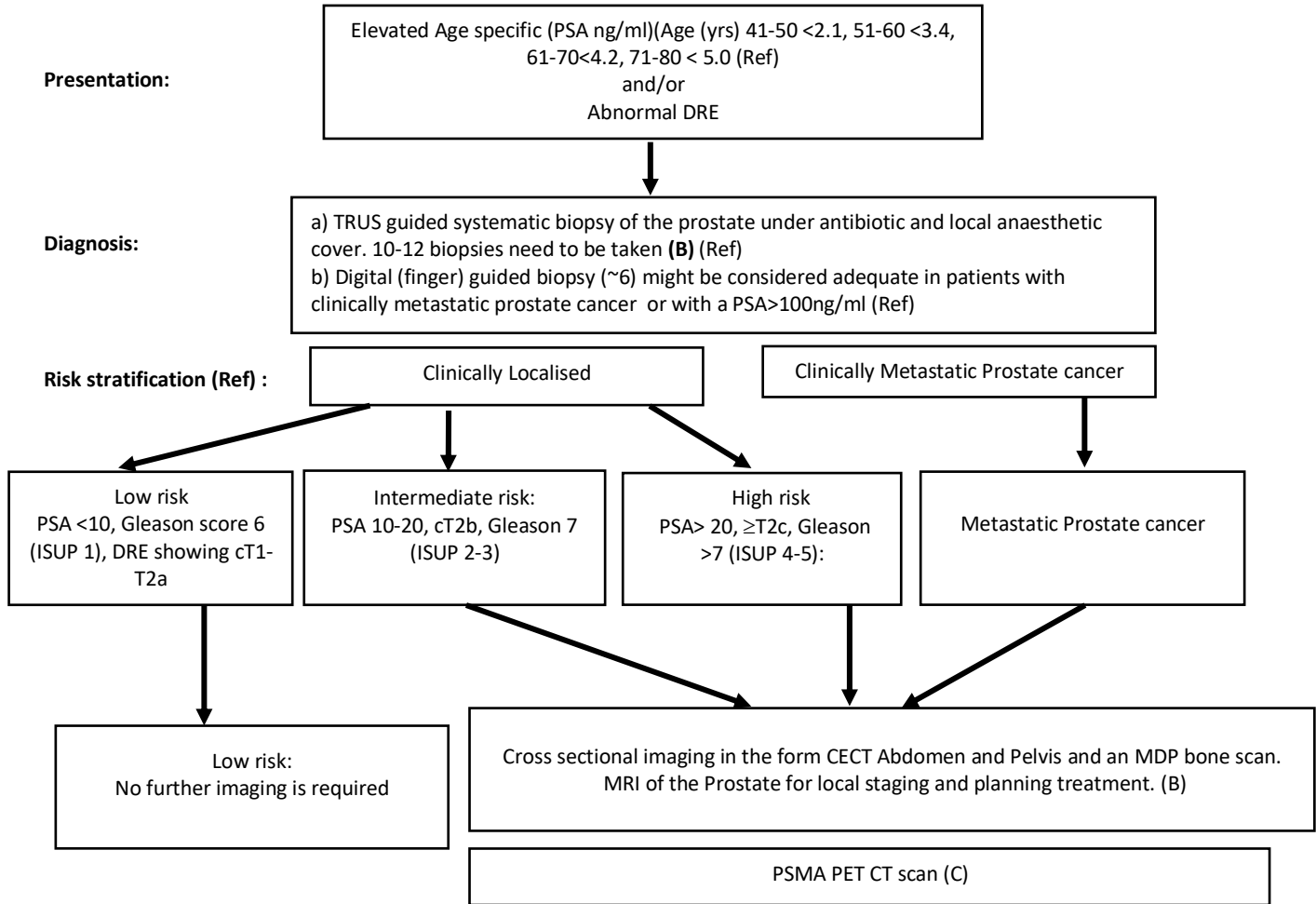
