Reduction of Rectal Toxicity after Injection of an absorbable Polyethylene Glycol Hydrogel between Prostate and Rectum before Radiation Therapy of the Prostate:

Results of the Multicenter Prospective Phase II Study

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Background: High-dose RT of the prostate, while sparing adjacent OARs, in particular the rectum, poses a huge challenge. The SpaceOAR hydrogel forms a reversible spacer between rectum and prostate after injection The objective of a multicenter European study was to demonstrate the clinical safety and tolerance through a reduction of the dose to the rectum. **Methods:** 52 men with prostate cancer (cT1, cT2) were included in this multicenter prospective phase II study (Heidelberg, Aachen, Amsterdam, Geneva). Before initiating RT, the patients received a perineal injection of the spacer gel, an absorbable polyethylene glycol (PEG) hydrogel, which expands the space between prostate and rectum. All patients had a CT/MRI before injection of the gel and a CT after the injection. Contouring and planning was done in both scans and a dose comparative study was performed. RT was delivered according to the spacer gel plan. A total dose of 78 Gy in 39 fractions was administered with IMRT. Primary endpoints were the functional success, which was achieved with an additional space of ≥7.5 mm between rectum and prostate, and the clinical success, which was achieved with a reduction of rectal V70 by ≥ 25%. Secondary endpoint was the GU/GI toxicity during the therapy as well as 3, 6, and 12 months after the therapy (RTOG/EORTC). A rectoscopy was performed after 12 months. Several procedural improvements were implemented approximately mid-way through the study. These improvements included the required use of a side-fire transrectal ultrasound (TRUS) probe and a stand-off balloon for improved visibility of the perirectal space, and a stepper to hold and stabilize the probe. In addition, the amount of gel per patient was limited to 10ml. Therefore, the analysis was performed in 2 cohorts. 23 patients were in cohort 1 and 29 in cohort 2 (after improvements). **Results**: Four patients (from Cohort 1) were excluded from the Per-Protocol Population. Reasons were no hydrogel injection (n=2), inadvertent rectal wall injection (n=1) and improper polymer reconstitution. Two additional patients were included in all analyses performed using the Per-Protocol Population except the clinical success, due to unavailable dosimetry plans. Finally, 48 patients were evaluated regarding the functional success and 46 regarding the clinical success. Functional success, with an additional space of ≥7.5 mm between rectum and prostate, was achieved in 95.8%. Clinical success rate with a reduction of rectal V70 by ≥25% was 95.6%. On average, a reduction by 60.3% was achieved. 19 patients (39.6%) developed acute grade 1 GI toxicity, 6 (12.5%) developed acute grade 2 GI toxicity. No one developed grade 3 or 4 toxicity. 20 (41.7%) had acute grade 1 GU toxicity, 17 (35.4%) had grade 2, and 1 patient (2.1%) had acute grade 3 GU toxicity. No patient had late GI or GU toxicity > grade 1 at the time of the follow-up. **Summary:** The use of the spacer gel is a safe way to reduce the toxicity to the rectum.