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High- vs low-dose pre-operative ipilimumab and nivolumab in locoregionally advanced urothelial cancer (NABUCCO cohort 2)

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Background

Standard treatment for patients (pts) with stage III (cT3-4aN0M0 or cT1-4aN1-3M0) urothelial cancer (UC) is cisplatin (cis)-based chemotherapy followed by radical surgery. A substantial number of pts is unfit for cis-based chemotherapy. In NABUCCO cohort 1, 24 pts were treated with pre-operative day 1 ipilimumab 3 mg/kg (ipi 3), day 22 ipi 3 + nivolumab 1 mg/kg (nivo 1), and day 43 nivolumab 3 mg/kg (nivo 3), showing encouraging efficacy (46% pathological complete response (pCR, ypT0N0)). Recent data in pre-operative trials for other cancer types suggests that a lower dose of ipilimumab has equal activity and is better tolerated. In cohort 2, we set out to identify if this is also true in stage III UC, by testing two different dosing schedules for ipi + nivo.

Methods

NABUCCO is a multicentre, phase Ib/II, pre-operative trial. In cohort 2, thirty stage III, cis-ineligible (or refusal) UC pts were randomly assigned (1:1) to arm A: two cycles ipi 3 + nivo 1 (day 1, 22) and nivo 3 (day 43); or arm B: two cycles ipi 1 + nivo 3 (day 1, 22) and nivo 3 (day 43). The primary endpoint was pCR rate. Secondary endpoints include feasibility (resection within 12 weeks) and grade 3–4 immune-related adverse events (irAEs).

Results

Thirty pts were randomly assigned to arm A (n=15) or arm B (n=15). 26/30 (87%) pts received all 3 treatment cycles. Four pts missed one or more cycles of therapy due to irAEs. 26/30 pts underwent radical surgery, 24 within twelve weeks after start of treatment. One patient (arm B) progressed before surgery (evaluable, non-response) and three pts (1x arm A and 2x arm B) refused radical surgery while responding radiologically; one of these (arm B, baseline cT4aN3) had a lymph node dissection showing a micrometastasis (evaluable, non-response). Response was evaluable in 28 pts. In arm A, 6/14 (43%) pts had a pCR; 8/14 (57%) had a pCR or ypTisN0. In arm B, 1/14 (7%) had a pCR whereas 3/14 (21%) had a pCR or ypTisN0.

Conclusions

We observed a pCR in 6/14 (43%) evaluable pts treated with ipi 3 + nivo 1 (arm A). In contrast, a pCR was observed in 1/14 (7%) evaluable pts treated with ipi 1 + nivo 3 (arm B). Our data suggest that ipi 3 + nivo 1 is more efficacious than ipi 1 + nivo 3 as pre-operative treatment in stage III UC. *Data for toxicity will be added in the presentation.*

Clinical trial identification

NCT03387761.

Legal entity responsible for the study

The Netherlands Cancer Institute.

Funding

Bristol Myers Squibb.

Disclosure

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