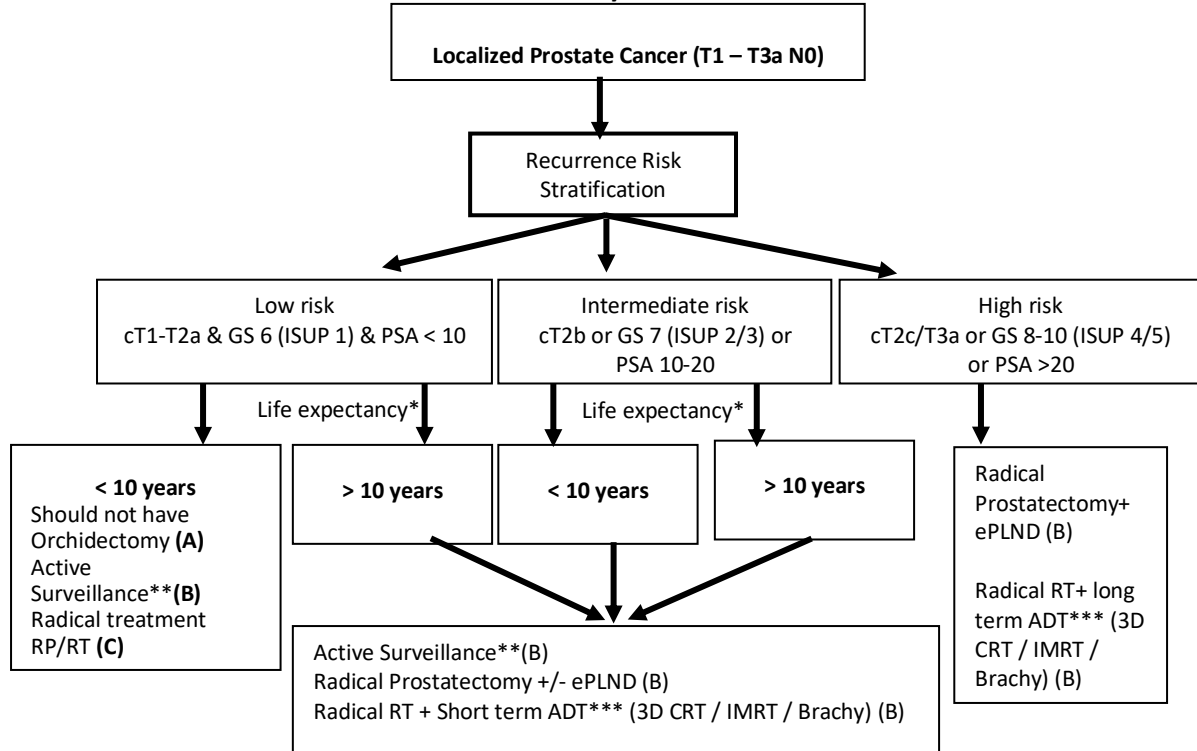


