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Cancer Center

Multimodality Therapy for High Risk Disease – The Surgical Perspective

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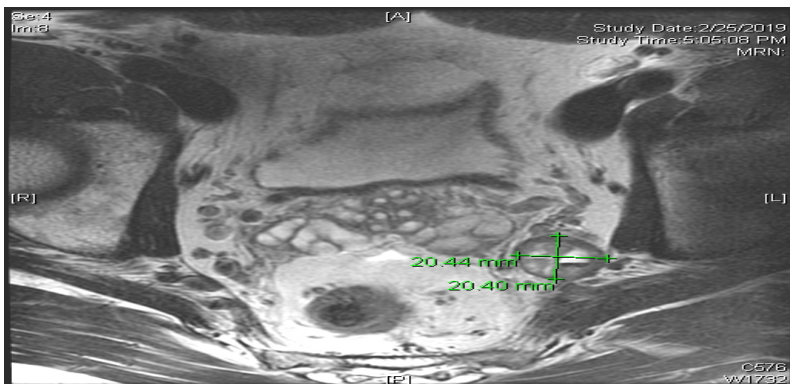
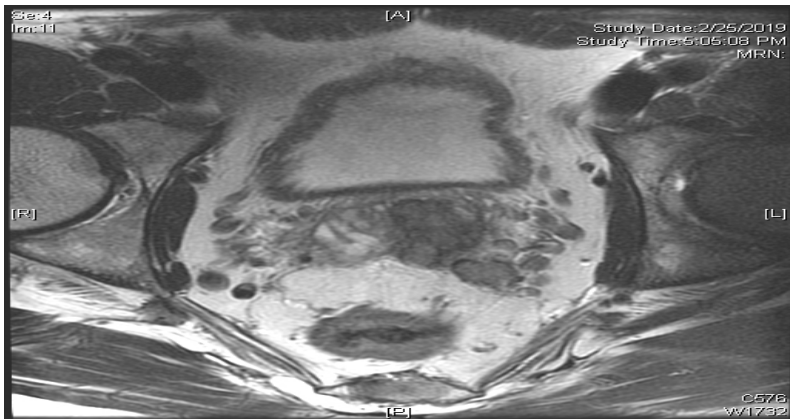
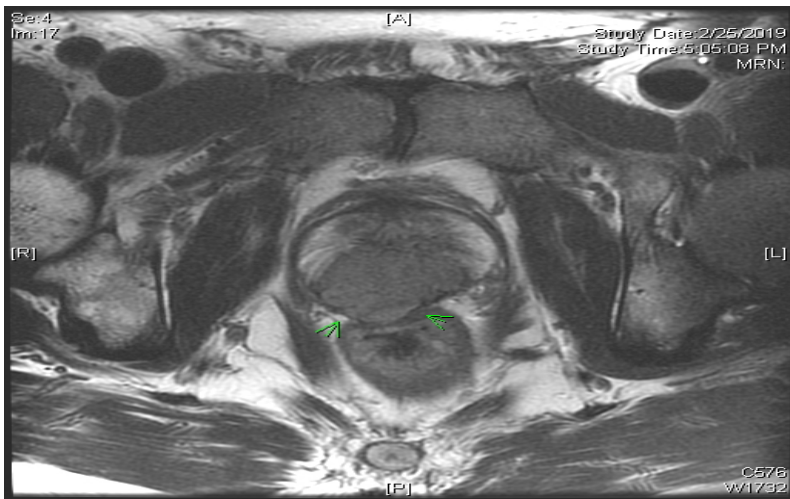
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New York, NY



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❖ 53 yo asymptomatic man with a PSA of 4.8 and family history of a father with prostate cancer.

❖ 14/18 biopsies showing Gleason Grade 10 (5+5) – 100% core involvement. (Two separate path reviews – no small cell.

