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Multimodal chemo-hormonal-radiation treatment with use of high-dose-rate brachytherapy with Ir192 of localized high- or very-high-risk or locally advanced prostate cancer

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Introduction & Objectives: Treatment high and very high risk prostate cancer is very complicated. Radiation therapy (RT) with long-term ADT is a gold standard, however, low treatment efficiency compared to that in the group of intermediate and low-risk prostate cancer makes us seek new therapeutic approaches. Analysis of publications and reviews of complex treatment with and without chemotherapy, and various types of RT showed a higher efficiency of multimodal therapy.

Materials & Methods: Several randomized phase I-II studies examined the role of neoadjuvant chemotherapy before EBRT/radical psostatectomy (RP) in patients with localized PCa, or as part of a trimodal approach in combination with EBRT/ADT. Phase III studies examined the role of chemotherapy in adjuvant treatment after radical treatment (STAMPEDE, GETUG-12, RTOG 0521). Adjuvant chemotherapy with docetaxel (STAMPEDE) improves progression-free survival (PFS) (HR 0.60; 95% CI 0.45-0.80; P <0.001); 8-year PFS (GETUG-12) was 62% in the combination group (ADT + Docetaxel + Estramustine) versus 50% in the ADT alone group. With a median follow-up of 5.5 y. (RTOG 0521), the addition of docetaxel to ADT significantly improves OS and PFS with tolerable toxicity.
Multimodal treatment of 15 subjects with localized or locally-advanced high- and very-high-risk PCa with neoadjuvant ADT and docetaxel was performed: Degarelix 240 mg at start, then 80 mg monthly; Docetaxel 75 mg/m2 every 3 weeks - 4 cycles. After follow-up examination, patients underwent combined RT: a course of 3D-conformal EBRT to the prostate - 46 Gy in 23 fractions; then, 2 weeks after the first stage - high-dose-rate brachytherapy with Ir^{192}, 15 Gy in one fraction. ADT for all patients is continued (to a total of at least 2 years). Tumor stage was T2c in 2 subjects, T3a in 4 subjects, T3b in 9 subjects.
5 subjects continue treatment (thus 20 subjects were enrolled)

Results: Median PSA before treatment was 51 ng/ml (11.26-300.7 ng/ml); after neoadjuvant therapy - 1.36 ng/ml (0.042-5.61 ng/ml). Median prostate volume before treatment was 45 cm^3 (19-96 cm^3), after neoadjuvant treatment - 25 cm^3 (14-66 cm^3). All patients achieved PSA nadir <0.2 ng/ml after the completion of RT. Observation period is 1-24 months after completion of RT course and 4-27 months from the start of treatment. Biochemical recurrence was never observed.

Conclusions: The combination of taxane-based chemotherapy, ADT with LHRH-antagonists and radiation therapy with the use of HDR-brachytherapy with Ir^{192} or combined RT is very promising. First treatment results at our center confirm high efficiency in terms of PSA decrease and prostate volume. Follow-up and PSA-control are continued. New patients are included in the study with planned 30-patients treatment group

and 30-patients control group of long-term ADT with LHRH-agonists + EBRT.

Long-term results are awaited.