Bladder Cancer: Invasive V

Podium 36

Sunday, April 30, 2023 **3:30 PM-5:30 PM**

PD36-01

NECTIN-4 PROTEIN EXPRESSION IN MUSCLE INVASIVE BLADDER CANCER - SELECTIVE PREDICTOR OR CONSISTENTLY EXPRESSED IN TUMOR TISSUE?

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INTRODUCTION AND OBJECTIVE: Nectin-4, a membrane protein involved in cell adhesion, has been recently introduced as a target of the novel antibody drug conjugate Enfortumab-Vedotin (EV). However, uniform Nectin-4 overexpression in BC was reported and no predictive capacity from Nectin-4 staining was reported. In the present trial we aimed to determine expression in two independent BC cohorts and further evaluate an alternative IHC interpretation approach for Nectin-4 in advanced BC.

METHODS: The study included two independent cohorts consisting of n=97 and 103 patients (70x male, median age 65.5 years, 31x T≤2 – 43x T3 – 23x T4, 76x G>2, 11x M1 and 79x male, 69 years, 31x T≤2 – 48x T3 – 24x T4, 78x G>2, 9x M1, median follow-up 44.5 months, respectively) who underwent radical cystectomy for invasive BC. Tissues from histologically proven BC and from benign urothelium (n=22 and 39) were processed to a tissue microarray and immunohistochemically stained by reported methods (polyclonal rabbit antibody, dilution 1:2000, incubation 16h at 4°, quantified by the histochemical scoring system/H-score 0-300). Results were transferred into four classes: Each cohort was divided into four 25%-classes of successive increasing staining and distribution was demonstrated for each the two BC cohorts. Results were compared to clinical and pathological features.

RESULTS: Mean expression scores in BC and parallel benign urothelium tissue were 133 and 81/157 and 114 ($p<0.005/0.002$) with benign urothelium expression correlated with that of corresponding BC (<0.02). The expressions within each patient cohort are lined up as follows: Expression in 25% of the cohort scored low (0-99), of 25% 100-119, of 25% 120-189 and of 25% strong (190-300) in the first cohort, the second distributed low (0-99) of 25%, 25% 100-165, 25% 166-209 and 25% strong 210-300. There were no significant associations of Nectin-4 expression to demographic or clinical patients' data. Moreover, there was no clinical association between Nectin-4 expression and survival.

CONCLUSIONS: Nectin-4 overexpression in BC is accompanied by parallel strong expressing benign urothelium in the same individual. While the distributions of expression in independent BC cohorts are similar, the assumption of Nectin-4 overexpression in all BC may be overestimated. A considerable share of even advanced BCs exhibit Nectin-4 only to a low or a medium level. This observation may support efforts of adapted reintroduction of Nectin-4 as a predictive biomarker for EV.

Source of Funding: Sources of Funding are coming from University Hospital Tuebingen

PD36-02

A COMPOSITE BIOMARKER APPROACH TO SPARE NEOADJUVANT CHEMOTHERAPY IN SELECT MUSCLE-INVASIVE BLADDER CANCER PATIENTS

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INTRODUCTION AND OBJECTIVE: Clinical guidelines recommend neoadjuvant chemotherapy (NAC) for the treatment of muscle-invasive bladder cancer (MIBC). However, NAC prior to radical cystectomy (RC) is associated with treatment-related toxicity and confers a modest survival benefit. Here, we aimed to identify MIBC patients who may avoid NAC by combining circulating tumor cell status and molecular subtypes in a composite biomarker approach.

METHODS: TURBT tissue specimen were collected from clinical stage T2-T4aN0-N1M0 MIBC cases that were included within the *CirGuidance* study (NL3954), a prospective trial that analyzed circulating tumor cell (CTC) status in a patient's blood sample using the CELLSEARCH system. For the present study, transcriptome-wide expression profiling was performed on 234 TURBT samples using an array-based approach. Molecular subtypes, long non-coding RNA (lncRNA) based FGFR3+ status and gene signatures were determined as described previously (de Jong *et al.*, Genome Med. 2019). The primary endpoint of this study was cancer-specific mortality (CSM), calculated as the date of study inclusion till date of bladder cancer related death. Median follow-up was 28.8 (IQR: 16.6-40.2) months.

RESULTS: Of 234 patients, 21 (9%) were treated with NAC and RC, while 213 (91%) received RC alone. A CTC-negative status was observed in 172 (81%) of RC-only cases. Molecular subtyping identified 28 luminal FGFR3+ cases with high FGFR3, SHH and p53 pathway activity, and lower EMT hallmark scores. Adjusting for clinical risk factors, both CTC and FGFR3+ status were significant predictors for cancer specific mortality on MVA ($p<0.05$). Of interest, the subgroup of FGFR3+ cases that were CTC-negative (N=26) showed most favorable outcomes with only one CSM event after a median of 33.4 (IQR: 24.8-44.5) months of follow-up.

CONCLUSIONS: Using a composite biomarker approach of blood-based CTC status and molecular subtyping, we identified a biologically distinct subgroup of MIBC with favorable prognosis after RC-only, validating the performance of a previously developed lncRNA based FGFR3+ classifier. Clinical trials which withhold NAC from CTC-negative, FGFR3+ MIBC patients are warranted.

Source of Funding: Gene expression profiles were generated using the Decipher Bladder assay

PD36-03

VESICAL IMAGING REPORTING AND DATA SYSTEM (VI-RADS) COULD PREDICT THE PROGNOSIS OF BLADDER CANCER PATIENTS RECEIVED RADICAL CYSTECTOMY

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INTRODUCTION AND OBJECTIVE: Vesical Imaging Reporting and Data System (VI-RADS) has shown a good potential in determining muscle-invasive bladder cancer (MIBC) patients. However, whether the VI-RADS could predict the prognosis of radical cystectomy (RC) patients has not been reported.

METHODS: We retrospectively analyzed the information of bladder cancer patients admitted to our center from June 2012 to June 2022. All patients who underwent multiparametric magnetic resonance imaging (mpMRI) and underwent RC were included. The exclusion criteria were: 1) Pathology was not urothelial carcinoma. 2) Receive neoadjuvant chemotherapy. 3) VI-RADS could not be evaluated. 4) The follow-up data was incomplete. VI-RADS were scored by two radiologists, blinded to clinical data. Patients' clinical features,