# PROSTATE CANCER

## Investigations for Prostate cancer



## Treatment Pathway for Localized disease



\*Life expectancy: Estimation of life expectancy has to be based on based patients' comorbidity and health assessment using validated tools like Geriatric 8 (G8) screening tool (Ref) (B)

\*\*Active surveillance: All patients need a mpMRI of the prostate within 3 months of biopsy before formal confirmation of Active surveillance pathway

- Any abnormality noted on mpMRI needs to be further assessed using targeted biopsy before confirmation of active surveillance especially in patients with life expectancy of >10 yrs.

**Follow up :** PSA testing every 3 months in the first year

- DRE every 12 months
- mpMRI every 12-18 months

**Progression:** PSA rise greater 50% in 12 months or PSA doubling time of <3 yrs warrants repeat biopsy or radical treatment

- Any significant rise in PSA, or abnormal DRE or mpMRI warrants a biopsy or consideration of radical treatment

### \*\*\*ADT: Androgen Deprivation therapy

- Short term ADT: Neo / concomitant / adjuvant for 4-6 months
- Long term ADT : Neo / concomitant / adjuvant for 2-3 years

### Radical RT : Radical Radiation therapy

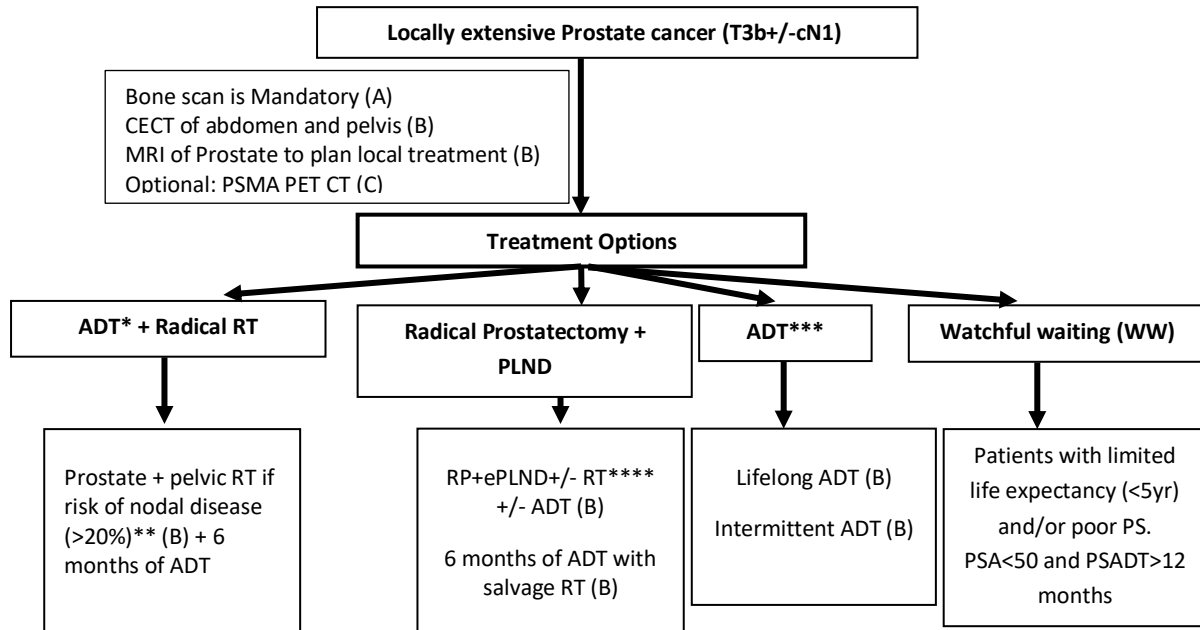
- Low Risk: 3 D CRT / IMRT / Brachytherapy : 70-74Gy
- Intermediate Risk : 3 D CRT / IMRT +/- Brachytherapy : 74 Gy /30 fractions or equivalent
- High Risk: 3 D CRT / IMRT +/-Brachytherapy : >74 using conventional / moderate hypofractionation
- SBRT for low and Intermediate risk prostate cancer (C)

**(RT Doses > 74 Gy mandates a component of Image Guided Radiotherapy)**

### Radical Sx : Radical Surgery

- RP: Radical prostatectomy
- ePLND: Pelvic lymph nodal dissection: When the risk of lymph node involvement is >5% either by using nomogram or Roach formula. Assessment of nodal risk using Roach formula:  $N+=2/3*PSA+(GS-6) \times 10$

**Monthly Intravenous Zoledronic acid is not required in Localised Prostate cancer treatment (A)**



**Monthly Intravenous Zoledronic acid is not required in Localised/Locally extensive Prostate cancer treatment (A)**

\*ADT in locally advanced disease is started as neoadjuvant treatment and is continued for 1836 months overall

\*\*Assessment of nodal risk using Roach formula:  $N = 2/3 * PSA + (GS - 6) \times 10$

\*\*\* In patients not fit and not willing for radical treatment

\*\*\*\* Neoadjuvant ADT is not recommended before radical prostatectomy (A)

\*\*\*\* Adjuvant RT after RP: If Capsule invasion or cut margins positive on final HPR (Ref.: 14,15) or PSA persistence post radical prostatectomy (B)

Early Salvage RT: Radiotherapy in post surgery setting with three consecutive raises of PSA with PSA 0.2-0.5 ng/ml (B)

In staging of post primary treatment recurrence disease PSMA PET is the investigation of choice (B)

Post-operative RT to Prostate bed: 60-66 Gy with 3D CRT / IMRT

**RT: Radiation therapy**

- ▶ Prostate only fields include Prostate + SV with margins
- ▶ Prostate + pelvic fields include Prostate + SV with margins and pelvic nodal regions

**Metastatic Hormone sensitive Prostate cancer**

Bone scan is Mandatory (A)  
CECT of abdomen and pelvis  
and Thorax (B)  
PSMA PET CT (C)

**Life- long ADT (A)**

Orchiectomy (A)  
LHRH agonist +Antiandrogen for flare for 3 weeks (B)  
LHRH antagonist (C)  
+

As per disease burden  
(Referral to medical  
oncologist)

