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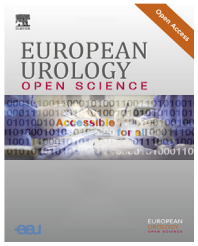

European Association of Urology

Prostate Cancer

A Feasibility Study of the Therapeutic Response and Durability of Short-term Androgen-targeted Therapy in Early Prostate Cancer Managed with Surveillance: The Therapeutics in Active Prostate Surveillance (TAPS01) Study

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Abstract

Background: Active surveillance (AS) is a preferred management option for men with prostate cancer with favourable prognosis. However, nearly half of men on AS switch to treatment within 5 years, so therapeutic strategies to prevent or delay disease progression could be considered. The androgen receptor is the pre-eminent oncogenic driver in prostate cancer.
Objective: To explore image-based tumour responses and the patient impact of short-duration androgen-targeted therapy (ATT) to abrogate disease progression during AS.
Design, setting, and participants: Men on AS with Cambridge Prognostic Group 1 & 2 (low and favourable intermediate risk) prostate cancer and lesions visible on magnetic resonance imaging (MRI) were recruited to an open-label, single-centre, phase 2 feasibility study of short-term ATT (the TAPS01 study).
Intervention: Apalutamide 240 mg was administered for 90 days.
Outcome measurements and statistical analysis: MRI-measured tumour volume (TV), gland volume (GV), and the TV/GV ratio were calculated at baseline, at day 90 (end of treatment), and at 6- and 18-month follow-up. Quality of life metrics were measured at day 0, day 90, and 6 weeks after ATT.
Results and limitations: Eleven patients (40% of eligible men approached) agreed to participate, of whom nine completed treatment. At day 90, the median percentage reduction was −38.2% (range −51.8% to −23.5%) for GV, −54.2% (range −74.1%

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to −13.8%) for TV, and −27.2% (range −61.5% to −7.5%) for TV/GV (all $p < 0.0001$). At 6 mo, while GV had returned to baseline ($p = 0.95$) both TV (−31.9%; $p = 0.0007$) and TV/GV (−28.7%; $p = 0.0009$) remained significantly reduced. This reduction was sustained at 18 months (TV −18%, TV/GV −23.8%; $p = 0.01$). European Organization for Research and Treatment of Cancer QoL core 30-item questionnaire scores for global, physical, role, and social functioning decreased during treatment, but all were recovering by 6 weeks. EQ-VAS scores were unchanged compared to baseline.
Conclusions: TAPS01 has demonstrated feasibility and patient tolerability for short-term ATT in men on AS. Our data suggest a selective and durable antitumour effect in the short term and support a larger-scale randomised trial.
Patient summary: We investigated the feasibility of short-term treatment with an androgen inhibitor to prevent or delay disease progression for men on active surveillance for prostate cancer. Results for a small group of patients show that 90-day treatment led to a sustained decrease in tumour volume over 18 months. The findings warrant a larger clinical trial for this approach, which could allow patients to delay or even avoid longer-term active treatments.

1. Introduction

Active surveillance (AS) is an increasingly accepted strategy for the management of prostate cancer with favourable prognosis [1–3]. More than 20% of men will progress to active treatment while on AS within a median of 2–3 yr [4,5]. Within 5 yr, up to 40% of men will have converted to active treatment, which is a high attrition rate for what should be favourable disease [4,5]. There is understandable concern among both clinicians and patients about not treating disease that may evolve over time. Conversely, the only current alternative is radical or ablative treatment, which carry the risks of side effects and complications [1]. This "all or nothing" approach offers an ideal opportunity to consider alternative therapeutic strategies. One of these is the concept of disease-modifying drugs that may delay or prevent progression so that men might never require active treatment [6].

Modern AS practice has been revolutionised by recent advances including precision baseline diagnostics, image-based follow-up, and better risk-stratified approaches to disease classification [7–11]. High-quality imaging with multiparametric magnetic resonance imaging (mpMRI) in particular offers an unprecedented ability to monitor real-time changes in tumour growth [9,12]. This, coupled with a better understanding of men who are at the highest risk of progression, positions AS a unique space for testing therapeutics to alter the natural trajectory of early disease [7,11]. Indeed, the US Food and Drug Administration have recently conducted a workshop on relevant endpoints for this new therapeutic space [13].

The concept of abrogating disease progression while on surveillance is an attractive one for both clinicians and patients [14]. The most promising target for therapy remains the androgen signalling pathway, with 5α reductase inhibitors (5ARIs) the option most often tested to date [15]. A recent meta-analysis involving more than 2000 men concluded that 5ARIs could delay disease progression, although many of the studies included were noted to be of low quality [16]. More recently, it has been reported that 5ARI treatment reduces MRI-defined lesion conspicuity and tumour volume in men on AS [17]. However, concerns that long-term androgen therapy may induce tumour adaptation have so far reduced enthusiasm for adopting 5ARI or other androgen-targeted therapy (ATT) in routine practice [18]. By contrast, short-term ATT may have the desired specific antitumour effects without the risk of longer-term tumour adaptation [19–21].

We hypothesised that short-term ATT, particularly with more selective next-generation antiandrogens, may be a potential therapeutic intervention to reduce tumour progression on AS. We further considered that mpMRI-based imaging would be ideal for noninvasive measurement of the response and clinical durability of any effect. To test our hypothesis, we undertook a feasibility study using apalutamide, a next-generation androgen receptor antagonist that does not also act as an agonist [22–24]. Apalutamide binds to the androgen receptor with seven- to tenfold greater affinity in comparison to bicalutamide, and studies have shown good tolerability profiles in men with prostate cancer [22–24]. Its pure antagonistic properties and good tolerability profile make apalutamide a very attractive agent for a short-term intervention strategy to block androgen receptor signalling for men on AS.

Our goal was to assess the feasibility of trial recruitment, drug efficacy, and patient tolerance and hence to evaluate if a formal future trial testing this approach in men on AS would be justified.

2. Patients and methods

2.1. Study cohort

Therapeutics in Active Prostate Surveillance 01 (TAPS01) was a single-centre, single-arm, open-label, phase 2 feasibility trial (NCT03365297, REC 18/EE/0047) to test the selective tumour response to short-term apalutamide treatment. Following written informed consent, men aged

≥18 yr and on AS with Cambridge Prognostic Group 1 or Cambridge Prognostic Group 2 prostate cancer were invited to participate [7]. The 5 strata Cambridge Prognostic Groups (CPG) have recently been adopted as the new standard for risk-classification of prostate cancer by the UK National Insititute for Health and Care Excellence (NICE) replacing the older-3 tier model (https://www.nice.org.uk/guidance/ng131/resources/prostate-cancer-diagnosis-and-management-pdf-66141714312133). CPG1 and 2 are comparable to low and favourable-intermediate risk disease. Men had to have been on AS for at least 6 months beforehand and a similar time since any prior biopsy event to be considered eligible. Other inclusions were Eastern Cooperative Oncology Group performance status of 0–2 and diagnostic mpMRI demonstrating a visible tumour (Likert score ≥3) congruent with diagnostic biopsy. Exclusion criteria included any contraindication to apalutamide (or its excipients), any change in study baseline mpMRI in comparison to previous imaging, prior treatment, and contraindication to MRI/contrast agents. No man was on prior 5ARI therapy. The trial opened to recruitment on June 5, 2018, with the last visit by the last patient on July 25, 2019. The trial was monitored by an independent trials steering committee. Adverse events were reported according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. A follow-on study to monitor the durability of response commenced with the latest imaging follow-up completed in January 2021 (REC 20/LO/0264). As of last follow-up, no patient had features of disease progression or opted for treatment.

2.2. MRI protocol

The mpMRI protocol included standard T2-weighted imaging, diffusion-weighted imaging (DWI), and dynamic contrast enhancement (DCE), as previously reported [12] (Supplementary Table 1). Patients underwent prostate MRI using a 3-T HDx Discovery MR750 HDx scanner (GE Healthcare, Waukesha, WI, USA) with a 32-channel phased array coil. Hyoscine butylbromide (Buscopan, 20 mg/ml, Boehringer Ingelheim, Ingelheim, Germany) was administered intravenously to reduce peristaltic movement. Axial T2-weighted imaging used a slice thickness of 3 mm and a gap of 0 mm; DWI and DCE imaging were matched in the axial plane (slice thickness 3–4 mm, gap 0 mm). DWI was performed using a spin-echo echo-planar imaging pulse sequence with b values of 150, 750, 1000, 1400, and 2000 s/mm^2, with apparent diffusion coefficient maps automatically calculated. DCE images were acquired following a bolus injection of gadobutrol (Gadovist, Bayer Healthcare, Berlin, Germany) via a power injector at a rate of 3 ml/s (dose 0.1 mmol/kg) with temporal resolution of 7s. Lesions were characterised at baseline using a 5-point Likert scale [12].

