostate cancer. *Cancer*. 2013;119:2990-2998.
12. Hernandez RK, et al. Estimating high-risk castration resistant prostate cancer (CRPC) using electronic health records. *Can J Urol*. 2015;22:7858-7864.
13. Average exchange rate 2021. https://www.banxico.org.mx/

Presented at the International Society for Pharmacoeconomics and Outcomes Research Europe 2022, Vienna, Austria, 6–9 November, 2022

Barbara Ruiz: barbara.ruiz@astellas.com