SC70 The feasibility and prognostic value of sequential evaluation of EGFR cell expression in bladder washings after transurethral resection of Non-Muscle Invasive Bladder Cancer: A new potential tool to identify patients at higher risk of disease progression

F. Di Maida, A. Mari, C. Scalici Gesolfo, A. Cangemi, R. Tellini, S. Sforza, A. Cocci, R. Allegro, L. Masieri, A. Russo, M. Carini, A. Minervini, V. Serretta (*Firenze*)

Aim of the study: The prognosis of non-muscle-invasive bladder cancer (NMIBC) is not homogeneous. Although the management of NMIBC has significantly improved during the past few years, it remains difficult to predict the oncologic outcomes of such tumors, especially if high-grade NMIBC is present. Aim of the study was to investigate the feasibility of Epidermal Growth Factor Receptor (EGFR) measurement in bladder washings of patients affected by NMIBC and its prognostic role in identifying risk subgroups and predicting disease recurrence and progression.
Materials and methods: Patients with NMIBC treated with trans-urethral resection of bladder tumor (TURBT) from 2012 and 2015 were enrolled. 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, performed by a miRNeasy Mini Kit (Qiagen®). 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. EGFR overexpression was defined as a ≥2.0 folds of change increase compared to healthy controls.
Results: An adequate cellular pellet was obtained in 50 (86.2%) of 58 patients and in 18 (85.7%) of 21 controls. Patients had a median 2.5-, a 1.6- and a 2.8-fold EGFR expression compared to controls before, during and after adjuvant treatment. Overall, 18 (36%) patients had EGFR overexpression before adjuvant treatment and 21 (42%) patients had an increasing trend of EGFR expression after adjuvant treatment. Patients at higher risk had a significantly higher EGFR expression compared to patients at low and intermediate risk when EGFR was measured during (p = 0.04) and after (p = 0.001) adjuvant therapy. At a median follow-up of 35.5 (IQR 19.0–54.8) months, in the high-risk group patients with overexpression had a significantly lower recurrence-free survival (27.9% vs 58%), progression-free survival (75.9% vs 90.2%) and cancer-specific survival (77.7% vs 93.3%) [Figure 1]. At multivariable analysis, EGFR overexpression was an additional independent prognostic factor to the EORTC scoring system of disease recurrence (HR 1.98, 95% CI 1.32–2.97) and progression (HR 1.84, 95% CI 1.27–2.65).

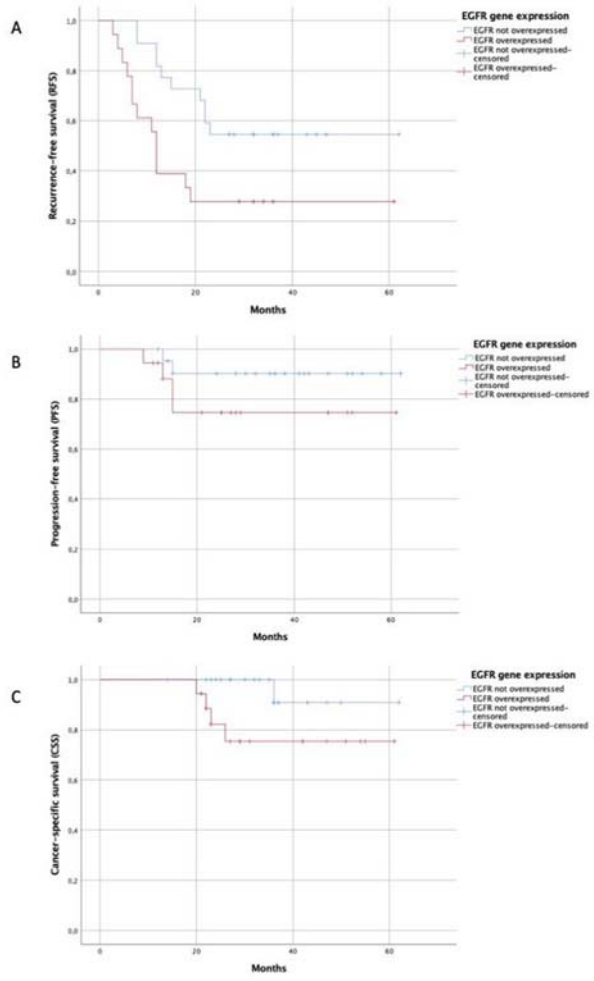

Figure 1: Kaplan-Meier curves depicting recurrence-free survival (A), progression-free survival (B), and cancer specific survival (C), in 40 high-risk patients according to EGFR expression

Discussion: The choice between conservative management and radical surgery in high risk NMIBC remains uncertain. EGFR evaluation in bladder washings might represent an additional parameter to the current clinical tools for an individualized risk stratification.