IMPACT testing (on biopsy):

34 somatic mutations

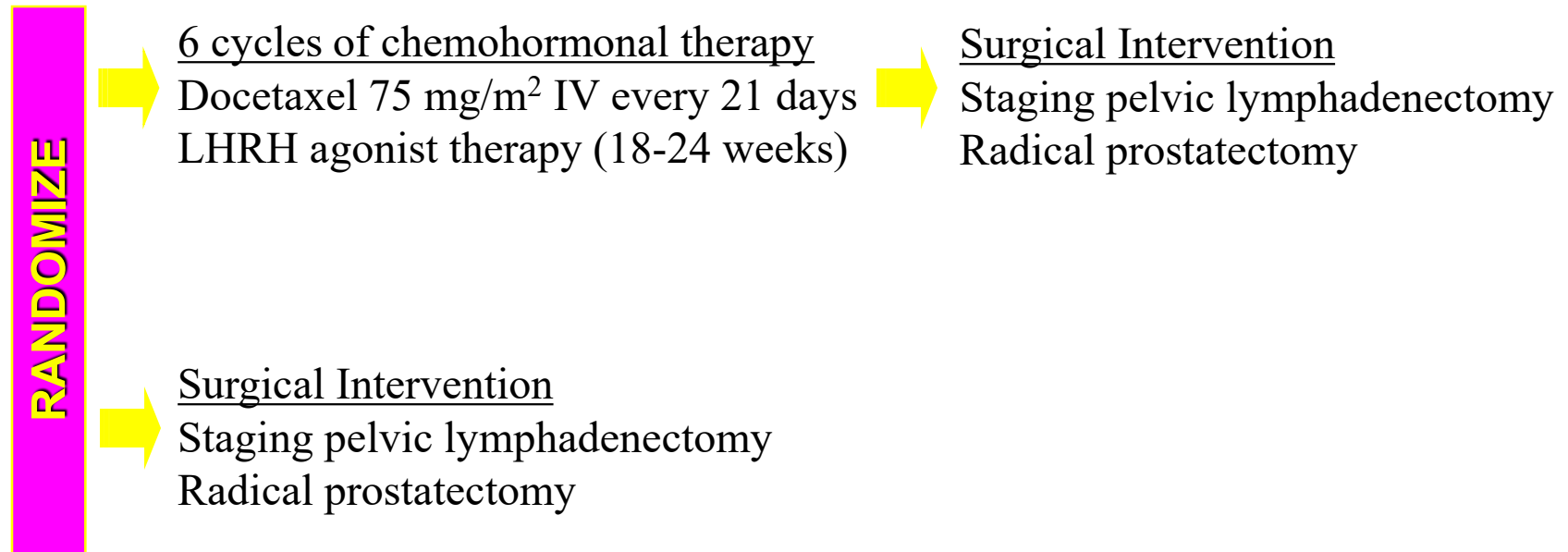
- Tumor mutation burden of 26.3 per megabase

