Early Results of Unilateral Prostatic Artery Embolization as a Focal Therapy in Patients with Prostate Cancer under Active Surveillance: Cancer Prostate Embolisation, a Pilot Study

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Early results of unilateral prostatic artery embolization as focal therapy in patients with prostate cancer under active surveillance: CaPEmbol, a pilot study

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Conflict of interest statement

The authors have no conflict of interest to disclose in relation with the present work.

Author contributions statement

Julien Frandon: conceptualization, data curation, formal analysis, interpretation of data, funding acquisition, project administration, supervision, writing original draft, writing review and editing, final approval of the manuscript; Elsa Bey: data curation, investigation, writing review and editing, final approval of the manuscript; Aymeric Hamard: data curation, investigation, final approval of the manuscript; Hélène Mohammad: data curation, investigation, final approval of the manuscript; Samia Gonzalez: data curation, investigation, final approval of the manuscript; Joël Greffier: data curation, investigation, writing review and editing, final approval of the manuscript; Thierry Chevallier: conceptualization, methodology, final approval of the manuscript; Hélène de Forges : interpretation of data, writing original draft, writing review and editing, final approval of the manuscript; Jean-Paul Beregi: conceptualization, interpretation of data, funding acquisition, project administration, supervision, writing review and editing, final approval of the manuscript; Stéphane Droupy: conceptualization, interpretation of data, funding acquisition, project administration, supervision, writing review and editing, final approval of the manuscript.

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Early results of unilateral prostatic artery embolization in patients with prostate cancer under active surveillance

Running Title: PAE under active surveillance

Abstract

Purpose: To evaluate the feasibility of prostatic artery embolization (PAE) in patients with low-risk prostate cancer (PC) under active surveillance (AS).

Methods: This monocentric prospective pilot study running from 06/2018 to 06/2019 included 10 patients, median age 72 years (62-77), with low-risk PC under AS, with a unilateral focal lesion visible on MRI with PIRADS≥3/5, confirmed by mpMRI targeted biopsy, Gleason score 6. Patients underwent unilateral PAE with 300-500 µm Embospheres® in the affected prostatic lobe. The primary endpoint was technical feasibility (prostate and no off-target ischemia on the imaging). Secondary endpoints included safety, negative biopsies / MRI response / functional outcomes at 6 months and oncologic efficacy at 1 year.

Results: Embolization was successfully achieved in all patients: prostate ischemia was confirmed on mpMRI and no off-prostate ischemia was reported. No major complications were reported. Four patients (40%) presented both negative targeted and systematic biopsies at 6 months. No lesions were seen on the MRI in 30% of patients. At baseline, mean IPSS and IEFF were 7 and 19 respectively and 5 and 20 at 6 months with no significant difference. Nine patients (90%) were still under AS at one year. One patient (10%) had PC progression outside the target lesion and was switched over to curative radiotherapy.

Conclusions: Prostate artery embolization is feasible and appears safe for prostate cancer patients under active surveillance, with no impact on erectile function or continence status. These results justify the pursuit of further studies.

Keywords: Prostatic artery embolization; low-risk prostate cancer; active surveillance; mpMRI; target lesion; focal therapy; fusion biopsy

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Introduction

Prostate cancer is the second most common cancer in men worldwide, with 29.3 new cases per 100,000 men in 2018 (1). Its incidence has increased due to greater life expectancy and a better detection of this asymptomatic localized low-risk disease with the widespread use of prostate-specific antigen (PSA) screening. Management of these very low- or low-risk patients with a life expectancy >10 years is based on active surveillance (AS) (2). Eligibility for AS varies according to recommendations and includes a PSA level <10ng/mL, stage T1 or T2 and a Gleason score of 6 or 7 (3+4) (International Society of Urological Pathology (ISUP) score 1 or 2) on up to 2 positives biopsy cores <3mm (2,3). AS aims to reduce overtreatment and postpone curative radical treatment (radiotherapy and prostatectomy) which induce side-effects on sexual quality of life (QoL) and urinary continence, with no major improvement in overall survival (4–6). A recent study randomized 1643 patients between radiotherapy, surgery and AS[7]. The cancer-related mortality rate at 10 years was not significantly different between groups. However, disease progression, including the occurrence of metastasis, was significantly higher in patients under AS.

The rate of patients who switch over to radical treatment due to disease progression, grade reclassification or patient decision greatly varies from 37% to 73% at 10 years (3,7,8). Focal therapies have thus emerged as an alternative to radical curative treatment (9,10), including thermal therapies such as cryotherapy (11) and high-frequency focused ultrasound (HIFU) (12), or a new vascular-targeted photodynamic therapy called Tookad® which induces local thrombosis within the blood

vessels leading to ischemia (13,14). A phase III randomized trial compared Tookad® with standard AS in low-risk patients and showed a longer time to progression and a lower disease progression rate with Tookad®. More patients presented negative biopsy results at 24 months after treatment (13). Locoregional ischemia-based therapies have thus demonstrated their efficiency in prostate cancer treatment.

