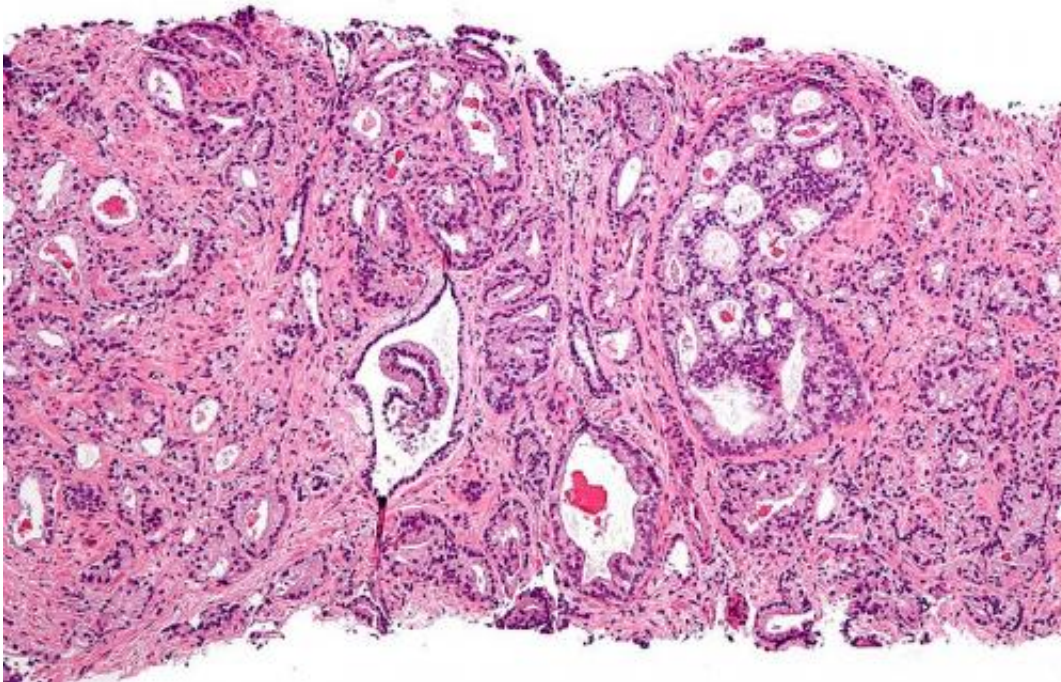


New meta-analysis may help guide treatment planning for patients with high-risk prostate cancer

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Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Results of a large study led by UCLA Jonsson Comprehensive Cancer Center researchers could help guide treatment planning for patients with high-risk prostate cancer.

An international effort consisting of a consortium of 16 research centers in collaboration with two international cooperative trial groups found that patients receiving high-dose external beam radiation therapy alone may benefit from [androgen deprivation therapy](#) (ADT) lasting longer than 18 months, while those with external beam radiation therapy and a brachytherapy boost—the implantation of radioactive seeds to deliver a higher total dose to the prostate—may be optimally managed with 18 months of ADT or possibly less. Results are published in the Jan. 20 issue of *JAMA Oncology*.

"Adding androgen deprivation therapy to radiation therapy has been consistently shown to improve survival when treating men with high-risk prostate cancer. However, lowering testosterone levels is associated with a number of side effects, including not only a decrement in quality of life, but possibly more serious adverse events when longer durations are used. While it has long been hypothesized that by delivering extremely high doses of radiation, one might be able to shorten the required duration of ADT, this has never been proven," said lead author Amar Kishan, MD, associate professor and vice chair of clinical and translational research in the Department of Radiation Oncology at UCLA and a researcher at the UCLA Jonsson Comprehensive Cancer Center.

The researchers analyzed individual patient data from three cohorts of patients: a retrospective cohort of patients from 16 cancer treatment referral centers between 2000 and 2014 who received either high-dose external beam radiotherapy or external beam radiotherapy with a brachytherapy boost; a cohort of patients enrolled in a randomized phase 3 trial that included patients from 23 treatment centers in Australia and New Zealand; and a cohort of patients enrolled in a randomized phase 3 trial conducted across 10 treatment centers in Spain. This is the only analysis to include both retrospective and prospective data in evaluating optimal ADT duration in high-risk prostate patients receiving these two

forms of radiation therapy.

"Because of androgen deprivation therapy's unpleasant side effects, it is often underutilized, with men receiving considerably shorter durations of ADT than might be recommended. To discern the ADT duration thresholds that provide the greatest metastasis-free survival benefit for these patients, we analyzed a multi-institutional database of patients, developed hypotheses, and then evaluated our findings by analyzing individual patient data from randomized trials," said Kishan.

"The consistency of our results across multiple different patient cohorts greatly strengthens our findings," said Tahmineh Romero, senior statistician in the UCLA Department of Medicine Statistics Core and the senior author of the article.

In the retrospective cohort—looking at ADT durations of less than six months, six to 18 months, and greater than 18 months—a significant interaction was seen between treatment type and ADT duration. A duration of 18 months or more was associated with improved outcomes, relative to shorter durations, for patients receiving high-dose external beam radiation therapy without a brachytherapy boost. In contrast, among patients receiving radiation therapy and brachytherapy, an ADT duration of at least six months but less than 18 months was associated with improved metastasis-free survival and overall survival, compared to receipt of less than six months of ADT. But there appeared to be no improvement in metastasis-free survival for those receiving both forms of radiation therapy and more than 18 months of ADT.

With further analysis, the researchers determined that for patients receiving radiation therapy without brachytherapy, the optimal ADT duration was 26.3 months; for those treated with radiation therapy and a brachytherapy boost, the minimum threshold was 12 months. Their hypotheses drawn from the retrospective study appeared to be supported

by effects observed in the randomized [clinical trials](#).

"Contrary to findings in a previous study, our results suggest that optimal duration of ADT for patients receiving high-dose radiation therapy may be more than 18 months. This is implied by findings from all the cohorts we analyzed. A secondary conclusion, based on the retrospective dataset, is that ADT duration shorter than 18 months may be sufficient for patients undergoing both [radiation therapy](#) and brachytherapy. Although current and future studies will continue to offer clarification, individual patient meta-analyses incorporating data from various trials may provide the best current guidance for doctors and [patients](#). We have additional studies underway to explore this concept further," said Kishan.

More information: The Interplay of Radiotherapy Dose and Androgen Deprivation Therapy Duration for High Risk Prostate Cancer: An Individual Patient Data Analysis of Three Cohorts, *JAMA Oncology* (2022). [DOI: 10.1001/jamaoncol.2021.6871](https://doi.org/10.1001/jamaoncol.2021.6871)

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