MP08-03

PROGRESSION-FREE SURVIVAL AS SURROGATE ENDPOINT IN HIGH-RISK NON-MUSCLE INVASIVE BLADDER CANCER STUDIES: RESULTS FROM A MACHINE LEARNING-BASED ANALYSIS OF A LARGE MULTI-INSTITUTIONAL DATABASE

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INTRODUCTION AND OBJECTIVE: Progression-free survival (PFS) is often used as surrogate endpoint in clinical trials investigating treatment effectiveness in patients affected by high-risk non-muscle invasive bladder cancer patients (HR-NMIBC). However, the goodness of such surrogate endpoint and its association with overall survival (OS) is challenged by conflicting results showing lack of OS advantage, even in presence of PFS improvement. We aimed to test the effect of time-to-progression on OS in a large cohort of HR-NMIBC treated with intravesical BCG.

METHODS: We included patients at first diagnosis of T1 HR-NMIBC after TURB. All procedures were performed at 18 different tertiary institutions between 2002 and 2012. Progression was defined as the time form HR-NMIBC to muscle invasive bladder cancer (MIBC) development. All patients who experienced a progression underwent radical cystectomy. Machine learning approach, based on random survival forest (RSF) was used to rank covariates based on OS prediction. Then survival tree data mining technique was used to obtain classes based on time-to-progression. Finally, Cox-regression models were deployed.

RESULTS: Overall, 1510 patients were included. During a median follow up of 49 months, 485 patients progressed to MIBC, while 163 patients died. The median time to progression was 82 months. In RSF time-to-progression and age were the most predictive covariates of OS. The C-index resulted to be 0.814 on the training set and 0.726 on the test set. Survival tree including these two covariates defined 5 groups of risk: PFS $\geq$62.5 months and age $<$77.5 years (reference), PFS $\geq$62.5 months and age $\geq$77.5 years (HR: 9.0, $p<0.001$), PFS between 10.5 and 62.5 months and age $<$79.5 years (HR: 14.3, $p<0.001$), PFS $<$10.5 months and age $<$79.5 (HR: 44.9, $p<0.001$) and PFS $<$62.5 month and age $\geq$ 79.5 years (HR: 58.7, $p<0.001$). In multivariable Cox's regression models accounting for progression status as time-dependent covariate, longer PFS (as continuous covariate) was associated with longer OS (HR: 0.9, $p<0.001$). Results were virtually the same after PFS stratification (PFS$\geq$ 10.5 months as reference): PFS between 10.5 and 62.5 months (HR: 0.4, $p<0.001$) and PFS $\geq$62.5 months (HR: 0.2, $p<0.001$).

CONCLUSIONS: Our results suggest that PFS represent a good surrogate endpoint of OS considering its strong independent predictor status and the high accuracy. Future studies evaluating the efficacy of HR-NMIBC treatments can safely rely on PFS as surrogate of OS.

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MP08-04

USE OF ANTIBIOTICS IN PATIENTS UNDERGOING FOLLOW-UP FOR NON-MUSCLE INVASIVE BLADDER CANCER WITH EITHER FLEXIBLE CYSTOSCOPY OR THE URINARY BIOMARKER TEST XPERT® BLADDER CANCER MONITOR: A SECONDARY OUTCOME FROM A RANDOMISED CLINICAL TRIAL

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INTRODUCTION AND OBJECTIVE: Patients with non-muscle-invasive bladder cancer (NMIBC) have a high recurrence rate, which leads to frequent flexible cystoscopies (FC). Aside from the burden of undergoing FC, there is a risk of urinary tract infection (UTI) following FC. Follow-up of NMIBC with non-invasive urinary biomarker tests could reduce the number of FCs, and thus potentially the need for antibiotics due to UTI. Furthermore, because UTIs are among the most common infections, any reduction in incidence could reduce development of multiresistant uropathogenic bacteria.In this study, a secondary outcome from the DaBlaCa-15 trial is reported. The objective was to compare the number of patients with collected prescriptions for antibiotics for UTI in patients followed with FC versus patients followed primarily with the urinary biomarker test Xpert® Bladder Cancer Monitor (XBCM) (CE-IVD. In Vitro Diagnostic Medical Device. May not be available in all countries. Not available in the United States.).

METHODS: A two-arm randomised non-inferiority trial enrolling 392 patients with previous high-grade NMIBC was conducted. In the intervention arm, patients were followed with XBCM every four months with only one yearly pre-scheduled FC. Patients in the control arm underwent FC every four months for two years. The number of patients who collected prescriptions for UTI during the study period was compared both peri- and post-FC and for visits where a FC was not pre-scheduled.

RESULTS: During follow-up, 23.7% of patients in the intervention arm collected a prescription compared to 31.0% in the control arm (RR 0.76; 95% CI 0.55-1.06; $p=0.11$). When analysing visits without a pre-scheduled FC, 6.3% of patients in the intervention arm collected a prescription in the 14 days after a visit versus 13.4% in the control arm (RR 0.47; 95% CI 0.25-0.90; $p=0.02$). Similarly, the peri-FC use of antibiotics was 7.9% in the intervention arm, compared to 15.0% in the control arm (RR 0.53; 95% CI 0.29-0.94; $p=0.03$). A reduction in the number of FCs performed in the intervention arm was observed (39.1% versus 98.3%; $p<0.0001$).

CONCLUSIONS: The findings of the present study support the hypothesis that replacing cystoscopy with XBCM can reduce the use of antibiotics for UTI during follow-up of NMIBC. Thus, the morbidity of follow-up of NMIBC with FC can be reduced, resulting perhaps in less development of multiresistant uropathogenic bacteria and increased quality of life.

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MP08-05

PHASE 1A/B STUDY OF INTRAVESICAL INSTILLATION OF TARA-002 IN ADULTS WITH HIGH-GRADE NON-MUSCLE INVASIVE BLADDER CANCER

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INTRODUCTION AND OBJECTIVE: Bladder cancer is the most common malignancy involving the urinary system, resulting in ~18,000 US deaths/year; ~70% of new urothelial bladder cancer cases are classified as non-muscle invasive bladder cancer (NMIBC). TARA-002 is a lyophilized biological preparation for instillation

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