SC71 Possible role of 5-alpha reductase inhibitors in non-invasive bladder urothelial neoplasm: Multicentric retrospective study

A. Pastore, C. De Nunzio, M. Balzarro, Y. Al Salhi, A. Fuschi, A. Martoccia, G. Velotti, N. Amigoni, A. Tubaro, W. Artibani, A. Carbone (*Latina*)

Aim of the study: About 75% of urothelial carcinoma of the bladder are non-invasive (non-muscle-invasive bladder cancer, NMIBC), therefore limited to mucosa (Ta or CIS) or sub-mucous (T1). Several studies have shown that androgens are implicated in bladder carcinogenesis: the increase in androgen expression and androgen receptors have a positive effect on oncogenic expression, which can lead to an increase of those specific proteins that promote the proliferation, invasiveness and motility of neoplastic cells. The aim of the study was to evaluate whether 5-alpha reductase inhibitors (5-ARI) have a role in NMIBC.
Materials and methods: The retrospective analysis was conducted on 293 patients diagnosed with NMIBC who underwent transurethral resection of the bladder (TURB), from 2013 to 2018. The study was

conducted evaluating demographic characteristic of each patient, intraoperative and postoperative parameters. We analyzed the number of resections, number of total recurrences, time of recurrences, and histopathology details. The population was divided into two main groups: treated and untreated whit 5-ARIs. Patients were treated with dutasteride for lower urinary tract symptoms due to prostatic hyperplasia (mean treatment time 16.8 months) The patients were followed according to EAU follow-up guidelines for NIMBC. Mean follow-up time was 29.5 months (range 24–50 months).
Results: No significant differences were observed among the different groups at baseline. The group treated with 5-ARIs presented a lower rate of recurrences (14.78%) than the untreated group (37.11%). Regarding the mean number of recurrences statistically significant difference was observed between the untreated (1.944 ± SD 0.141) and the treated group (1.235; ± SD 0.206; p-value: 0.0066), respectively. Furthermore, evaluating the recurrences, the 5-ARIs group showed a lower T stage when compared to the untreated group (p-value = 0.037). No significant differences were obtained regarding the grade of the recurrences (p-value = 0.756).
Discussion: Long-term treatment with 5-alpha-reductase inhibitors might play a role in reducing the risk of tumour recurrence and pT and extension of the lesions. Starting from this experience, a long-term, randomized prospective study could definitively assess the possible role of this widely used drugs in NMIBC.

SC72 Bladder cancer and aploidentical bone marrow transplant with immunotherapy: Which is the relationship?

J. Rossi de Vermandois, G. Casarola, A. Carotti, G. Cochetti, M. Del Zingaro, A. Boni, I. Soli, M. Martelli, B. Falini, E. Mearini (*Perugia*)

