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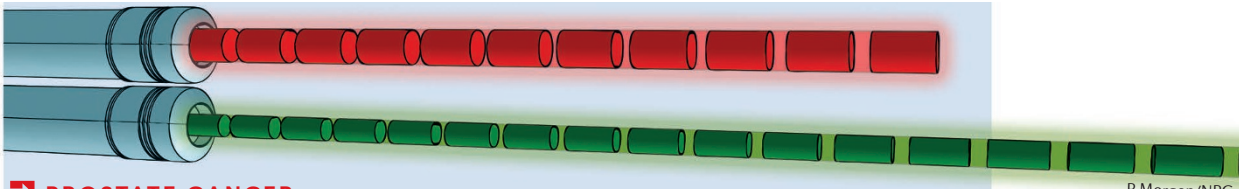

P. Morgan/NPG

PROSTATE CANCER

Hypofractionated radiotherapy confirmed effective and safe

Recently published long-term results of two multicentre phase III trials demonstrate that moderately hypofractionated radiotherapy (MHRT) is effective and safe in patients with prostate cancer. Implementation of such shortened treatment regimens might increase patients' convenience and decrease treatment costs in comparison with the use of conventionally fractionated radiotherapy.

Adjustments to the fractionation of radiotherapy by reducing the number of treatment sessions but increasing the individual radiation doses are thought to augment antitumour toxicity while protecting adjacent nonmalignant tissues. HYPRO and CHHiP, two large phase III trials performed in Europe, were conducted to investigate whether regimens of MHRT would result in efficacy and toxicity outcomes that are similar to conventional schedules. The investigators of HYPRO and CHHiP randomized 820 men and 3,216 men with mostly high-risk or mostly intermediate-risk prostate cancer, respectively, to receive MHRT (57–64.6 Gy in 19–20 fractions) or conventional radiotherapy (78 Gy or 74 Gy in 39 or 37 fractions, respectively).

Both studies have now published their 5-year follow-up data in *The Lancet Oncology*. HYPRO found relapse-free survival outcomes of 80.5% for the MHRT group and 77.1% for the control group (HR 0.86, 95% CI 0.63–1.16; $P = 0.36$). CHHiP found biochemical-failure-free or clinical-failure-free rates of 85.9% in the 57 Gy MHRT group, 90.6% in the 60 Gy MHRT group and 88.3% in the control group; only MHRT with 60 Gy was noninferior to conventional treatment (HR 0.84, 90% CI 0.68–1.03; $P = 0.0018$). Overall, the trials showed almost identical survival curves for MHRT and conventional radiotherapy, apart from the 57 Gy MHRT group in the CHHiP trial. The investigators of CHHiP recommend their 60 Gy regimen as a new standard of care for their patient population, in contrast to the investigators of HYPRO, who conclude that their 64.6 Gy MHRT regimen cannot be regarded as such.

"The most important difference between the two trials is that CHHiP is a noninferiority trial (that is, the main hypothesis is that MHRT is not worse than conventional fractionation), whereas HYPRO hypothesized that MHRT is superior to conventional fractionation," comments Ronald Chen, MD MPH, Associate Professor of Radiation Oncology at the University of North Carolina at Chapel Hill, USA. "For this reason, the two trials reached different formal conclusions, although the efficacy figures in both reports qualitatively show the same finding. Importantly, a noninferiority trial, such as CHHiP, requires high numbers of patients to test the noninferiority hypothesis. Thus, although HYPRO showed similar efficacy outcomes in its two arms, the trial probably did not have sufficient power (patient numbers) to fully demonstrate noninferiority."

In the CHHiP trial, adverse event profiles at the 5-year follow-up interval based on both physician-assessed toxicity and patient-reported outcomes were similar in the MHRT groups and the conventional group. The investigators of HYPRO did not report adverse events in their current publication.

Considering the future of MHRT as a routine treatment for prostate cancer, Chen told *Nature Reviews Urology*: "I think for many low-risk patients, active surveillance and brachytherapy are probably even more attractive options than MHRT. For intermediate-risk patients, MHRT performed as in the CHHiP trial should be considered a standard of care, but stereotactic body radiotherapy might offer an even shorter treatment course in the future. For high-risk patients, MHRT needs to be compared to combination external beam radiotherapy (EBRT) for 5 weeks plus brachytherapy. Both are short treatments and the latter seems to result in better disease control outcomes compared with EBRT based on randomized data."

Clemens Thoma

ORIGINAL ARTICLES Dearnaley, D. *et al.* Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial. *Lancet Oncol.* http://dx.doi.org/10.1016/S1470-2045(16)30102-4 (2016) | Incrocci, L. *et al.* Hypofractionated versus conventionally fractionated radiotherapy for patients with localised prostate cancer (HYPRO): final efficacy results from a randomised, multicentre, open-label, phase 3 trial. *Lancet Oncol.* http://dx.doi.org/10.1016/S1470-2045(16)30070-5 (2016)

FURTHER READING Arcangeli, S. *et al.* Hypofractionated radiotherapy for organ-confined prostate cancer: is less more? *Nat. Rev. Urol.* http://dx.doi.org/10.1038/nrurol.2016.106 (2016)