P2-05

THE NEXT GENERATION TRIAL – ASSESSING ^{18}F-PSMA-1007 POSITRON EMISSION TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING IN THE PRIMARY STAGING OF PROSTATE CANCER PATIENTS

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INTRODUCTION AND OBJECTIVE: Prostate specific membrane antigen (PSMA) is a type II transmembrane protein which demonstrates overexpression in the vast majority of prostate cancers and correlates with the aggressiveness of the tumor. PSMA PET imaging has been shown to be superior to conventional imaging (CT/Bone scan) in the workup of prostate cancer. The objective of this study is to determine the accuracy and role of ^{18}F-PSMA-1007 PET and mpMRI in the primary locoregional staging of intermediate and high-risk prostate cancer.

METHODS: The Next Generation Trial (NCT05141760) was a Phase II prospective validating paired-cohort trial assessing ^{18}F-PSMA-1007 PET/CT and mpMRI for locoregional staging of prostate cancer, with final histopathology as the gold standard comparator in 134 patients undergoing prostatectomy. Radiologists, nuclear medicine physicians, and pathologists were blinded to preoperative clinical, pathology, and imaging data. The primary outcome was correct identification of the prostate cancer tumor ('T') stage. The secondary outcomes were correct identification of the dominant nodule, laterality, extracapsular extension, and seminal vesical invasion.

RESULTS: PSMA PET was superior to mpMRI for the accurate identification of the final pathological T stage (45% vs. 28%, $p=0.003$). PSMA PET was also superior to MRI for the correct identification of the dominant nodule (94% vs. 83%, $p=0.007$), laterality (64% vs. 44%, $p=0.001$), and extracapsular extension (75% vs. 63%, $p=0.014$), but not for seminal vesicle invasion (91% vs. 85%, $p=0.065$). On a per tumor nodule analysis, PSMA PET detected more GGG2 or greater nodules than MRI (86% vs. 62%, $p<0.001$).

CONCLUSIONS: In this trial, 18F-PSMA-1007 PET/CT was superior to mpMRI for the locoregional staging of prostate cancer. These findings support the use of PSMA PET in the preoperative workflow of intermediate- and high-risk tumors.

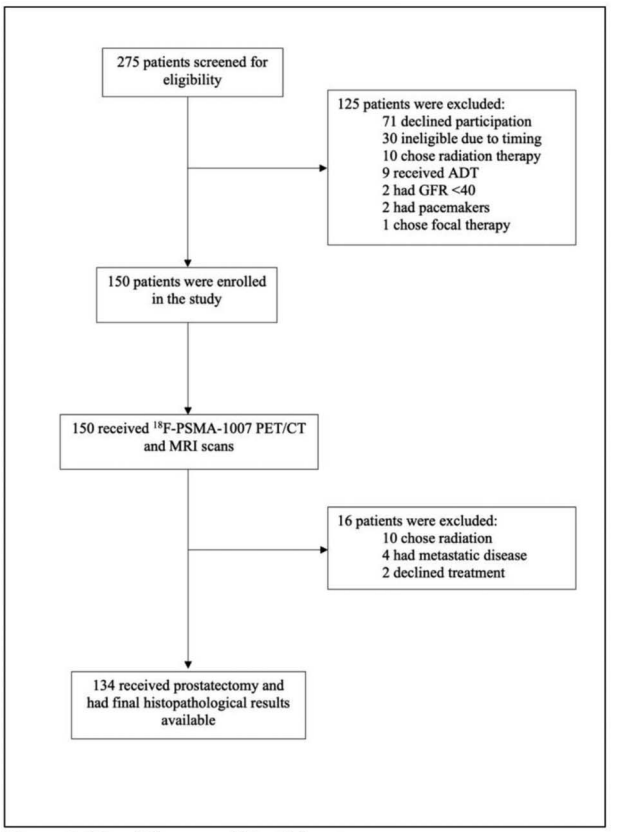

Figure 1. Flow Diagram of Participants.

Table 1. Clinical and Pathological Characteristics at Time of Radical Prostatectomy.

