

Radiotherapy (RT) is an alternative treatment for localized prostate cancer (PC) **with the same cure rates as radical prostatectomy (RP)**. Radiation dose is directly related to disease control; however, toxicity is a limitation. Androgen deprivation therapy (ADT) has a **cytotoxic effect** on tumor cells, **which associated with RT has a synergistic effect, increasing sensitivity to radiation, enhancing its effect and improving oncological results.**

CURATIVE TREATMENT

Who are the candidates and what are the RT options?

<p>Low and favorable intermediate risk External beam radiation therapy (EBRT) or brachytherapy if good urinary function (IPSS < 12 and Qmax 15 ml/s). No indication of ADT in combination or as monotherapy.</p>	<p>Unfavorable intermediate risk EBRT + ADT* or trimodal therapy (more long-term urinary complications could occur). There is no indication for ADT monotherapy.</p>	<p>High, very high and locally advanced risk EBRT + ADT, trimodal therapy or ADT monotherapy**. In very high-risk patients, it is recommended to add docetaxel (DOC) for 6 cycles or abiraterone (ABI) for 2 years or until progression. In locally advanced patients, ABI could be added for 2 years both to patients who receive RT and to those who do not.</p>
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* Contraindication or non-acceptance of ADT: EBRT or EBRT + brachytherapy

** Patients not suitable for RP/RT if, in addition, PSA doubling time (PSADT) < 12 months and PSA > 50 ng/mL or poor tumor differentiation, also in symptomatic locally advanced patients.

Why add ADT?: reduces biochemical recurrence (BCR), improves progression-free survival (PFS), cancer-specific survival (CSS), metastasis-free survival (MFS), and overall survival (OS).

How long?: short cycles (**4 – 6 months**) at intermediate risk and long cycles (**18 months – 3 years**) at high risk and beyond.

¿Adjuvant or neoadjuvant ADT?: the superiority between two options is not definitive. Two recent meta-analysis favor the use of **adjuvant ADT** in terms of PFS and MFS without being affected by RT dose, risk group (NCCN), or age.

What are the ADT options?: **LHRH agonists with or without first-generation antiandrogens, or LHRH antagonists.**

¿When to indicate radiotherapy and/or ADT after radical prostatectomy?

UNDETECTABLE PSA

Patients **pN0** and pT3/T4 + ISUP 4-5 with/without positive margins (especially if there is >10 mm involvement or ≥3 positivity sites), benefit from receiving **adjuvant EBRT**.

If not, **monitoring** with PSA is a valid option. The threshold for early rescue is a repeat PSA level >0.1 ng/mL.

DETECTABLE PSA

It is considered detectable if PSA is ≥ 0.1 ng/ml 4-8 weeks after the RP. This population may have a higher risk of metastasis and death and worse PFS.

PET-PSMA helps to differentiate between regional or distant involvement. If metastases are ruled out, **salvage RT + ADT**.

Performing PET-PSMA or indicating salvage therapy depends on patient characteristics such as PSA nadir level and prior to surgery, PSADT, clinical-pathological data, age and comorbidities. A Decipher® score > 0.6 (high risk) could be useful in this scenario and in RBQ after RP.

BIOCHEMICAL RECURRENCE

What is biochemical recurrence?: after RP, **PSA > 0.2 ng/ml with a second confirmatory level. After RT, PSA ≥ 2 ng/ml above the nadir.**

How to make the assessment after recurrence?: imaging assessment helps to detect regional and/or distant involvement. **PET-PSMA** is the best tool (especially if PSA > 0.2 ng/ml).

Prostate mpMRI in patients undergoing RT provides useful information that also helps guide subsequent prostate biopsy.

Which patients are indicated treatment?: after ruling out metastases, consider life expectancy and comorbidities. **EAU high-risk** patients benefit from active treatment. Observation is an option in EAU low-risk or those considered palliative.

EAU High risk BCR

RP: pathological ISUP grade 4-5 or PSADT < 1 year
RT: interval to BCR < 18 months or biopsy ISUP grade 4-5

EAU Low risk BCR

RP: pathological ISUP grade < 4 and PSADT > 1 year
RT: interval to BCR > 18 months and biopsy ISUP grade < 4

What are the active treatment options?: after RP, **salvage radiotherapy** is ideally indicated with PSA levels < 0.5 ng/mL. In BCR after RT and positive biopsies, **salvage prostatectomy, brachytherapy, cryotherapy or HIFU** could be chosen, ideally with PSA < 5 ng/mL. If biopsy was negative, these patients could undergo **observation or ADT**.

Is it necessary to combine with ADT?: consider ADT with salvage RT, if there are risk factors (pT3b-T4 + ISUP > 4 or pT3b-T4 + PSA > 0.4 ng/mL). Salvage interventions in BCR after RT are not indicated in combination with ADT.