Apalutamide for High-Risk Localized Prostate Cancer Following Radical Prostatectomy (Apa-RP): A Multicenter, Open-Label, Single-Arm Phase 2 Study

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Disclosures

- Jason Hafron has been a consultant and speaker for Janssen Biotech, Inc. and a consultant for Myovant Sciences Inc.

Patients with High-Risk Localized Prostate Cancer Experience Increased Rates of Disease Recurrence

- In 2024, it is estimated there will be nearly 300,000 new cases of prostate cancer in the US; ~15% will be diagnosed as having high-risk disease[1–3*]
- Approximately, 45–65% of patients with high-risk disease experience recurrence within five years of undergoing radical prostatectomy[4–7]
- Apalutamide is a selective, androgen receptor inhibitor approved for patients with nonmetastatic castration-resistant prostate cancer and metastatic castration-sensitive prostate cancer[8]
- Apalutamide is being investigated in two registrational trials in patients with high-risk localized prostate cancer receiving a prostatectomy (PROTEUS; NCT03767244) or radiation therapy (ATLAS; NCT02531516)
- Apa-RP is a Phase 2 study that investigated apalutamide plus ADT adjuvant to radical prostatectomy in patients with high-risk localized prostate cancer

*NCCN define high-risk disease as having at least one of the following: T3a or higher disease, a Gleason Score ≥8 or a PSA level of ≥20 ng/mL.[9]

ADT, antigen deprivation therapy; NCCN, National Comprehensive Cancer Network; PSA, prostate-specific antigen; US, United States.

1. Siegel RL, et al. *Cancer Statistics* 2024;74:12; 2. Cooperberg MR, et al. *World J Urol* 2008;26:211; 3. Cooperberg MR, et al. *J Clin Oncol* 2010;28:1117; 4. Briganti A, et al. *Urol Oncol* 2015;33:163.e7;
5. Murata Y, et al. *Int J Urol* 2018;25:284–289; 6. Walz J, et al. *BJU Int* 2011;107:765–770; 7. Martini A, et al. *Eur Urol Oncol* 2019;2:456–463;
8. Apalutamide FDA label. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/210951s007lbl.pdf (Accessed March 21, 2024);
9. NCCN guidelines. Prostate cancer, version 2 2024. Available at: https://www.nccn.org/guidelines (Accessed March 21, 2024).

Apa-RP: a Multicenter, Open-Label, Single-Arm, Phase 2 Study

Key Inclusion Criteria:

- High-risk localized prostate cancer*
- Candidate for RP or between Days 29 and 90 post-RP
- Post-RP PSA ≤0.2 ng/mL
- No prior treatment for prostate cancer
- No evidence of metastatic prostate cancer
- ECOG PS 0–1

Radical prostatectomy

Main study (n=96)

Apalutamide 240 mg/day + ADT

(12 cycles; 28 days per cycle)

Post-treatment follow-up every 6 months

Endpoints:

- **1°** BCR-free survival at 24 months†
- **2°** BCR-free survival at 12 months; serum testosterone recovery rate to ≥150 ng/dL at 18 and 24 months‡
- **Exploratory:** unconfirmed BCR‖

*High risk was defined based on PSA ≥20 ng/mL or Gleason Score ≥9 in any core, or Gleason Score ≥8 (4+4 or 5+3) in >80% of 2 cores, or Gleason Score 8 (4+4 or 5+3) in 1 core if ≥5 cores had a minimum Gleason Score of 4+3; †12 months after completion of treatment; confirmed BCR was defined as two sequential (measured within 3-4 weeks) PSA levels of >0.2 ng/mL; ‡6 and 12 months after the completion of adjuvant treatment with apalutamide plus ADT; ‖Patients with a PSA >0.2 ng/dL and no subsequent PSA value during the trial.

ADT, androgen deprivation therapy; BCR, biochemical recurrence; ECOG PS, Eastern Cooperative Oncology Group performance status; PSA, prostate-specific antigen; RP, radical prostatectomy.