**Low Volume \***

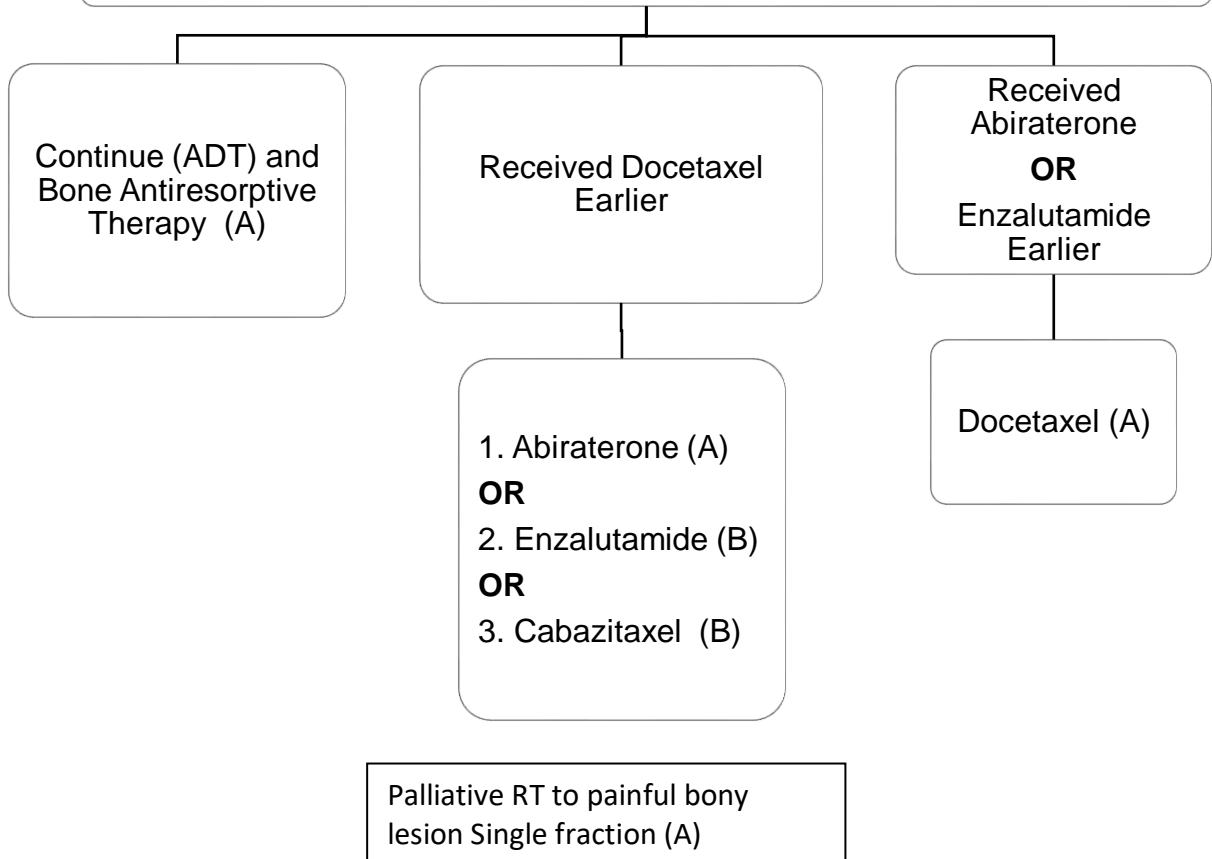
Docetaxel chemotherapy for 6 cycles in  
patients with good PS and GC (B)  
Prostate + Pelvic RT (B)  
Prostate + Pelvic RT + Enzalutamide (C)

