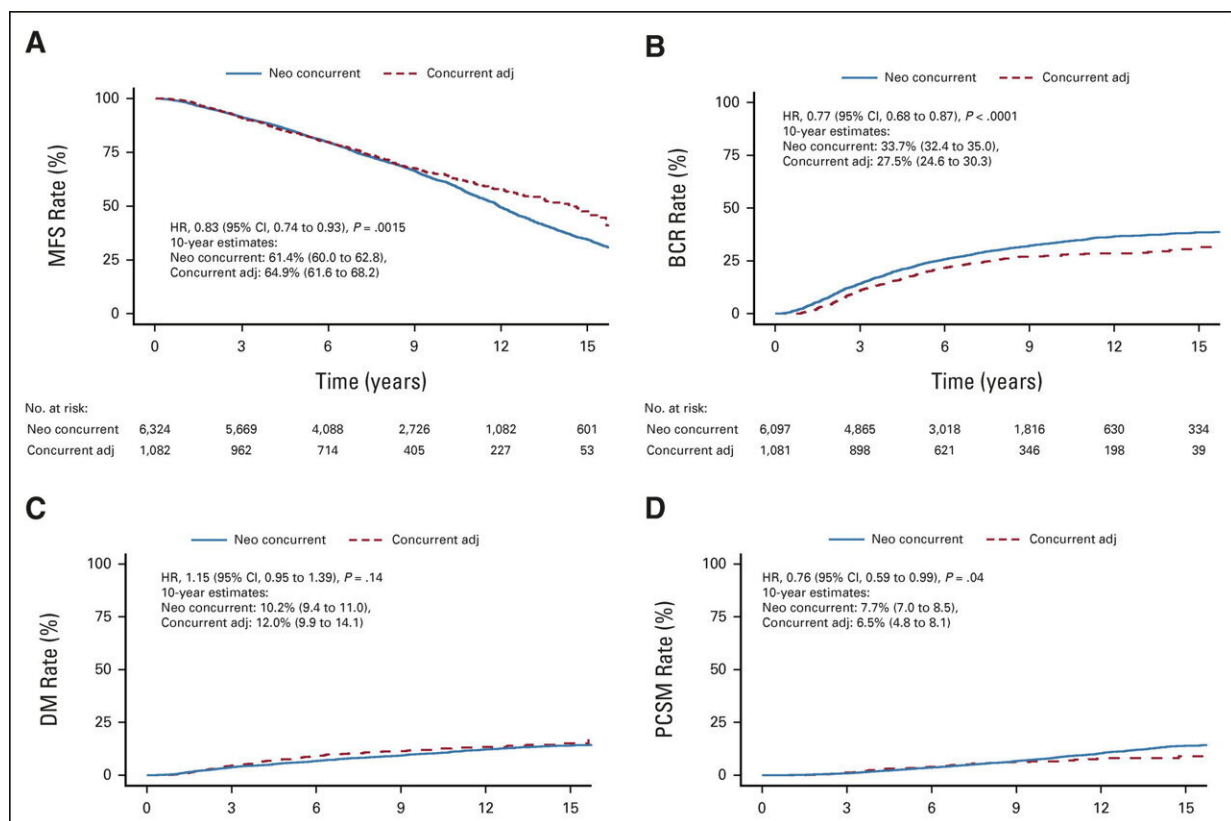


Timing androgen-deprivation therapy with radiation therapy improves outcomes in localized prostate cancer

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Unadjusted Kaplan-Meier and cumulative incidence curves evaluating the associations between concurrent/adjvant versus neoadjuvant/concurrent ADT sequencing and oncologic outcomes in the overall cohort. Oncological outcomes included (A) metastasis-free survival, (B) biochemical recurrence, (C) distant metastasis, (D) prostate cancer-specific mortality, (E) other-cause mortality, and (F) overall survival. The neoadjuvant/concurrent ADT group was used as the

reference when calculating HRs. ADT, androgen-deprivation therapy; BCR, biochemical recurrence; concurrent adj, concurrent/adjuvant; DM, distant metastasis; HR, hazard ratio; MFS, metastasis-free survival; neo concurrent, neoadjuvant/concurrent; OCM, other-cause mortality; OS, overall survival; PCSM, prostate cancer–specific mortality. Credit: *Journal of Clinical Oncology* (2022). DOI: 10.1200/JCO.22.00970

Men with prostate cancer who are receiving radiation often benefit from adding to the treatment androgen deprivation therapy, a form of medication that reduces testosterone. Historically, men have been placed on androgen deprivation therapy prior to beginning radiation. In a large analysis of more than 7,000 men treated internationally across 12 randomized trials, Dr. Kishan and colleagues have shown that it is almost universally optimal for men to begin androgen deprivation therapy when starting radiation, so that most of the period of having a low testosterone is "backloaded" after radiation is complete.

