TPS9610 Poster Session

A phase 2 study to determine the clinical and pathological (path) response to neoadjuvant nivolumab (nivo) and relatlimab (rela) in stage II to IV (M0) resectable cutaneous squamous cell carcinoma (Neo-SCC).

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Background: Cutaneous squamous cell carcinoma (cuSCC) is the second most common skin cancer worldwide (Bray et al. 2018). While 90% of cases are cured surgically (Kauvar et al. 2015), approx. 5% spread regionally or distantly, with an OS rate $<$ 20% at 10 years if regional lymph nodes (LN) are involved (Ogata et al. 2019). Immunotherapy trials have shown efficacy in advanced disease. Neoadjuvant therapy (NAT) is a powerful treatment platform to rapidly assess drug activity in resectable cancers. In melanoma, a major path response to immunotherapy ($\leq$10% viable tumor) correlates with low risk of recurrence in resectable stage III disease (Menzies et al. 2021), and improved OS and EFS when anti-PD1 monotherapy or in combination with anti-CTLA-4 is given neoadjuvantly vs. monotherapy adjuvant (adj) treatment (Patel et al. 2023; Blank et al. 2024). In a study of NAT anti-PD1 monotherapy with cemiplimab, in pts with resectable stage III or IV (M0) cuSCC (N = 20), 55% of pts had a path complete response (pCR) (0% viable tumour) (Ferrarotto et al. 2021). In a larger NAT cemiplimab trial (N = 79) 51% pts achieved pCR (Gross et al. 2022). The De-Squamate cuSCC trial, evaluating NAT anti-PD1 monotherapy with pembrolizumab (N = 27), showed a 63% combined rate of pCR and clinical complete response (CCR) resulting in the de-escalation of surgery and post operative radiotherapy (RT) in 48% of pts, and avoidance of post-operative RT in 15% of pts (Ladwa et al. 2024). The Neo-SCC trial will evaluate if combined PD-1 plus lymphocyte-activation 3 (LAG3) checkpoint inhibition achieves high path response, while allowing for response-driven surgical and RT de-escalation in pts with resectable cuSCC. **Methods:** Pts with histologically confirmed, resectable cuSCC AJCC (8th ed, head/neck) or UICC (9th ed, non-head/neck) clinical stage II, III or IV (M0) are eligible (N = 20). All pts undergo resection (RES) at week 6 following NAT with 2 doses of nivo (480 mg, IV) plus rela (160 mg, IV) at week 0 and 4. LN disease pts undergo baseline index-LN marking and RES at week 6, with subsequent total LN RES if there is no pCR in the index-LN. Synchronous primary/in-transit metastases undergo wide excision during index-LN resection. Non-LN disease pts showing CCR at week 6 receive an incisional biopsy of the baseline tumor site. All non-LN pts undergo definitive excision except those with CCR or pCR on biopsy. RT follows standard care. Imaging includes CT and FDG PET/CT at BL, prior to RES, and during the 5-year follow-up period. Tumor, blood and faecal samples are collected at BL, RES, and recurrence. The primary endpoint is the pCR rate at RES. The sample size is powered to detect a difference $>$ 25% in pCR rate with the historical control. Secondary endpoints include surgical/RT de-scalation rates, RFS, OS, safety/tolerability, surgical outcomes, QOL, and biomarker analyses. Clinical trial information: NCT06288191. Research Sponsor: Bristol Myers Squibb (drug only).