EDU 20 - Optimizing Post-Prostatectomy Radiotherapy: A Multi-Disciplinary Perspective.

Emmanuel Antonarakis, MD, Robert Den, MD, Stephen Freedland, MD, Drew Moghanaki, MD, MPH

## Question 1:

The 2013 ASTRO/AUA Guidelines for Adjuvant and Salvage Radiotherapy after Prostatectomy provides the following recommendation for patients with an undetectable PSA, but a positive margin:

- a) Deliver adjuvant radiotherapy to all of these patients
- b) Deliver adjuvant androgen deprivation therapy to all of these patients
- c) Deliver radiotherapy + androgen deprivation therapy to all of these patients
- d) Offer radiotherapy but deliver only after the shared decision making process has been completed

### Answer:

d) Offer radiotherapy but deliver only after the shared decision making process has been completed

## Feedback:

The ASTRO/AUA Panel emphasized that ART should be offered to all patients at high risk of recurrence because of adverse pathological features. By "offered", the Panel means that the patient, his family, and the multi-disciplinary treatment team should engage in a shared decision-making process in which the patient is advised to consider the possibility of additional treatment (i.e., radiotherapy). Whether ART is likely to benefit a particular patient and should be administered is a decision best made by the multidisciplinary treatment team and the patient with full and thoughtful consideration of the patient's history, current functional status, values, and preferences, and his tolerance for the potential toxicities and quality of life effects of radiotherapy.

## Reference:

Thompson et al, Adjuvant and Salvage Radiotherapy After Prostatectomy: AUA/ASTRO Guideline. J. Urology, 2013

-- End of Question 1 ---

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# Question 2:

The PORTOS gene signature is a predictive of:

- a) Response to chemotherapy
- b) Response to radiation therapy
- c) Response to androgen deprivation therapy
- d) All of the above

#### Answer:

b) Response to radiation therapy.

#### Feedback:

PORTOS is a 24-gene predictor of response to postoperative radiotherapy in prostate cancer. There is no currently published genomic response to chemotherapy. For androgen deprivation therapy, luminal/basal subtyping has demonstrated association with response.

## Reference:

Zhao et al. Development and validation of a 24-gene predictor of response to postoperative radiotherapy in prostate cancer: a matched, retrospective analysis, Lancet Oncology, November 2016.

--- End of Question 2 ---

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# Question 3:

When considering post-operative radiation therapy for patients with pathologic T3 or positive margins, the following statements are **true**:

- a) Patients with a high Decipher score have no reduction in metastasis with radiotherapy
- b) Patients with a high Decipher score have lower rates of metastases with adjuvant radiotherapy
- c) A Decipher test is indicated for patients with castrate resistant disease
- d) A Decipher test is indicated for patients with metastatic disease

### Answer:

b) Patients with a high Decipher score have lower rates of metastases with adjuvant radiotherapy as compared to observation

## Feedback:

Patients with high Decipher score had an 80% reduction in cumulative incidence of metastases with adjuvant as compared to salvage radiation therapy. Decipher is currently also indicated for patients with localized hormone sensitive prostate cancer.

#### Reference:

Den et al. Genomic classifier identifies men with adverse pathology after radical prostatectomy who benefit from adjuvant radiation therapy. JCO 2015 Mar 10;33(8):944-51.

--- End of Question 3 ---

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## Question 4:

According to the ASCO Guidelines on adjuvant radiation, which patients stand to derive the **greatest** benefit from adjuvant radiation?

- a) Those with Gleason 6 or 7 disease (grade group I-III)
- b) All patients with positive margins
- c) Those with seminal vesicle invasion
- d) Those with extracapsular extension

### Answer:

c) Those with seminal vesicle invasion

#### Feedback:

While clinical trials have shown that adjuvant radiation reduces the *relative* risk of recurrence by ~50%, the *absolute* risk reduction is derived by knowing the risk of recurrence without radiation (i.e. men at the greatest stand to benefit the most). Thus, the ASCO guideline panel identified men at the greatest risk of recurrence to include men with extensive positive margins, Gleason 8-10 disease (grade group 4-5), seminal vesicle invasion, and detectable post-operative PSA.

## Reference:

Freedland et al, Adjuvant and Salvage Radiotherapy after Prostatectomy: American Society of Clinical Oncology Clinical Practice Guideline Endorsement, JCO 32 (34): 3892-3898, 2014

--- End of Question 4 ---

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## **Question 5:**

Choose the correct statement below based upon prospective randomized trial data:

- a) Adjuvant radiation has never been prospectively compared to early salvage radiation in a phase III trial
- b) Phase III data has shown adjuvant radiation improves survival vs early salvage radiation
- c) Phase III data has shown adjuvant radiation improves biochemical control but not survival vs early salvage radiation
- d) Phase III data has shown adjuvant radiation neither improved biochemical control or survival vs early salvage radiation

#### Answer:

a) Adjuvant radiation has never been compared to salvage radiation

### Feedback:

While multiple trials have examined adjuvant radiation, the control arm was observation with salvage radiation left to the discretion of the investigator. Collectively, these studies show adjuvant radiation reduces biochemical recurrence and may improve survival (in one study, but not in others). However, no study to date has compared adjuvant vs. early salvage radiation directly.

## Reference:

Thompson et al, Adjuvant and Salvage Radiotherapy After Prostatectomy: AUA/ASTRO Guideline. J. Urology, 2013

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