MULTI-MODALITY TREATMENT



Neoadjuvant Chemo-hormonal Therapy Prior to Radical Prostatectomy

CALGB 90203



Eligibility: Kattan Pre-operative nomogram prediction of < 60%

OR

Biopsy Gleason Sum 8-10

Sample size: 750



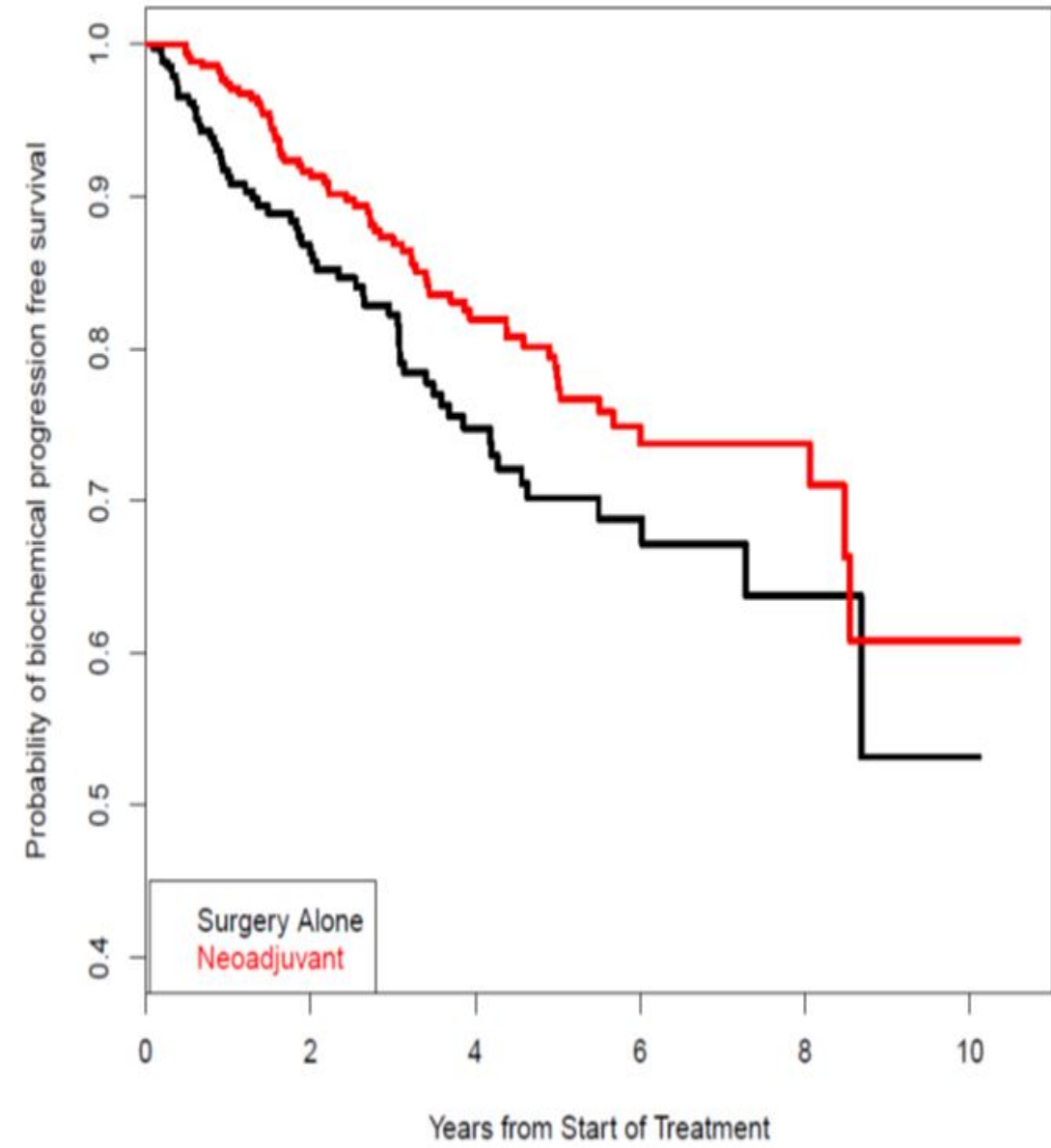


TABLE NEOADJUVANT CHEMOHORMONAL THERAPY VS. SURGERY FOR PCa

	Patients undergoing neoadjuvant CHT	Patients undergoing surgery
Pathologic T3/T4 disease rate	60%	77%
Seminal vesicle invasion rate	32%	41%
Positive lymph nodes	20%	30%
Positive surgical margins	18%	45%

Source: James Eastham, MD

Biochemical Progression Free Survival





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Establishing a Cure Paradigm for Locally Advanced and Low Volume Metastatic Disease

Multimodality Therapy



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Clinical trials with neoadjuvant enzalutamide and/or abiraterone

Cancer Therapy: Clinical

Clinical
Cancer
Research

Neoadjuvant Enzalutamide Prior to Prostatectomy

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ORIGINAL REPORT

Intense Androgen-Deprivation Therapy With Abiraterone Acetate Plus Leuprolide Acetate in Patients With Localized High-Risk Prostate Cancer: Results of a Randomized Phase II Neoadjuvant Study

Mary-Ellen Taplin, Bruce Montgomery, Christopher J. Logothetis, Glenn J. Bubley, Jerome P. Richie, Bruce L. Dalkin, Martin G. Sanda, John W. Davis, Massimo Loda, Lawrence D. True, Patricia Troncoso, Huihui Ye, Rosina T. Lis, Brett T. Marck, Alvin M. Matsumoto, Steven P. Balk, Elahe A. Mostaghel, Trevor M. Penning, Peter S. Nelson, Wanling Xie, Zhenyang Jiang, Christopher M. Haqq, Daniel Tamae, NamPhuong Tran, Weimin Peng, Thian Kheoh, Arturo Molina, and Philip W. Kantoff

original report

Evaluation of Intense Androgen Deprivation Before Prostatectomy: A Randomized Phase II Trial of Enzalutamide and Leuprolide With or Without Abiraterone

