982. Local antiandrogen therapy, a novel treatment strategy for localized prostate cancer (LPC)

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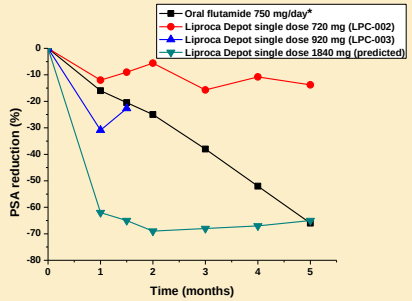
Objectives: The aim of this study (LPC-003) was to evaluate the safety and efficacy of a novel parenteral controlled release (CR) formulation of 2-hydroxyflutamide (2-HOF) (Liproca® Depot) after a single dose injected into the prostate in patients with LPC in terms of local antitumour effect based on histopathology of the surgically removed prostatic tissue, magnetic resonance (MR) imaging (MRI), proton (1H) single-voxel spectroscopy (MRS) and spectroscopic imaging (MRSI).

Materials & Methods: An open, single dose, antitumour effect study where 2-HOF CR-formulation was injected transrectally under ultrasound guidance into the peripheral zone on the affected side of the prostate in patients with LPC (n=18). Patients were followed for 6 weeks after the injection of 920 mg (600-1300 mg) of 2-HOF. At the end of LPC-003, the patient underwent radical prostatectomy. Effect of local antiandrogen therapy was determined by changes in the prostate tissue concentrations of choline, creatine, citrate and polyamines by MR spectroscopy. The efficacy was also measured as change of and prostate volume (PV) and was compared with an earlier phase IIa study (LPC-002). Safety and quality of life were monitored throughout the study.



* Stone NN, Clejan SJ.
J Androl. 1991;12(6): 376-80

Fig. 1. The effect on PSA.

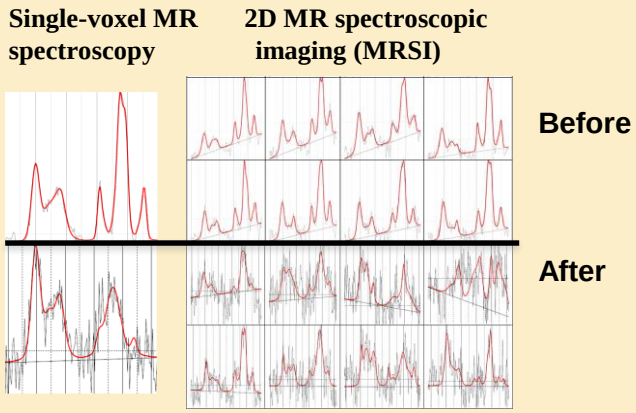


Fig. 2. The effect on prostate tissue metabolites.

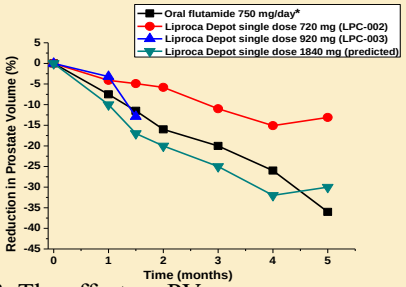


Fig. 3. The effect on PV.

Results: The mean nadir (±SD) reduction of PSA and the prostate volume were 33.1±15.6% and 16.3±12.5%, respectively. No effect was observed on the serum testosterone and plasma concentrations of 2-HOF remained low (< 100 ng/ml). The mean dose of 2-HOF was 920 mg, 28 % higher dose than in the previous Phase IIa trial (720 mg) (LPC-002). The onset of effect was more rapid than after oral treatment (Fig. 1). Local antiandrogen therapy decreased concentration of all MR-detectable metabolites (citrate from 16.2 mM to 6.2 mM) in the whole prostate (global influence) because significant decrease of metabolite-to-water and signal-to-noise ratio can be seen in the all spectra (Fig. 2). Most patients did not report any side effects. Hematuria, typically occured a few days after injection, but disappeared in a few days.

Conclusions: A clear effect was observed on prostate tissue concentrations of metabolites such as citrate, PSA and prostate volume following local antiandrogen treatment.