

AB025. Evaluation of potential therapeutic immunohistochemical targets with experimental or FDA-approved therapies in thymic epithelial tumor microarrays

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Background: Thymus epithelial tumors (TETs) are rare malignancies of the anterior mediastinum. The current standard of care for metastatic TETs is a combination of platinum-based chemotherapy. Here, we have evaluated the experimental and FDA-approved makers in a large TET tissue array with the hope of identifying a new therapeutic option.

Methods: A tissue microarray (TMA) containing ninety malignant thymic tumors (A, AB, B1 and B2, n=62, B2/B3 and B3, n=16, and thymic carcinoma, n=12) and seven normal adult thymus were assembled. The protein expressions of GLUT1, TROP2, PSMA, ROS1, ALK, HER2, and PDL-1 were tested with immunohistochemical assays. Expression was quantified using a “staining score (SS)”, which is a 0–3 numerical score that results from the product of the intensity of expression: 0= negative, 1= weak, 2= moderate, 3= strong, and the area of expression in fractions of a percent (0= no expression, 1= 100% area). Expression of HER2 and PDL-1 was quantified according to existing guidelines [HER2 score and combined positive score (CPS)].

Results: Trop-2 had the highest expression in thymic

carcinoma (TC) (100%, SS 2.6±0.6) followed by thymoma B2/B3 (78%, SS 1.3±1.3), types A/AB/B1 (54%, SS 1.1±1.1) (P=0.01). In TC, all patients with squamous histology had immunohistochemistry (IHC) SS of 3. Patients with thymoma who had Trop-2 expression experienced significantly worse survival [hazard ratio (HR): 3.3, P=0.008]. GLUT1 was highly expressed in TC (81.8%, SS: 2.1±1, TC *vs.* normal thymus, P=0.0003). PDL-1 was expressed in all TET tissues (mean, 2.5–52 CPS). No significant expression of ALK, ROS1, or HER2 observed in normal thymus or TETs.

Conclusions: Trop-2 expression is a prognostic marker in TETs. High expression of Trop-2 protein in thymoma and TC appears a promising therapeutic target for Trop-2 antibody-drug conjugates.

Keywords: Thymic tumor; TROP2; PSMA; PDL-1

Acknowledgments

We thank Indiana University Tissue Bank, Rema Tanib, HT, IUH Immunohistochemistry Laboratory Supervisor, for performing the immunohistochemical studies.

Funding: This work was supported by Indiana University career development Alumni Award 2021.

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://med.amegroups.com/article/view/10.21037/med-23-ab025/coif>). F.A.L. reports having used the Indiana University Alumni Award 2021 for this project. P.J.L. reported Composition finding material for diagnosis, prognosis, and treatment of thymic epithelial tumors. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Indiana University IRB and Ethic Board Committee under the protocol number of CTO-IUSCCC-0764.

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doi: 10.21037/med-23-ab025

Cite this abstract as: Ardeshir-Larijani F, Loehrer PJ, Maniar R, Hou T, DeBrock V, Mesa H. AB025. Evaluation of potential therapeutic immunohistochemical targets with experimental or FDA-approved therapies in thymic epithelial tumor microarrays. *Mediastinum* 2023;7:AB025.