INTRODUCTION

In non-small cell lung cancer (NSCLC), the MET tyrosine kinase receptor can be dysregulated by mutations and/or gene amplification. The most common MET mutation is in exon 14 (METex14), leading to impaired receptor degradation and increased MET-mediated signaling causing sustained tumor proliferation. MET amplification also leads to continued MET signaling and oncogenesis and can be a mechanism of resistance to targeted therapy. We sought to compare the genomic landscape of METex14 and high-level MET amplified tumors, both of which can be targeted with tyrosine kinase inhibitors.

METHODS

Tumor mutation burden (TMB), neoantigen load, PD-L1, and the proportion of immune cell subtypes were evaluated from patient derived genomic profiles of NSCLC. PDL1 status was determined by IHC. Differences between groups were assessed by Chi-squared/Fisher’s Exact tests or Kruskal-Wallis tests. Prevalence of gene alterations was compared with false-discovery correction for multiple testing. Analyses were two-sided with statistical significance evaluated at the 0.05 alpha level or 0.05 q level.

RESULTS

**MET gene expression higher in METamp**

MET gene expression was higher in METamp compared to METWT (p < 0.001).

**PD-L1 expression lowest in METamp**

PD-L1 expression was lowest in METamp (p < 0.001).

**METex14 exhibited lower TMB and Neoantigen Burden**

METex14 tumors exhibited differences in IO biomarkers and the somatic landscape compared to non-METex14 NSCLC tumors.

**Variation in immune profiles may affect immunotherapy selection in MET-altered NSCLC and require further exploration**

**SUMMARY**

- METex14 tumors exhibited differences in IO biomarkers and the somatic landscape compared to non-METex14 NSCLC tumors
- Variation in immune profiles may affect immunotherapy selection in MET-altered NSCLC and require further exploration

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**CORRESPONDENCE**

baschnagel@humonc.wisc.edu

**Table 1.** Comprehensive genomic profiles from 18,047 NSCLC tumors were queried for METex14 mutations and high MET amplification defined as copy number gain (CNG) ≥10.

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Genomic comparison of MET exon 14 skipping and MET amplified non-small cell lung cancer

Rachel Minie BS1, Natalie Luo BS1, Anne Traynor, MD2, Minxuan Huang PhD3, Luisina DeTullio PhD1, Jen Goddern PharmD1, Melissa Stoppler MD3, Randall J. Kimple MD PhD1, Andrew M. Baschnagel MD1

1Department of Human Oncology, School of Medicine and Public Health, University of Wisconsin, Madison, WI; 2Tempus Labs, Inc., Chicago, IL; 3Division of Hematology/Oncology, Department of Medicine, School of Medicine and Public Health, University of Wisconsin, Madison, WI