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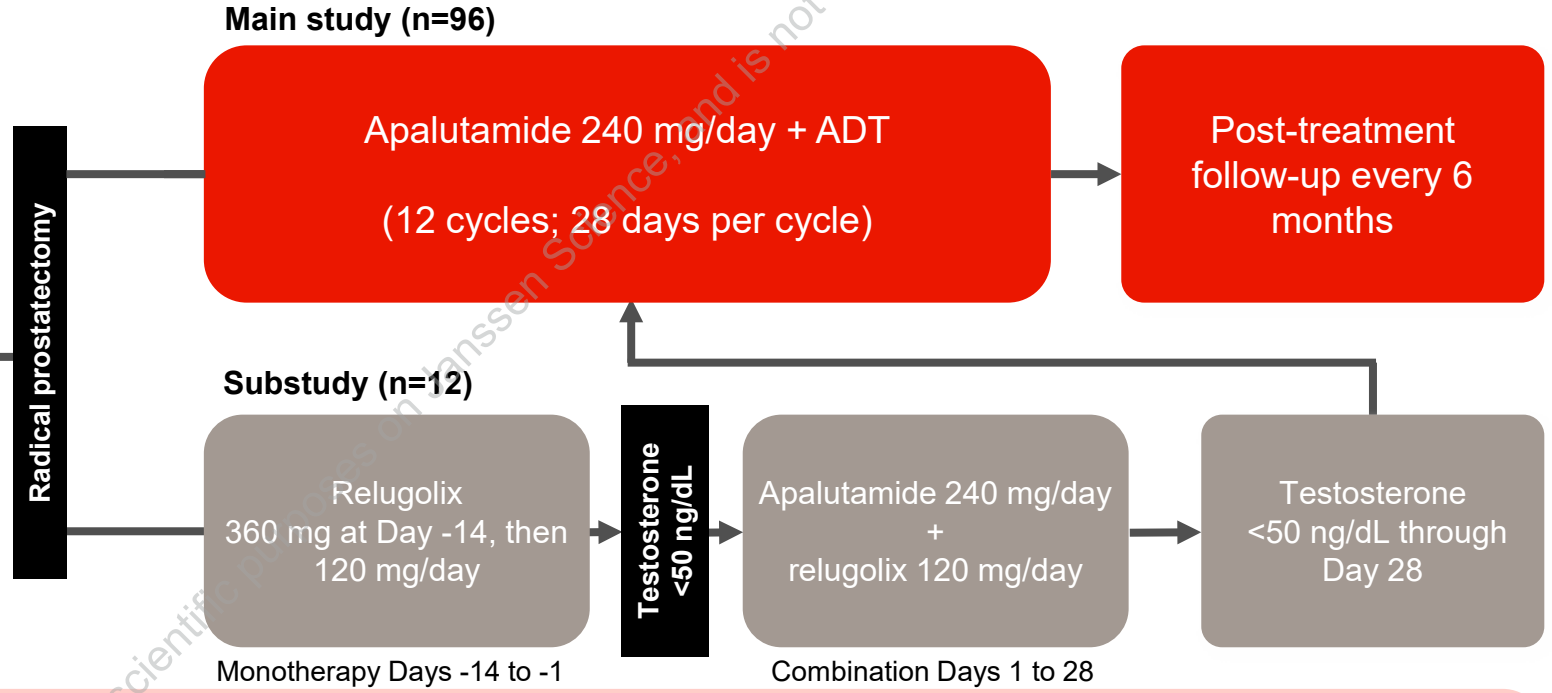

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Apa-RP Statistical Analysis Plan

Primary Endpoint	BCR-Free Survival at 24 Months
Statistical hypothesis	10% absolute increase compared with control
Historical control[1]	76% BCR-free rate at 24 months
One-sided α / Power	0.05 / 80%
Minimum number of patients	94

- The null hypothesis, derived from Martini, et al.[1], assumed a 76% BCR-free rate at 24 months in patients with high-risk localized prostate cancer who underwent radical prostatectomy. The null hypothesis would be rejected if the lower limit of the 90% CI crossed 76%
- To ensure 80% power for the primary hypothesis, the study aimed to enroll 96 patients to account for potential attrition

BCR, biochemical recurrence; CI, confidence interval; US, United States.

