Pre- and Post- Immune phenotype assessed by artificial intelligence (AI)-powered tumor-infiltrating

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Background/Aims: A phase II trial (NCT03737968) evaluated the effect of preoperative durvalumab with or without tremelimumab in pts with resectable HNSCC. Further analysis with an AI-powered TIL analyzer revealed that dual immune blockade induces a dynamic shift towards an inflamed immune phenotype (IIP), resulting in favorable clinical outcomes. We aimed to investigate if immune phenotype (IP) can affect clinical outcomes in pts receiving preoperative cytotoxic chemotherapy (CTx).

Methods: We retrospectively reviewed pts with locally advanced HNSCC, treated with neoadjuvant platinum-based CTx followed by surgery at Severance Hospital in Seoul, Korea. H&E-stained whole-slide images (WSIs) of pre- and post-treatment tumor specimens from HNSCC pts were collected and 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.

Results: From Jan 2019 to Apr 2021, a total of 53 pts were diagnosed with potentially resectable HNSCC and treated with cisplatin-based CTx. Of these 41 paired tumor samples of pre- and post-treatment WSIs were available for analysis. Among these, 32 pts with stage II-IVA were included. The majority (15/32, 46.9%) had HPV-positive oropharyngeal cancer. Favorable response was observed in 75% (24/32). Pathologic complete response was achieved in 21.8% (7.32) and down staging were occurred in 65.6% (21/32). Pre- or post-treatment samples classified as IIP were 37.5% (12/32), respectively. Four pts, initially classified as ID or IE, changed to IIP. Interestingly, pts with post- IIP showed superior 2-yr disease-free survival (100% vs. 65%, p=0.025). Among 13 pts (40.7%) without postoperative treatment, there was no recurrence in the 7 with post- IIP, but 4 of the 6 with post- IE or ID relapsed.

Conclusions: IP changes could also be observed in platinum-based CTx group. Confirmed post-treatment IIP seems to be associated with a favorable clinical outcome and may have a role in determining postoperative treatment. Analysis of a larger number of pts and the mechanism of IP change should be further investigated.

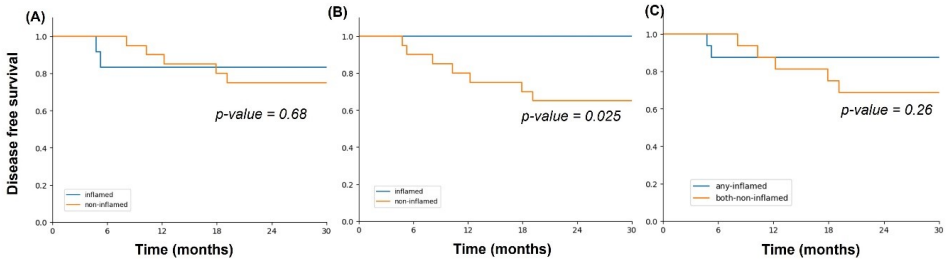

Figure 1. Disease-free survival by (A) pre- IP status, (B) post- IP status, and (C) pre- and post- IP status

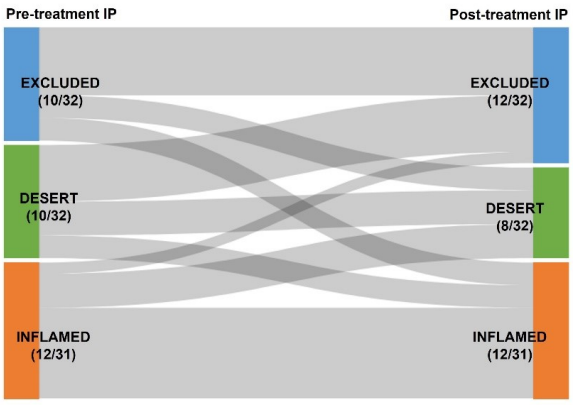

Figure 2. Sankey diagram showing pre- and post- immune phenotype changes