

De Barros H.A.¹, Van Beurden I¹, Droghetti M.¹, Wilthagen E.A.², Özman O.¹, Bergman A.M.³, Aluwini S⁴, Van Moorselaar R.J.A.⁵, Donswijk M.L.⁶, Van Leeuwen P.J.¹, Van Der Poel H.G.¹

¹The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Dept. of Urology, Amsterdam, The Netherlands, ²The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Scientific Information Service, Amsterdam, The Netherlands, ³The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Dept. of Medical Oncology and Oncogenomics, Amsterdam, The Netherlands, ⁴University Medical Centre Groningen, Dept. of Radiation Oncology, Groningen, The Netherlands, ⁵Amsterdam University Medical Center, VU University, Dept. of Urology, Amsterdam, The Netherlands, ⁶The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Dept. of Nuclear Medicine, Amsterdam, The Netherlands

Introduction & Objectives: Emerging data suggest a survival benefit for patients with low metastatic burden who are treated with prostate-directed therapy (PDT) and/or metastasis-directed therapy (MDT). It remains unclear whether these results also apply to men with hormone-sensitive de novo or recurrent prostate cancer metastasized to non-regional lymph nodes (M1a). We aim to systematically summarize the literature regarding oncologic outcomes of de novo and recurrent M1a PCa patients treated with PDT and/or MDT.

Materials & Methods: This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria. We searched Medline (Ovid), Embase and Scopus for English language study reports published up to December 2021 reporting on oncologic outcomes of de novo or recurrent hormone-sensitive M1a PCa patients treated with PDT and/or MDT with or without androgen deprivation therapy (ADT). Patients with castration-resistant PCa and/or who had previously received chemotherapy were excluded. A descriptive data synthesis and methodological quality assessment using the Newcastle-Ottawa Scale (NOS) were performed to evaluate the impact of PDT and/or MDT on overall survival (OS), cancer-specific survival (CSS), ADT-free survival, recurrence-free survival, and progression-free survival in M1a PCa patients.

Results: A total of 6136 articles were screened, and 24 studies were included in this systematic review. Studies were categorized according to the disease stage into de novo and recurrent disease (using conventional- or novel imaging techniques), and according to the treatment modality into PDT (i.e., radical prostatectomy or radiotherapy), MDT (i.e., [stereotactic] nodal radiotherapy and salvage lymph node dissection) and a multimodal strategy including both PDT and MDT. In de novo M1a PCa patients, PDT was associated with improved oncologic outcomes compared to no PDT (NPDT). In recurrent M1a PCa, MDT could delay the need for systemic treatment in a selection of patients, but high-level evidence from prospective phase III randomized controlled trials is still awaited.

Conclusions: PDT plus systemic therapy improved oncologic outcomes for de novo M1a PCa. MDT to distant lymph node metastases delayed the need for systemic therapy in recurrent disease, but robust data are lacking. The predominantly retrospective nature of the included studies and significant heterogeneity in study designs limit the strength of evidence.