Rana R. McKay, MD^{1,2}; Huihui Ye, MD²; Wanling Xie, MS²; Rosina Lis, MD²; Carla Calagua, MD³; Zhenwei Zhang, MD, PhD²; Quoc-Dien Trinh, MD²; Steven L. Chang, MD²; Lauren C. Harshman, MD²; Ashley E. Ross, MD, PhD⁴; Kenneth J. Pienta, MD⁴; Daniel W. Lin, MD⁵; William J. Ellis, MD⁵; Bruce Montgomery, MD²; Peter Chang, MD, MPH²; Andrew A. Wagner, MD²; Glenn J. Bubley, MD²; Adam S. Kibel, MD²; and Mary-Ellen Taplin, MD²

Montgomery B et al. *Clin Cancer Res.* 2017 May 1;23(9):2169-2176.
McKay RR et al. *J Clin Oncol.* 2019 Apr 10;37(11):923-931.
Taplin ME et al. *J Clin Oncol.* 2014 Nov 20;32(33):3705-15.



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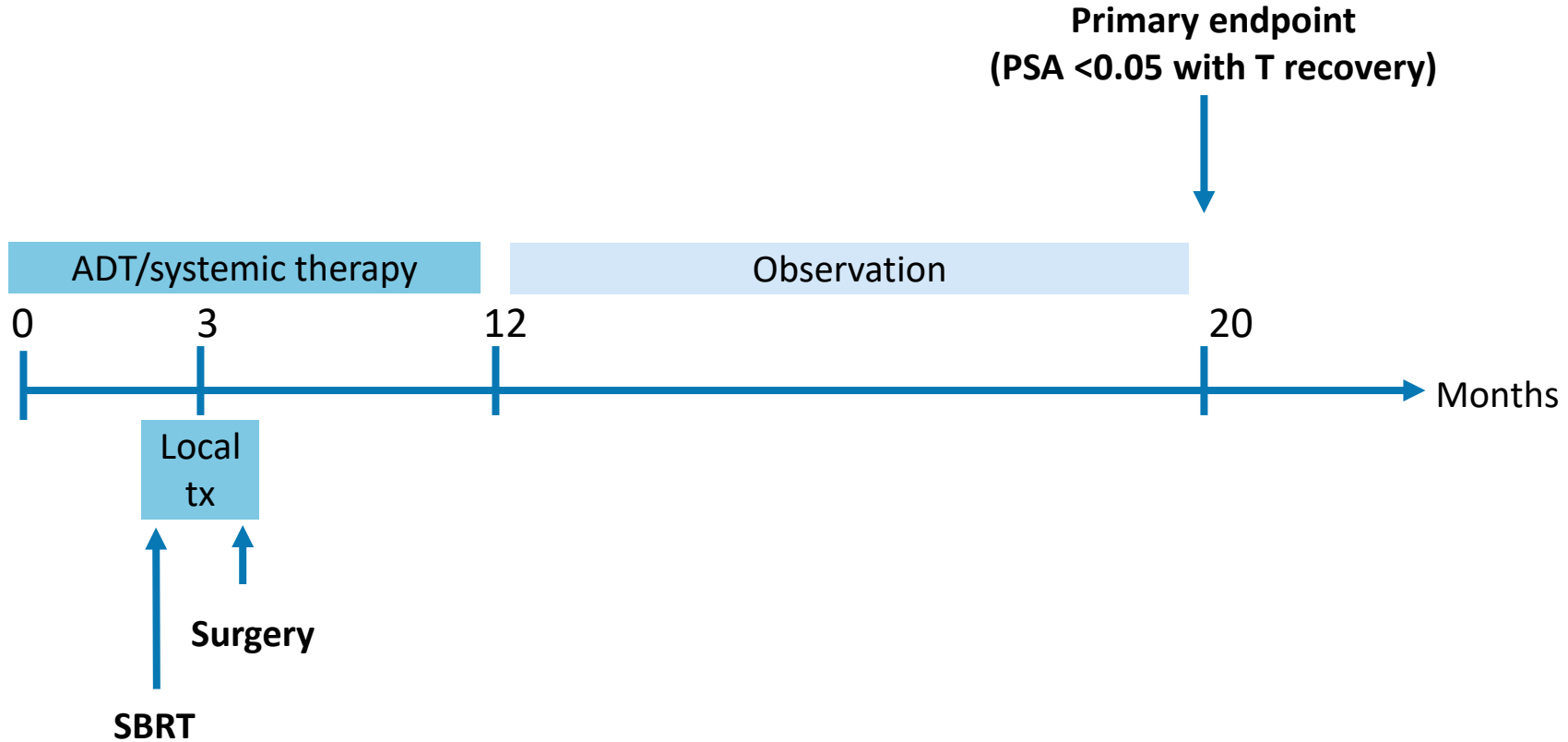


Can a Combined Modality Approach Eliminate Low-volume Metastatic Disease?

