RUTGERS
Cancer Institute
of New Jersey

Interim analysis of phase 2 randomized prospective study on neoadjuvant apalutamide/abiraterone acetate with prednisone and the feasibility of performing nerve-sparing radical prostatectomy in men with high-risk prostate cancer (NCT02949284).

Joshua Sterling M.D., Kevin Chua M.D., Hiren V. Patel M.D., Ph.D., Tina Mayer M.D., Biren Sariya M.D., Isaac Yi Kim M.D., Ph.D., M.B.A.

Disclosures

- This work is supported by an Investigator Initiated Study grant from Janssen Scientific Affairs, LLC and NCI Cancer Center Support Grant (P30CA072720)

Background

- Neoadjuvant systemic therapy is a widely established treatment paradigm for many malignancies
  - Use of androgen deprivation is not widely endorsed in the non-castrate resistant setting
- Neoadjuvant hormone therapy (NHT) has been shown to improve pathologic outcomes
  - Labire et al. 1995. NHT decreased positive surgical margins (7.8% Vs 33.8% in the control), and increased incidence of organ confined disease (77.8% Vs 49.3% in the control)
- Early NHT studies found significant improvement in pathologic but not in survival outcomes.

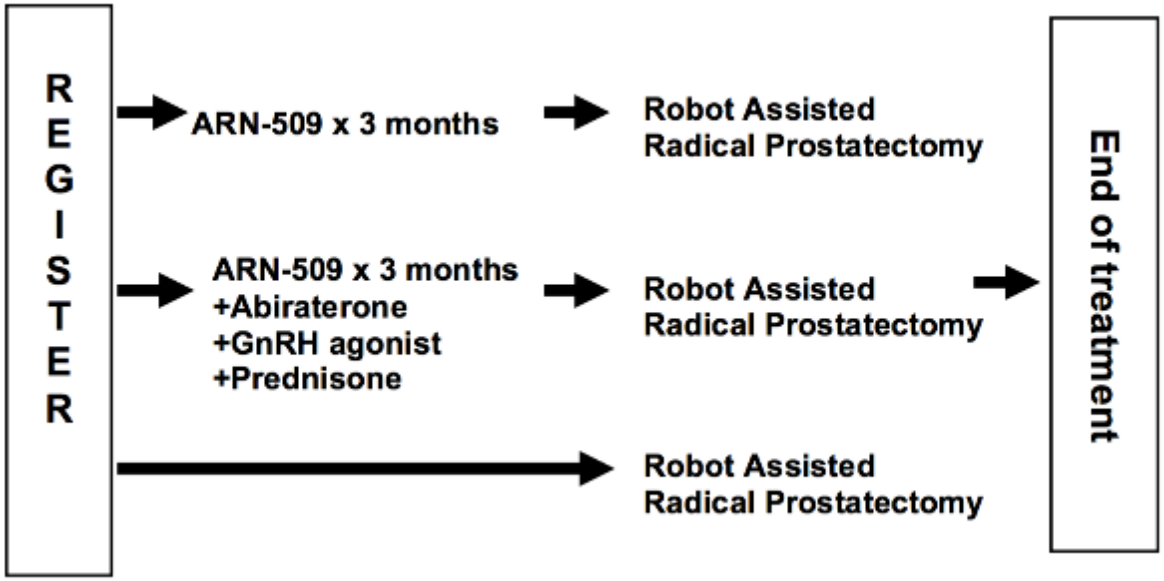
Study Rational

- Men with high-risk PCa are unlikely to be cured with just extirpative treatment; ~50% will have a BCR within 10-15 years
- NHT does reduce tumor burden which can allow for a nerve-sparing approach in men with high-risk disease, increasing post-surgical quality of life outcomes
- The newer generations of anti-androgens are more effective at rendering patients castrate, which may improve oncologic outcomes not seen in early studies
- There are currently no head to head comparisons of neoadjuvant treatment, using the latest generation of anti-androgen medications, followed by radical prostatectomy to immediate radical prostatectomy.

Study Design

Randomized three arm phase II prospective trial with a planned post-operative follow up of 2 years.

Primary Objective: evaluate the effect of neoadjuvant androgen deprivation treatments on the feasibility of performing nerve-sparing radical prostatectomy in men with high-risk prostate cancer.



Outcomes

- Primary outcome
  - Post-surgical potency rate at 12 months defined as being to penetrate and complete sexual intercourse satisfactorily in more than 50% of the attempts.
    - Each of the experimental arms will be compared to the surgery-only arm, so each test will be a 2.5% level one-sided test to control for the fact that there are two comparisons
- Secondary outcomes
  - Change in tumor volume on pelvic MRI after neoadjuvant therapy [Time Frame: Baseline to week 13]
    - Will be correlated with clinical outcomes before and after androgen receptor antagonist ARN-509 or androgen receptor antagonist ARN-509, GnRH agonist, prednisone plus abiraterone acetate.
  - biochemical recurrence rate defined using the Prostate Cancer Clinical Trials Working Group 2 definition [Time Frame: Up to 5 years]
  - pathological T0 rate
  - positive surgical margins rate.
  - Postoperative continence rate (pad-free).
  - Quality of life as assessed by the EPIC questionnaires [Time Frame: Up to 24 months after surgery]

Results

- Patient enrollment (11/2019): 32 patients
  - 4 withdrew following randomization, 1 declared ineligible, 3 still receiving neoadjuvant treatment, 24 in the follow up phase
  - 10, 7, and 7 in arms 1, 2, and 3 respectively.
- No significant difference in OR time
- Median reduction of tumor volume
  - Arm I: 32.4%; Arm II: 55.7%
- Positive surgical margin
  - Arm I = 3; Arm II = 1; Arm III = 3
- Potency Achieved
  - Arm I = 50%; Arm II = 14.2 %; Arm III = 28.5%
- BCR
  - Arm I = 1; Arm II = 2; Arm III = 0