Androgen-deprivation therapy (ADT), also called hormone-suppression therapy, has consistently been shown to improve [survival rates](#) when added to [radiation](#) therapy (RT) for lower-risk patients with localized [prostate](#) cancer. However, the optimal sequencing of ADT for these patients remains controversial. Two previous studies suggested that ADT beginning with RT and continuing afterward may be superior to the before-and-during RT sequencing option, but both randomized trials had limitations that made it difficult to infer broad conclusions, according to the authors.

Based on those trials, this study's researchers theorized that concurrent/adjuvant ADT sequencing would offer improved metastasis-free survival compared with neoadjuvant/ concurrent ADT sequencing in patients receiving short-term (four to six months) therapy in a RT

field size-dependent manner.

This [meta-analysis](#) was designed to investigate how the sequencing of ADT combined with RT administered via prostate-only RT or whole-pelvis RT might impact outcomes for prostate cancer patients.

The analysis examined more than 7,400 patient records, including 6,325 patients who had received ADT before and during (neoadjuvant/concurrent) their radiation therapy and 1,084 patients who received ADT during and after (concurrent/adjuvant) undergoing RT. The median follow-up period was 10.2 years.

Researchers observed a significant interaction between ADT sequencing and RT field size for all study endpoints except overall survival. For patients receiving prostate-only RT, ADT occurring during and after radiation was associated with improved metastasis-free survival compared with neoadjuvant/concurrent ADT.

However, with patients receiving whole-pelvis RT, no significant difference was observed with ADT sequencing, except greater distant metastasis occurrence among those who had concurrent/adjuvant ADT. However, that finding should be interpreted with caution due to details on how the individual trials were structured.

The study appears in the *Journal of Clinical Oncology*.

The authors concluded that ADT sequencing demonstrated a significant impact on clinical outcomes with a strong correlation to RT field size. They believe that concurrent and adjuvant ADT should be the standard of care where short-term ADT is indicated in combination with prostate-only RT.

The researchers conducted a new analysis of individual patient data from

12 [randomized trials](#) in which patients received short-term ADT either before and during their radiation therapy or during and after for localized prostate cancer. Data was obtained through the Meta-Analysis of Randomized Trials in Cancer of the Prostate (MARCAP) Consortium, a first-of-its-kind repository for worldwide clinical trials involving patients with prostate cancer. The consortium was co-founded in 2020 by Drs. Amar Kishan of the UCLA Jonsson Comprehensive Cancer Center and Daniel Spratt with University Hospitals Seidman Cancer Center in Cleveland.

Their analysis included performing inverse probability of treatment weighting (IPTW) with propensity scores derived from factors such as age, initial PSA score, Gleason score, T stage, RT dose and mid-trial enrollment year. Metastasis-free survival and overall survival were assessed by Cox regression models adjusted for IPTW and analyzed independently for men receiving prostate-only RT versus whole-pelvis RT. Adjusted Fine and Gray competing risk models were built to evaluate distant metastasis (DM) and prostate cancer-specific mortality.

"To our knowledge, this study represents the first time a significant association has been demonstrated between concurrent and adjuvant ADT sequencing and overall survival rates among prostate [cancer](#) patients," said Kishan, corresponding author for the study. "For patients receiving prostate-only RT, concurrent/adjuvant sequencing is associated with optimal outcomes."

Kishan, who is vice-chair of Clinical and Translational Research and chief of genitourinary oncology for Radiation Oncology at UCLA, noted that the results should be "considered practice-changing with regards to how ADT is sequenced with radiation for patients getting short courses of ADT with prostate radiation."

He says future trials currently in the pipeline may yield more answers

about the benefit of neoadjuvant/concurrent ADT sequencing with whole-pelvis RT in patients with intermediate- and high-risk [prostate cancer](#).

More information: Ting Martin Ma et al, Sequencing of Androgen-Deprivation Therapy of Short Duration With Radiotherapy for Nonmetastatic Prostate Cancer (SANDSTORM): A Pooled Analysis of 12 Randomized Trials, *Journal of Clinical Oncology* (2022). [DOI: 10.1200/JCO.22.00970](#)

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