

85. Focal drug therapy, a novel treatment strategy for localized prostate cancer

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Objectives: The primary objective of this study was to evaluate the efficacy of a single, intra prostatic injection of Liproca® Depot (a novel controlled release formulation of 2-hydroxyflutamide; “2-HOF”) in patients with localized PCa. Secondly, to evaluate safety, quality of life and to determine the pharmacokinetic and pharmacodynamic profiles of Liproca® Depot.

Materials & Methods: The study design was an open, multicenter study. Patients with localized prostate cancer (T1-T2) were being followed to progression or during at the longest 6 months after the injection. Liproca® Depot is administered by local injection, via rectum, with ultrasound guidance, into one of the lobes of the prostate gland where tumor foci had been localized from biopsy mapping.

Efficacy was measured primarily as the proportion of patients showing PSA nadir, and secondly as time to PSA nadir and prostate volume (PV) change.

Results : All planned 24 patients have been included in the study. As of January 18, 2011 data from 20 patients, treated at least 3 months, were accessible for evaluation. The mean (\pm SEM) amount of the Liproca® Depot formulation (paste) given per patient was 3.6 ± 0.2 ml and the mean dose of 2-HOF was 720 mg. A PSA nadir was found in 75% of the treated patients. The mean (\pm SEM) PSA- and PV-reduction, at nadir, of those responding are shown in Fig. 1. The duration of the effect on PSA and prostate volume (mean \pm SEM) are shown in Fig. 2-3. Before the study it was estimated that the mean effect on PSA reduction should be 30-40%, as only a part of one lobe was treated.

There was no effect on the serum testosterone levels nor on IPSS. The plasma exposure of 2-HOF were low compared to oral administration (~5%) (Fig. 4). Most patients have not reported any side effects. Hematuria, typically occurs a few days after injection, but disappears in a few days. Two SAEs have been reported, which both were local infections in the prostate caused by the transrectal injection. The patients recovered completely after antibiotic treatment.

Conclusions: There was a clear antiandrogen response, although in some patients the dosing in relation to the tumor location has not been optimal. It is important to note that the new formulation was administered only to one prostate lobe in this study. Imaging techniques will be of utmost importance in future clinical development and in clinical practice to optimize the dose planning accuracy and thus the treatment effect.

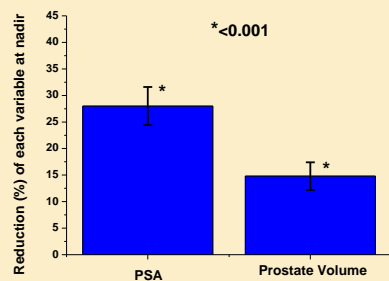


Fig. 1. The effect of Liproca® Depot on PSA nadir and prostate volume

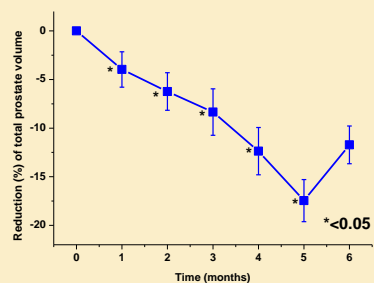


Fig. 2. The effect (mean \pm SEM) of Liproca® Depot on PV

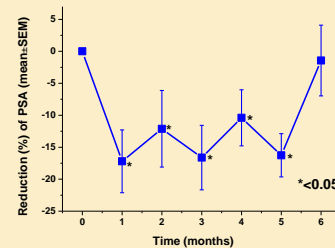


Fig. 3. The effect (mean \pm SEM) of Liproca® Depot on PSA

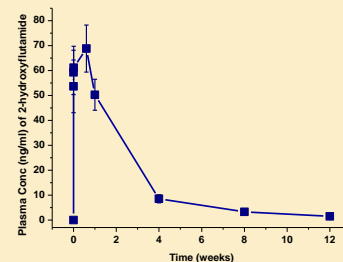


Fig. 4. The mean (\pm SEM) plasma concentration of 2-HOF