2.3. Intervention and measurements

Apalutamide 240 mg was given for 90 days with MRI measurement of tumour volume (TV), gland volume (GV), and the TV/GV ratio at baseline and after treatment. In cases with more than one lesion, the lesions were combined for a total TV measurement. Image-based volumetric measurements were performed using lesion outlining and gland segmentation with Dynacad software by a single expert uroradiologist (>3000 MRI read) (TB). Follow-up imaging using the same measurements and by the same radiologist was done at 6 months and then at 18 months. Changes were expressed as a percentage change compared to baseline for each measurement. Quality of life (QoL) was measured using the European Organization for Research and Treatment of Cancer QoL core 30-item questionnaire (EORTC QLQ-C30) functional scale and the Euro-Qol 5-dimenison 5-level (EQ-5D-5L) QoL questionnaire and global visual analogue scale (VAS). QoL metrics were measured at baseline and 30, 60, and 90 days, and then 6 weeks after treatment completion.

2.4. Sample size and statistical analysis

The primary outcome was a physiological response, defined as achieving tumour volume downsizing in at least 50% of the cohort as determined via mpMRI at 90 days from the start of treatment. The a priori sample size was calculated as follows: for a significance level (one-sided) of 5% and 80% power, using the A'Hern method, eight patients would be required to test the response rate of ≤10% (H_0) versus ≥50% (H_1). If three or more patients were to be classified as achieving a reduction, the null hypothesis H_0 would be rejected. An interim analysis was performed to examine the size of the treatment effect when 50% of the cohort had been recruited and had completed the study. Secondary endpoints were tolerability and side effects assessed using patient-reported outcomes for urinary and sexual function and overall wellbeing. Standard descriptive summary statistics were used for the data summaries. Follow-up imaging at 6 and 18 mo was compared to baseline for each case. Summary statistics were reported to one decimal place greater than the original data. The software package SAS v9.4 (SAS Institute, Cary, NC, USA) was used to produce all summaries. Comparisons between time points and baseline were performed using two-tailed paired-sample *t* tests ($p < 0.05$).

3. Results

3.1. Cohort profile

The study recruited 11 patients in total, representing 40% of the eligible men who were approached regarding study participation. Reasons for not taking part were usually related to satisfaction with AS or personal circumstances. One patient did not proceed because of screening failure and another man stopped therapy after 34 d because of an asymptomatic unexplained decrease in neutrophil count, which resolved quickly after treatment cessation (CTCAE grade 3). No patients dropped out because of drug intolerance or physical side effects. Nine patients were evaluable and completed the treatment, assessments, and follow-up. The patient characteristics and demographics are shown in Table 1. Five patients were classified as Cambridge Prognostic Group 1 and four as Cambridge Prognostic Group 2. Prior AS duration ranged from 6 mo to 84 mo, and eight out of nine men had Likert 4–5 lesions. The median initial GV and TV were 39.2 cm^3 (range 30.5–135.7) and 0.85 cm^3 (range 0.21–1.83), respectively (Table 1).

3.2. Therapeutic response

At day 90 (end of treatment) the median percentage reduction was −38.2% (range −51.8 to −23.5%; $p < 0.0001$) for GV and −54.2% (range −74.1% to −13.8%; $p < 0.0001$) for TV (Table 2). The median change in TV/GV ratio was −27.2% (range −61.5 to −7.5%; $p < 0.001$; Table 2). At 6 mo after treatment, GV had largely returned to baseline (median change 0%; $p = 0.95$; Table 2). Both TV (median −31.9%; $p = 0.0007$) and the TV/GV ratio (median −28.7%; $p = 0.0009$) remained smaller than at baseline (Table 2 and Fig. 1). At a median of 18 mo after treatment, both TV and the TV/GV ratio continued to be smaller than at baseline by a median of −18% and −23.8%, respectively ($p = 0.01$; Table 2 and Fig. 1). Figure 2 and Supplementary Figure 1 shows exemplar images for two patients at baseline, day 90, and 6 mo and 18 mo after treatment. Patient-level data

Table 1 – Individual baseline characteristics of the cohort.

Case	Grade Group	CPG category	PSA (ng/ml)	Prior AS Duration (mo)	PI-RADS score	GV[a] (cm^3)	TV[a] (cm^3)	TV/GV ratio
1	2	2	8.4	6	5	58.1	1.83	0.031
2	1	2	11.59	13	5	135.7	0.70	0.005
3	1	1	5.9	24	4	39.2	1.07	0.027
4	1	1	8.2	84	4	46.7	0.21	0.004
5	1	1	3.94	15	4	32.7	0.94	0.03
6	2	1	3.34	15	3	35.7	0.47	0.013
7	2	2	5.8	6	5	32.3	0.43	0.013
8	1	1	4.96	6	4	30.5	0.93	0.03
9	1	2	10.37	7	5	120.7	0.85	0.007

AS = active surveillance; CPG = Cambridge prognostic group; GV = gland volume; PI-RADS = Prostate Imaging-Reporting and Data System (version 2); PSA = prostate-specific antigen; TV = tumour volume.
[a] Gland and tumour image-based volumetric measurements were performed using lesion and gland outlining with Dynacad software.

Table 2 – Percentage change in gland volume, tumour volume, and TV/GV ratio from baseline after 90 days of apalutamide.[a]

	Change from baseline (%)		
	Day 90 (end of treatment)	6 month post-tx-MRI)	18 month (post-tx-MRI) [b]
Gland volume			
Mean	−36.1	−5.6	−1.88
Median (range)	−38.2 (−51.8 to −23.5)	0 (−33.4 to 7.4)	−2.52 (−36.0 to 17.3)
Tumour volume			
Mean	−52.4	−30.24	−20.2
Median (range)	−54.2 (−74.1 to −13.8)	−31.9 (−50.6 to −2.3)	−18.0 (−54.8 to 2.5)
TV/GV ratio			
Mean	−28.7	−25.6	−19
Median (range)	−27.2 (−61.5 to −7.5)	−28.7 (−54.0 to 6.25)	−23.8 (−38.9 to 6.6)

post-tx MRI = post-treatment magnetic resonance imaging; TV/GV = tumour volume/gland volume.
[a] Gland and tumour image-based volumetric measurements were performed using lesion and gland outlining with Dynacad software by a single expert uroradiologist.
[b] The 18-month MRI assessment allowed for a 3-mo time window (median 18 months, range 15–20).

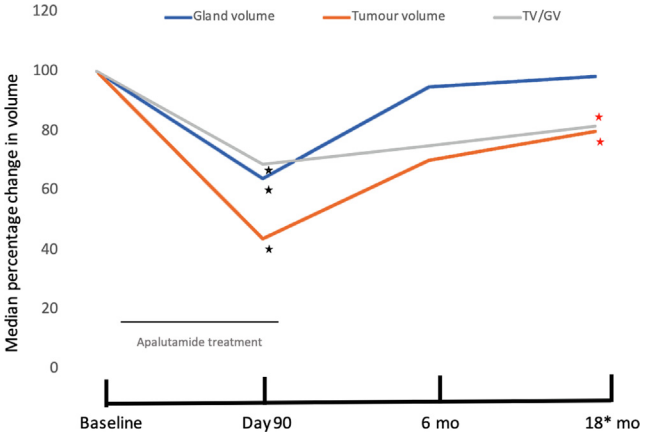

Fig. 1 – Composite graphical representation of the median percentage changes in gland volume (GV), tumour volume (TV), and the TV/GV ratio during and apalutamide treatment. Day 90 is the end of the treatment period. Gland and tumour image-based volumetric measurements were performed using lesion and gland outlining with Dynacad software by a single expert uroradiologist who also performed all the comparative measurements. * The 18-month magnetic resonance imaging assessment allowed for a 3-month time window (median 18 months, range 15–20). The black stars denote $p < 0.0001$ and the red stars, $p = 0.01$.

for each case are listed in Supplementary Table 2 (TV and GV) and Supplementary Table 3 (prostate-specific antigen [PSA] density). Although there were individual variations in response, median PSA density levels, despite showing the expected fall during apalutamide treatment, mostly returned to pretreatment level by 6 mo. In one case the PSA drop was sustained up to 18 mo after treatment (Supplementary Table 3).

3.3. QoL measures

QoL assessments were conducted at baseline, at day 90, and at 6 weeks after treatment. Across EORTC QLQ-C30 domains there were reduced scores for global, physical, role, and social functioning between baseline and day 90, but all started to recover by 6 wk after treatment (Table 3). However, there were no changes in emotional or cognitive functioning (Table 3). The mean EQ-5D-5L score was 0.07 points lower at day 90 and remained so at 6 wk (Table 4). However, the EQ VAS, a global measure of health, remained unchanged at day 90 day and at 6 weeks after treatment compared to baseline. The main side effects reported were fatigue ($n = 5$ men), rash ($n = 4$), and breast pain ($n = 4$) during treatment and all resolved or were resolving by 6 weeks after the end of drug dosing. No patient discontinued the drug or did not complete the study because of these symptoms.

4. Discussion

In this feasibility study, we observed a specific cytoreductive effect in response to short-term apalutamide as evalu-

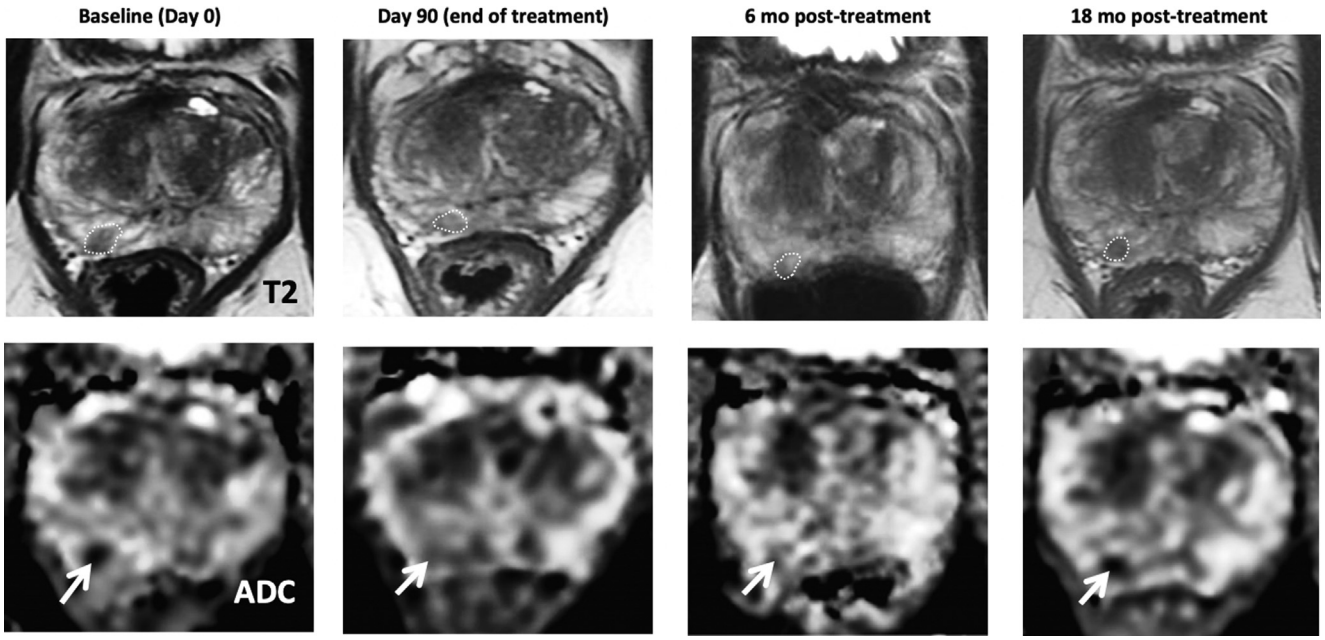

Fig. 2 – Exemplar (case 1) of magnetic resonance imaging (MRI) scans showing changes from baseline in the MRI-defined tumour volume after 3 mo of apalutamide treatment and during follow-up. Gland and tumour image-based volumetric measurements were performed using lesion and gland outlining with Dynacad software. Lesions are outlined in the top images and denoted by arrows in the bottom images. T2 = T2-weighted imaging; ADC = apparent diffusion coefficient.

Table 3 – EORTC QLQ-C30 functional scores during treatment and at the 6-wk review visit (n = 9 patients for all domains and time points).