- Objective:** Complete elimination of detectable disease
- Eligibility:** Low volume M1 prostate cancer:
Bone: 3 or fewer **radiation portals**
Nodal: Maximum 4 cm; no visceral mets
- Intervention:** Induction with systemic therapy (**total 8 months**), radiation to metastatic sites, treatment of the primary tumor.
- Endpoint:** Proportion with undetectable PSA (PSA0) at 20 months and non-castrate testosterone levels (NED).
- Statistics:** Pilot study; N=20
- Conclusions:** PSA0 rate as binary response indicator of treatment efficacy.



Treatment Schema

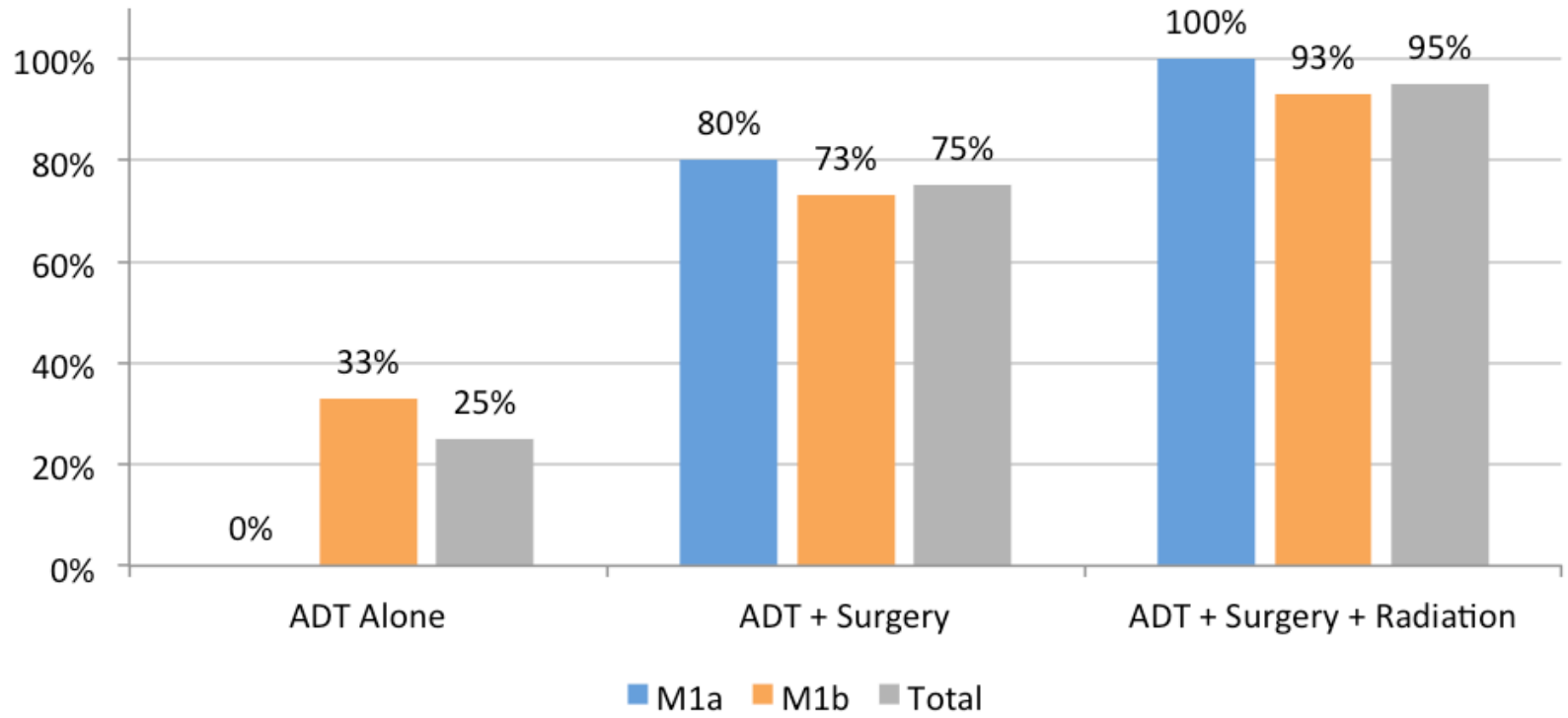


Surgery: intended to resect all gross disease, including RP nodes >2 cm

SBRT was considered for patients with metastatic bone lesions. Lesions were treated to total doses ranging from 2000-3000 cGy delivered over 1-5 fractions.



