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THE POWER OF SHARED PURPOSE: Transforming Gynecologic Cancer Care

Evaluation of the somatic and immunologic landscapes of primary and metastatic cervical cancer to better inform future clinical trial development

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INTRODUCTION

Adding angiogenesis inhibitors and immuno-therapy to chemotherapy in metastatic cervical cancer improves overall survival. Whether metastatic sites are differentially sensitive to these therapies is unknown. We investigated the somatic and immunologic landscape of cervical primary vs metastatic tumors to evaluate potential therapeutic implications.

METHODS

- De-identified cases of patients with squamous cell cervical cancer sequenced with the Tempus xT assay were selected from the Tempus Database (2016-2023).
- Included 136 samples (73 primary and 24 lung, 13 liver, and 26 lymph node metastases). No metastatic sites had a matched primary sample.
- Median (IQR) from time of diagnosis to time of biopsy of each site was: 0 days (0,0) for cervix, 425 days (109,826) for lung, 455 days (141,592) for liver, and 194 days (1,367) for lymph node.
- Pathogenic somatic mutations and gene expression patterns of immune cells (B, T [CD4+, CD8+], NK cells, and macrophages) were evaluated to predict relative intra-tumor abundance.
- Immune cell percentages, tumor mutational burden (TMB), and neoantigen burden were compared across primary and metastatic sites.
- Chi-squared/Fischer's exact tests or Kruskal-Wallis tests were used to assess statistical significance ($p<0.05$, $q<0.05$ for false discovery rate correction for multiple testing).

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SUMMARY

- Molecular and immune profiling of primary and metastatic lesions in this cervical cancer cohort revealed similar phenotypes, suggesting that predominant biologic pathways are preserved.
- Further interrogation of the molecular landscape across paired and serial samples is needed to better inform the development of novel therapies.

RESULTS

Figure 1. Comprehensive Molecular Markers Across Primary and Metastatic Sites

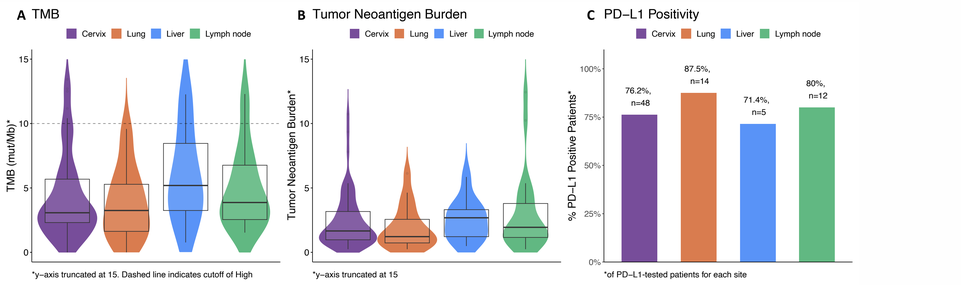

Figure 1. A) High TMB (≥ 10 mut/Mb) was seen in 9.6% (9% primary, 0% lung, 17% liver, 17% lymph node, p=0.2). B) Median tumor neoantigen burden was 1.71 (IQR 0.98, 3.20). C) PD-L1 status from internal IHC was positive in 78% (76% primary, 88% lung, 71% liver, and 80% lymph node, p=0.8).

Figure 3. Somatic Alteration Landscape Across Primary and Metastatic Sites

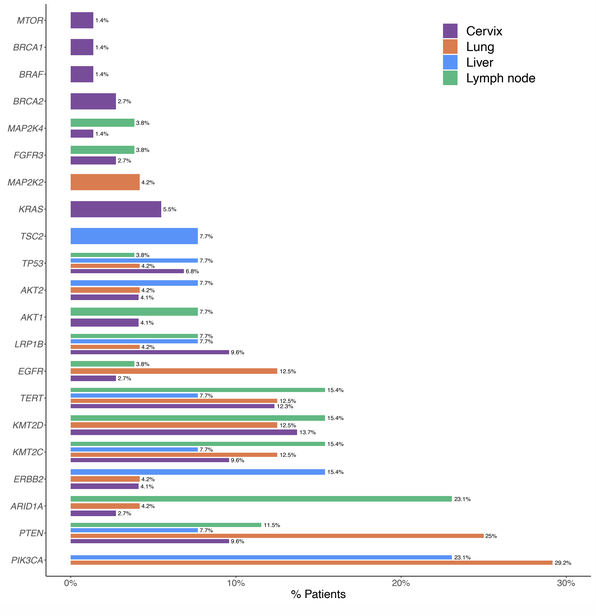

Figure 3. PIK3CA was the most common pathogenic/likely pathogenic somatic alteration but was not statistically different across sites (primary 36%, lung 29%, liver 23%, nodes 42%, q>0.9). ARID1A was more commonly seen in nodes and MAP2K2 more commonly in lung but neither were significantly different (q=0.2, 0.4).

Figure 2. Immune Cell Percentages Across Primary and Metastatic Sites

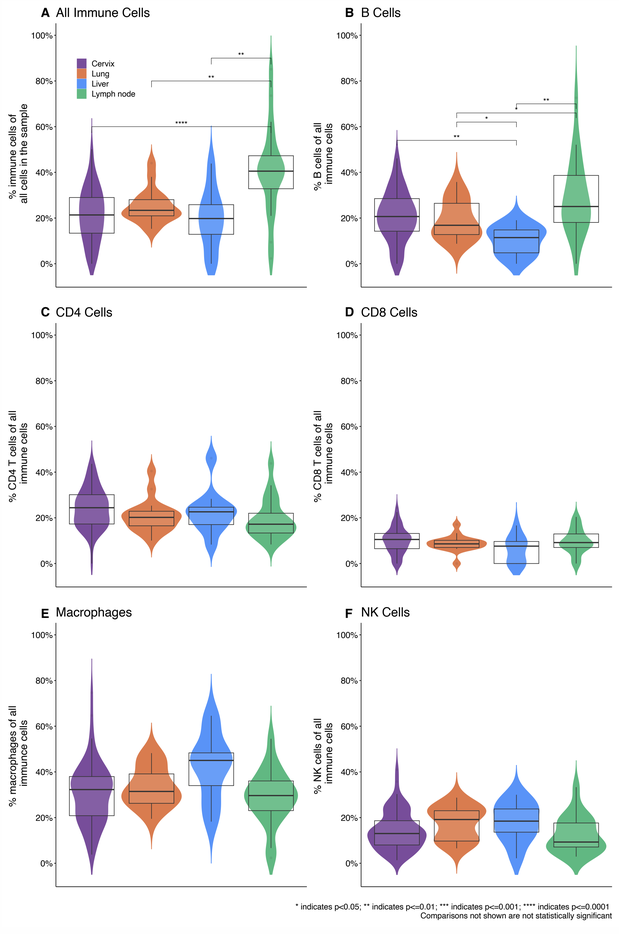

Figure 2. Immune cell percentages did not suggest one site was more or less immunogenic. However, liver lesions had the lowest percentage of B cells (p=0.001) with a trend towards a higher percentage of macrophages (p=0.053) compared to all sites. There was a trend towards lower percentages of CD4 cells (p=0.053) and NK cells (p=0.090) in lymph nodes compared to all sites.

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