PATCH - Prostate Adenocarcinoma: TransCutaneous Hormones. A randomised comparison evaluating cardiovascular morbidity and mortality of transdermal oestradiol versus Luteinising Hormone-Releasing Hormone Agonists in advanced prostate cancer

Introduction

Androgen deprivation therapy with luteinising hormone-releasing hormone agonists (LHRHa) suppresses testosterone but also depletes oestradiol, leading to long-term toxicities including osteoporosis. Transdermal oestradiol (tE2) should avoid the cardiovascular (CVS) toxicity associated with oral oestrogen, while mitigating oestradiol depletion-related toxicities.

Patients and Method

PATCH is an ongoing randomised trial comparing efficacy and safety of tE2 against LHRHa (allocation ratio 2:1<21/2/2011, then 1:1). Men with advanced hormone-naïve prostate cancer but no significant CVS disease are eligible. tE2 is delivered as 100mcg/24hr oestradiol patches; LHRHa administered as per local practice. The Independent Data Monitoring Committee has permitted release of the CVS morbidity and mortality data. Treatment effect on CVS risk was estimated using Cox models, stratified by recruitment before/after allocation ratio change.

Results

1127 (621 tE2, 506 LHRHa) men recruited between 14/08/07 and 21/11/16. Baseline characteristics were similar between groups; overall median age 74(IQR 68–79) years, PSA 39(17–106) ng/mL, 40% metastatic disease, 59% current/previous smokers. Median follow-up was 3.2(IQR 0.9-5.1) years.

At 3 months, 94.0% of tE2 group and 93.8% LHRHa had testosterone concentrations≤1.7 nmol/L. 100 CVS events were reported, 60 in 57 (9.2%) tE2 patients and 40 in 36 (7.1%) LHRHa; hazard ratio comparing tE2 vs LHRHa 1.19 (95%CI 0.78-1.81, P=0.432). 18/60 (30%) CVS events in tE2 group occurred >6 months after patients stopped treatment with tE2.

Conclusions

Rates of CVS toxicity were similar between tE2 and LHRHa. A tE2 arm was recently added to the STAMPEDE trial platform to speed up the efficacy evaluation on prostate cancer outcomes.

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