**High Volume\***

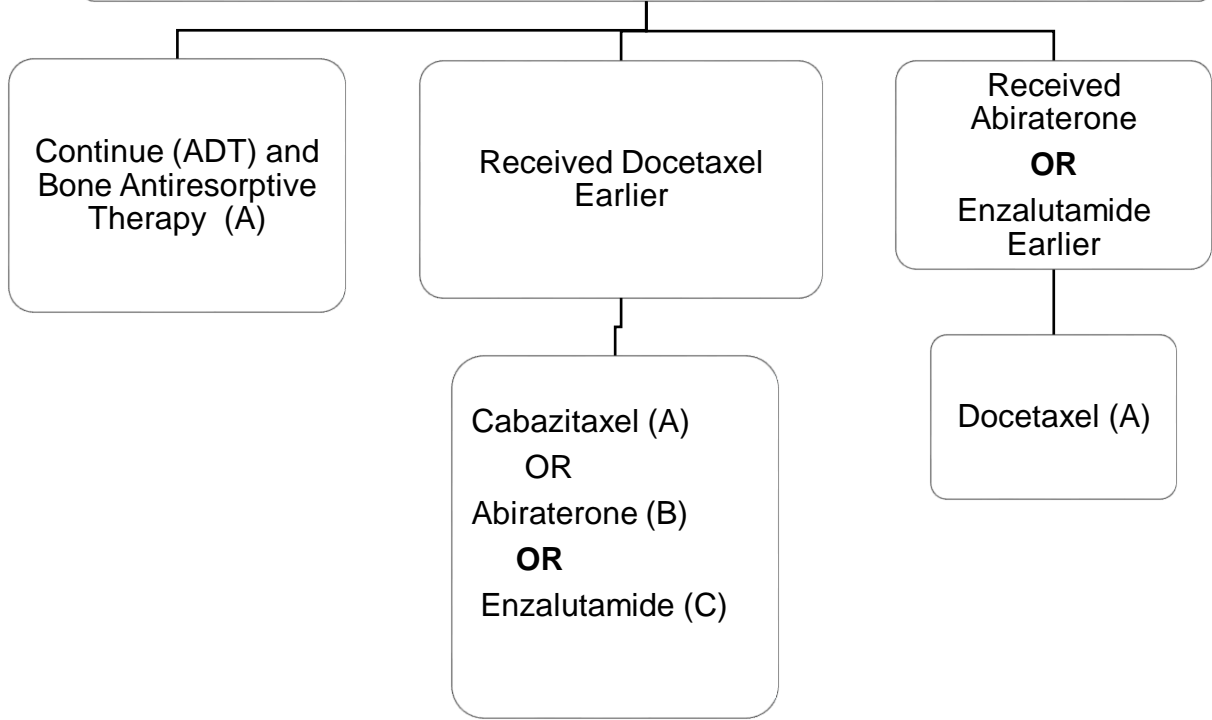
Docetaxel for 6 cycles (A) in  
patients with good PS and (A)  
Abiraterone +Prednisolone till  
progression (A)

\*Based on Bone scan and cross sectional imaging in the form of CT/MRI scan-  
High volume disease is defined as more than four lesions with one of the  
lesions being extra axial or any visceral metastasis

