Background Post-FDA approval immune therapy for cancer becomes widely used for locally advanced or metastatic urothelial carcinomas. There are patients that may suffer severe side effects from these immune checkpoint blockades (ICBs). The aim of this study was to identify patients that will achieve response or those who do not achieve response to these ICBs.

Methods Pretreatment normalized ribonucleic acid (RNA) Sequencing (Seq), clinical and other data for patients with advanced UC receiving PD-1 axis inhibitors were downloaded from gene expression omnibus (GEO) datasets project PRJNA735749.1 This data also included responses to treatment data. Responders were categorized as patients with either complete response (CR), partial response (PR), or stable disease (SD) while non-responders comprised patients with progressive disease (PD). The data set was split 70/30 for training and test sets for the deep-learning algorithm. Four distinct algorithms were developed using a complete gene expression profile, targeted normalized RNA or high vs low RNA expression (upper or lower than the 75 percentile) with non-RNA Seq data; total mutational burden (TMB), clinical characteristics of the patient (including age, TNM staging, etc.) and FGFR mutational status. The performance of each of the algorithms was assessed by comparing a matrix of test set accuracy, sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV), and area under the receiver-operating curves.

Results A total of 89 patients of were selected from a total of 103 that had complete RNASeq, DNA and clinical data. The complete RNASeq + non-RNASeq data showed test set; accuracy (18.5%), sensitivity (100%), specificity (0.0%), PPV (25%), NPV (undefined*). The targeted RNASeq + non-RNA Seq data showed test set; accuracy (70.4%), sensitivity (0.0%), specificity (100%), PPV (undefined), NPV (70.4%). The targeted RNASeq (Hi/Low cutoff) + non- RNASeq data using a Multilayer Perceptron (MLP) classifier showed test set; accuracy (81.5%), sensitivity (20.0%), specificity (95.5%), PPV (50.0%), NPV (84.0%). The targeted RNASeq (Hi/Low cutoff) + non-RNASeq data using a TensorFlow (TF) classifier showed test set; accuracy (77.8%), sensitivity (20.0%), specificity (90.9%), PPV (33.3%), NPV (83.3%) see table 1.

Conclusions The MLP/deep-learning classifier for targeted normalized high vs low RNA expression with TMB, clinical characteristics, and FGFR mutational status shows better overall results compared to other algorithms. However, we can these results need external validation and with a larger dataset, we may also be able to predict responders.

REFERENCE