

## **SAT-418: Finding the Needles in the Haystack: Harnessing the Electronic Health Record to Find Thyroid Immune Related Adverse Events**

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**Background:** Immune checkpoint inhibitors (CPIs) are being used to effectively treat a growing number of cancers but can cause immune related adverse events (irAE). Thyroid dysfunction is the most common endocrine irAE. A meta-analysis of clinical trials estimated that following CPI exposure, 6.6% will become hypothyroid and 2.9% will have hyperthyroidism<sup>1</sup>. It is unclear if this reflects the real-world incidence of these irAEs. We used electronic health record (EHR) data to identify patients who developed thyroid dysfunction after CPI to estimate the real-world incidence of these irAEs.

**Methods:** Data were derived from the EHR of a large U.S. academic center. We identified subjects treated with CPIs between 2012 and 2018 and excluded those with thyroid cancer or pre-existing thyroid disease. Thyroid dysfunction was identified as either a TSH > 10, an abnormal free T4 or a prescription for thyroid hormone replacement or anti-thyroid medication. Those with thyroid dysfunction were then categorized as having pre-existing disease or a new-onset thyroid irAE based on the timing of CPI initiation. Logistic regression was used to evaluate the association of thyroid irAE with age, gender, CPI and type of cancer.

**Results:** In total, 1146 individuals without pre-existing thyroid disease that received CPIs were assessed. Pembrolizumab was the most common treatment (45%), followed by nivolumab (20%). Less than 10% of subjects received atezolizumab, durvalumab, ipilimumab monotherapy, combined ipilimumab/nivolumab, or other combinations of CPIs. Melanoma was the most common cancer treated (32%), followed by non-small cell lung cancer (13%). The prevalence of any other cancer was < 10% each. Overall, 19% developed thyroid irAEs. After adjustment for gender and age, the type of cancer was significantly associated with new onset thyroid dysfunction ( $p=0.01$ ). The rates of thyroid irAEs ranged from 10% in glioblastoma to 40% in renal cell cancer. Although there was no significant association between irAEs and specific CPIs in the overall analysis, thyroid irAEs were more common in subjects who received combined ipilimumab/ nivolumab (31%) compared to pembrolizumab (18%,  $p=0.03$ ), nivolumab (18%,  $p<0.01$ ) and ipilimumab (15%,  $p=0.02$ ).

**Conclusion:** Thyroid irAEs are much more common in real world practice than in clinical trials and there is emerging evidence that certain cancer types incur a higher risk of thyroid irAEs even after adjustment for CPI exposure. Clinicians and patients should be educated about these risks. Future work should focus on exploring the reasons underlying the differing rates of thyroid irAEs among different cancers including effect on cancer outcomes.

1. Barroso-Sousa et al. Incidence of Endocrine Dysfunction Following the Use of Different Immune Checkpoint Inhibitor Regimens. *JAMA Oncol.* 2017; 02215: 1–10.