Safety and effectiveness of apalutamide for the treatment of Non-Metastatic Castration-Resistant Prostate Cancer (nmCRPC):

Preliminary results from an Open-Label Expanded Access Protocol (EAP)

S. Campos-Gomez[1], J. J. C. Ochoa[2], F. M. Cruz[3], A. C. A. Mota[4], J. A. Rinck Junior[5], A. Bhaumik[6] , M. Grings[7], A. C. L. Acerbi[7], K. N. Salomão[7], V. C. Fabrício*, R. Gidekel[8]

[1]Centro Oncológico Estatal - Instituto de Seguridad Social del Estado de México y Municipio, [2]Hospital Pablo Tobón Uribe, [3]IBCC Oncologia, [4]AMO Clinic, [5]Departamento de Oncologia Clínica do A C Camargo Cancer Center, [6]Janssen U.S., [7]Janssen Brasil, Brazil, [8]Janssen Argentina, *Former Janssen Brasil employee

ABSTRACT

Background: When apalutamide was not commercially available, expanded access protocols were key to provide treatment access and evidence generation. These preliminary results from EAP aims to describe safety and effectiveness of apalutamide plus androgen deprivation therapy (ADT) for the treatment of nmCRPC.

Methods: This multicenter, open-label, EAP included patients ≥18 years with confirmed nmCRPC-. Participants received oral apalutamide 240 mg once daily plus ADT until disease progression, unacceptable toxicity, withdrawal of consent, study closure or death. Baseline characteristics and serious treatment-emergent adverse event (TEAE), all grade ≥3 adverse events (AEs) and AEs of special interest were collected. The data was summarized using descriptive statistics, with median and range, as well as mean and standard deviation (SD).

Results: 51 patients were included with a median age of 76 (50-89) years old and mean follow-up of 13 (SD 6.3) months. 52.9% of the patients were from Brazil, 37.3% from Mexico and 9.8% from Colombia. After 12 weeks of treatment, patients presented a median prostate-specific antigen (PSA) reduction of 93.7% (-100% - 22.2%; n=40) that continued up to the 24-week, with a median of 95% (-99.9% - 8.1%; n=21). Considering the best response in 24 weeks, patients had a median PSA decline of 97% (-100%-265.8%; n=50), with 76% of them reaching more than 90% of maximum PSA reduction. 51% presented at least one TEAE, 11.8% experiencing serious TEAEs, 23.5% grade 3 TEAEs and 5.9% patients discontinued treatment due to TEAEs. No deaths or grade 4 AEs were reported. 33.3% patients had at least one TEAE of special interest: 15.7% had skin rash, 13.7% hypothyroidism and 7.8% fall with no fractures. Of them, only 5.9% experienced grade 3 TEAE, all related to skin rash.

Conclusions: The results showed a low proportion of serious and grade ≥3 TEAEs, with a small number of patients discontinuing treatment. Also, it was possible to observe a fast and intense overall reduction on PSA levels. The results suggest that apalutamide plus ADT has a good safety and effectiveness profile for the treatment of nmCRPC comparable with phase 3 data.

RATIONALE

Apalutamide is an inhibitor of the ligand-binding domain of the androgen receptor has been approved in many countries indicated for the treatment of nmCRPC (non-metastatic castration-sensitive prostate cancer). Shortening of the prostate-specific antigen doubling time (PSADT) and no distant metastases on imaging in the setting of on-going androgen deprivation therapy (ADT) characterize these patients. Without further treatment, patients with nmCRPC invariably progress to metastatic disease, with significant morbidity and mortality. Association of direct inhibition of androgen receptor and ADT might potentialize the androgen signals block enhancing the patient's outcomes. When apalutamide was not commercially available, expanded access protocols (EAP) were key to provide treatment access and generate real world evidence for safety .