Characteristic	N=134
Mean Age at Prostatectomy, years (standard deviation)	62 (5.7)
Median Preoperative PSA, ng/mL (IQR)	7.8 (6.7-10.9)
Final Pathology Gleason Group, n (%)	Benign – 1 (1) GG 1 – 0 (0) GG 2 – 94 (70) GG 3 – 33 (25) GG 4 – 1 (1) GG 5 – 5 (4)
Final Pathological T Stage, n (%)	pT0 – 1 (1) pT2a – 5 (4) pT2b – 4 (3) pT2c – 59 (44) pT3a – 44 (33) pT3b – 21 (16) pT4 – 0 (0)
Final Pathological N Stage, n (%)	N0 – 130 (97) N1 – 4 (3)
Median Pathological Prostate Volume, cc (IQR)	39 (31-47)
MRI PI-RADS Score, n (%)	≤2 – 16 (12) 3 – 0 (0) 4 – 45 (34) 5 – 73 (54)
PSMA PET modified PROMISE Scores, n (%)	0 – 0 1 – 54 (40) 2 – 42 (31) 3 – 38 (28)

Table 2. Correct Identification of Pathological Parameters by Pre-operative ^{18}F-PSMA-1007 PET/CT and MRI.

Pathological Variable	MRI (n=134)	PSMA PET/CT (n=134)	P Value
Final Pathological T Stage, n (%)	38 (28)	61 (45)	**0.003**
Dominant Nodule, n (%)	112 (83)	126 (94)	**0.007**
Laterality, n (%)	60 (44)	86 (64)	**0.001**
Extracapsular Extension, n (%)	84 (63)	100 (75)	**0.014**
Seminal Vesical Invasion, n (%)	115 (85)	122 (91)	0.065

Table 3: Nodule Level Detection by Multiparametric MRI and ^{18}F-PSMA-1007 PET/CT Stratified by Gleason Grade Group of Individual Prostate Cancer Nodules.

Gleason Grade Group	MRI	PSMA PET/CT	P Value
1, n (%)	6/54 (11)	15/54 (28)	0.02
≥2, n (%)	144/232 (62)	201/232 (86)	<0.001

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P2-06

HIFI TRIAL: HIFU VS RADICAL PROSTATECTOMY FOR LOCALIZED PROSTATE CANCER IN 3328 CASES. FINAL RESULTS

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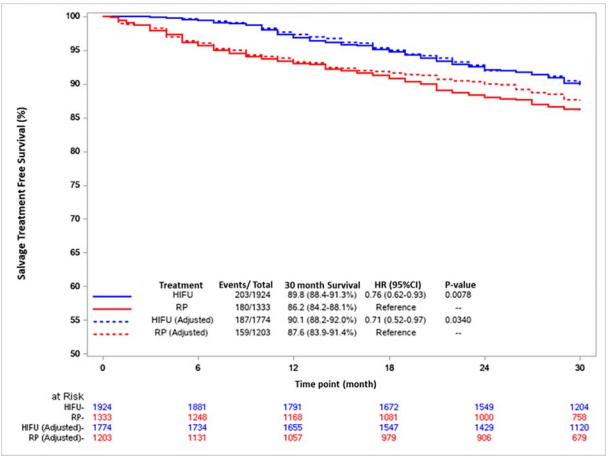
INTRODUCTION AND OBJECTIVE: High-intensity focused ultrasound (HIFU) has emerged as an interesting ablative alternative to standard treatments such as radical prostatectomy (RP) or radiation therapy (RT) for localized prostate cancer (PCa). However no prospective comparative data has been published.

METHODS: HIFI trial (NCT 04307056) is a non-inferiority, prospective, non-randomized, nationwide study performed in 46 French centers comparing HIFU vs RP. Inclusion criteria were age > 69 years in the HIFU arm (2014 French guidelines), low and intermediate risk PCa (cT1-2 NxM0, GG 1 or 2, PSA<15 ng/ml), not eligible for active surveillance, with a maximum of 4/6 positive sextants at post mpMRI systematic biopsies. HIFU (Focal One, Edap TMS, Vaux-en-Velin) was to treat at least 70% of the gland depending on MRI and biopsies. HIFI was conducted under IRB and ethical committee approval (IDRCB:2013-A01042-43). Primary endpoint was salvage treatment-free survival (STFS) defined by the use of any salvage treatment for progression as follows: RP, RT and/or androgen blockade (AB). Salvage treatment was triggered by PSA progression (confirmed nadir PSA+2) or significant cancer at post HIFU for cause biopsies and in the RP arm detectable PSA and/or significant positive margins > 3mm and/or pT3b. All decisions were validated by a local tumor board and reviewed by the national scientific board of the study. Secondary endpoints were metastasis, specific and overall survival (OS), safety and functional outcomes. Patients were followed for at least 30 months.

RESULTS: From April 2015 to September 2019, 3328 patients were included (1967 consecutive HIFU and 1361 RP). Median PSA was 7.1 vs 6.9 (p=0.54), GG2 were 50% (p=0.25), in HIFU and RP arms respectively. 1859 patients had 1 HIFU session (94.7%) while 108 had 2 sessions (5.5%). Median follow up for censored patients was 30 months in both treatment groups. The 30-month STFS rate was significantly higher in the HIFU arm (89.8%) compared with the RP arm (86.2%; HR 0.76; 95%CI 0.61-0.96, p=0.008). This result was confirmed by using a pre-planned propensity score matching, including age and other covariates (BMI, ASA score, Prostate volume, PSA level, Grade Group, and ICS score at baseline) and an adjusted analysis using the same covariates in a regression Cox model for survival analysis (HR 0.71; 95% CI 0.52-0.97, p=0.03) (Fig 1). There was no influence of age on salvage treatment decision. No distant metastasis or PCa-specific death was reported. When adjusted on age, there was no OS difference between groups (HR=2.53; 95% CI 0.95-6.73, p=0.06). Complications >IIIa were reported in 2.7% and 2.1% of patients after HIFU and RP, respectively (p=0.26). At 12 months, urinary continence (UPS score ≤1) was better in the HIFU group (RR=0.76; 95%CI 0.70 -0.83 p<0.001). IIEF-5 score decreased significantly less after HIFU than after RP (median Δ = - 4 vs - 9 , p<0.001). There was no statistical difference in quality of life (EORTC QLQC-30) despite an age difference of 9.6 years between the two arms.

CONCLUSIONS: The HIFI trial is the first prospective study comparing HIFU vs RP as primary treatment for localized prostate cancer. Salvage therapy-free survival after HIFU was not inferior to that reported after RP at the pre- planned 30-month follow-up. Patient-reported outcomes showed a significant lower negative impact of HIFU on functional outcomes such as urinary continence and erectile function.

Promoter: Association Française d'Urologie



Source of Funding: French Ministry of Health

P2-07

APALUTAMIDE FOR HIGH-RISK LOCALIZED PROSTATE CANCER FOLLOWING RADICAL PROSTATECTOMY IN APA-RP: A MULTICENTER, OPEN-LABEL, SINGLE-ARM PHASE 2 STUDY

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INTRODUCTION AND OBJECTIVES: Approximately 25% of patients (pts) with high-risk localized prostate cancer (HR LPC) experience disease recurrence within 2 years following radical prostatectomy (RP). The Apa-RP study (NCT04523207) investigated adjuvant treatment with apalutamide and androgen deprivation therapy (ADT) to determine if this combination improved the biochemical recurrence (BCR)-free rate in participants with HR LPC who had undergone RP, compared with historical data from pts with RP alone.

METHODS: In this multicenter, open-label, single-arm, Phase 2 study conducted at 27 US community urologic practices, treatment-naïve pts with HR LPC who had undergone RP were treated with apalutamide (240 mg; once daily) and ADT for 12 cycles (1 cycle=28 days). The primary endpoint was confirmed BCR-free rate at 24 months, where BCR is defined as two sequential prostate-specific antigen (PSA) levels >0.2 ng/mL. Secondary endpoints included testosterone recovery rate and safety. Modified intention-to-treat analysis set is reported.

RESULTS: 108 pts were enrolled; the median age was 66.0 (range 46.0-77.0) years. The median pre-operative PSA and testosterone at baseline were 7.6 (range 2.2-62.7) ng/dL and 340.0 (range 43.0-939.0) ng/dL, respectively. Confirmed BCR-free rate was 100% at 24 months (90% confidence interval [CI] 93.0, 100.0) (Figure 1A); unconfirmed BCR-free rate at 24 months was 98.4% (90% CI 92.2, 99.7) (Figure 1B). The serum testosterone recovery (≥150 ng/dL) event rate was 76.4% (95% CI 65.0-84.5) at 12 months following treatment completion. Treatment-emergent adverse events (TEAEs) were reported by 99.1% (n=107) of pts during the study; 22.2% (n=24) were Grade 3 -4, and 14.8% (n=16) were serious AEs. 13.0% (n=14) and 10.2% (n=11) of pts required treatment dose reduction/interruption or discontinuation due to AEs, respectively.