BACKGROUND/METHODS

Most patients would defer using androgen deprivation therapy (ADT) with radiation therapy (RT) when the number-needed-to-treat (NNT) exceeds 25 persons to prevent 1 from developing metastasis, corresponding to an absolute benefit (AB) of 4%. However, no tools for estimating personalized NNT or AB from ADT exist. We aimed to quantify personalized AB and NNT for persons receiving ADT added to single modality RT.

The clinical cell-cycle risk (CCR) score combines the University of California, San Francisco’s Cancer of the Prostate Risk Assessment and the cell cycle progression molecular score to accurately assess prostate cancer aggressiveness. The effect of ADT added to RT was modeled using a 10-year risk of metastasis as a function of continuous CCR score for patients treated with RT alone (Table 1). The relative benefit of ADT added to RT to reduce distant metastasis was modeled using published data from The Meta-Analysis of Randomized Trials in Cancer of the Prostate (MARCAP) which utilized several prospectively randomized RT±ADT trials. Methods for calculating absolute benefit from risk and relative benefit are shown in Figure 1. The average absolute benefit was calculated for patients with CCR scores above and below a prespecified multimodality treatment threshold (MMT; CCR = 2.112) using the distribution of scores in a cohort of patients commercially tested by Myriad Genetics.

The CCR score can accurately predict an individual’s absolute risk reduction for metastasis by using multimodality ADT+RT over RT alone, regardless of NCCN risk group.

The Multimodality Treatment Threshold is consistent with patient attitudes about when to use or omit ADT and can be a useful guideline for treatment intensification discussions.

RESULTS

• The average absolute benefit of adding ADT to RT in the commercially tested cohort was 0.86% (NNT=116) in patients below the multimodality benefit threshold (MMT), and 8.2% (NNT=12) for patients with CCR scores above the MMT.

• Patients with CCR scores precisely at the MMT had a predicted absolute benefit of 3.7% (NNT=27).

• The individualized risk of metastasis for each CCR score for patients treated with RT alone and with RT+ADT is shown in Figure 2. Figure 3 shows the absolute risk reduction and number needed-to-treat for ADT added to RT for each CCR score.

Table 1: Characteristics of men with prostate cancer from Single-Mode RT Cohort (N=467) and Commercial Cohort (N=56,485).

Figure 1: Overview of statistical methods to model ADT benefit as a function of CCR score.

Figure 2: Risk of metastasis as a function of CCR score assuming a relative benefit of ADT of 41% (Kishan 2022) with simulated 95% confidence intervals.

Figure 3: Absolute benefit of ADT added to RT with corresponding NNT as a function of CCR score assuming a relative benefit of ADT of 41% with simulated 95% confidence intervals.

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1. Huntsman Cancer Institute, University of Utah, Salt Lake City, UT2. Myriad Genetics, Inc.

Email questions to: jonathan.tward@hci.utah.edu

@prostatemd