Discovery of plasma protein biomarkers associated with overall survival in R/R DLBCL patients treated with loncastuximab tesirine

Francesco Vallania1, Victoria Cheung1*, Anupriya Tripathi1, Maggie Louie1, Thomas Snyder1, Jimmy Lin2, Karin Havenith2, Yajuan Qin1, Serenaio Pantano3, Jens Wuerthner3, Patrick van Berkel4

1Freenome, 279 East Grand Avenue, 5th Floor, South San Francisco, CA, USA; 3ADC Therapeutics SA, Biopole, Route de la Corniche 3B, 1066 Epalinges, Switzerland

*Authors contributed equally to the work 1Affiliation at the time the work was conducted

INTRODUCTION AND OBJECTIVES

- Plasma proteomics is a non-invasive approach towards the discovery of biomarkers associated with cancer treatment outcomes, including disease progression and overall survival (OS)
- Loncastuximab tesirine (lonca) is an antibody-drug conjugate, composed of a humanized anti-CD19 antibody conjugated to a pyrrolobenzodiazepine dimer cytotoxin, currently approved for the treatment of relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL)
- Here, we investigated the association of plasma protein biomarkers measured at baseline with OS in the LOTIS-2 phase 2 trial (NCT0369469; data cut March 1st 2021)

METHODS

- Abundances of 888 plasma proteins, including inflammation, cancer and DNA repair associated markers, were measured for 62 patients with R/R DLBCL from plasma samples collected at baseline
- Protein markers predictive of overall survival (OS) were identified using an L1-regularized Cox Proportional Hazard model that incorporates survival time and censoring status
- To better characterize underlying biology and identify set of proteins associated with OS, we applied an L2-regularized (Ridge) Cox Proportional Hazard model. Gene Set Enrichment Analysis (GSEA) with the MSigDB gene sets was performed on the coefficients of this model.

RESULTS

- Using an L1-regularized Cox proportional hazard model with 3-fold cross-validation, we identified 5 proteins markers associated with survival using a final model with L1 tuning parameter λ selected per the 1SD rule.
- CV accuracy was measured by the Harrel C-index (y-axis) as a function of the log of λ (x-axis) with max (left) and 1SD (right) values indicated by dashed lines. Corresponding number of identified protein markers is shown above.
- Coefficients of identified proteins are shown, with positive sign indicating increased hazard (reduced survival time)

CONCLUSIONS

- Using our platform, we characterized a cohort of R/R DLBCL patients at baseline with lonca using plasma proteomics
- Our results identified plasma protein markers associated with overall survival of patients with R/R DLBCL treated with lonca, highlighting the potential of plasma proteins as a source of relevant biomarkers
- Our analysis revealed a protein set reflective of changes in KRAS signaling to be associated with overall survival.
- Future studies with our platform may enable targeted precision medicine applications and support therapeutic decisions