First results of NURE-Combo: A phase 2 study of neoadjuvant nivolumab (NIVO) and nab-paclitaxel (ABX) followed by postsurgical adjuvant NIVO in patients (pts) with muscle-invasive bladder cancer (MIBC).

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Background: MIBC is a systemic disease with a high risk of recurrence after radical cystectomy (RC), that represents the standard of care (SOC) for cisplatin-ineligible pts. Initial data suggest that ABX is active in combination with pembrolizumab in advanced urothelial carcinoma (UC; PMID:32979512). We report results from a phase 2 trial of NIVO + ABX followed by RC and adjuvant NIVO in pts with MIBC (NCT04876313). **Methods:** Eligible pts who were cisplatin unfit or declined cisplatin-based treatment had previously untreated MIBC (clinical stage T2-T4a, N0-1, M0, assessed via CT and MRI scan), Eastern Cooperative Oncology Group performance status ≤ 1, and predominant (> 50%) UC histology. Pts received 4 cycles of NIVO 360 mg Q3W + ABX 125 mg/m2 on Day 1 and 8, Q3W, followed by RC and by 13 administrations of adjuvant NIVO 360 mg Q3W. The primary endpoint was the pathologic complete response rate (ypT0N0; H0: ≤20% and H1≥ 38% in a 2-stage design: ≥9 ypT0N0 were required in stage 1+2). Secondary endpoints were major pathological response (ypT≤1N0), safety (CTCAE v5.0) and event-free survival (EFS). Tumor biomarkers included comprehensive genomic profiling (CGP) and PD-L1 expression, and circulating tumor DNA monitoring (Signatera). **Results:** 31 pts were enrolled from 12/2021 to 06/2023; 17 (54.8%) had a cT3-4 stage, 14 (45.2%) a cT2, 2 (6.4%) had N1 stage, 15 (48.4%) had a variant histology component. All 31 pts concluded the neoadjuvant treatment, 29 having pathological response at data cutoff. A total of 4 pts (14.8%) received <4 cycles of neoadjuvant treatment due to treatment-related adverse events (TRAEs). Four patients had G3 TRAEs, including neutropenia (2), asthenia (1), increased AST/ALT (2), neurotoxicity (1) and acute renal failure (1). The median time from start treatment to RC was 4 months (IQR: 3-4). In total, 11 pts (38%; 95%CI 20.3-55.6) achieved an ypT0N0 response and 21 (72%; 95%CI 55.3-88.3) an ypT≤1N0 response. No disease progressions (PD) occurred during neoadjuvant treatment. After a median follow-up of 10.6 months (IQR: 8-16), one pt had a PD: 12-month EFS was 96.4% (95%CI: 89.9-100). Mean tumor mutational burden (TMB) was 12.3 mut/Mb for ypT0N0 responders vs 5.8 mut/Mb for non-responders. All pts with MRI complete response had a ctDNA-negative assay post neoadjuvant NIVO-ABX. **Conclusions:** The first results from Nure-Combo trial suggest that this novel chemo-immunotherapy combination with NIVO+ABX could be an effective and safe perioperative strategy in pts with MIBC with sustained efficacy post-RC. These results could expand the opportunities of chemotherapy combinations in cisplatin-ineligible pts. Results also strengthen the role of clinical complete response to envision organ-sparing approaches. Clinical trial information: NCT04876313. Research Sponsor: None.