1. Martini A, et al. *Eur Urol Oncol* 2019;2:456–463.

Apa-RP Enrolled a Diverse Patient Population

- Patients were on study from Aug 2020 to Oct 2023 and were enrolled from 27 community urology sites

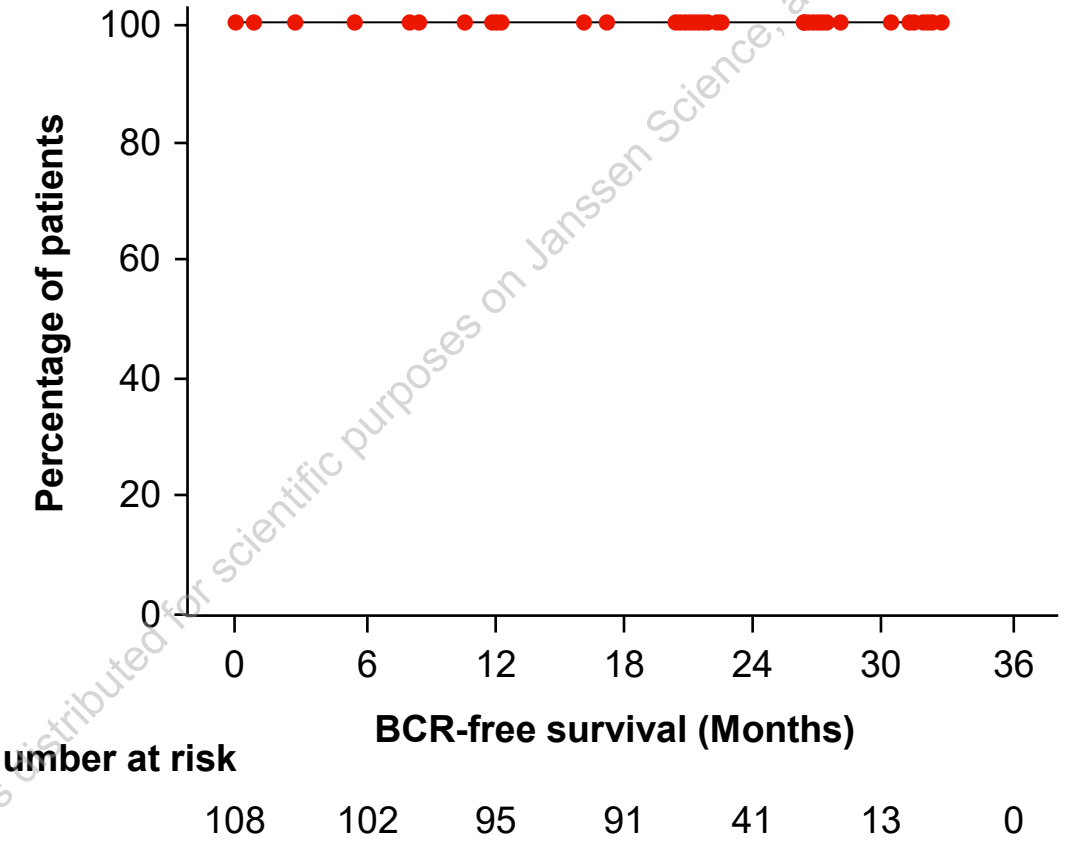
	Apalutamide + ADT (N=108)
Age, years, median (range)	66.0 (46–77)
Male, n (%)	108 (100)
Race, n (%)	
Asian	4 (3.7)
Black or African American	15 (13.9)
White	88 (81.5)
Unknown	1 (0.9)
Time from initial diagnosis to enrollment, months, median (range)	4.62 (1.5–26.0)
Time from prostatectomy to enrollment, months, median (range)	2.0 (0.6–5.0)
ECOG PS, n (%)	
0	102 (94.4)
1	6 (5.6)
Gleason Score at diagnosis, n (%)	
7	11 (10.2)
8	32 (29.6)
9	62 (57.4)
10	3 (2.8)
PSA at pre-operative screening visit, ng/mL, median (range)	7.6 (2.2–62.7)
Testosterone, ng/dL, median (range)	340.0 (43.0–939.0)

ADT, androgen deprivation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; PSA, prostate-specific antigen.

No Patients had a Confirmed BCR at 2+ Years Following Radical Prostatectomy

Confirmed BCR-free rate* at 24 months was 100% (90% CI: 93.0–100.0)