	Day 0	Day 90	6 weeks post-treatment
Global health status/QoL			
Mean (SD)	89.8 (11.6)	79.6 (11.1)	81.5 (13.7)
Median (range)	91.7 (66.7–100)	83.3 (58.3–100)	83.3 (58.3–100)
Interquartile range	83.3–100	75–83.3	75–83.3
Physical functioning			
Mean (SD)	99.3 (2.2)	91.8 (14.8)	92.6 (15.4)
Median (range)	100 (93.3–100)	100 (60–100)	100 (53.3–100)
Interquartile range	100–100	93.3–100	93.3–100
Role functioning			
Mean (SD)	100 (0)	83.3 (23.6)	92.6 (22.2)
Median (range)	100 (100–100)	100 (33.3–100)	100 (33.3–100)
Interquartile range	100–100	66.7–100	100–100
Emotional functioning			
Mean (SD)	94.4 (8.4)	94.5 (11)	95.4 (11.1)
Median (range)	100 (83.3–100)	100 (66.7–100)	100 (66.7–100)
Inter-quartile range	83.3–100	91.7–100	100–100
Cognitive functioning			
Mean (SD)	90.7 (8.8)	92.6 (12.1)	90.7 (12.1)
Median (range)	83.3 (83.3–100)	100 (66.7–100)	100 (66.7–100)
Interquartile range	83.3–100	83.3–100	83.3–100
Social functioning			
Mean (SD)	100 (0)	87 (23.2)	88.9 (22.1)
Median (range)	100 (100–100)	100 (33.3–100)	100 (33.3–100)
Interquartile range	100–100	83.3–100	83.3–100

EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer QoL core 30-item questionnaire; QoL = quality of life; SD = standard deviation.

ated via MRI prostate tumour measurements. This effect appeared to be durable over the short term despite rapid recovery of overall GV and PSA values. Patient tolerance and self-reported impact on QoL were within expected limits and had started to recover within 6 wk of completing treatment. These findings strongly support the hypothesis that short-duration ATT is a potential therapeutic intervention that warrants further investigation.

Serial prostate MRI is now an indispensable tool in modern AS practice [9,10,12]. Changes on MRI are already considered an important trigger to review AS management and there is significant interest in using MRI as a sole measure to detect tumour progression to avoid repeat biopsies [8,10,12]. MRI is noninvasive, well tolerated by patients, and a more direct measure of tumour changes than PSA alone [8,10,12]. All these attributes make MRI an attractive

Table 4 – EQ-5D-5L and Visual Analogue Scale scores during treatment and at the 6-wk review visit.

	Day 0	Day 90 (end of Tx)	6 weeks post treatment
EQ-5D-5L score			
Patients (*n*)	9	8[a]	9
Mean (SD)	0.97 (0.09)	0.9 (0.12)	0.9 (0.1)
Median (range)	1 (0.74–1)	0.96 (0.71–1)	0.88 (0.77–1)
Interquartile range	1–1	0.81–1	0.84–1
Visual Analogue Scale			
Patients (*n*)	8[a]	9	9
Mean (SD)	87 (10)	87 (8)	87 (11)
Median (range)	90 (75–100)	90 (75–95)	90 (65–100)
Interquartile range	75–95	80–95	80–95

EQ-5D-5L = EuroQol 5-dimenison 5-level quality-of life questionnaire; SD = standard deviation; Tx = treatment.
[a] One patient did not fill in the questionnaire at this time point.

and valuable surrogate for investigating and monitoring novel therapy effects in clinical trials. Previously, the use of imaging after ATT was considered challenging because of the significant effect on prostate tissue architecture. However, work by ourselves and others has shown that modern functional MRI methods such as DCE and DWI can reliably detect and measure tumour regions of interest before and after ATT [17,25]. In this study we were able to exploit these innovations to provide a direct noninvasive method for monitoring changes in tumour response over time. Interestingly, while reductions in TV and GV were matched by PSA reductions during treatment, PSA recovery afterwards did not follow changes in TV and were the most variable parameter. This probably reflects the fact that PSA in early cancers is mainly a measure of GV rather than TV dynamics, underscoring its limited utility as an AS monitoring tool in isolation.

QoL changes were, not unexpectedly, seen during treatment. Reference standards for the minimally important difference (MID) to interpret group-level changes in this therapeutic context are unknown [26]. QoL tools are also dependent on the cancer stages in which they are tested [27]. However, if the mean and standard deviation for the group at baseline were used as a measure, then the scores at 90 days and 6 wk were well within that range for each of the three tools used here. Some comparisons from previous studies may also provide context. Pickard et al [26] established an MID for UK cancer patients using the EQ-5D scale of between 0.10 and 0.12, which is notably higher than the values in our study. For the EQ VAS they reported an MID of 8–12, while we observed no changes in mean VAS scores. It is known that apalutamide crosses the blood-brain barrier and has been associated with central nervous system effects [28]. In this study, however, we did not find any significant change in emotional or cognitive scores, which may be a further advantage of the short-duration ATT approach, potentially reducing long-term drug exposure that affects cognition.

The notion of using ATT for early prostate cancer is not new. The Early Prostate Cancer study conducted more than 15 yr ago did not show a survival benefit when bicalutamide was given in early disease [29]. However, this was given as long-term therapy and predates the modern AS era, in which the clinically important endpoint is not survival but avoiding active treatment for disease progression [1,2,5]. Interest in this area has now re-emerged with a better understanding of disease prognosis, the acceptance of AS for mainstream management, and better selective ATT drugs [19]. The ENACT study, for example, has treated men on AS with enzalutamide (NCT02799745) or placebo. As reported in a recent abstract presentation, early data show that at 1 yr the use of enzalutamide increased the negative biopsy rate by 46% and delayed PSA progression by 6 mo compared to placebo. This study did not include state-of-the-art imaging-targeted biopsies or MRI surveillance in the protocol [30]. Schweizer et al [21] reported on short-term ATT with apalutamide in 22 men on AS in the USA using systematic biopsy outcomes as the primary endpoint. The concept of direct intraprostatic antiandrogens has also been recently published by the well-respected AS group from Toronto [31]. In that study the primary measure was a reduction in PSA, but MRI, mainly used to look at the effect on gland volumes, did reveal a reduction in Prostate Imaging-Reporting and Data System score in nine out of61 men.

Our study has clear limitations as a single-centre small cohort trial of treatment feasibility. Our goal was to establish proof of principle for the treatment approach and the method for monitoring. Therefore we can draw no conclusions at this stage on the longer-term benefit from short-term ATT. As we did not include repeat biopsies, we cannot comment on whether the effect on tumour volume observed is matched by histopathological changes. In the study by Schweizer et al [21], 13/22 men (59%) had no cancer on post-treatment biopsy (day 90) and seven out of 22 (37%) had no residual cancer at 1 yr. Importantly from the safety point of view, no man in our study experienced disease progression and patient acceptance and tolerability were high. Although our median follow-up was only 18 months, we are the first to report the potential durability of the cytoreductive effect of short-term ATT. These preliminary data support progression to a formal, well-powered trial using clinically relevant endpoints in AS and with MRI as an important component in measuring tumour response. Certainly, the ability to optimally characterise and noninvasively monitor tumours at the outset and during AS is potentially unique in oncological trial design, alongside the ability to detect early nonresponders and to rapidly convert patients to radical treatment. This might be particularly attractive for men on AS who are known to be at higher risk of progression [4–7]. To this end we will be starting a multicentre randomised trial to test the clinical efficacy of short-term ATT as a means of reducing progression rates on AS. If proven, there is also the possibility that this approach may be suitable for repeat challenges as intermittent therapy to prolong the durability and limit side effects, a method that has been effective in men who require permanent long-term androgen deprivation therapy [32].

5. Conclusions

In summary, we report the successful completion of an exploratory study looking at short-term ATT in men on

AS, and the first to use modern AS methods including MRI as a monitoring tool. The study confirms the acceptability, tolerability, and safety of short-term ATT for patients. We demonstrated early signals of a potentially clinically meaningful and durable therapeutic effect, which we hypothesise may translate into longer-term benefits. We are now taking this forward in a formal clincial trial to test this hypothesis.

Author contributions: Vincent Gnanapragasam had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Gnanapragasam.
Acquisition of data: Barrett, Pacey, Leonard, Funingana.
Analysis and interpretation of data: Gnanapragasam, Wulff, Pacey, Barrett.
Drafting of the manuscript: Gnanapragasam.
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Data sharing statement: Data are available on request from the corresponding author.

Appendix A. Supplementary data

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