**METASTATIC CASTRATION RESISTANT PROSTATE CANCER  
- SECOND LINE**

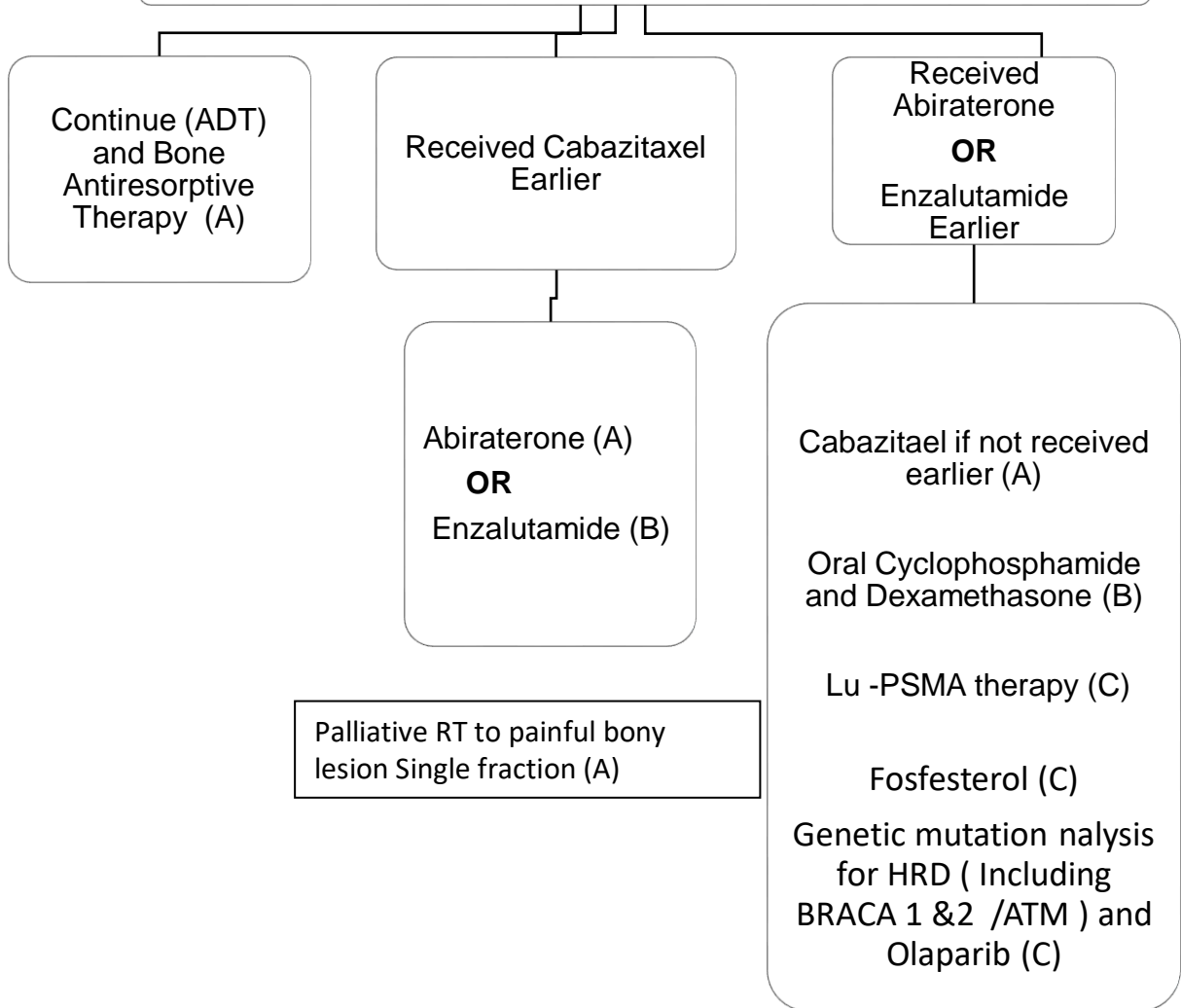


**METASTATIC CASTRATION RESISTANT PROSTATE CANCER  
- THIRD LINE**



Palliative RT to painful bony lesion Single fraction (A)

**METASTATIC CASTRATION RESISTANT PROSTATE  
CANCER - BEYOND THIRD LINE**



Continue (ADT)  
and Bone  
Antiresorptive  
Therapy (A)

Received Cabazitaxel  
Earlier

Abiraterone (A)  
**OR**  
Enzalutamide (B)

Palliative RT to painful bony  
lesion Single fraction (A)

Received  
Abiraterone  
**OR**  
Enzalutamide  
Earlier

Cabazitael if not received  
earlier (A)

Oral Cyclophosphamide  
and Dexamethasone (B)

Lu -PSMA therapy (C)

Fosfesterol (C)

Genetic mutation nalysis  
for HRD ( Including  
BRACA 1 &2 /ATM ) and  
Olaparib (C)

