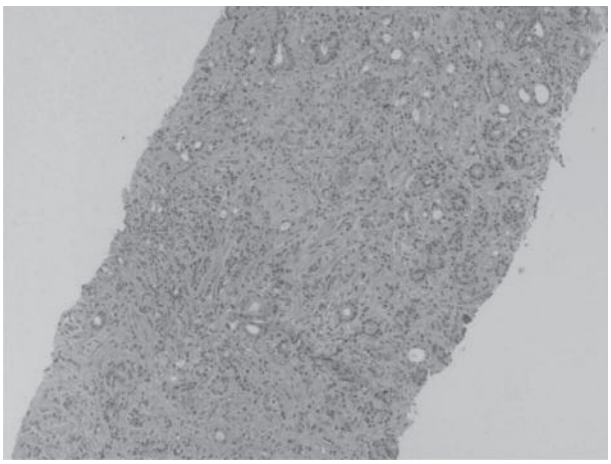

Figure 1. *First diagnosis (biopsy). Fragments of prostate tissue with evidence of differentiated atypical glandular proliferation coherent with adenocarcinoma Gleason Score 4+5=9 (grade group 5). Nuclear morphological detail appears characterized by evident nucleolar expression.*

Figure 2. *Re-biopsy after long-course ADT. Glandular population consisting of small cells, for the most part monomorphic, with a central nucleus and nucleus-cytoplasm ratio shifted in favor of nucleus. Poor nucleolar evidence. Immunohistochemistry: positivity to test for chromogranin confirmed a neuroendocrine origin of lesion.*

adenocarcinoma: rapidly progressive visceral disease, relative low serum PSA concentration and high response rate to platinum-based chemotherapy (1). In the case reported, a re-biopsy was performed for the suspicion of trans-differentiation: local progression and no distant metastases. The new diagnosis has allowed a more correct antiblastic therapy. Many patients undergo for years to hormonal therapies and often are used second-line drugs. It thus increase the time of androgen suppression and therefore the possibility of inducing differentiation. However, the re-biopsy is not a routine. But due to the low complication rate, it can be widely indicated after long course ADT. Nouri *et al*. studied pathways of epithelial-to-mesenchymal transition arguing that androgen-targeted therapy induces epithelial– mesenchymal plasticity and neuroendocrine transdifferentiation in prostate cancer (2). Understanding tumor cell plasticity will be important in further defining the rational use of hormonal therapies. With increasing recognition of cancer as a multifaceted process, the identification and characterization of specific cell phenotypes or the diagnosis of a trans-differentiation occurred, can help clinicians to make more targeted therapies, an opportunity for intervention to prolong survival in metastatic prostate cancer patients (3).

86

LOWER RESPONSE TO INTRAVESICAL ADJUVANT THERAPY IN HIGH-RISK BLADDER CANCER COULD BE RELATED TO THE UROTHELIAL EXPRESSION OF EGFR

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Introduction: Studies on the role of EGFR in non-muscle-invasive bladder cancer (non-MIBC) are lacking. EGFR expression has been determined mainly in tissue specimens of MIBC and its overexpression has been associated with worse prognosis and shorter survival. Urothelial EGFR status after transurethral resection (TUR) of non-MIBC could indicate the risk of recurrence and progression. We investigated the feasibility of EGFR measurement in bladder washings of patients undergoing intravesical adjuvant therapy for non-MIBC and its usefulness in identifying risk subgroups. *Patients and Methods:* Our prospective study included patients after TUR of non-MIBC and healthy controls. Samples of bladder washings were centrifuged at 4°C for 10 minutes at 1500 rpm, washed in cold phosphate buffer saline solution and centrifuged again obtaining a cellular pellet stored at −80°C until RNA extraction was performed by miRNeasy Mini Kit (Qiagen®). A Nanodrop ND-2000 spectrophotometer was used

