Material and methods We have designed an interventional project included in the HoTBreast trial: the extended use of HT as an NA for breast cancer patients who refuse surgery or are considered inadequate to receive it, in the context of close surveillance. In this group of extended NA treatment patients, different hormone treatment strategies (aromatase inhibitor and tamoxifen) are allowed to be used, depending on tumour response and patient quality of life. During treatment, clinical and imaging (ultrasound) follow-up will be implemented every two to three months in the first 3 years and every four to six months after that. The treatment option can be changed at any time if considered appropriate, based on disease response or progression and the patient’s quality of life. This group will be randomly divided into two subgroups, one who will receive hormone treatment alone and a second one who will receive HT and aspirin. Aspirin plays the role of an anti-inflammatory controller and it is not clear what the relation between chronic inflammation processes and breast cancer is – this is a new approach for cancer treatment with a strategy targeting the tumour microenvironment. Our secondary objective is to understand if the local disease presents the same response as the systemic one (in cases where this also exists) or if it can be used as an independent predictor of disease behaviour.

Results and discussions We believe that HoTBreast Trial can give some answers about the best practice for treating early BC. We also expect that it can shed some light on the question of the role of surgery in early BC and the use of aspirin in BC patients. We acknowledge the hypothesis that aspirin can improve the treatment of BC patients in a safe, well tolerated and inexpensive way.

Conclusion Efforts should be made to better communicate to patients that NA HT is a valid option and sometimes the most appropriate for the specific patient. The decision should depend on the patient, based on an informed understanding of the benefits and risks of avoiding surgery.

**PO-259** IDENTIFICATION OF A CLINICALLY MEANINGFUL SITE-SPECIFIC STEROID ROADMAP IN PROSTATE CANCER.

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**Introduction** In prostate cancer the genotype of the tumour does not always predict clinical behaviour and disease aggressiveness after castration therapy. Additional factors might be important. Here we hypothesise that there is a site-specific steroid profile roadmap after castration that is of clinical significance.

**Material and methods** Steroid profiles in blood plasma (BP) and bone marrow aspirate plasma (BMA) from 120 castrated patients with prostate cancer were evaluated with mass spectrometry. We studied the steroid ligand-receptor interactions in prostate cancer adrenal metastases (PCAM) because they represent a steroid-rich environment. Adrenalectomy specimens from 3 castrated patients with PCAM were analysed.

**Results and discussions** It is known that normally BP/Adrenal vein plasma testosterone (T) concentration ratio is approximately 1:1 and cortisol (C) ratio is roughly 1:3. We measured similar T levels in BP and BMA. The levels of C were significantly lower in BMA compared to BP. Our data suggest that T levels are uniform but there is a C concentration gradient between the different compartments. Cortisol acts through GR and in the presence of T is a partial AR inhibitor.

All PCAM samples had functional androgen receptor (AR) (wild-type (wt), no copy number changes) and glucocorticoid (GR), but no progesterone receptor (PR). No DHT was detected. Patient 1 tumour was able to synthesise T and had above castrate intra-tumoral T levels. The tumour lacked enzymes to synthesise C, but was able to catabolise C. The levels of C were within the normal BP range. Gene expression of AR was normal. Patient 2 and 3 samples had castrate T and high C levels (3-fold BP), but AR gene expression was remarkably high. All patients had PTEN and RB deletions, while patients 2 and 3 had mutant (m) p53.

Addition of 40 ng/dl T increased growth in vitro in a xenograft PCAM model (propagated in matrigel) derived from patient 1. When C was concomitantly added at high levels such as those in patients 2 and 3, PCAM growth returned to baseline (no steroids), suggesting that almost all T or C activity were lost. Moreover, proliferation in VCAP cells (High AR/GR+) decreased when high C was added in low T, but remained well above baseline, generating the hypothesis that this steroid combination mostly inhibits AR/GR tumours with non-amplified AR (e.g. early in castration).

**Conclusion** There is a clinically meaningful site-specific steroid roadmap. The PCAM steroid profile may serve as a useful model to elucidate tumour interactions with the steroid environment.