Prostatic artery embolization (PAE) is used in the treatment of lower urinary tract symptoms related to benign prostatic hyperplasia treatment and has been shown to be safe and efficient (15–17). Randomized trials comparing PAE with standard treatment have reported few adverse effects, with preservation of erectile and urinary functions (15). PAE was recently used in prostate cancer patients in two studies, with no significant results. Patients included had advanced-stage prostate cancer (T2c/T3) under treatment or were in a palliative situation (18,19). This pilot study evaluated the feasibility, safety and efficacy of unilateral PAE in patients under AS with low-risk prostate cancer presenting a focal lesion visible on MRI with PIRADS ≥3/5 confirmed by mpMRI target biopsy.

Materials and Methods

Study design and objectives

The primary objective of this prospective monocentric pilot study was to evaluate the feasibility of unilateral PAE in patients with localized low-risk prostate cancer under AS. Secondary objectives were to evaluate safety, response of the target lesion on biopsy and multiparametric Magnetic Resonance Imaging (mpMRI), PSA level, functional outcomes and short-term oncologic efficacy *i.e.* switching over to radical treatment. All patients signed an informed consent and the study was approved by an ethical review board. The study was performed according to Good Clinical Practice requirements and the Helsinki Declaration and registered on ClinicalTrials.gov (NCT03407963). After inclusion of 5 patients, an independent surveillance committee was formed to evaluate safety and before allowing the study to continue.

Study population

Patients with unilateral low-risk prostate cancer (d'Amico classification) at clinical stage <T2b were included. The main inclusion criteria were: age 18 to 80 years old, life expectancy >10 years; focal lesion on MRI, PIRADS (Prostate Imaging Reporting and Data System) v2 ≥3/5; positive mpMRI target lesion; PSA level <10ng/mL (or ≥10ng/mL in the event of a large prostate volume); presence of unilateral positive MRI-targeted biopsies; Gleason score ≤6 (ISUP 1) with <3 positive biopsies and <50% of positive biopsy length. The main criteria for non-inclusion included the patient's ineligibility or refusal to undergo active surveillance, contraindication for MRI (incompatible pacemaker, claustrophobia, hip prosthesis or metallic implanted device) or for administration of the study products, a tumor on both lobes or a hemostasis disorder.

From June 2018 to June 2019, 10 patients of median age 72 years (range: 62-77) were included in the study. Baseline patient and tumor characteristics of prostate biopsies are reported in Table 1.

Technical procedures

Biopsy

Biopsies were performed at baseline and 6 months after PAE by one experienced operator: 1 to 3 mpMRI-targeted biopsies in the target lesion region under real-time transrectal ultrasonographic (TRUS) guidance and visual real-time matching between MRI target lesions and prostate image (Toshiba, Applio 500^{TM} smart fusion) and 9 to 12 TRUS standard systematic biopsies (20).

Prostatic artery embolization

PAE was performed by one interventional radiologist (JF, with 10 years of experience and more than 30 cases of PAE performed) under local anesthesia. Both Digital Subtraction Angiography (DSA) and cone-beam computed tomography (CBCT) were performed using a pump injection to evaluate the iliac vessels and identify the prostatic arteries. Prior to PAE, each artery was controlled by CBCT to assess which part of the prostate was vascularized and avoid off-target prostate ischemia. Unilateral embolization was performed using Trisacryl® microspheres (Embosphere, 300-500µm, Merit Medical System, South Jordan, USA) until the prostatic artery was completely occluded. The volume of microspheres injected was reported and compared with the embolized prostate volume. PAE was performed on an ALLURA Xper FD20 (Philips Healthcare) and the radiation dose, *i.e.* total Kerma-Area Product was collected for all patients.

A follow-up angiography was performed to check for any prostatic lobe blood supply after PAE. Patients were discharged on the following day.

Imaging

An mpMRI was performed at baseline, at 2 weeks and 6 months after PAE, using a 3.0-T scanner (Magnetom Skyra, Siemens, Erlangen, Germany) with a pelvic phased-array coil. 3DT2-weighted (T2WI), diffusion-weighted (DWI), and dynamic contrast-enhanced (DCE) imaging sequences were acquired according to European guidelines (21).

