2578 **Poster Session**

Dynamic change of immune phenotype assessed by artificial intelligence (AI)-powered analysis of tumor-infiltrating lymphocytes (TILs) during neoadjuvant durvalumab with or without tremelimumab (D+/-T) in head and neck squamous cell carcinoma (HNSCC).

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Background: The results of a phase II trial evaluating preoperative durvalumab with or without tremelimumab (D+/-T) in resectable HNSCC (NCT03737968) suggest that the neoadjuvant immunotherapy is associated with pathologic tumor regression with manageable safety profiles. Here, we applied AI-powered spatial TIL analyzer, Lunit SCOPE IO, to tumor specimens of the patients included in the trial to assess the impact of spatial TIL density and inflamed immune phenotype (IIP) on immunotherapy responses. **Methods:** H&E-stained whole-slide images (WSIs) of pre- and post-treatment tumor specimens from HNSCC pts enrolled in the aforementioned D+/-T trial were collected. Patients with locally advanced but operable HNSCC were randomly assigned in 1:1 to receive a single dose of D (1,500mg) or D+T (1,500mg+75mg) followed by surgery, at Severance Hospital in Seoul, Korea. Lunit SCOPE IO was used to segment tumor epithelium and stroma to identify and quantify intratumoral TIL (iTIL) and stromal TIL. IIP was defined as the proportion of high iTIL area more than 33.3% of analyzable area. Clinical data and the combined positive scores (CPS) of PD-L1 were also collected. **Results:** A total of 39 paired tumor samples of pre- and post-treatment WSI (23 from D+T and 16 from D) were included. Overall, tumor regression grade 2 (TRG2, $\geq$ 50% of tumor regression) was achieved in 15.4% (6/39) pts, and downstaging after treatment was achieved in 35.9% (14/39) pts. By pre-treatment WSIs, 38.5% (15/39) samples were classified as IIP, and subgroups of D+T and D had 34.8% (8/23) and 43.8% (7/16), respectively. In the D+T arm, the proportions of TRG2 were 25% (2/8) in IIP versus 13.3% (2/15) in non-IIP, whereas D arm had 28.6% (2/7) TRG2 in IIP, but no TRG2 in non-IIP (0/9), respectively. Comparing the WSI of pre- and post- D+/-T samples, the proportion of IIP was significantly increased to 66.7% from 38.5 (p = 0.015). The increase in IIP proportion was prominent in the D+T arm (34.8% to 69.6%, p = 0.043), but not in the D arm (43.8% to 62.5%, p = 0.37). Similarly, PD-L1 CPS increased after therapy, especially in the D+T group (mean CPS 6.0 to 20.7, p = 0.009). Interestingly, pts who remained non-IIP in both pre- and post-treatment (25.6%, 10/39) had significantly poor prognosis compared to the others, as the 12-month disease-free survival (DFS) rate was 50.0% vs 93.1% (median DFS 13.4m vs not reached, hazard ratio [HR] 4.26, 95% confidence interval [CI] 1.32-13.8, p = 0.009). This prognostic impact was prominent in the D+T arm (HR 6.75, 95% CI 1.49-30.6, p = 0.004). **Conclusions:** Neoadjuvant durvalumab +/- tremelimumab promotes dynamic change toward inflamed immune phenotype, resulting in favorable clinical outcomes. Resistance mechanism of stand-still-non-inflamed patients even on D+/-T should be further investigated. Clinical trial information: NCT03737968. Research Sponsor: AstraZeneca; National Research Foundation of the Republic of Korea (NRF-2019M3A9B6065231 to Hye Ryun Kim, 2020R1F1A1073692 to Hyun Je Kim, 2021R1A2C2094629 to Hye Ryun Kim, and 2021R1I1A1A01059271 to Chang Gon Kim) funded by the Ministry of Science and ICT of Republic of Korea, and Information and Communications Technology and Severance Hospital Research Fund for Clinical Excellence (SHRC 2022-0001) funded by Yonsei University College of Medicine.