Confirmed BCR was defined as two consecutive PSA values >0.2 ng/mL

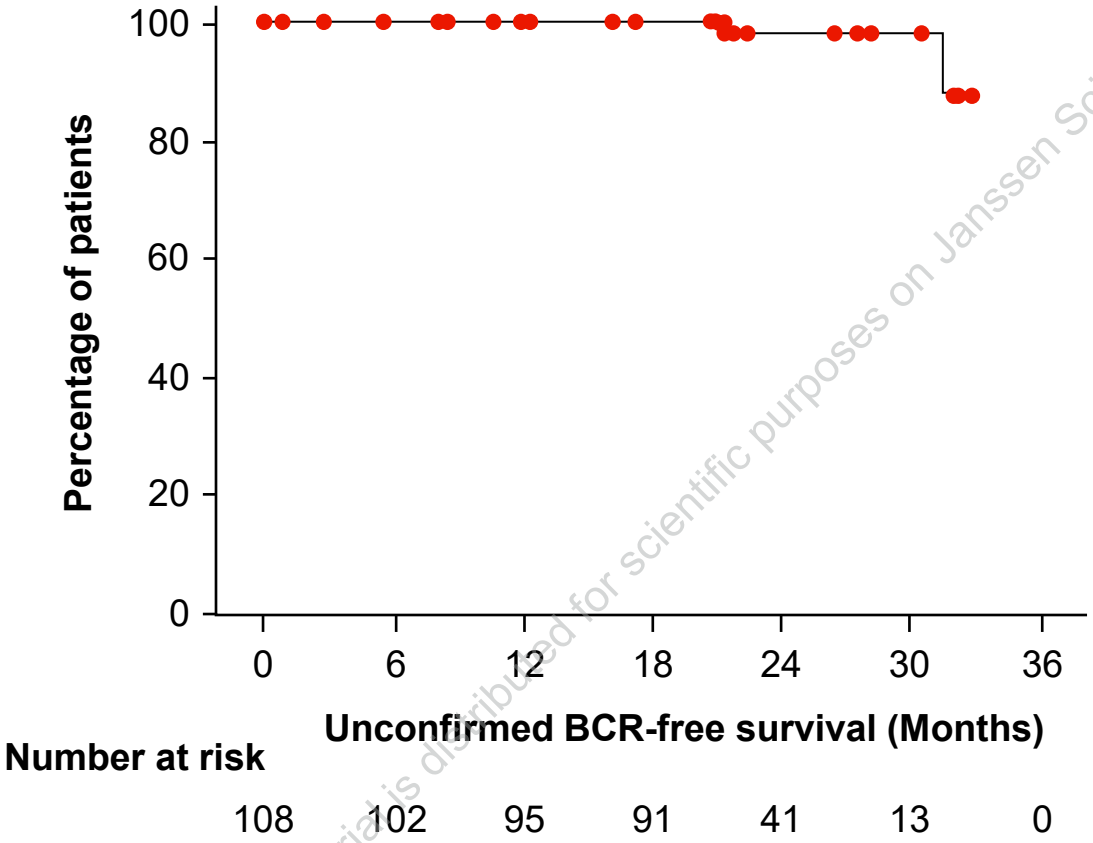


*mITT population; enrolled patients who met all eligibility criteria, received ≥1 dose of apalutamide, had a baseline PSA and ≥1 PSA value after initiating treatment.

BCR, biochemical recurrence; mITT, modified intention-to-treat; PSA, prostate-specific antigen.

Two Patients Had an Unconfirmed BCR at 2+ Years Following Radical Prostatectomy

Unconfirmed BCR-free rate at 24 months was 98.4% (90% CI: 92.2–99.7)



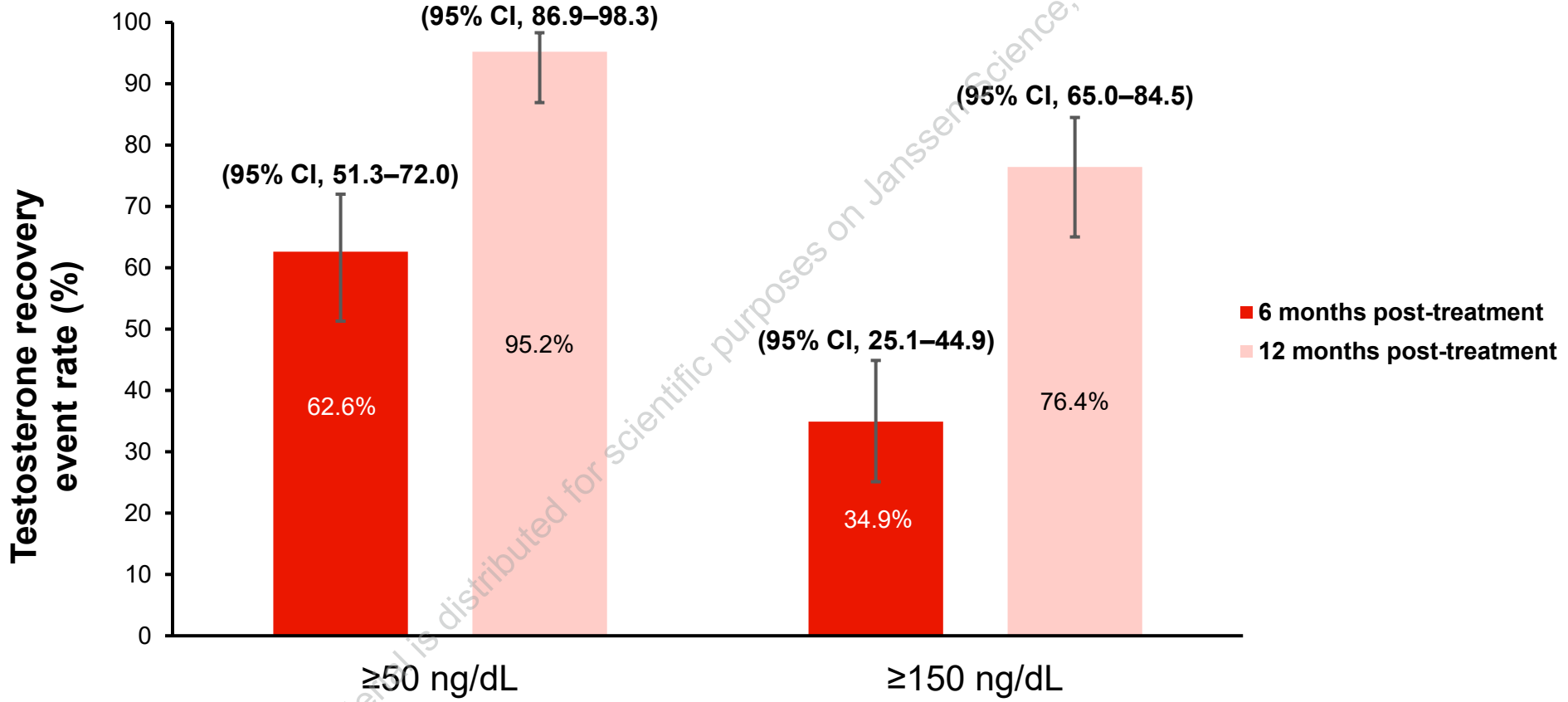
Two patients had elevated PSA levels just prior to the end of the study; confirmatory PSA measurements could not be obtained

Patient	Timepoint	PSA (ng/mL)
1	24 Months	0.39
2	30 Months	0.22

BCR, biochemical recurrence; PSA, prostate-specific antigen.

Secondary Endpoint: Serum Testosterone Recovery at 6 and 12 Months Following Treatment Completion

76% of patients had testosterone recovery to 150 ng/dL at 12 months following treatment completion



CI, confidence interval.

The Safety Profile of Apalutamide + ADT was Consistent with Previous Reports

Most common TEAEs (≥10% of patients) n (%)	Apalutamide + ADT (N=108)		
	Any grade	Grade 3	Grade 4
Hot flush	74 (68.5)	1 (0.9)	0 (0)
Fatigue	58 (53.7)	4 (3.7)	0 (0)
Rash‡	23 (21.3)	3 (2.8)	0 (0)
COVID-19	19 (17.6)	2 (1.9)	0 (0)
Arthralgia	18 (16.7)	0 (0)	0 (0)

n (%)	Apalutamide + ADT (N=108)		
	Any grade	Grade 3	Grade 4
Number of patients with TEAEs*	107 (99.1)	20 (18.5)	4 (3.7)
SAEs†	16 (14.8)	11 (10.2)	4 (3.7)
TEAEs leading to treatment discontinuation	11 (10.2)	5 (4.6)	1 (0.9)
TEAEs leading to treatment dose reduction or interruption	14 (13.0)	5 (4.6)	1 (0.9)
TEAEs leading to death	0 (0)	-	-

*Adverse events of any cause that occurred from the time of the first dose of the study treatment through 30 days after the last dose. Adverse events were graded according to National Cancer Institute Common Toxicity Criteria for Adverse Events, version 5.0; †Treatment-emergent SAEs included: syncope (2.8%), COVID-19 (1.9%), atrial fibrillation (1.9%), transient ischemic attack (0.9%), acute cholecystitis (0.9%), hypertransaminemia (0.9%), colon cancer (0.9%), squamous cell carcinoma of the tongue (0.9%), bladder neck obstruction (0.9%), hydronephrosis (0.9%), hypertension (0.9%), hypertensive crisis (0.9%), abdominal incarcerated hernia (0.9%), chest pain (0.9%), post-procedural hemorrhage (0.9%), Stevens–Johnson syndrome (0.9%); ‡Rash refers to a combination of preferred terms.