Endpoints and assessments

The primary endpoint was technical feasibility, defined as blood flow arrest assessed by angiography, ischemia of the prostatic lobe on the imaging at 2 weeks and the absence of specific risks, especially off-target ischemia (penis, bladder, rectum) assessed at Day 1, Day 5 (follow-up phone call) and Day 15 (clinical evaluation at the time of the MRI) and at 1, 3 and 6 months. Secondary endpoints were: safety (Clavien-Dindo classification), negative targeted and systematic biopsies at 6 months; mpMRI response of the target lesion at 6 months (PIRADS v2 score); functional outcomes evaluated using validated questionnaires/tests at baseline, 1, 3 and 6 months after PAE: urinary-specific QoL (International Prostate Symptom Score, IPSS), incontinence (24-hour Pad test in the event of urinary leakage), erectile dysfunction (Index of Erectile Function, IIEF-6) and QoL (EQ-5D); early oncologic efficacy at one year *i.e.* the rate of patients switching over to radical treatment (with the decision being made at a multidisciplinary meeting after mpMRI, biopsies and biology results).

~~*Study population*~~

~~From June 2018 to June 2019, 10 patients of median age 72 years (range: 62-77) were included in the study. Baseline patient and tumor characteristics of prostate biopsies are reported in Table 1.~~

Statistical considerations

Considering the study design and lack of literature data, no formal calculation was made to determine the number of required subjects, but 10 patients were included. Quantitative variables are presented using medians and ranges. Qualitative variables are presented with numbers and percentages. Values were compared using Mann-Whitney U tests.

Results

Feasibility and safety

Embolization was successfully achieved in all patients. The median embolization procedure time was 50 min. (31-125) and the median radiation dose received was 101 666mGy.cm^2 (39 666-211 118) (Table 2). The artery selected for embolization was confirmed by CBCT (Figure 1). Prostate ischemia was confirmed by mpMRI at 2 weeks. No off-prostate ischemia was reported and no target lesions were seen on the angiography.

No major complications were reported. Minor complications (Clavien-Dindo I or II) occurred in 3 patients (30%). Patient 3 reported a Grade II urinary infection on Day 3, successfully treated with ofloxacine (200 mg) twice a day for 10 days; patient 5 had Grade I prostatic pain just after embolization which resolved within 5 days on prednisolone (20 mg) combined with omeprazole (20 mg) once a day and paracetamol (1000 mg) four times a day; patient 6 had a Grade I superficial hematoma at the puncture site 2 days after embolization, with spontaneous resolution and no clinical consequences. All patients were discharged the day after embolization according to protocol requirements.

Biopsy and imaging results

At baseline, 8 patients (80%) reported 1 positive targeted biopsy, 2 patients (20%) 2 positive targeted biopsies, and 2 patients (20%) also reported 1 positive systematic biopsy (Table 3). Six months after PAE, 3 patients (30%) had targeted biopsies in the area where the tumor was previously located as no target lesion was visible on mpMRI (Table 3 and Figure 2). In these 3 patients (30%) with complete response on mpMRI (no visible PIRADS v2 lesion, Table), 2 reported negative biopsies performed in the former target location. Overall, 4 patients (40%) reported both negative targeted and systematic biopsies. One patient's PC (10%) had progressed on a systematic biopsy at 6 months (Gleason score 7, 3+4), outside the target lesion.

The size of the target lesion on mpMRI, 10mm (7-16) at baseline, was stable. Ischemia of the prostatic lobe was partial and heterogeneous, involving 20% (10-40) of tissue (Figure 2 and Table 4). Ischemia was visible at 2 weeks after PAE, not at 6 months.

PSA levels were similar before and after embolization. As expected, the prostatic volume decreased from 67.5cm^3 (31-111) at baseline to 54.0cm^3 (37-95) at 6 months (p=0.344) (Table 4).

Functional outcomes

Overall, functional outcomes were improved after PAE: no urinary incontinence was reported, and patients showed better urinary status (IPSS: 5 (1-16) at baseline and 1 (1-19) at 6 months) (Table 5). No erectile dysfunction was reported after embolization either.

Early oncologic efficacy

At one year**,** 9 patients (90%) were still under AS and the patient whose PC had progressed on a systemic biopsy, outside the target, was reclassified and switched over to curative external beam radiotherapy.

Discussion

Results show that therapeutic unilateral PAE in patients under AS for low-risk prostate cancer with a focal lesion visible on MRI with PIRADS ≥3/5 confirmed by a targeted mpMRI biopsy is feasible and seems safe and promising. PAE is already used for the treatment of benign prostatic hyperplasia with good results in terms of safety and efficacy (16). PAE was assessed in patients with low-risk prostate cancer under AS to postpone switching over to radical treatment and limit the side-effects on erectile and urinary functions.

It was decided to perform unilateral PAE for various reasons. First, patients were addressed for unilateral prostate cancer and not for low urinary tract symptoms. Secondly, unilateral PAE represented a shorter procedure time with potentially fewer side effects. Thirdly, it would allow us to study the locoregional effect of PAE in greater depth. The feasibility of unilateral PAE for these patients was demonstrated as partial prostatic ischemia was achieved for all of them. This non-invasive treatment was performed in a short time (median duration 50min), with discharge the following day. If complete safety is confirmed, an ambulatory setting may be possible. The PAE procedure has advantages compared to other focal therapies developed as alternatives to radical treatment. Indeed, most other therapies published are costly, require specific logistics (dark room etc.) and adverse events such as erectile dysfunction and other complications related to off-target tissue ablation have been reported. Also, some prostate locations such as anterior sites or those close to the apex or urethra are either inaccessible or too risky for other focal therapies (22). In this study, PAE was possible in many prostate locations as the procedure consists of embolizing the whole prostate lobe with no off-target ischemia.

In this study, safety was as good as for other studies on PAE for HBP which reported very few complications (23). Functional outcomes were good, with no incontinence or sexual dysfunction, in agreement with other results on PAE for HBP reported (15,16). PAE may also have the potential benefit of relieving emotional stress in patients who are anxious about their untreated cancer. The two previous studies on PAE in prostate cancer showed significant complications with equivocal oncologic results. Mordarsini *et al.* reported Grade 3b partial bladder wall necrosis in two patients and infected

lymphocele (grade 3a) (19), as for Pisco *et al.* who reported off-target necrosis (bladder wall) (18). They also reported Grade 2 incontinence and sexual dysfunctions (18,19). They used smaller microspheres (100-300µm) which could induce higher morbidity (24). Also, Pisco *et al.* performed bilateral chemoembolization with docetaxel in advanced cancer patients, which may explain this higher toxicity (18). In this study, unilateral PAE was performed in patients with low-risk cancer and limited symptoms at baseline (median IPSS of 5). Overall, these results are encouraging as the purpose of AS is precisely to avoid or postpone side-effects induced by radical treatments (25). It is thus essential that new focal therapies, proposed as an alternative to AS, do not induce important side-effects.

Focal treatment during AS is debated (26) and therefore patient selection was an important issue in this study. Only patients under AS presenting consequent lesions visible on mpMRI (median index lesion 10mm, upper Gleason 3+3 score) confirmed by targeted biopsy were included. Very low-risk patients weren't included (26). Indeed, these patients with lesions found on the MRI have a poorer disease evolution and oncologic outcome which justifies proposing focal therapy during AS (27). Targeted biopsies have been shown to lead to better identification of patients under AS who can benefit from hemi-ablative focal therapies (28). Indeed, targeted biopsies enabled us to carefully select patients, thus avoiding misclassifications during systematic follow-up biopsies (29,30).

Although recent literature has highlighted the crucial role of mpMRI in AS follow-up (31), this study seems to report limitations in the use of mpMRI for these patients. Indeed, 4 patients had negative systematic, targeted biopsies and 2 of them had a visible target on the imaging. It seems that the response on mpMRI may be delayed compared with the biopsy results. Moreover, one patient with a complete response on mpMRI reported a positive biopsy in the former target location. This emphasizes the limitations of concordance between the PIRADS V2 classification and oncologic results (32). These results also suggest that both targeted and systematic biopsies are important; indeed, in the one patient whose disease had progressed, this was detected with systematic biopsies and not with the targeted biopsy (33). However, it is possible that the lesion was missed by the systematic biopsies, and that this patient may initially have been understaged.

Azzouzi *et al.* reported similar results with Tookad®. They showed a 28% progression rate and switch to radical treatment and 49% negative biopsies at 2 years (13). It seems that ischemic strategies do not achieve complete success rates, probably due to complex prostate vascularization, modified by the tumor (34). This may explain a heterogeneous distribution of the embolization microspheres and the partial, heterogeneous ischemia reported in the study. It is also possible that the number of microspheres injected plays a role in this random distribution of particles in the prostate volume. This raises the question of performing bilateral embolization in refractory patients who may have developed contralateral arterial anastomoses. As PAE is a safe procedure, it may be possible to repeat PAE in the event of failure. Pisco *et al.* have shown the efficacy of such a strategy: among 3 patients who had biochemical failure of their first chemoembolization at 6 months and underwent a second procedure, 2 achieved biochemical success afterwards (18).

Usual focal treatments are based on high focal energy deposits mainly using thermal ablation (HIFU or, cryotherapy) (22). One reason why they cannot be used for all lesions may be the necessity to obtain clear margins, especially when close to regions at risk. This study opens new perspectives with this new targeted vascular therapy. PAE is a different concept based on vascular territories, which may be used for patients with difficult-to-access lesions or regions at risk. It may also lead to the possibility of using chemotherapy-loaded particles that could be administered directly within the prostate, reducing the side-effects of systemic chemotherapy. Moreover, potential radiotherapy treatment may still be possible after PAE in the event of disease progression; indeed, the 6-month MRI showed complete regression of the ischemic effect of PAE.

This study shows certain limitations, including those inherent to the pilot study design as this was a mandatory stage before conducting further studies. The main limitations are the small number of patients included, and the short follow-up (1 year) required due to the safety design. A 5-year follow-up would be more clinically meaningful for oncological results, especially regarding the switch to radical treatment. Another limitation is the absence of precise targeting of the lesion leading to the embolization of the entire prostatic lobe. Indeed, the lesions were not visible on the angiogram and this did not allow us to better target the embolization. Although there was a lack of a control group to

assess the magnitude of treatment effect, these results are promising and warrant further investigations to determine the right number of microspheres to use and explore the long-term efficacy of PAE in these patients.

In conclusion, this pilot study showed that prostatic artery embolization is feasible and appears safe in patients with low-risk prostate cancer and a visible lesion on MRI PIRADS ≥3/5 confirmed by mpMRI targeted biopsy under active surveillance. This procedure offers patients eligible for AS a "reinforced active surveillance" as an alternative to focal therapy before eventually switching over to radical treatment. Early results with 40% of negative targeted biopsies and 90 % of patients still under AS at one year are encouraging and justify the pursuit of further studies. Randomized multicentric studies with, as an endpoint, the proportion of patients switching over to radical treatment, would help to confirm the interest of this promising procedure.

Data availability statement

All data supporting the findings of this study are available from the corresponding author, upon reasonable request.

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Morphologic Changes in Periprostatic Arteries Have an Influence on Prostatic Artery Embolization? Eur. Urol. 2019; **75**: e110–e113.

Figure and Table legends

Figure 1: Feasibility of prostatic artery embolization: mpMRI of Patient 6 with the target lesion (white arrow) visible on T2WI (A) and ADC map (B) as a well circumscribed hypo-intensity in the right peripheral zone measuring 10 mm. DSA with injection in the internal iliac artery (IIA) (panel C) showed the right prostatic artery (PA) arising from the anterior trunk (AT). The CBCT angiography performed in the prostatic artery (D) confirmed the tumor feeding artery with vascularization of the right prostatic lobe (white circle). Successful embolization was defined by the complete stasis of flow in the PA on the post embolization angiography (E). DCE MRI at 15 days (F) confirmed partial and heterogeneous ischemia of the right prostatic lobe (white circle), visible on T2WI (G) as a diffuse unilateral hypo-intensity (white arrow), and a heterogeneous iso intensity on the ADC map (H).

Figure 2: Efficacy of the procedure: At baseline, patient 2's mpMRI showed a PIRADS 4 target lesion of 9 mm in the right apex (white arrow) with a circumscribed homogenous T2 hyposignal (A), markedly hypo intense on ADC map (B) with a positive focal enhancement on DCE (C). At 6 months after PAE, no more circumscribed hypo signal is visible on T2WI mpMRI (white arrow head, D), ADC map (E) and no focal enhancement is visible on DCE (F).

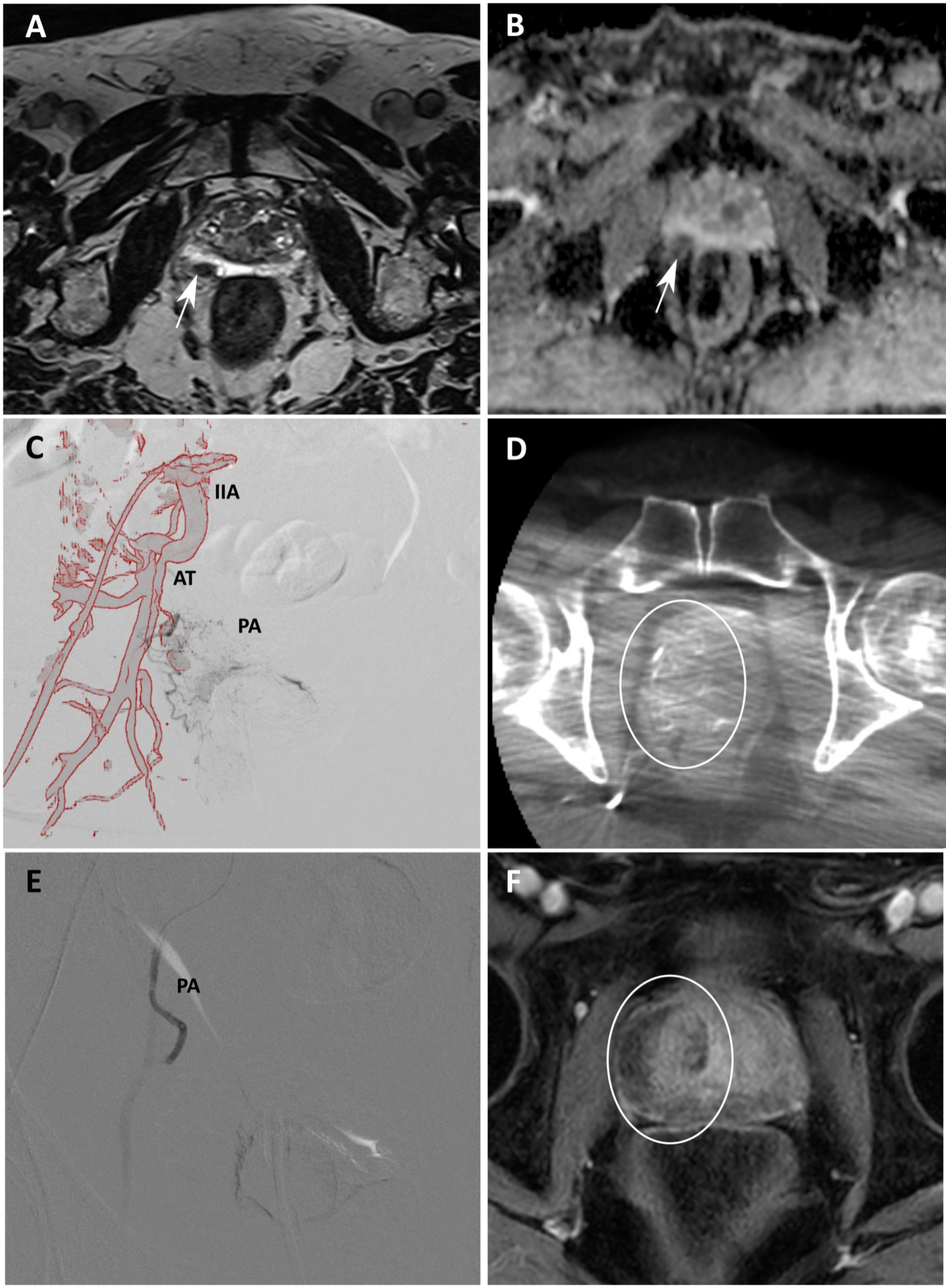
Table 1: Patients' characteristics at baseline

Table 2: Technical and angiographic data

Table 3: Biopsy results at baseline and 6 months after prostatic artery embolization

Table 4: MRI target at baseline, and at 2 weeks and 6 months after prostatic artery embolization

Table 5: Functional outcomes at baseline and at 1, 3 and 6 months after prostatic artery embolization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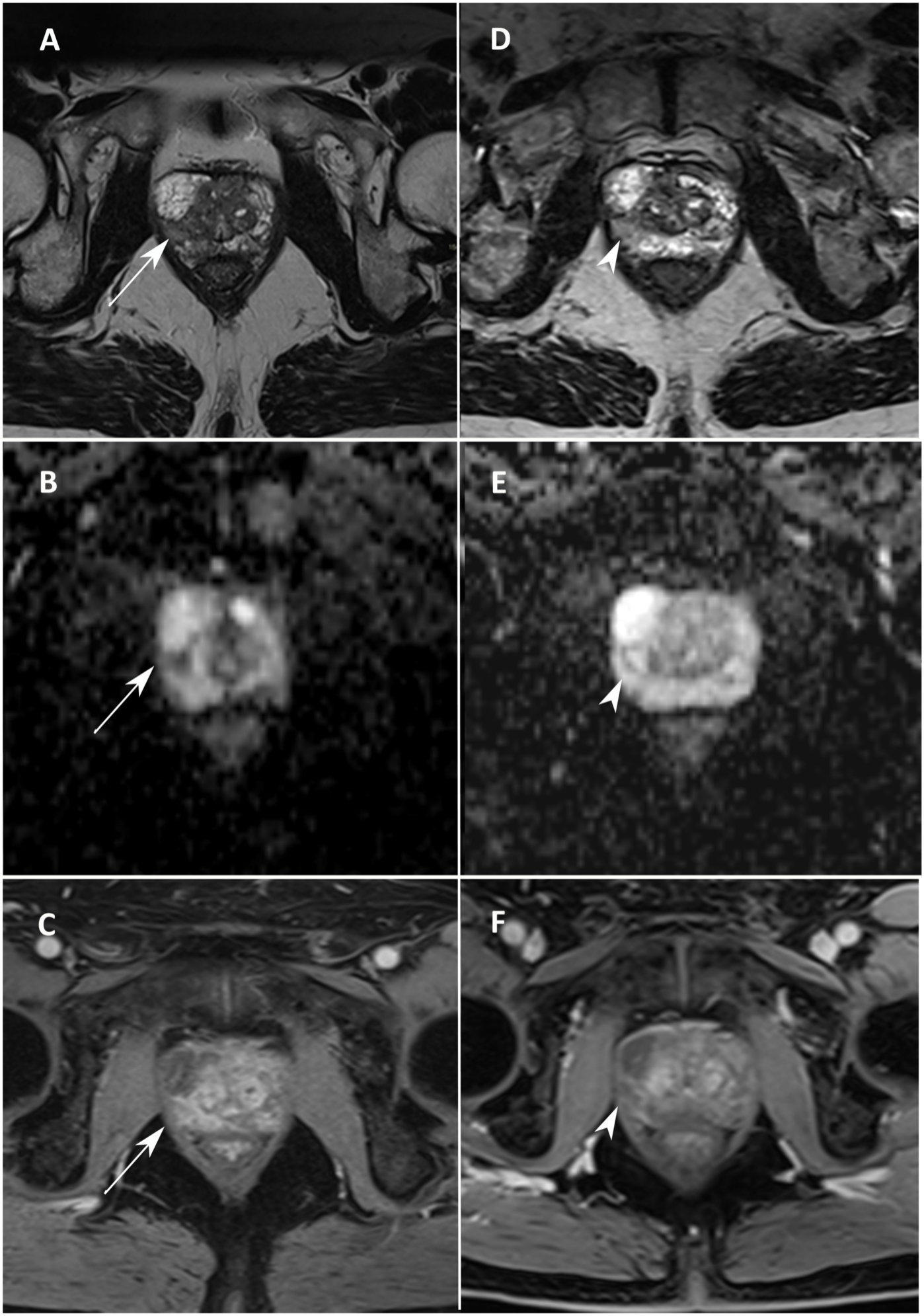
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Table 1: Patients' characteristics at baseline

	N=10
Age, median (range)	72 (62-77)
BMI, median (range)	24.5 (21.3-35)
Ethnical origin, n (%)	
Caucasian	9 (90)
North African	1 (10)
MRI prostate volume, cm^3, median (range)	67.5 (31-111)
PSA level, ng/mL, median (range)	6.22 (3.28-10.14)
Rectal examination, n (%)	
Soft	5 (50)
Firm	2 (20)
Nodular	3 (30)
T clinical stage, n (%)	
T1c	5 (50)
T2a	5 (50)
Localization, n (%)	
Side	
Left	3 (30)
Right	7 (70)
Anatomical region	
Apex	5 (50)
Medial	3 (30)
Basal	2 (20)
Anterior	5 (50)*
Posterior	6 (60)*
Peripheral zone	6 (60)
Transitional zone	4 (40)
MRI focal lesion size, mm, median (range)	10 (7-16)
PIRADS score, n (%)	
3	1 (10)
4	9 (90)
5	0
Number of positive biopsies, n (%)	
1	6 (60)
2	2 (20)
3	2 (20)**
Gleason score, n (%)	
6	10 (100)
7 (3+4)	0 (0)

BMI: Body Mass Index; MRI: Magnetic Resonance Imaging; PSA: prostate specific antigen; PIRADS: Prostate Imaging Reporting and Data System

* Patient 2: focal lesion both posterior and anterior

** Patients 4 and 7: 2 positive biopsies in the target lesion and one next to it, in systematic biopsies.

Table 2: Technical and imaging data

Patient	Embolized prostatic artery number, side, origin	Volume of Microspheres injected (mL)	Procedure duration (min)	Total Kerma Area Product ($mGy.cm^2$)
1	1, right, superior vesical artery	3	35	184 329
2	**1, right, rectal artery**	**3**	**85**	**138 930**
3	1, left, superior vesical artery	5	31	58 316
4	1, left, superior vesical artery	4.5	51	82 396
5	2, right, obturator artery x 2	4 (2 + 2)	55	120 937
6	1, right, superior vesical artery	3	50	39 666
7	1, right, gluteal artery	4	69	69 743
8	**1, right, obturator artery**	**4**	**47**	**139 687**
9	**1, left, superior vesical artery**	**3.5**	**46**	**71 089**
10	**2, right, pudendal and obturator arteries**	**7 (3+4)**	**125**	**211 118**

Bold: No positive biopsy reported in the targeted or systemic biopsies at 6 months

Embolization was performed with a mixture of 12 mL of contrast media, 8 mL of saline, and 2 mL of microparticles (Embosphere, 300-500µm, Merit Medical System, South Jordan, USA).

Table 3: Biopsy results at baseline and at 6 months after prostatic artery embolization

	Baseline					At 6 months				
	Number of positive biopsies / number of biopsies performed		Max core length (mm)	Gleason score	PSA level (ng/mL)	Number of positive biopsies / number of biopsies performed		Max core length (mm)	Gleason score	PSA level (ng/mL)
	Targeted biopsies	Systematic biopsies				Targeted biopsies	Systematic biopsies			
Patient 1	1/1	1/11	5	6	3.3	1/2	1/10	3	6	2.9
Patient 2	**1/1**	**0/12**	**1**	**6**	3.4	**0/1***	**0/11**	**/**	**/**	0.3
Patient 3	1/1	0/11	1	6	7.1	1/2	1/10	4	7 (3+4)**	6.0
Patient 4	2/2	0/10	3	6	6.8	2/2	1/12	6	6	6.3
Patient 5	1/1	0/11	1	6	8.7	1/2	0/10	4	6	6.8
Patient 6	1/1	0/11	1.5	6	10.1	2/2*	0/10	5	6	5.1
Patient 7	2/2	1/12	8	6	8.5	1/3	0/9	1	6	7.6
Patient 8	**1/1**	**0/12**	**1**	**6**	5.6	**0/1***	**0/11**	**/**	**/**	3.6
Patient 9	**1/1**	**0/12**	**2**	**6**	1.9	**0/3**	**0/9**	**/**	**/**	2.9
Patient 10	**1/1**	**0/12**	**2**	**6**	4.3	**0/2**	**0/10**	**/**	**/**	2.9

* Patients 2, 6 and 8: no target lesion was visible on MRI at 6 months, target biopsies were performed in the area where the tumor was previously located.

** Patient 3 progressed outside of target lesion

Bold: No positive biopsy reported in the targeted or systemic biopsies at 6 months

Table 4: MRI target at baseline, and at 2 weeks and 6 months after prostatic artery embolization

	Baseline				At 2 weeks				At 6 months			
	PIRADS score*	Target lesion size, mm	Necrosis of the prostatic lobe, %	Prostate volume, cm^3	PIRADS score*	Target lesion size, mm	Necrosis of the prostatic lobe, %	Prostate volume, cm^3	PIRADS score*	Target lesion size, mm	Necrosis of the prostatic lobe, %	Prostate volume, cm^3
Patient 1	4+	7	/	80	3+	7	30	83	3+	7	0	58
Patient 2	4+	9	/	31	4	9	10	30	**CR**	**CR**	0	37
Patient 3	4+	16	/	111	4+	18	20	121	3+	10	0	95
Patient 4	4+	10	/	75	4+	9	10	84	4+	10	0	70
Patient 5	4+	10	/	82	Ø assessable	Ø assessable	40	60	2+	5	0	64
Patient 6	4+	10	/	50	4+	7	40	46	**CR**	**CR**	0	38
Patient 7	4+	13	/	57	Ø assessable	13	20	61	4+	13	0	50
Patient 8	4+	11	/	72	3	Ø assessable	20	67	**CR**	**CR**	0	69
Patient 9	3	12	/	38	3	11	20	39	3	11	0	39
Patient 10	4+	10	/	63	3	7	40	53	3	10	0	45

* Dynamic contrast enhancement is reported with a +

Ø assessable: target lesion not clearly identifiable because of ischemic remodeling

MRI: Magnetic Resonance Imaging; CR: complete tumor response (no target lesion visible on MRI)

Table 5: Functional outcomes at baseline and at 1, 3 and 6 months after prostatic artery embolization

	Baseline (N=10)	1 month (N=9*)	p**	3 months (N=9*)	p**	6 months (N=10)	p**
IPSS (/35), median (range)	5 (1-16)	2 (1-16)	0.179	2 (1-9)	0.197	1 (1-19)	0.321
Urinary symptoms QoL (/6), median (range)	2 (0-4)	1 (0-4)	0.189	1 (0-3)	0.486	1 (0-3)	0.365
IIEF-6 (/30), median (range)	24 (1-30)	24 (0-30)	1.000	27 (1-30)	0.528	27 (0-30)	0.970
EQ-5D score (/100), median (range)	90 (40-100)	90 (50-95)	0.855	90 (40-95)	0.486	90 (40-100)	0.786

IPSS: International Prostate Symptom Score; QoL: Quality of life; IIEF-6: International Index of Erectile Function;
EQ-5D: European Quality of Life (EuroQoL) questionnaire
*: Data missing for one patient at 1 month (patient 5) and for one patient at 3 months (patient 7)

**: compared to baseline