Operative outcomes

	Arm 1 (apalutamide)	Arm 2 (GnRH agonist + apalutamide + abiraterone + prednisone)	Arm 3 (surgery alone)
N	10	7	7
Surgery length (minutes)			
Median (IQR)	298.0 (254.3-301.8)	273.0 (249.0-305.5)	291.0 (266.5-347.0)
EBL (mL)			
Median (IQR)	150.0 (150.0-237.5)	250.0 (125.0-285.0)	200.0 (75.0-525.0)
Length of stay (days)			
Median (IQR)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.5)
Pathologic T stage			
T2	4	2	4
T3a	4	3	1
T3b	2	2	2
Positive surgical margins	3	1	3
Lymph node yield			
Median (IQR)	22.0 (17.0-27.8)	21.0 (20.5-30.5)	26.0 (21.0-31.0)
Number of patients with lymph node involvement	2	2	1

*GS not given due to therapeutic effect.

	Arm 1 (apalutamide)	Arm 2 (GnRH agonist + apalutamide + abiraterone + prednisone)	Arm 3 (surgery alone)
N	10	7	7
Median age at time of surgery (IQR)	66.0 (61.8-70.5)	62.0 (60.5-67.0)	64.0 (61.5-66.5)
Demographics			
White	7	5	5
Black	2	0	0
Asian	0	1	1
Other/Unidentified	1	1	1
Grade Group from prostate biopsy			
Median (IQR)	4.0 (4.0-4.8)	5.0 (4.0-5.0)	4.0 (3.5-4.0)
Highest measured PSA			
Median (IQR)	11.8 (8.8-16.7)	19.9 (15.6-25.0)	8.9 (7.7-17.8)
Median PSA reduction after neoadjuvant Therapy (IQR)	11.2 (8.5-15.2)	19.8 (15.4-24.8)	NA
Side effects From neoadjuvant therapy			
Grade 1	8	7	NA
Grade 2	1	0	NA
Grade 3	1	0	NA
Median PIRADS of initial MRI (IQR)	5.0 (5.0-5.0)	5.0 (5.0-5.0)	4.0 (3.0-5.0)
Median tumor size on initial MRI (IQR)	36.2 (30.5-56.7)	52.2 (32.6-55.2)	42.9 (33.2-48.0)
Median tumor size reduction after neoadjuvant therapy (IQR)	11.2 (7.2-19.8)	27.7 (15.1-31.7)	NA
Median percent tumor size reduction after neoadjuvant therapy (IQR)	32.4 (24.4-34.7)	55.7 (46.2-62.0)	NA
Median serum testosterone level			
Testosterone pretreatment (IQR)	334 (281-551)	370 (296-536)	NA
Free testosterone pretreatment (IQR)	8.64 (6.535-8.64)	7.1 (5.6-10.3)	NA
Testosterone pre-surgery (IQR)	1015 (855-1040)	7 (7-7)	370 (269-415)
Free testosterone pre-surgery (IQR)	17.45 (12.2-22.4)	0.04 (0.04-0.04)	8.07 (5.44-10.4)
Testosterone 1 yr post surgery (IQR)	397.5 (319-491)	470 (300.5-821)	277.5 (65.5-431.5)
Free testosterone 1 yr post surgery (IQR)	8.8 (7.875-10.44)	7.91 (7.07-11.18)	5.41 (2.19-9.04)

	Arm 1 (apalutamide)	Arm 2 (GnRH agonist + apalutamide + abiraterone + prednisone)	Arm 3 (surgery alone)
N	10	7	7
Follow up time			
Median (IQR) (months)	11.6 (5.0-11.9)	8.9 (5.4-13.6)	12.1 (4.8-14.1)
Achieve potency			
yes	5 (p=0.25)	1 (p=0.21)	2
No; last FU <12 months since surgery	1	3	1
No, Last FU >12 months since surgery	3	3	3
Achieve continence			
Yes	7 (p=0.14)	5 (p=0.22)	3
Incontinent <6 months post-op	1	1	1
Incontinent >6 months post-op	1	1	2
SHIM			
Last FU <6 months since surgery - median (IQR)	1.5 (1.3-1.8)	4.0 (3.5-4.5)	21.0 (21.0-21.0)
Last FU 6-12 months since surgery - median (IQR)	2.0 (1.0-19.0)	2.5 (1.8-3.3)	20.0 (20.0-20.0)
Last FU >12 months since surgery - median (IQR)	11.5 (6.3-16.8)	2.0 (1.5-13.5)	1.0 (1.0-1.5)
AUAss			
Last FU <6 months since surgery - median (IQR)	6.5 (5.3-7.8)	9.0 (9.0-9.0)	13.0 (13.0-13.0)
Last FU 6-12 months since surgery - median (IQR)	7.0 (2.0-11.0)	3.5 (3.3-3.8)	5.0 (5.0-5.0)
Last FU >12 months since surgery - median (IQR)	8.0 (7.5-8.5)	2.0 (1.0-3.0)	1.5 (0.8-5.3)
BCR	1	2	0
Time to BCR			
Median (IQR) (months)	11.7 (11.7-11.7)	13.4 (12.7-14.1)	NA
Received/Planned for XRT after surgery	1	1	2

Conclusion

- Early results indicate that neoadjuvant therapy prior to RP resulted in reduction of tumor volume.
- Possibly improved potency preservation without an adverse effect on positive surgical margin rates.

Citations

- Labrie F, Cusan L, Gomez JL, et al. Downstaging by combination therapy with flutamide and an LHRH agonist before radical prostatectomy. *Cancer Surv.* 1995;23:149-156.