Aim of the study: Lymphocytes T replete Aploidentical Transplantation (AT) after bone marrow ablation by radiotherapy and chemotherapy is the gold standard treatment for haematological cancer when an allogeneic transplantation is necessary. Nevertheless, this type of AT is affected by high rate of recurrence and potentially lethal infections. For this reason, an immunotherapy including an inoculation of lymphocytes T-regulator and T-conventional was added in order to decrease the risk of transplant rejection and the Graft versus host disease leading to survival improvement. Primary aim was to analyze the incidence of secondary urological neoplasms in patients undergone bone marrow transplant from Hla aploidentical donor for haematological cancer. Secondary aim was to investigate the potential relationship between bone marrow transplant from Hla aploidentical donor and secondary urological malignancies.
Materials and methods: Patients undergone AT with lymphocytes T regulator and T-conventional were prospectively enrolled from September 2008 to December 2018. Those who had previous or synchronous malignancies were excluded. The demographic and pathological data were analyzed focusing on the age at the time of tumor diagnosis, the haematological disease that led to bone marrow transplantation, the timing between the transplantation and the urological tumor diagnosis, the histological type, the immunosuppressive regimen, any episode of rejection, the age and sex of the donor, any early and late complication and finally the cancer specific survival related to haematological and urological cancer. For statistical analysis, the software SPSS ver. 21 (SPSS Inc., Chicago, IL, USA) assuming significance cut-off value $P < 0.05$.
Results: All data were resumed in table. 179 patients (86 female and 93 male) were included. Of these, 17 (24%) underwent TURB for bladder cancer. Histologic examination revealed 16 low-grade urothelial carcinoma and one case of recurrence of lymphatic acute leukemia with atypical localization. These secondary bladder neoplasms arose after mean time of 30.7 months (3–77) from bone marrow transplantation. The Wilcoxon test revealed that the patients undergoing bone marrow transplantation had a significant correlation with the development of bladder cancer (p = 0.011).

Age group	18-34 y	34-49 y	50-65 y
n.° patient	48 (26.8%)	60 (33.5 %)	71 (39.7%)
Ematologic desease	34 LMA 13 LLA 1 LH	36 LMA 18 LLA 4 LH 2 MM	53 LMA 13 LLA 1 LH 4 MM
Follow-up	32.2 months (1-119)	32.95 months (1-113)	25.76 months (1-111)
secondary malignacy	0 (0%)	0 (0%)	17 (24%)
Time secondary malignacy			30.7 months (3-77)

Discussion: To our knowledge, the incidence of urological tumor secondary to bone marrow transplantation for haematological cancer was evaluated for the first time in Literature. We found a significant correlation between AT with lymphocytes T regulator and T-conventional and the development of bladder cancer.

SC73 Comparison of 2 newly developed bladder cancer tests in the follow up of patients with non muscle invasive bladder cancer (NMIBC)

C. D'Elia, E. Trenti, S. Pycha, C. Mian, C. Schwienbacher, E. Hanspeter, A. Pycha (*Bolzano*)

Aim of the study: Cystoscopy is the most efficient method currently available for the diagnosis of primary or recurrent Bladder cancer (BC), but it is invasive and causes significant discomfort to the patient. Furthermore, flat tumors or carcinoma in situ may be difficult to detect. Urinary cytology is not invasive and very effective in diagnosing high grade lesions but it has a low sensitivity in low grade tumours. The limitations of both, cytology and cystoscopy, for monitoring patients with bladder cancer led to the development of new urine tests for the early detection of BC. The aim of this study was to compare the diagnostic value of two newly developed urine tests, the mRNA based Xpert BC Monitor and the DNA methylation based Bladder Epicheck in patients under follow-up after TUR.
Materials and methods: 230 patients (median age 73 yrs, range 43–90) under follow up for NMIBC were studied prospectively. Samples were analyzed with the Bladder Epicheck Test, the Xpert BC Monitor and voided urinary cytology. Subsequently to urine collection, the patient underwent cystoscopy and if cystoscopically positive, a TUR-B. Cytologies were evaluated according to the Paris System of reporting cytology. For the Bladder Epicheck Test a software calculates the EpiScore, a number between 0 and 100 representing the overall methylation level of the sample. If the EpiScore is equal or above 60 it is considered positive. The results of the Xpert BC Monitor are interpreted by the GeneXpert® Instrument System and given as LDA totals and Analyte Results on the Test Report. A cut-off is set at a LDA of >0.5. Sensitivity, specificity, PPV and NPV of Bladder Epicheck, Xpert BC Monitor and cytology were calculated using cystoscopy/histology as gold standard.
Results: 9.3% of the patients had to be excluded due to insufficient DNA in the Bladder Epicheck Test. 53 out of 230 remaining patients had histologically verified BC of the bladder, 33 low grade (LG) and 20 high grade (HG); 177/230 patients were negative cystoscopically and/or histologically. Of the 53 patients with BC, 31 (58.5%) were found positive for Bladder Epicheck and 34 (64.1%) for Xpert BC Monitor and 15 (28.3%) for cytology. The sensitivity of Bladder Epicheck increased from 45.5% for LG to 80% in HG tumours, whereas the sensitivity of