

A pilot study of endorectal magnetic resonance imaging and magnetic resonance spectroscopic imaging changes with dutasteride in patients with low risk prostate cancer

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OBJECTIVE

- To evaluate the effects of dutasteride on treatment-naïve prostate cancer in men using serial magnetic resonance imaging (MRI) and magnetic resonance spectroscopic imaging (MRSI) in this pilot study.

PATIENTS AND METHODS

- This investigator-initiated prospective single-arm study was approved by the institutional committee on human research ethics board.
- The target accrual was 10 patients. Newly diagnosed prostate cancer patients with low risk disease either with symptomatic benign prostatic hypertrophy or deemed to require pre-brachytherapy androgen suppression therapy were eligible. In the latter group, dutasteride was used to achieve cytorreduction.
- All patients received 6 months of dutasteride 3.5 mg daily and underwent baseline blood work, health-related quality of life indices and MRI/MRSI, which were repeated at 1, 3 and 6 months.
- MRSI spectra were examined and scored as healthy or cancerous. The change

What's known on the subject? and What does the study add?

While not approved by the Food and Drug Administration (FDA) for chemoprevention, dutasteride has been shown in a large randomized trial to reduce the overall risk of developing prostate cancer.

In our pilot study, one third of patients demonstrated a significant reduction in the volume of their prostate cancer as measured by magnetic resonance spectroscopic imaging.

in cancerous volumes over time was evaluated.

RESULTS

- Of the 10 patients enrolled, nine patients completed the entire study. One patient withdrew after 3 months because of drug-related toxicity.
- Because a significant decrease in citrate and polyamines on MRSI spectra was noted at 1 month compared with baseline, healthy tissue appeared to be more like cancer and thus created a false impression that the cancer had grown after 1 month. To reduce this bias, comparisons were made between the 1-month and 6-month scans.
- The median MR cancer volumes at 6 months and 3 months were 100% and 101% of the 1-month value, respectively. Three of the nine patients had a 30–45% decrease in cancer volume at 6 months relative to 1-month measures. Of the others, two had no

change in cancer volume and four had an increase (range 65–167% of the 1-month value).

- The median cancer volume (range) at baseline was only 0.5 (0.1–5.6) mL.

CONCLUSIONS

- The inclusion of only men with low volume disease may have limited our ability to accurately assess response rates after dutasteride due to the background effects on normal prostate metabolism. Despite this, one-third of patients had a 30–45% reduction in cancer volume at 6 months.
- Future studies including men with larger volume disease may enable estimates of response rates to be made more accurately.

KEYWORDS

prostate cancer, magnetic resonance spectroscopy, dutasteride

INTRODUCTION

In general, early localized prostate cancers are androgen-sensitive. The most effective and widely used class of androgen suppression therapy is LHRH agonists. However, by virtue of their mechanism of action, LHRH agonists expose men to a number of potentially significant side-effects [1]. Aside from hot flashes, decreased libido and erectile dysfunction, there is increasing recognition of long-term toxicities such as osteoporosis, neurocognitive changes and metabolic syndrome [1].

Data from the Prostate Cancer Prevention Trial (PCPT), a multicentre placebo-controlled phase 3 study, showed that finasteride, a type 2 5- α -reductase-inhibitor (5ARI), can reduce the risk of prostate cancer by 25% [2]. Equally important, this was achieved with minimal toxicities and a favourable safety profile, which is in sharp contrast with LHRH agonists. These findings compelled the American Society of Clinical Oncology and AUA to jointly issue guidelines recommending that asymptomatic men with PSA ≤ 3.0 ng/mL consider a 5ARI for chemoprevention [3].

5ARIs act by inhibiting the 5- α -reductase (5AR) enzyme from converting testosterone, the major circulating androgen, to dihydrotestosterone (DHT), the major intracellular androgen. The first-generation compound was finasteride, which is US Food and Drug Administration (FDA) approved for the treatment of benign prostatic hyperplasia and alopecia and is a selective inhibitor of the type 2 isoenzyme of 5AR. Dutasteride, a second-generation 5ARI, is a non-selective inhibitor of 5AR, resulting in near total suppression of testosterone conversion to DHT [4]. In the ARIA2001 multi-institutional, double-blind phase 2 trial, finasteride reduced serum DHT by 70.8%, whereas dutasteride 0.5–5 mg once-daily doses reduced DHT by at least 94.7%. Both agents preserved normal serum testosterone levels [4]. Dutasteride is currently FDA approved for the treatment of benign prostatic hyperplasia. Phase 2 and 3 studies have shown that the most commonly reported drug-related adverse reactions were erectile dysfunction (<10%), decreased libido (<5%), ejaculatory disorders (<5%) and gynaecomastia (<3%) [5]. Recently, the results of the multicentre placebo-controlled phase 3 REDUCE trial demonstrated that dutasteride reduced the incidence of prostate cancer by 23% in a high risk population [6].

Although these data clearly demonstrate the hormonal effects of dutasteride, the impact on prostate cancer itself is unclear. MRI and magnetic resonance spectroscopic imaging (MRSI) can provide non-invasive measures of the prostate and its metabolism. Numerous studies have demonstrated the value of a combined MRI/MRSI examination to detect cancer in untreated patients and in patients after therapy [7–11]. MRI without spectroscopy can identify cancer by a decrease in signal intensity on T2-weighted images with high sensitivity (79%) but only moderate specificity (55%) [11]. MRSI measures chemical compounds in the tissue with healthy prostatic glandular tissue demonstrating high levels of citrate and low levels of choline, and cancerous tissues demonstrating low citrate and potentially high choline levels [7]. The addition of MRSI to MRI improves the specificity and accuracy of detecting cancer [7,11]. One limitation of MRSI is its relatively low spatial resolution (0.04–0.08 mL), limiting its role for very small cancers.

The aim of the present pilot study was to evaluate the effects of dutasteride on prostate cancer in men with low risk, previously untreated disease using serial MRI and MRSI in combination with serum measures and health-related quality of life (HRQL) assessments.

PATIENTS AND METHODS

PATIENT ELIGIBILITY

This investigator-initiated, single-institution pilot study received institutional review board approval in June 2005. Ten study patients were recruited from June 2005 to June 2008 from untreated patients seen at the University of California San Francisco. The eligibility criteria included men with low risk prostatic adenocarcinoma (must have all of the following: T1b–T2a, Gleason score ≤ 6 , pretreatment PSA <10 ng/mL) who had baseline MRSI scans that demonstrated measurable spectroscopic malignancy within the prostate gland, and who were on active surveillance or deemed to require neo-adjuvant hormones for prostate shrinkage prior to permanent seed prostate brachytherapy. Measurable disease as seen on MRSI was defined as the presence of at least three contiguous voxels with a score of 4 or 5 (see MRSI technique section below),

suggesting malignancy [12]. In addition, patients had to have at least an IPSS of 8 (i.e. mild urinary symptoms), or an IPSS of 0–7 with the intention of commencing pre-brachytherapy hormones. Participation in the present study meant that dutasteride, rather than other hormonal agents such as an LHRH agonist, was used for cytoreduction. Ineligibility criteria included nodal or metastatic disease, prior prostate cancer treatment including hormones (e.g. LHRH agonists, antiandrogens, oestrogens or surgical castration, and concurrent and/or previous use of 5ARI and herbal supplements, such as selenium, vitamin E, saw palmetto, PC-SPES), pelvic radiotherapy, chemotherapy or radical prostatectomy.

STUDY TREATMENT

Dutasteride was administered at a dose of 3.5 mg once daily as an oral soft gelatine capsule. Although this dose is higher than the approved dose for benign prostatic hyperplasia, it remains within the range of safe doses as determined by the phase 2 study ARIA2001 [5]. This dose was chosen to maximize any potential dose–response effects.

EVALUATIONS DURING STUDY

Patients were seen at baseline and 1, 3 and 6 months after commencing dutasteride. Each visit included a history and physical examination, Karnofsky performance status, complete blood count, renal function tests, liver function tests, serum testosterone and DHT levels, serum-free and total PSA levels, MRSI scan and HRQL assessments by the five-item version of the International Index of Erectile Function (IIEF-5), the Spitzer Quality of Life Index (SQLI), Functional Alterations due to Changes in Elimination (FACE) and the IPSS. Additionally, toxicities from dutasteride were recorded at each follow-up visit using the National Cancer Institute's Common Terminology Criteria for Adverse Events toxicity scale version 3.0. At our biochemistry laboratory, the minimum detectable DHT level is 2.0 ng/dL. Also, the free PSA is performed only when the total PSA is between 2.5 and 10 ng/mL.

The IPSS and IIEF-5 represented symptom indices. The IPSS is a validated seven-item questionnaire designed to quantify irritative and obstructive urinary symptoms, and is

scored out of 35 (the higher the score, the more the symptoms) [13]. The IIEF-5 is an abridged five-item version of the original IIEF 15-item questionnaire designed to evaluate erectile function, based on a definition arrived at by the National Institutes of Health Consensus Panel [14,15]. The IIEF-5 is scored from 5 to 25, with lower scores indicating erectile dysfunction.

The HRQL indices included FACE and SQLI. FACE is a 14-item questionnaire designed to evaluate the effects of changes in urinary and bowel elimination on daily functioning. It is scored out of 56, with higher scores reflecting poorer HRQL. SQLI is a validated five-item questionnaire evaluating global HRQL [16]. It is scored out of 10, with lower scores indicating poorer HRQL.

MRSI TECHNIQUE AND RESPONSE ASSESSMENT

MR anatomical images and spectroscopic images were obtained at baseline, and at 1, 3 and 6 months after the start of dutasteride therapy. Patients were scanned using a combined endorectal probe (MedRad Inc., Indianola, PA, USA, or USA Instruments Inc., Aurora, OH, USA) and a pelvic phased array coil on GE MR scanners (GE Medical Systems, Milwaukee, WI, USA). Nine patients were scanned at 3 T and one was scanned at 1.5 T. The baseline MR scan for two of the patients scanned at 3 T was acquired with a rigid probe made by USA Instruments in conjunction with the GE Torso phased array. The MR anatomical imaging included axial T1-weighted images and fast spin-echo T2-weighted images with an echo train length of 16, a field of view of 140 mm and a slice thickness of 3 mm. The 16 × 8 × 8 three-dimensional MRSI used a point resolved spectroscopy (PRESS) sequence incorporating dual-band spectral spatial pulses [17]. Spectra were zero-filled in two dimensions resulting in an analysed spatial resolution of 0.04 mL for 3 T cases (TR/TE = 1300 ms/85 ms) and 0.08 mL for the 1.5 T case (TR/TE = 1000 ms/130 ms). Spectra were baseline, frequency and phase corrected before analyses.

Peripheral zone spectra were labelled as cancerous if choline was higher than creatine in part based upon established criteria for labelling MR spectra for untreated patients [12]. Spectra adjacent to the urethra were excluded as were any deemed unusable due to

Characteristic	Median (range) or n (%)	TABLE 1 Patient characteristics at baseline
Age (years)	65 (57–78)	
Clinical stage		
T1c	7 (70)	
T2a	3 (30)	
Total PSA (ng/mL)	5.05 (2.14–11.74)	
Serum testosterone (ng/dL)	343 (170–500)	
Serum dihydrotestosterone (ng/dL)	33 (18–50)	
Prostate volume (mL)	47.3 (22.0–75.2)	Normal ranges: testosterone, 185–800 ng/dL; DHT, 4–22 ng/dL.
MRSI cancer volume (mL)	0.5 (0.1–5.6)	
IPSS (out of 35)	10 (1–15)	

seminal vesicle or lipid contamination. In one case with a central gland tumour measured with MR apparent diffusion coefficient (ADC), the region with low ADC was labelled as cancerous and its volume was manually measured. Spectra were excluded from all time points if excluded or not covered in the PRESS selected region for any time point. Numbers of voxels of cancerous spectra were recorded for each time point.

To assess changes in prostate volume, at each time point regions of interest were manually drawn around the prostate across its full three-dimensional extent on the T2-weighted MR images. To compare results across patients, all data were presented as a percentage of the baseline value. Additionally, the number of cancerous spectral voxels was also presented as a percentage of the 1-month values.

STATISTICAL ANALYSES

The sample size was chosen to be 10 patients as this was a pilot feasibility study to determine whether MRI could be used to quantify metabolic and other changes due to dutasteride. The primary endpoint of the present study was MRI- and MRSI-measured prostate cancer volume changes at 6 months. Other study endpoints included the toxicities of dutasteride; temporal changes in serum-free and total PSA, DHT and testosterone; and temporal changes in HRQL indices. Temporal MR, biochemical and HRQL changes were analysed using anova methods for repeated measures with measurements at baseline and 1, 3 and 6 months after the start of treatment. Analyses included linear tests for trends and *post hoc* pairwise comparisons using the Newman–Keuls test. Statistical analyses were performed using Statistica v6 (StatSoft Inc., Tulsa, OK, USA).

RESULTS

PATIENT CHARACTERISTICS

Ten patients were enrolled in the study. Patient characteristics are listed in Table 1. One patient withdrew from the study after 3 months because of toxicities.

MRSI CANCER VOLUME RESPONSE

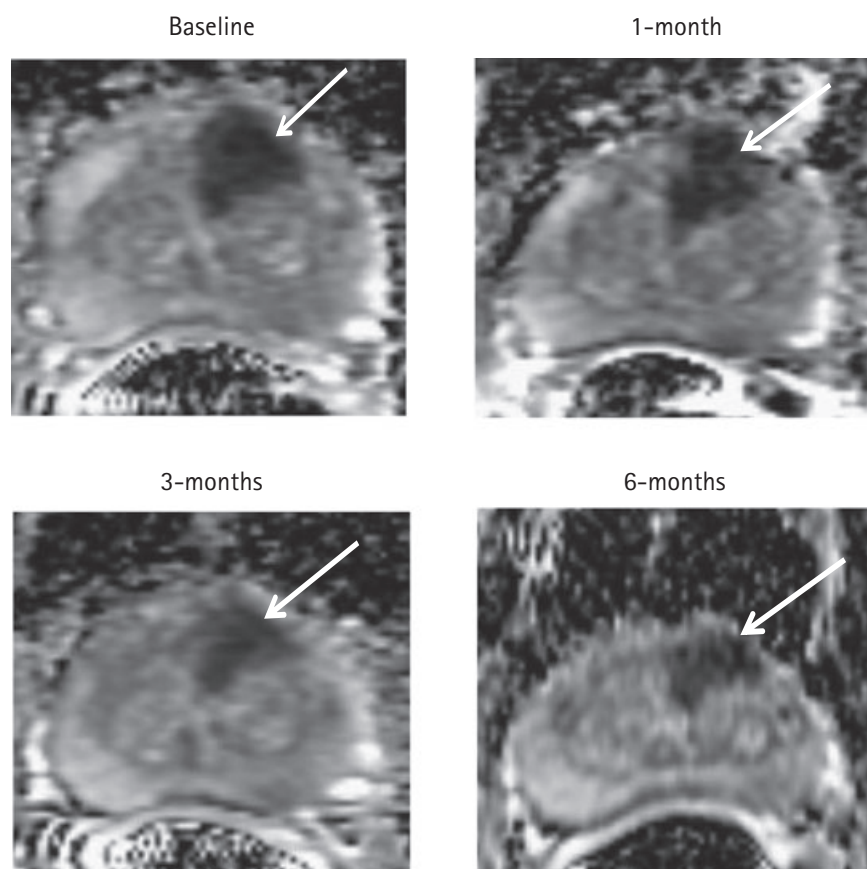
Across all the patients, changes in MRSI-measured cancer volumes did not reach statistical significance. Overall, because this is a low risk cohort of patients, the cancers were generally small with a median volume at baseline of 0.5 mL and a 6-month volume of 1.3 mL.

MRSI-measured cancer volume responses varied in this population. With dutasteride, it was noted that healthy regions had a decrease in citrate and polyamines compared with pre-dutasteride, making the spectra appear more similar to cancer. Accordingly, the number of MRSI voxels classified as cancerous compared with baseline was high and varied. At 6 months, the median value was 200% (range 50–933%) of baseline with a median increase of 0.7 mL.

However, when the number of MRSI voxels classified as cancerous was compared with 1-month values to address the effect of citrate and polyamine reduction, the median cancer volume did not change at 6 months and was 100% (range 55–267%) of the 1-month value. Similarly, the 3-month median value was 101% (range 82–218%) of the 1-month value.

Three of nine patients who completed the study had a decrease in cancer volume at 6 months vs baseline (50%, 60% and 61% of baseline) which was similarly observed vs 1-month measures (55%, 67% and 70% of 1-

FIG. 1. Representative patient with Gleason score 3 + 3 cancer (depicted by white arrow) located in the central gland by MR ADC maps. Images show temporal changes from baseline to 1, 3 and 6 months of dutasteride. Size and intensity of images are on the same scale.



month measure, respectively). One of these three was the patient with the central gland tumour measured with MR ADC in which the MR ADC identified cancer volume decreased at 6 months to 61% of baseline, whereas the overall prostate gland volume decreased only to 76% of baseline (see Fig. 1). Relative to 1-month imaging measurements, two other patients had virtually no change in the volume of their disease at 6 months (96% and 100% of 1-month value) and four showed an increase of 165–267% of 1-month measures. The median cancer volume at baseline was 0.5 mL for both the subsets of patients with an increase and those with a decrease in cancer volume at 6 months.

TOXICITIES

Of the 10 patients enrolled in the present study, nine completed 6 months of dutasteride as per the study protocol. One patient developed an eczematous rash after 3 months and was withdrawn from the study. The rash was located on his back and arms and resolved after discontinuing the dutasteride. An attempt to re-start dutasteride at a lower dose led to return of the rash.

None of the patients experienced any hot flashes. Of the five patients who reported normal erectile function at baseline, none developed erectile dysfunction when on dutasteride. Three of the five patients with normal erectile function experienced decreased ejaculate volume. None of the five patients experienced decreased libido.

There was no significant change in haemoglobin, white blood cell count, platelets, liver function test or renal function tests over time (data not shown).

CLINICAL AND BIOCHEMICAL RESPONSE

Table 2 shows the temporal changes in total PSA, testosterone, DHT and prostate volume. At 6 months, the mean total PSA significantly decreased by 47% (*post hoc* test, $P = 0.01$), DHT decreased significantly by 92% (*post hoc* test, $P < 0.001$), testosterone levels increased by 44% (*post hoc* test, $P = 0.07$), and prostate volumes significantly decreased by 25% (*post hoc* test, $P < 0.001$). For all three biochemical parameters, a response was seen as early as 1 month. An example illustrating the prostate volume shrinkage with time is shown in Fig. 2.

Table 3 lists the effects of dutasteride on symptoms and HRQL indices. Although there

TABLE 2 Biochemical and clinical response to dutasteride over time

Mean (SD)	Baseline (n = 10)	1 month (n = 10)	3 months (n = 10)	6 months (n = 9)	ANOVA, linear trend, P
Total PSA (ng/mL)	5.44 (2.90)	4.33 (2.23)	2.85 (1.49)	2.59 (1.06)	0.001
Testosterone (ng/dL)	356.5 (109.3)	418.4 (155.7)	443.2 (132.1)	484.3 (106.0)	0.027
DHT (ng/dL)	33.5 (8.9)	5.2 (5.5)	2.5 (0.8)	2.5 (0.8)	<0.001
Prostate volume (mL)	44.7 (19.0)	40.2 (17.6)	36.4 (15.1)	30.9 (11.9)	<0.001

TABLE 3 HRQL indices over time

Mean (SD)	Baseline	1 month	3 months	6 months	ANOVA, linear trend, P
IPSS	8.8 (3.8)	6.6 (3.0)	7.9 (4.4)	5.9 (4.3)	0.25
IIEF-5	16.4 (7.8)	17.0 (8.7)	16.0 (7.9)	15.3 (8.6)	0.22
FACE	4.6 (2.5)	4.7 (1.2)	5.0 (1.9)	4.8 (1.3)	0.71
SQLI	9.7 (0.7)	9.9 (0.3)	9.6 (0.7)	9.9 (0.3)	0.79

was a downward trend in the IPSS from 8.8 at baseline to 5.9 at 6 months, this was not statistically significant ($P=0.25$). Additionally, there was no significant linear trend in the IIEF-5, FACE and SQLI.

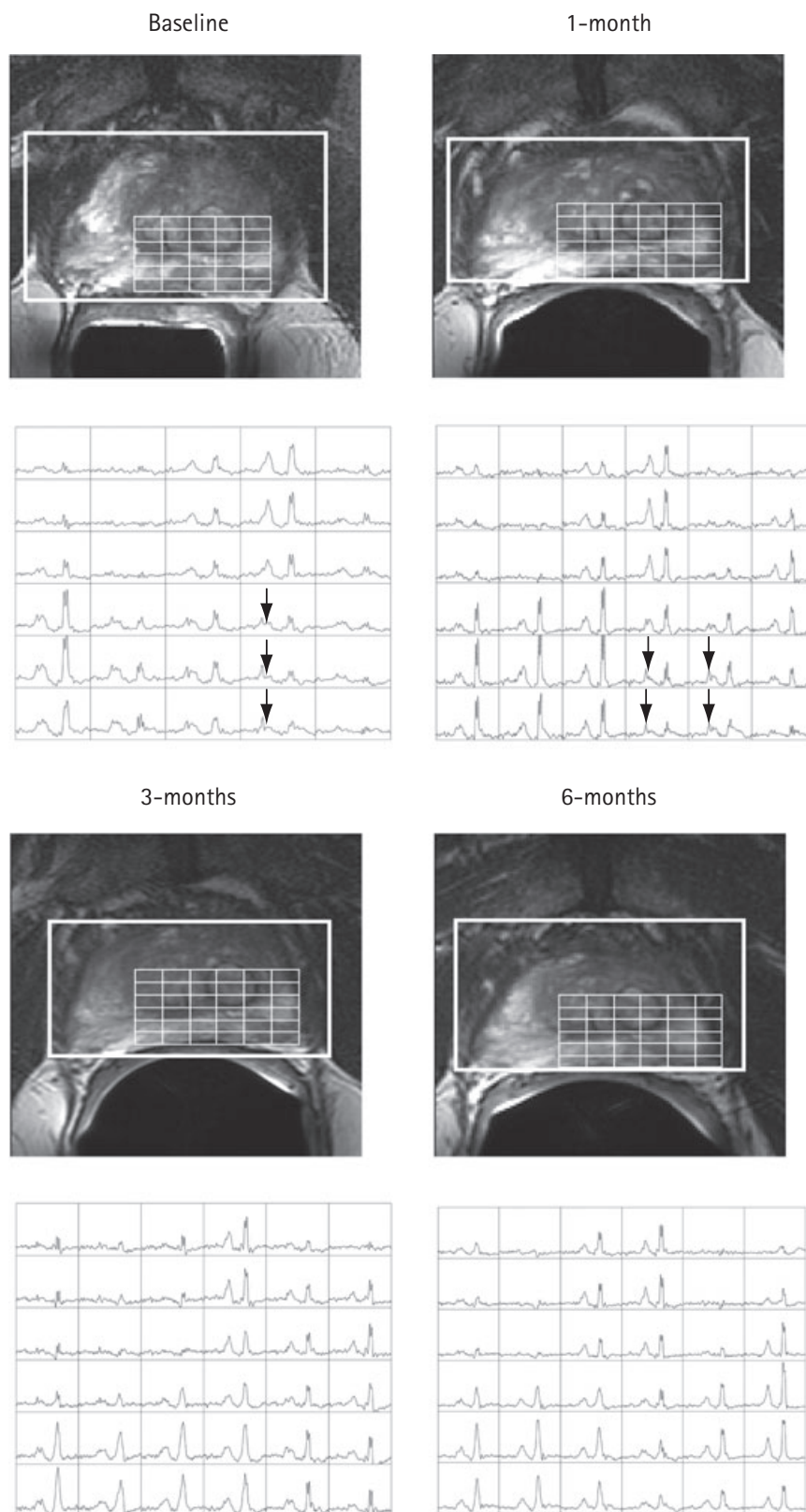
DISCUSSION

DHT, the dominant intracellular androgen, is converted from testosterone by the isoenzyme 5AR. Currently, there are two commercially available products, finasteride, a type 2 inhibitor, and dutasteride, a type 1 and type 2 inhibitor, that inhibit this enzyme. Both have received FDA approval for the treatment of symptoms related to BPH. Moreover, data from the PCPT study demonstrated that finasteride reduced the incidence of prostate cancer [2]. Similarly, recent results from the REDUCE trial demonstrated that dutasteride reduced the incidence of prostate cancer by 23% in a high risk population [6]. Unlike LHRH agonists, the 5ARI preserves testosterone levels and so worrisome complications with prolonged LHRH agonist use, such as osteoporosis, erectile dysfunction and metabolic syndrome, are uncommon. These findings led us to hypothesize that dutasteride, a dual type 1 and 2 and more potent inhibitor of 5AR, may have activity against prostate cancer, culminating in this proof-of-principle pilot study.

We deliberately confined the eligibility criteria to symptomatic low risk patients, where active surveillance remains a management option. Inclusion of higher risk patients would have been unethical in the absence of any data showing a drug response. Patients who indicated that they wished for low-dose-rate brachytherapy alone were also eligible for the present study as long as it was determined that their prostate required cytoreduction via androgen suppression therapy. Rather than the usual LHRH agonists, prostate downsizing was achieved using the study drug.

The study dose chosen (3.5 mg) was higher than the standard dose (0.5 mg) prescribed for BPH. In the ARIA2001 phase 2 study, 399 patients with symptomatic BPH were randomized to 24 weeks of placebo, finasteride 5 mg once daily, or one of five dutasteride dosing group regimens (0.01, 0.05, 0.5, 2.5 or 5.0 mg once daily) [4]. ARIA2001 confirmed that dutasteride was superior to finasteride in the reduction of serum DHT, by 98.4% with 5.0 mg daily doses

FIG. 2. Representative patient with temporal reduction in cancerous volume on MR spectroscopy. Cancerous spectra (black arrows) were no longer visible at the 3-month scan.



and 94.7% with 0.5 mg daily doses compared with finasteride 5 mg once-daily dose which reduced DHT by 70.8%. Serum testosterone levels increased by 21.2% and 13.7% with dutasteride 0.5 mg and 5 mg daily doses, respectively. No dose-related toxicity trend for dutasteride from 0.01 mg to 5.0 mg was observed, except for more frequent decreased libido in the 5.0 mg cohort. In the present study, a specially formulated capsule containing 3.5 mg of dutasteride was used to avoid the possibility that an insufficient dose was used should the study turn out negative.

Overall, the MR measures demonstrated no significant change in cancer volume, with no change in median cancer volume at 6 months vs 1 month. Individual results varied: three patients showed a decrease of 30–45%, two were unchanged, and four demonstrated percentage increases ranging from 65% to 167%. This may reflect a differential response to dutasteride across individuals. The baseline volumes of cancer were similar in these groups (0.5 mL for those that decreased, 0.9 mL for the stable volume cases, and 0.5 mL for those that increased in MR cancer volume). ARTS, a phase 3 placebo-controlled trial, is currently accruing and evaluating the effects of dutasteride in patients with biochemical failure after radical treatment [18]. Completed accrual in 2007, REDEEM is another placebo-controlled phase 3 trial that is assessing whether dutasteride extends the time to progression of low risk prostate cancer in men on expectant management [19]. Another phase 3 study involving dutasteride is Therapy Assessed by Rising PSA (TARP), which is investigating the addition of dutasteride to bicalutamide in castrate-refractory prostate cancer [20].

MRI was able to consistently track the decrease in overall prostate volume with time. MR ADC was a clear indicator of apparent cancer volume decrease with time in one case of a central gland tumour in which the MR ADC was dramatically lower in intensity than surrounding tissues at baseline (see Fig. 1). MR ADC was not definitive for the three other cases for which it was measured in peripheral zone cancers, probably because of small volume and potentially low density cancers.

MRSI interpretation was confounded by the observation that citrate and polyamines decreased in healthy tissues with dutasteride. This potentially confounded the choline and creatine relative estimates as the spectral

peak for polyamines is between and overlapping the choline and creatine resonance peaks. Thus, there was a bias to label healthy regions as probably cancer after dutasteride use, as demonstrated by the overall higher mean and median apparent cancer volume at 6 months compared with baseline. Those patients who demonstrated an increase in cancer volume vs baseline may have already had cancer in these areas at baseline, but masked by healthy tissue. As the most dramatic changes in MRSI occurred in the first month, the 1-month MRSI measures may be useful as an alternative baseline in which subtle cancers mixed with healthy tissue may be more apparent. Thus, the 6-month MRSI data were compared with 1-month values which demonstrated no overall median increase in cancer volume. MRSI data from patients taking dutasteride need to be interpreted in the context that healthy tissues appear more cancer-like. Although using 1-month values as baseline resulted in no change in overall cancer volume, there may still be bias to call healthy tissues cancerous at this time point. Other MRSI studies after antiandrogen therapy or after radiation have seen similar reductions in citrate and polyamines [8,10,21]. The full impact of this effect needs to be further evaluated.

In addition to the small sample size and relatively small cancer volumes at baseline (median 0.5 mL), other limitations were due to the MRSI interpretation process. With dutasteride, the signal to noise ratio decreased with time, furthering hindering interpretation of the MRSI data. Voxels with seminal vesicle and/or lipid contamination or adjacent to the urethra were visually identified and excluded. Because of this, some patients had only a subset of their likely cancer regions evaluated. Future studies to evaluate the effects of dutasteride on cancer will probably benefit from selecting patients with larger cancers, particularly those identifiable by MR ADC.

The biochemical response to dutasteride in the present study was similar to that observed in the ARIA2001 and ARIA3001 phase 2 and 3 trials [4,5]. Serum DHT decreased by 92% from baseline after 6 months, comparable to the 97.7% and 98.4% seen with 2.5 mg and 5.0 mg of dutasteride in ARIA2001 [4]. In ARIA2001, serum DHT reached its nadir after 4–8 weeks of starting dutasteride. Serum testosterone levels increased by 44% from baseline after 6 months in the present study,

which is consistent with the 19% (SD 50.3%) and 13.7% (SD 38.3%) observed with 2.5 mg and 5.0 mg respectively of dutasteride in ARIA2001. Consistent with the PCPT study and the ARIA3001 placebo-controlled phase 3 trial, total PSA decreased by approximately 50% in the present study [2,5].

Dutasteride 3.5 mg was well tolerated in our study cohort. Only one patient discontinued the study drug after developing a rash. In the ARIA2001 and ARIA3001 studies, rash was observed in less than 10% of patients [4,5]. Among the patients with normal erectile function at baseline, none developed erectile dysfunction and decreased libido with dutasteride. Three of five patients with normal erectile function experienced decreased ejaculatory volume. This is consistent with the ARIA3001 study that included 4325 patients, where only 7.3% experienced erectile dysfunction, 4.2% decreased libido and 2.2% decreased ejaculatory volume [5]. These findings are consistent with the lack of change seen in the IIEF-5 scores (see Table 3). In the present study, the IPSS decreased from 8.8 to 5.9, a mean decrease of 2.8, after 6 months ($P = 0.25$). In the ARIA3001 study, a difference in IPSS between the placebo arm (–2.5 from baseline) and the dutasteride arm (–3.2 from baseline) was not seen until 6 months [5].

In conclusion, the present study demonstrated no overall change in MRSI-measured cancer volumes, whereas the overall prostate gland volume decreased significantly by 1 month and continued to decrease over the 6-month study. Of the nine patients, three had at least a 30% decrease in their cancer volumes. Interpretation of MRSI data was limited by dutasteride-induced decreases in citrate and polyamines. Comparisons of MRSI data to 1-month measures appeared more appropriate than comparisons to baseline measures. As expected, the biochemical profile of PSA, testosterone and DHT values responded accordingly. Dutasteride was well tolerated and there were no significant changes in HRQL indices. More studies are warranted, and would benefit from including bulkier prostate cancers to assess response.

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CONFLICT OF INTEREST

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Abbreviations: PCPT, Prostate Cancer Prevention Trial; 5AR(I), 5- α -reductase (-inhibitor); DHT, dihydrotestosterone; FDA, Food and Drug Administration; MRSI, magnetic resonance spectroscopic imaging; HRQL, health-related quality of life; IIEF-5, five-item version of the International Index of Erectile Function; SQLI, Spitzer Quality of Life Index; FACE, Functional Alterations due to Changes in Elimination; PRESS, point resolved spectroscopy; ADC, apparent diffusion coefficient.