to check for good quality of RNA. RNA criteria to proceed with reverse transcription to cDNA: minimum 500 ng/ml, protein (260/280) solvents and organic compounds (260/230), contamination ratio 1.7-2.5. The cDNA obtained from RNA by High Capacity cDNA Reverse Transcription Kit (Life Technologies®) was used to perform a gene expression analysis by a real-time PCR, according to the method of the comparative quantification (ΔΔCt) with an endogenous control (cyclophilin). Every reaction was set in triplicate as a further guarantee of quality. The patients were grouped for EAU risk class and maintained in follow-up. *EGFR* expressions were statistically analyzed according to EAU risk groups and to patients' outcomes. *EGFR* gene expression values were expressed in folds of change compared to healthy controls (*EGFR*=1). *Results:* Fifty-eight patients and 21 healthy age-matched controls were entered. An adequate cellular pellet was obtained in 50 patients (86.2%) showing a median *EGFR* expression of 2.0-fold (IQR=0.6-4.3-fold, p=0.0004). The median level of *EGFR* varied considerably among the EAU risk classes. After TUR and adjuvant intravesical therapy, in 22 (55%) out of 40 high-risk patients, EGFR decreased to 1.3-fold (IQR=0.9-1.5-fold), while 18 (45%) showed elevated EGFR, median=4.7-fold (IQR=4.1-11.6-fold). At 25 months median follow-up (IQR=19.0-34.8 months), 20 (40%) patients experienced recurrence and six (12%) progression. Among patients with and those without *EGFR* gene increase, disease in nine (22.5%) and five (12.5%) recurred and in five (12.5%) and one (2.5%) progressed, respectively. *Conclusion:* In our experience *EGFR* expression measurement was feasible in more than 85% of patients and was related to EAU risk classes for recurrence and progression, showing different behavior during intravesical therapy. It was possible to identify a subgroup of high-risk patients overexpressing *EGFR* in spite of intravesical adjuvant therapy. *EGFR* evaluation in bladder washing could represent a repeatable and useful tool to identify a subgroup of patients at risk for progression predicted as not being responsive to intravesical adjuvant therapy and candidates for early radical cystectomy.

We wish to thank GSTU Foundation for data and statistical management.

87
STEREOTACTIC BODY RADIATION THERAPY AS A VIABLE OPTION FOR ELDERLY PATIENTS WITH LOCALIZED PROSTATE CANCER

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Introduction: Radiotherapy (RT) for the treatment of elderly patients with prostate cancer is associated with a cancer specific mortality risk reduction of 2.6% at 10 years, even after adjusting for several confounders, including 12 comorbid conditions. The aim of the present study is to evaluate the efficacy and toxicity of high-dose, non-invasive stereotactic body radiation therapy (SBRT) in a group of elderly patients affected by low and intermediate risk prostate cancer. *Patients and Methods:* Patients aged ≥75 years, with biopsy-confirmed prostate cancer were enrolled. Inclusion criteria were: initial prostate-specific antigen (PSA) ≤20 ng/ml, Gleason Score ≤7, International Prostate Symptom Score ≤7. SBRT was performed with gantry-based volumetric modulated arc therapy (VMAT) in its RapidArc form and the use of flattening filter-free beams. The treatment schedule was 35 Gy in five fractions delivered on alternate days. Planning target volume included the prostate for low-risk and prostate plus seminal vesicles for intermediate risk, with a 5 mm margin of expansion in all directions. Toxicity was recorded according to CTCAE criteria v4.0. Biochemical failure was calculated according to the Phoenix definition. The Expanded Prostate Cancer Index Composite questionnaire was used to record health-related quality of life. *Results:* From May 2012 to April 2016, 50 patients were enrolled in the trial. Twenty-five patients were classified in low-risk group and 25 in intermediate-risk group. The mean age was 78 (range=75-84) years; Gleason score was 6 in 26 and 7 in 24 patients. Median initial PSA was 6.43 (range=2.6-17) ng/ml. Median follow-up was 26 months. Acute toxicity was mild. Rectal toxicity was reported as grade 1 in five (10%) cases and grade 2 in one (2%) cases; grade 1 and grade 2 genitourinary toxicity was described in 13 (26%) and 14 (28%) patients, respectively. In the late setting, three (6%) patients reported rectal grade 1 toxicity. Genitourinary late effects were reported as grade 1 in 13 (26%) patients and grade 2 in two (4%) patient. When evaluating outcome, median nadir PSA was 0.51 ng/ml (range=0.01-3.12) ng/ml. No biochemical relapses were observed during follow-up and all patients were alive at the time of the analysis. *Conclusion:* Gantry-based SBRT with VMAT and flattening filter-free can be considered an effective, non-invasive and safe approach for elderly patients affected by prostate cancer at low and intermediate risk. Randomized trials comparing SBRT with other approaches in this setting are necessary.

88
DIFFERENT MOBILITY OF SEMINAL VESICLE AND PROSTATE

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