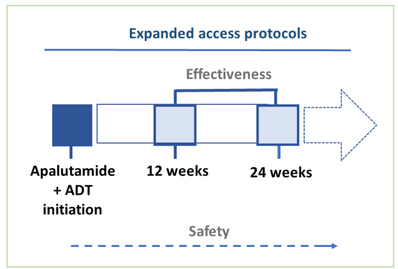
OBJECTIVE

These preliminary results from Apalutamide LATAM EAP aims to describe safety and effectiveness of apalutamide plus ADT for the treatment of nm-CRPC in Brazil, Colombia and Mexico.

METHODS

- This multicenter, open-label, EAP included patients ≥18 years with confirmed nmCRPC.
- Participants received oral apalutamide 240 mg once daily plus ADT until disease progression, unacceptable toxicity, withdrawal of consent, study closure or death.
- PSA concentration at baseline, 12 weeks and 24 weeks after treatment scheme initiation was assessed.
- Data on serious treatment-emergent adverse event (TEAE), all grade ≥3 adverse events (AEs) and AEs of special interest were collected (Figure 1).

Figure 1. Schematic study design



Statistical Methods

- The data was summarized using descriptive statistics, with median and range, as well as mean and standard deviation (SD).

RESULTS & DISCUSSION

At the time of this analysis, in total, 51 patients were included with mean duration of follow-up of 13 (SD 6.3) months and the median age of 76 (50-89) years old (table 1) with 60.1% over of them with more than 75 years old (figure 2).

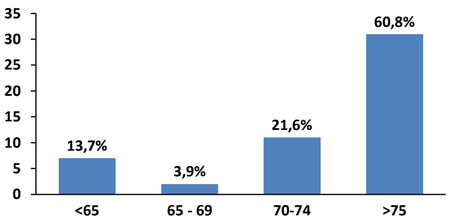
Table 1. At the time of this analysis, in total, 51 patients were included with mean duration of follow-up of 13 (SD 6.3) months and the median age of 76 (50-89) years old (table 1) with 60.8% of them with more than 75 years old (figure 2).

Table 1. Demographic characteristics of nmCRPC treating with apalutamide plus ADT

	Apalutamide
N*	51
Age, years	
Mean (SD)	75.2 (8.78)
Median	76.0
Race	
White	14 (27.5%)
Black or African American	9 (17.6%)
Multiple	2 (3.9%)
Other	26 (51.0%)
Not reported	0
Ethnicity	
Hispanic or Latino	50 (98.0%)
Not Hispanic or Latino	1 (2.0%)

*Intent-to-treat population

Figure 2 shows the percentage of patients per age stratification



Fifty three percent (53%) of the patients were from Brazil, 37% from Mexico and 10% from Colombia (figure 3).

Figure 3 shows the country distribution

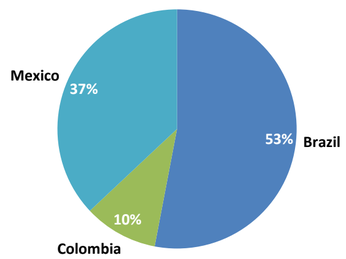


Table 2. After 12 weeks of treatment, patients presented a median prostate-specific antigen (PSA) reduction of 93.7% (-100% - 22.2%; n=40) that continued up to the 24-week, with a median of 95% (-99.9% - 8.1%; n=21) (figure 4). Considering the best response in 24 weeks, patients had a median PSA decline of 97% (-100%-265.8%; n=50), with 76% of them reaching more than 90% of maximum PSA reduction (table 2).

Table 2. PSA measurement at baseline, 12 weeks and 24 weeks after treatment scheme initiation

	Apalutamide
	Apalutamide
PSA at baseline (ng/mL)	
N	51
Mean (SD)	26.72 (64.278)
Median	7.88
Range	(0.1; 393.0)
PSA at 12 weeks/ET[a] (ng/mL)	
N	40
Mean (SD)	2.57 (6.241)
Median	0.60
Range	(0.0; 36.5)
Percent change from baseline at 12 weeks/ET	
N	40
Mean (SD)	-83.61 (26.743)
Median	-93.73
Range	(-100.0; 22.2)
PSA at 24 weeks/ET[b] (ng/mL)	
N	21
Mean (SD)	0.65 (0.778)
Median	0.36
Range	(0.0; 2.6)
Percent change from baseline at 24 weeks/ET	
N	21
Mean (SD)	-87.23 (26.467)
Median	-95.36
Range	(-99.9; 8.1)
Maximum percent[c] decline from baseline at any time on study	
N	50
Mean (SD)	-79.39 (56.326)
Median	-97.04
Range	(-100.0; 268.5)

a ET: End of treatment. For subjects who discontinued study treatments prior to 12 weeks, their last PSA results prior to 12 weeks was included and summarized.
b ET: End of treatment. For subjects who discontinued study treatments prior to 24 weeks, their last PSA results prior to 24 weeks was included and summarized.
c A negative percent indicates a decline in PSA, whereas a positive percent indicates that the subject never has a decline in PSA.

Table 3. Shows the adverse events reported during this period: 51% presented at least one TEAE, 11.8% experiencing serious TEAEs, 23.5% grade 3 TEAEs and 5.9% patients discontinued treatment due to TEAEs. No deaths or grade 4 AEs were reported. 33.3% patients had at least one TEAE of special interest: 15.7% had skin rash, 13.7% hypothyroidism and 7.8% fall with no fractures. Of them, only 5.9% experienced grade 3 TEAE of interest, all related to skin rash. Data showed that the rate of adverse event (51% vs. 97%) and treatment discontinuation (5.9% vs. 13.6%) was lower in the present real-world data with apalutamide compared to SPARTAN study, respectively.

Table 3. Overall Summary of Treatment-emergent Adverse Events

	Apalutamide
Patients (N)	51
Number of subjects with TEAEs[b]	26 (51.0%)
Drug-related[a]	16 (31.4%)
Number of subjects with Grade 3-4 TEAEs	12 (23.5%)
Drug-related[a]	4 (7.8%)
Number of subjects with SAEs[b]	6 (11.8%)
Drug-related[a]	1 (2.0%)
Grade 3-4	5 (9.8%)
Number of subjects with TEAEs leading to treatment discontinuation	3 (5.9%)
Drug-related[a]	2 (3.9%)
Number of subjects with TEAEs leading to death	0
All deaths within 30 days of last dose	0
Discontinued study treatment	9 (17.6%)
Reasons for Discontinuation	
Adverse Event	3 (5.9%)
Progressive Disease	3 (5.9%)
Withdrawal by Subject	2 (3.9%)
Physician Decision	1 (2.0%)

[a] Adverse event is categorized as related if assessed by the investigator as possible, probable, and very likely related to study drug.
[b] Excludes Grade 5 events.
Note: Percent is based on the Safety population.
Note: Treatment-emergent adverse events are those that occurred between the date of 1st dose of study drug and date of last dose of study drug+30 days. For each category, subjects are counted only once, even if they experienced multiple events in that category
TEAEs: treatment-emergent adverse event

CONCLUSION

The results showed a low proportion of serious and grade ≥3 TEAEs, with a small number of patients discontinuing treatment. Also, it was possible to observe a fast and meaningful overall reduction on PSA levels. The results suggest that apalutamide plus ADT has a good safety and effectiveness profile for the treatment of nmCRPC in real world setting of patients, consistent with SPARTAN phase 3 trial results.

REFERENCES

1. R. Given et al., "Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer," pp. 1–12, 2019,
2. P. N. Mainwaring, et al., "Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer," pp. 1–10, 2018,
3. B. A. Hadaschik et al., "Apalutamide and Overall Survival in Prostate Cancer," vol. 9, pp. 1–9, 2020

Acknowledgment

Jose Alberto Regalado Ramos for his support on this publication

Janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson