**The Bristol Bladder Trial: Five-year outcomes in patients treated with neoadjuvant cabazitaxel and cisplatin chemotherapy for muscle invasive transitional cell carcinoma of the urinary bladder**

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**Background:** Neoadjuvant cisplatin-based combination chemotherapy (NAC) improves survival in muscle invasive bladder cancer (MIBC). However, response rates and survival remain suboptimal. We sought to evaluate the efficacy of cabazitaxel with cisplatin in this patient group. These patients have now been followed for survival status for 5 years post NAC and radical cystectomy.

**Methods:** This was a single arm (Simon 2 stage), phase 2 study. Patients with MIBC were included if fit to receive NAC and to undergo radical cystectomy. 26 evaluable patients were required to detect an objective response rate (ORR) of >35% with 80% power. ORR was defined as pathological complete response (pCR) plus partial response (pathological downstaging, ≥T2 at diagnosis to ≤T1 at cystectomy). Treatment was with cisplatin 70mg/m2 and cabazitaxel 15mg/m2 on day 1 of a 21-day cycle, for 4 cycles prior to surgery. Toxicity was recorded using CTCAE v.4.03. QoL data was assessed during and after chemotherapy using EQ-5D-5L and EORTC-QLQ-C30, BLM30 questionnaires. Patients were followed for 5 years post cystectomy for progression free survival (PFS) and overall survival (OS).

**Results:** ORR was seen in 15 out of 26 evaluable patients, 57.7%, with 24.6% achieving pCR. 1 out of 15 patients who achieved ORR died due to disease progression in the 5 year follow up period. The median PFS and OS were not reached by the 5 year follow up time point with a 5 year survival rate of 65.4% being seen in this patient cohort. Median OS in non-responders (11 patients) was 20.5 months and 5 year survival rate for the non-responders was 36.4% compared to 93.3% for responders.

**Conclusions:** Neoadjuvant cabazitaxel with cisplatin chemotherapy is an effective regimen with 65.4% patients alive and progression-free at 5 years. It also indicates that ORR (and not just pCR), is a good predictor of patient survival at 5 years post radical cystectomy with only 1 out of 15 patients who achieved ORR progressing and dying in this period. However, in current clinical practice, there are no validated predictive biomarkers regarding potential response to NAC. Taken together with our previously published data, cabazitaxel with cisplatin as neoadjuvant chemotherapy is a safe, well-tolerated and effective regimen and should be compared to the regimens e.g. cisplatin/gemcitabine considered as standard in this setting.