HIFI trial : Final results of a large multicentre cohort of 3,328 patients - HIFU vs RP

Monday, March 13th
10:45 at 12:15
Pink Area Coral 1

Presentation by **Pr Rischmann** during EAU session
"Active surveillance and focal therapy: Standard of care?"

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Objectives

Primary objectives: To compare the oncological efficacy of HIFU vs RP on salvage treatment-free survival (STFS) at 30 months.
Secondary objectives: Tolerance

Study design

Patient population : 3,328 patients (HIFU (1967) VS PR (1361)), 46 centres

PCa risk group: low & intermediate risks (GG<3). Not eligible for active surveillance, with < or equal to 4/6 sextants invaded and a prebiopsy mpMRI with or without target.

HIFU: Subtotal (at least 70%), Focal One®, EDAP TMS™, RP: robotic, laparoscopic, open

Treatment strategy : first line treatment

Key results

Primary endpoint: Salvage treatment free survival rate (%): At 30 months, the STFS was significantly higher in the HIFU arm (90.1%) compared with RP arm (86.8%) with a risk of salvage treatment > 1.2-fold higher after RP (HR: 0.78, 95% CI [0.64-0.96], p = 0.02).

Safety

Despite an age difference of 9.6 years between two arms (HIFU 74.7 VS RP 65.1 years):

Erectile dysfunction	70-74 yo: IIEF-5 score decreased significantly less after HIFU than after RP (median Δ = -4 vs -9 p < 0.001)
Incontinence	ICS score was signifcantly lower after HIFU
Quality of life	QLQC-30 summary score: no statistical difference

Performance - PSA & Biopsy

After HIFU, median PSA nadir was 0.34 ng/ml and the positive biopsy rate was 12.5%.

After RP, median PSA was 0.01 ng/ml and positive margins (PM) were reported in 26%.

Patient impact

In selected patient, this trial shows a benefit in favor of HIFU compared to RP.

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Introduction & Objectives

The HIFU study (NCT 04307056) compares sub-total high intensity focused ultrasound (HIFU) vs radical prostatectomy (RP) as a first line treatment in grade groups (GG) < 3 localized prostate cancer. The objectives were to compare oncological efficacy, functional and safety outcomes. Herein, we present the final analysis results at 30 months.

Materials & Methods

HIFI trial is a prospective, non-randomized, open-label, comparative and multicenter non inferiority study. Inclusion criteria were low or intermediate risk PCa (cT1-2 NxM0, GG 1 or 2, PSA < 15 ng/ml) not eligible for active surveillance, with < 4/6 sextants invaded and a pre-biopsy mpMRI with or without target. Patients were > 69 years old in HIFU arm (French guidelines) and had a life expectancy > 10 years in RP arm. HIFU (Focal One®, EDAP TMS, Vaulx-en-Velin) treated at least 70% of the gland (sub-total). HIFI was conducted under IRB and ethical committee approval (IDRCB:2013-A01042-43). Primary endpoint was salvage treatment-free survival (STFS). Detectable PSA for RP and significant cancer at post HIFU biopsies triggered salvage treatment. Secondary endpoints were functional outcomes (IPSS, ICS, IIEF-5 scores, EORTC-QLQC-30) and safety. Patients were followed for at least 30 months. All primary and salvage treatment decisions were validated by a local tumor board.

Results

From April 2015 to September 2019, 3328 patients (HIFU: 1967, RP: 1361) were included in 46 centres. Median age was 74.7 vs 65.1 years ($p > 0.0001$), median PSA was 7.1 vs 6.9 ($p = 0.54$), GG2 were 50% vs 51% ($p = 0.49$), in HIFU and RP arms respectively. At 30 months, the STFS was significantly higher in the HIFU arm (90.1%) compared with RP arm (86.8%) with a risk of salvage treatment > 1.2-fold higher after RP (HR: 0.75, 95% CI [0.64-0.96], $p = 0.02$). After HIFU, median PSA nadir was 0.34 ng/ml and the positive biopsy rate was 12.5%. After RP, positive margins (PM) were reported in 26% and median PSA was 0.01 ng/ml. There was no difference in IPSS and quality of life QLQC-30 summary scores. ICS score was significantly lower after HIFU (0 vs 1, $p < 0.001$). IIEF-5 score decreased significantly less after HIFU than after RP despite an age difference of 9.6 years between two arms (median Δ = -4 vs -9 $p < 0.001$). Clavien-Dindo SAE > 3a rates were 2.74% and 2.13% ($p = 0.49$), after HIFU and RP, respectively.

Conclusions

This large multicentric cohort is the first study comparing RP versus sub-total HIFU as primary treatment. Primary endpoint shows a 30 months SFTS benefit in favor of HIFU. Secondary endpoints show better continence and erectile function outcomes after HIFU. Sub-total HIFU should be discussed as first line treatment in well selected patients.