**BACKGROUND**

- Adjuvant chemotherapy (ACT) for ES-NSCLC provides only a modest improvement in survival and is associated with serious adverse effects. Thus, identifying subgroups of ES-NSCLC patients who will benefit from ACT is of high clinical relevance. Utilizing novel digital pathology algorithms, we evaluated relationship between pre-treatment tumor immune microenvironment and survival benefit from ACT in ES-NSCLC patients.

**METHODS**

- 451 tissue sections of formalin-fixed, parallel embedded surgical resection specimens from ES-NSCLC patients without ACT were tested with multiplexed fluorescence immunohistochemistry assay designed to detect key immune cell markers such as PD-L1, PD-1, CD4, CD8, CD20, FOPX1 and NIH2. Fluorescence images were acquired on the Vectra platform (Perkin Elmer) and analyzed with novel AQUA algorithms designed to accurately measure the correlation of PD-L1 and PD-1 (the Interaction Score, corrected for background signal of PD-L1 and activated (HET) T cell subsets).

**RESULTS**

- **Patients exhibiting high PD-1/PD-L1 Interaction Scores (≥ 643) and regulatory T cell burden (≥ 1%) in their pre-treatment tumors experienced significantly improved progression-free survival (p = 0.004) with ACT after surgery, whereas no survival difference was observed for patients who received surgery alone (p = 0.5).** Median PFS was not reached in biomarker positive patients vs 2880 days in biomarker negative patients. Interestingly, neither PD-1 or PD-L1 levels alone did not predict survival for surgery + ACT in all patient populations.

**High PD-1/PD-L1 Interaction score predicts survival in lung cancer patients receiving chemotherapy**

- **High regulatory T cell burden predicts survival in lung cancer patients receiving chemotherapy**

**CONCLUSIONS**

- **PD-1/PD-L1 Interaction Score and CD25/FOXP3 positive T cells are predictive of benefit from ACT in ES-NSCLC patients**

- **Significantly prolonged survival in patients exhibiting higher proportion of PD-1+ cells in close proximity with PD-L1+ cells is observed following adjuvant chemotherapy but not surgery alone.**

- **Chemotherapy augments the immune system likely by modifying tumor immunosuppression but only in patients harboring relevant lymphocytes within the tumor bed.**

- **Chemotherapy may be most beneficial in NSCLC patients whose tumors display signs of adaptive and tumor immune response evidenced by elevated PD-1/PD-L1 interaction and increased T cell activity.**

- **Ongoing independent validation studies will determine if these biomarker signatures can be used to select patients that may benefit from chemotherapy without compromising outcome.**

**REFERENCES**

1. Udayakumar D, Monika Khunger, Nathan A Pennell, James Stevenson, Monica Khunger, Christine Vaupel, Kurt A. Schalper, David Rimm and Vamsidhar Velcheti.

**AQUA ALGORITHMS**

- Precision Phenotyping of Classical Regulatory T cells and Activated T cells on Same Slide

**PD-1/PD-L1 Interaction Score Assessment**

- Representative Case Exhibiting High PD-1/PD-L1 Interaction and T regs

**RESULTS**

- **High PD-1/PD-L1 Interaction Score Plus T Reg Burden Predicts Best Survival Benefit to Chemotherapy**

**REFERENCES**