1. Mullerad M, Hricak H, Kuroiwa K, Pucar D, Chen HN, Kattan MW. Comparison of endorectal magnetic resonance imaging, guided prostate biopsy and digital rectal examination in the preoperative anatomical localization of prostate cancer. *J Urol* 2005;174(6): 2158-63.
2. Eichler K, Hempel S, Wilby J, Myers L, Bachmann LM, Kleijnen J. Diagnostic value of systematic biopsy methods in the investigation of prostate cancer: a systematic review. *J Urol* 2006;175(5):1605-12.
3. Billis A, Guimaraes MS, Freitas LL, Meirelles L, Magna LA, Ferreira U. The impact of the 2005 international society of urological pathology consensus conference on standard Gleason grading of prostatic carcinoma in needle biopsies. *J Urol* 2008;180(2):548-52; discussion 552-3.
4. Heidenreich A, Varga Z, Von Knobloch R. Extended pelvic lymphadenectomy in patients undergoing radical prostatectomy: high incidence of lymph node metastasis. *J Urol* 2002;167(4):1681-6.
5. Soloway MS, Soloway CT, Williams S, Ayyathurai R, Kava B, Manoharan M. Active surveillance; a reasonable management alternative for patients with prostate cancer: the Miami experience. *BJU Int* 2008;101(2):165-9.
6. Bill-Axelson A, Holmberg L, Filén F, Ruutu M, Garmo H, Busch C, Nordling S, Häggman M, Anderson SO, Bratell S, Spångberg A, Palmgren J, Adami HO, Johansson JE; Scandinavian Prostate Cancer Group Study Number 4. Radical prostatectomy versus watchful waiting in localized prostate cancer: the Scandinavian prostate cancer group-4 randomized trial. *J Natl Cancer Inst.* 2008;100(16):1144-54.
7. Ficarra V, Novara G, Artibani W, Cestari A, Galfano A, Graefen M, Guazzoni G, Guillonneau B, Menon M, Montorsi F, Patel V, Rassweiler J, Van Poppel H. Retropubic, Laparoscopic, and Robot-Assisted Radical Prostatectomy: A Systematic Review and Cumulative Analysis of Comparative Studies. *Eur Urol* 2009; 25 Jan.
8. Shelley M, Kumar S, Harrison C, Coles B, Wilt TJ, Mason MD. A systematic review and meta-analysis of randomized trials of neo-adjuvant hormone therapy for localized and locally advanced prostate carcinoma *Cancer Treatment Reviews* 2009; 35, 9– 17.
9. Zietman AL, DeSilvio M, Slater JD, Rossi CJ, Miller DW, Adams JA, Shipley WU. Comparison of conventional-dose vs high-dose conformal radiation therapy in clinically localized adenocarcinoma of the prostate. A randomized controlled trial *JAMA* 2005;294 (10):1233-9.
10. D'Amico A, Renshaw AA, Loffredo M, Kantoff PW. Androgen suppression and radiation vs radiation alone for prostate cancer; a randomized controlled trial. *JAMA* 2008;299 (3):289-95.
11. Bradley R, Pieters A, Djuna Z. Systematic review: Comparison of three radiotherapy modalities on biochemical control and overall survival for the treatment of prostate cancer: A systematic review. *Radiotherapy and Oncology* 2009; 93: 168–173.
12. Gustavo A Viani, Eduardo J Stefano, Sergio L Afonso. Higher-than -conventional radiation doses in localized prostate cancer treatment: a metaanalysis of randomized, controlled trials. *Int. J. Radiat. Oncol Biol. Phys.* 2009; 74 (5), 1405–1418.
13. M. Roach III, M. DeSilvio, C. Lawton et al. Phase III Trial Comparing Whole-Pelvic Versus Prostate- Only Radiotherapy and Neo-adjuvant Versus Adjuvant Combined Androgen Suppression:



Radiation Therapy Oncology Group 9413 :By Journal of Clinical Oncology, 2003; Vol 21, No 10 (May 15), pp 1904-1911

14. Bolla M, van Poppel H, Collette L, van Cangh P, Vekemans K, Da Pozzo L, de Reijke TM, Verbaeys A, Bosset JF, van Velthoven R, Maréchal JM, Scalliet P, Haustermans K, Piérart M; European Organization for Research and Treatment of Cancer. Postoperative radiotherapy after radical prostatectomy: a randomized controlled trial (EORTC trial 22911). *Lancet* 2005;366 (9485) 572-8.
15. Wiegel T, Bottke D, Steiner U, Siegmann A, Golz R, Storkel S, et al. Phase III, Post-operative adjuvant radiotherapy in patients with pT3 prostate cancer after radical prostatectomy with postoperative undetectable PSA – a randomized controlled trial. *J. Clin Oncol.* 2009; 27(18): 29, 4-30.
16. Hanks GE, Pajak TF, Porter A, Grignon D, Brereton H, Venkatesan V, Horwitz EM, Lawton C, Rosenthal SA, Sandler HM, Shipley WU; Radiation Therapy Oncology Group. RTOG 92-02: Phase III trial of long term adjuvant androgen deprivation after neoadjuvant hormonal cytoreduction and radiotherapy in locally advanced carcinoma of the prostate. *J Clin Oncol* 2003;21(21):3972-8.
17. Widmark A, Klepp O, Solberg A, Damber JE, Angelsen A, Fransson P, Lund JÅ, Tasdemir I, Hoyer M, Wiklund F, Fosså SD for the Scandinavian Prostate Cancer Group Study, the Swedish Association for Urological Oncology. Endocrine treatment, with or without radiotherapy, in locally advanced prostate cancer (SPCG-7/SFUO-3): an open randomized phase III trial. *Lancet* 2008;373 (9660):301-8.
18. Ghavamian R, Bergstralh EJ, Blute ML, Slezak J, Zincke H. Radical retropubic prostatectomy plus orchiectomy versus orchiectomy alone for pTxN+ prostate cancer: a matched comparison. *J Urol* 1999;161(4):1223-8.
19. Lawton CA, Winter K, Grignon D, Pilepich MV. Androgen suppression plus radiation versus radiation alone for patients with D1/pathologic nodepositive adenocarcinoma of the prostate: updated results based on a national prospective randomized trial, RTOG 85-31. *J Clin Oncol* 2005;23(4):800-7.
20. Medical Research Council Prostate Cancer Working Party Investigators Group. Immediate versus deferred treatment for advanced prostatic cancer: initial results of the Medical Research Council Trial. *Br J Urol* 1997;79(2):235-46.
21. Tangen CM, Faulkner JR, Crawford ED, Thompson IM, Hirano D, Eisenberger M, Hussain M. Ten-year survival in patients with metastatic prostate cancer. *Clin Prostate Cancer* 2003;2(1):41-5.
22. Hartsell WF, Scott CB, Bruner DW, Scarantino CW, Ivker RA, Roach M 3rd, et al. Randomized trial of short- versus long-course radiotherapy for palliation of painful bone metastases. *Natl Cancer Inst* 2005; 97 (11):798-804.
23. Saad F, Gleason DM, Murray R, Tchekmedyian S, Venner P, Lacombe L, Chin JL, Vinholes JJ, Goad JA, Chen B. A randomized, placebo-controlled trial of zoledronic acid in patients with hormone refractory metastatic prostate carcinoma. *J Natl Cancer Inst* 2002; 94 (19):1458-68.
24. Seidenfeld J, Samson DJ, Hasselblad V, Aronson N, Albertsen PC, Bennett CL, Wilt TJ. Singletherapy androgen suppression in men with advanced prostate cancer: a systematic review and meta-analysis. *Ann Intern Med* 2000;132 (7): 566-77.
25. de Leval J, Boca P, Yousef E, Nicolas H, Jeukenne M, Seidel L, Bouffieux C, Coppens L, Bonnet P, Andrianne R, Wlatregny D. Intermittent versus continuous total androgen blockade in the

treatment of patients with advanced hormone-naive prostate cancer: results of a prospective randomized multicenter trial. *Clin Prostate Cancer* 2002;1(3):163-71.

26. Boccon-Gibod L, Djavan WB, Hammerer P, Hoeltl W, Kattan MW, Prayer-Galetti T, Teillac P, Tunn UW. Management of prostate-specific antigen relapse in prostate cancer: a European Consensus. *Int J Clin Pract* 2004;58(4):382-90.

27. Roach III M, Hanks G, Thames jr H, Schelhammer P, Shipley WU, Sokol GE, Sandler H. Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: recommendations of the RTOG-ASTRO Phoenix consensus conference. *Int J Radiat Oncol Biol Phys* 2006;65 (4):965-74.

28. Oh WK, Kantoff PW. Management of hormone refractory prostate cancer: current standards and future prospects. *J Urol* 1998;160(4):1220-9.

29. Carthon BC and. Antonarakis ES. The STAMPEDE trial: paradigm-changing data through innovative trial design *Transl Cancer Res.* 2016 September ; 5(3 Suppl): S485–S490.

30) Ganpule AP et al. Age specific prostate specific antigen and prostate specific antigen density values in a community based Indian population. *Indian J Urol.* 2007 Apr-Jun; 23(2):122-125

31) Parker CC et al. Radiotherapy to the primary tumor for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. *Lancet.* 2018 Dec 1; 392(10162): 2353-2366

32) Sydes MR et al. Adding abiraterone or docetaxel to long-term hormone therapy for prostate cancer: directly randomised data from the STAMPEDE multi-arm, multi-stage platform protocol. *Ann Oncol.*2018 May; 29(5): 1235-1248

33) NW Clarke et al. Addition of docetaxel to hormone therapy in low and high burden metastatic hormone sensitive prostate cancer: long-term survival results from the STAMPEDE trial. *Annals of Oncol.* 2019 Sept; 1-12