Percentage of Patients Achieving Undetectable PSA following Multimodal Therapy



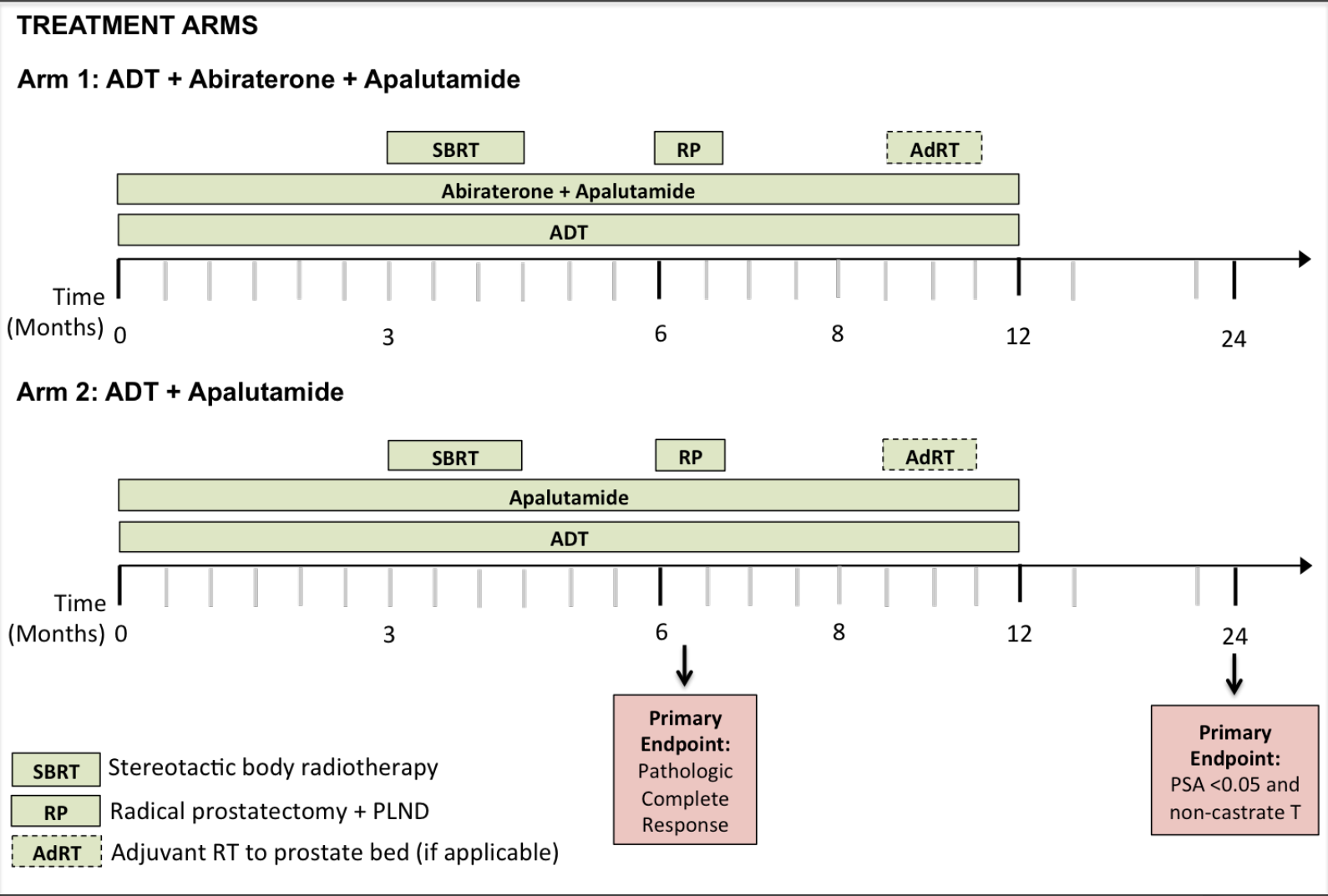


Final Results -

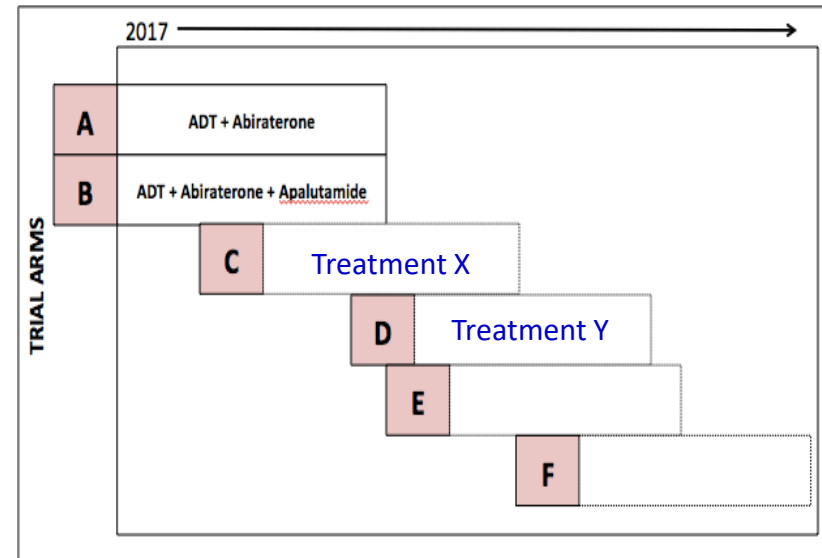
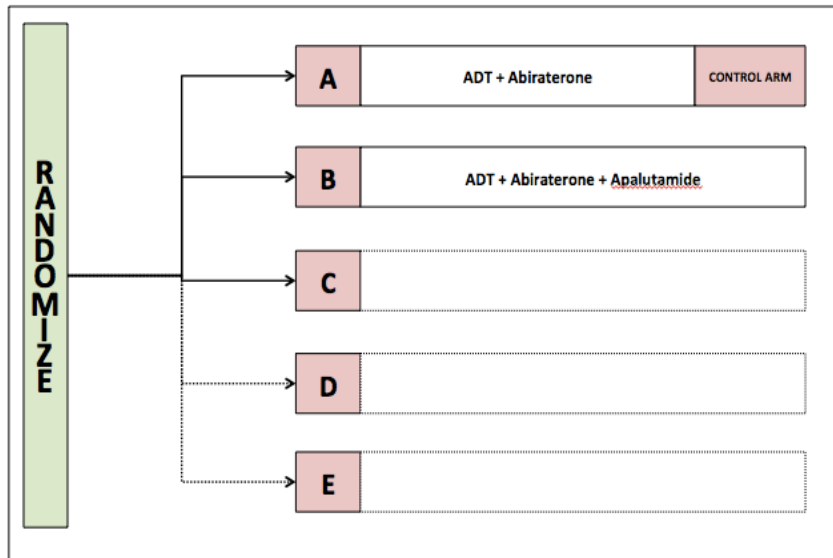
20% of patients (4/20)
had an undetectable PSA with
Non-Castrate Testosterone Levels
at 24 months.



A Combined Modality Randomized Phase 2 Design with Systemic Therapy, Stereotactic Body Radiotherapy and Radical Surgery

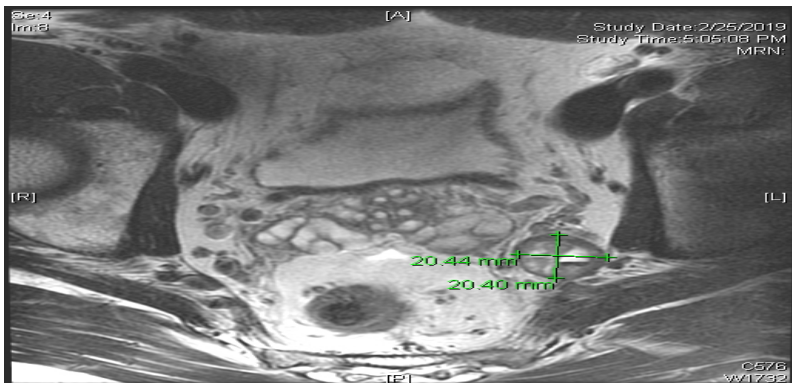
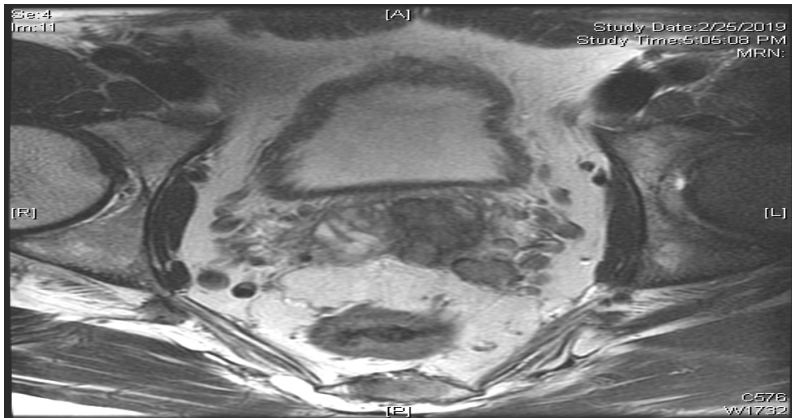
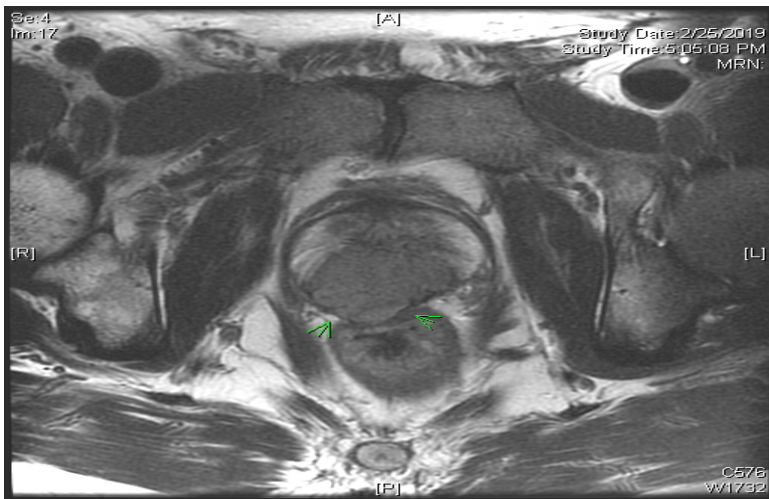


A MultiArm – MultiStage, Randomized , Phase 2 Design



New regimens (Treatment X or Y) can be added at any time without developing a new protocol using the continuously accruing control arm.





- ❖ 53 year asymptomatic man with a PSA of 4.8 and family history of a father with prostate cancer.
- ❖ 14/18 biopsies showing Gleason Grade 10 (5+5) – 100% core involvement. (Two separate path reviews – no small cell).
- ❖ Six months of Lupron, Abiraterone, Prednisone
- ❖ Radical Prostatectomy with extended lymph node dissection September





Pathology at surgery:

No residual tumor anywhere - including the prostate, seminal vesicles, tissue around the prostate, and 24 lymph nodes.

Only treatment related changes.



Ongoing trials with neoadjuvant hormones prior to surgery

NCT	Intervention	Phase	Status
NCT03971110	Goserelin + Bicalutamide	4	Not yet recruiting
NCT03860987	Goserelin + Abiraterone + Enzalutamide	2	Recruiting
NCT03412396	Apalutamide	2	Recruiting
NCT03124433	Apalutamide	2	Active, not recruiting
NCT03080116	Degarelix +/- Apalutamide	2	Recruiting
NCT02949284	Abiraterone + GnRH agonist +/- Apalutamide	2	Recruiting
NCT02903368	Leuprolide + Abiraterone +/- Apalutamide	2	Active, not recruiting
NCT02849990	Degarelix + Abiraterone + Apalutamide + Indomethacin	2	Active, not recruiting
NCT02789878	Goserelin + Abiraterone +/- Apalutamide	2	Recruiting
NCT02770391	Leuprolide + Apalutamide	2	Recruiting
NCT01990196	Degarelix + Enzalutamide +/- Trametinib or Dasatinib	2	Active, not recruiting
NCT01542021	Degarelix	Not applicable	Active, not recruiting
NCT03436654	GnRH agonist/antagonist + Apalutamide +/- Abiraterone	2	Recruiting