ADT, androgen deprivation therapy; SAE, serious adverse event; TEAE, treatment emergent adverse event.

Summary and Conclusions

- BCR-free rate was 100% at 24 months; two patients had unconfirmed BCR
- Serum testosterone recovery rates to ≥150 ng/dL were 34.9% at 6 months post-treatment and 76.4% at 12 months post-treatment
- Per FDA guidance, the enrolled population was reflective of the US population (~15% of patients enrolled in Apa-RP were Black)[1]
- The safety profile of apalutamide + ADT was consistent with what has been reported previously
- **Treatment intensification with 12 cycles of apalutamide + ADT could become an option for patients with high-risk localized prostate cancer who have undergone RP**

ADT, antigen deprivation therapy; BCR, biochemical recurrence; FDA, United States Food and Drug Administration; RP, radical prostatectomy.

1. Enhancing the Diversity of Clinical Trial Populations. https://www.fda.gov/media/168352/download?attachment (Accessed April 8, 2024).

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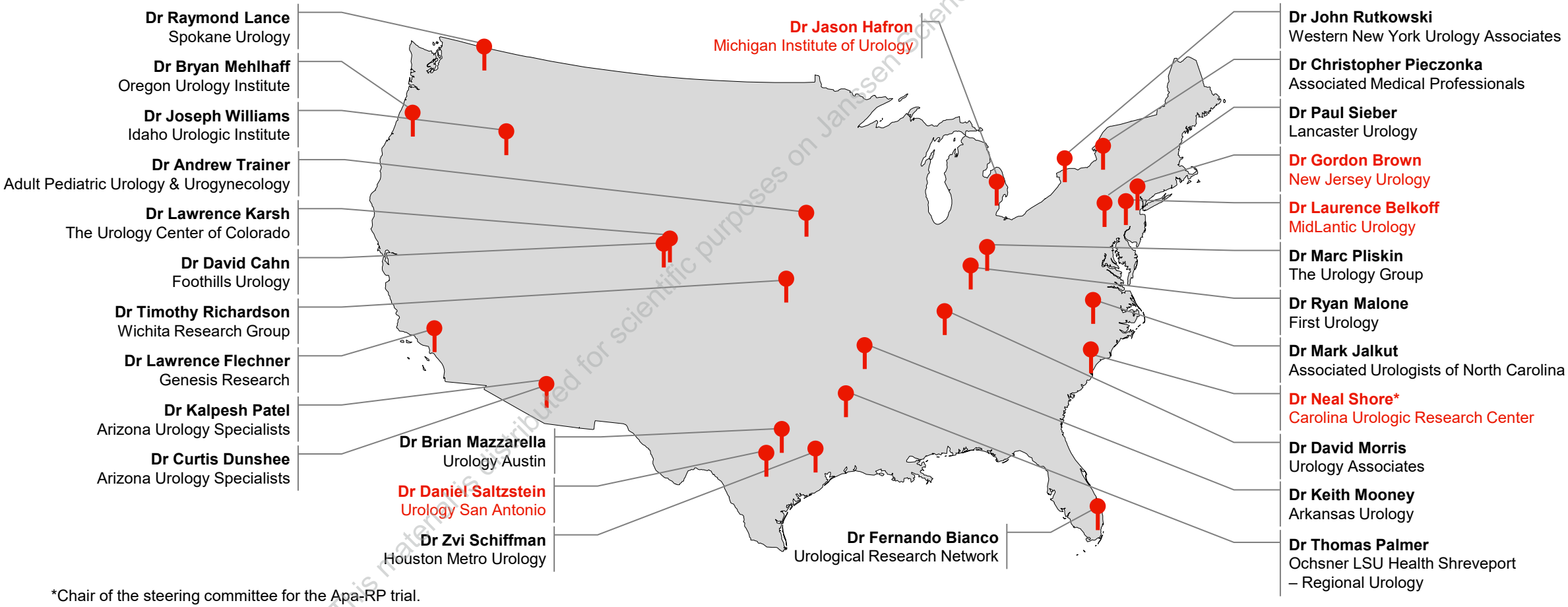

*Chair of the steering committee for the Apa-RP trial.

https://www.congresshub.com/Oncology/AUA2024/Apalutamide/Shore

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