Background

A prognostic model for overall survival (OS) was reported for patients treated with post-platinum atezolizumab for metastatic urothelial carcinoma (mUC) (Pond GR, GU ASCO 2018).

The model was limited due to small sample size and unclear applicability to other PD-1/PD-L1 inhibitors.

We created a robust prognostic model evaluating candidate factors and utilizing the combined atezolizumab cohort as the derivation dataset.

Validation of model was then performed on post-platinum mUC patients treated with avelumab or durvalumab.

Datasets

Derivation dataset comprised of 405 patients treated with atezolizumab on 2 phase III trials, IMvigor210 (Rosemberg JE, Lancet 2016) and PCDC9889g (Powles T, Nature 2014).

Avelumab validation dataset: 242 patients enrolled on phase III trial (Patel MR, Lancet Oncol 2018) who received post-platinum avelumab.

Durvalumab validation dataset: updated 1108 (Powles T, JAMA Oncol 2017) that evaluated durvalumab (n=198).

Methods

Cox regression modeling was used to identify factors prognostic of OS. All factors listed in the table were included as candidate factors. Forward stepwise selection was used to construct an optimal multivariable model.

Dichotomization of factors was performed as needed to ensure similar factors were available in both datasets.

Laboratory data was logarithmically transformed as appropriate for statistical normalization purposes.

Prognostic index (PI) was calculated using model coefficient estimates and risk groups are defined based on PI distribution quartiles the derivation dataset.

Validation was performed as per the methods of Royston and Altman (BMC medical research methodology, 2013).

Discrimination between Kaplan-Meier curves for risk groups are well separated as shown in figure above.

Conclusions and Next Steps

• A 5-factor prognostic model for OS is proposed in the setting of post-platinum PD-L1 inhibitors for mUC.

• The model was developed using a derivation dataset of 405 patients from 2 phase III trials receiving atezolizumab and validated using 2 independent datasets of 242 patients receiving avelumab and 198 patients receiving durvalumab.

• Model concordance appeared acceptable and Kaplan-Meier survival estimates of a priori defined risk groups showed good discrimination.

• This model may assist in prognostic stratification and interpreting non-randomized trials of post-platinum PD-1/PD-L1 inhibitors.

• Further clinical and statistical validation analysis including assessment of predicted vs. observed survival to be conducted.

• Further refinement of this model may be feasible by the incorporation of molecular variables.