Correlation Between Overall Survival and Bladder-Intact Event-Free Survival in Cystectomy-Ineligible/Refusal Non-Metastatic Muscle-Invasive Bladder Cancer Patients in Sweden

Kishan HM Ankri, Oscar Laurin, Simana Basileva, Sarah Côté, Simona Baculea, Robert Szulkin, Frida Schain, Christina V Jones, Markus Aly

INTRODUCTION

- Radical cystectomy is recommended treatment for non-metastatic muscle-invasive bladder cancer (MIBC). However, this surgical procedure is associated with significant risk for morbidity and mortality.
- In Sweden, patients considered medically unfit or those who refuse surgery are instead offered bladder-preserving treatment options instead including radiotherapy and/or chemotherapy.
- Bladder-intact event-free survival (BI-EFS) has been introduced as a primary endpoint in clinical trials assessing treatment outcomes for MIBC patients. It is defined as the survival from treatment initiation until histologically confirmed refractory/recurrent MIBC or nodal/metastatic disease, radiotherapy, or death.
- However, the relationship between BI-EFS and overall survival (OS), a well-established clinical endpoint in cystectomy-ineligible/refusal MIBC patients has not been established. This study evaluated the correlation between these endpoints in cystectomy-ineligible/refusal MIBC patients based on real-world data in Sweden.

METHODS

- **Data Sources**: Patients ≥ 18 years of age with bladder cancer were identified in the Swedish Cancer Register and linked to the National Patient Register, Prescribed Drug Register & Cause of Death Register.
- **Patient Population and Study Design**: The study population included patients (i) with a bladder cancer diagnosis registered between January 1st 2006 and December 31st 2017, (ii) who had tumor stage T2a-4 N0-3 M0 at diagnosis, (iii) were aged 18 years or above at primary treatment initiation (index date), and (iv) were followed-up for at least 2 years after diagnosis. Patients who underwent any subsequent radical surgery or were not followed-up for at least 2 years after diagnosis were excluded.
- **OS was defined as the time from index date until death from any cause or censoring (end of follow-up or emigration), whichever occurred first**.
- **BI-EFS was defined as survival time from index date to the date of earliest evidence of any of the following events: (i) histologically proven recurrence of MIBC and clinical evidence of nodal/metastatic disease using a register-based proxy defined as record of a new MIBC diagnosis or the initiation of systemic chemotherapy, immunotherapy and/or targeted therapy without concomitant radiotherapy, (ii) radical cystectomy, or (iii) death from any cause**.
- **An iterative multiple imputation method for censored outcomes measured the nominal scores rank correlation between BI-EFS and OS.**

RESULTS

- **Patient characteristics**: A total of 337 patients were included in the study, where 286 had T2 and 51 had T3 or T4a stage at diagnosis (Table 1).
- **Median age at diagnosis was 77 yrs (IQR 71-82), and 39.2% of patients had a Charlson Comorbidity Index of ≥3.**
- **BI-EFS events**: The most common BI-EFS event captured was death in both T2 patients (89%) and T3+T4a patients (77%) (Table 2).
- **Median BI-EFS was 0.85 yrs (95%CI 0.71-1.05) for T2 patients and 0.50 yrs (0.22-0.98) for T3+T4a patients** (Figure 1a).
- **Median time to BI-EFS event, m (95% CI)**
  - T2: 8.75 (7.14-10.30)
  - T3+T4a: 2.2 (2.6)

- **OS in cystectomy-ineligible/refusal MIBC patients**: Median OS was 1.11 yrs (95%CI 0.91-1.33) for T2 patients and 0.76 yrs (95%CI 0.51-1.40) for T3+T4a patients (Table 1).

- **Correlation between BI-EFS and OS**: The correlation between OS and BI-EFS was 0.82 (95%CI 0.77-0.85) for T2 and T3+T4a patients, respectively. The correlation was 0.84 (95%CI 0.80-0.87) for OS and the BI-EFS for T2 patients, and 0.85 (95%CI 0.44-0.79) for T3+T4a patients, respectively (Table 2).

- **Strong correlation supports the use of BI-EFS as a surrogate endpoint for OS in similar patient populations.**

CONCLUSIONS

- A strong correlation supports the use of BI-EFS as a surrogate endpoint for OS in similar patient populations.
- This real-world study included a heterogeneous population of MIBC patients, with varied treatment intent & comorbidities.
- High age and comorbidities in this patient group may have contributed to the short median survival time, and in turn the strong correlation between BI-EFS and OS.

REFERENCES: