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Duration of androgen deprivation therapy (ADT) with post-operative radiotherapy (RT) for prostate cancer: First results of the RADICALS-HD trial (ISRCTN40814031)

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Background

There is good evidence on the use of ADT with primary RT as initial treatment for prostate cancer. By contrast, there is uncertainty about the role and duration of ADT with RT after radical prostatectomy (RP).

Methods

RADICALS-HD, part of the RADICALS protocol, was a randomised controlled trial to assess use and duration of ADT with post-operative RT. Key eligibility criteria were indication for RT after previous RP and no previous post-op ADT. Prior to post-op RT, pts were randomised to either no ADT (“None”), 6mo ADT (“Short”) or 24mo ADT (“Long”). 3-way randomisation was encouraged, and 2-way randomisation between None-vs-Short or Short-vs-Long also allowed. The trial was powered for the two pairwise comparisons. The primary outcome measure was metastasis-free survival (MFS). Secondary outcomes included time to salvage ADT and overall survival (OS). Toxicity assessments focused on RT with RTOG scale. The Statistical Analysis Plan is at https://doi.org/10.5281/zenodo.6586525. All confidence intervals (CI) are 95%.

Results

From 2007 to 2015, 2839 pts, including 492 in the 3-way randomisation, joined RADICALS-HD from UK, Canada & Denmark: median age 66yrs; 23% pT3b/T4; 20% Gleason 8-10, median pre-RT PSA 0.22ng/ml. Of these, 1480 pts contribute to None-vs-Short and 1523 pts to Short-vs-Long. Arms were balanced within each comparison; risk factors were more favourable in None-vs-Short than Short-vs-Long. Median follow-up was 9yrs. In None-vs-Short, based on 268 MFS events, 6mo ADT did not improve MFS (HR 0.89; CI: 0.69-1.14; 79% vs 80% event-free at 10yrs). Time to salvage ADT was delayed (HR 0.54; CI: 0.42-0.70); OS was not improved (HR 0.88; CI: 0.65-1.19). In Short-vs-Long, based on 313 MFS events, 24mo ADT improved MFS (HR 0.77; CI: 0.61-0.97; 72% vs 78% at 10yrs). Time to salvage ADT was delayed (HR 0.73; CI: 0.59-0.91); OS was not improved (HR 0.88; CI: 0.66-1.17). Pre-specified subgroup analyses will be presented.

Conclusions

In pts having post-operative RT after RP, 24mo ADT vs 6mo ADT improved both time to salvage ADT and MFS; In contrast, 6mo ADT vs no ADT improved time to salvage ADT but did not improve MFS.

Clinical trial identification

ISRCTN40814031.

Legal entity responsible for the study

MRC Clinical Trials Unit.

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Disclosure

C.C. Parker: Financial Interests, Institutional, Invited Speaker: Bayer; Financial Interests, Personal, Invited Speaker: Janssen; Financial Interests, Personal, Advisory Board: Myovant, ITM Radiopharma; Financial Interests, Institutional, Advisory Board: AAA. C. Catton: Financial Interests, Personal, Advisory Board: Bayer, AbbVie; Financial Interests, Institutional, Research Grant: Tersera Corp. H. Payne: Financial Interests, Personal, Advisory Board: AstraZeneca, Astellas, Janssen, SanofiAventis, Ferring, Bayer, Novartis. All other authors have declared no conflicts of interest.