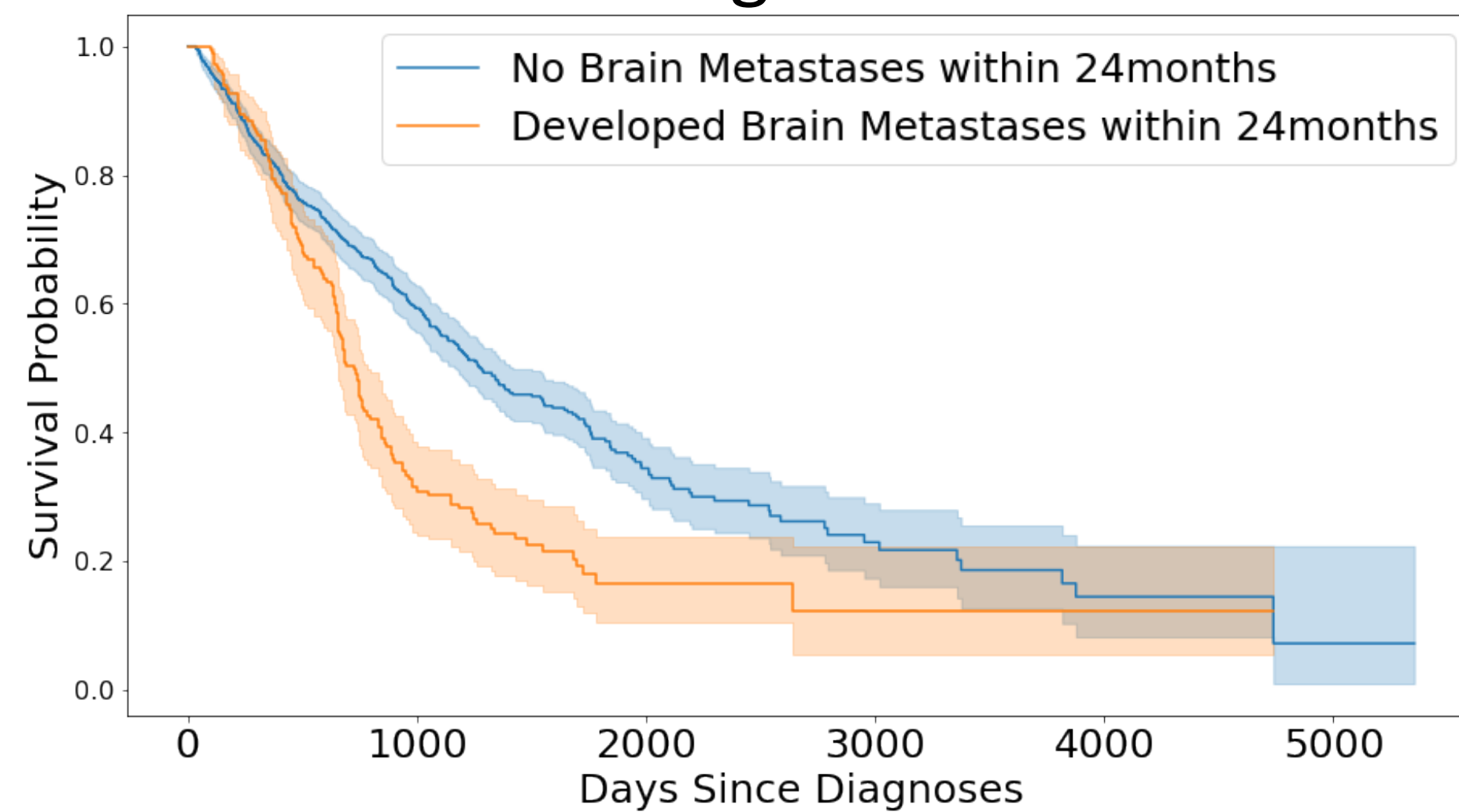


Abstract 2032: Clinical and Genomic Predictors of Brain Metastases in NSCLC

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Background

- 30-50% of patients with Non-Small Cell Lung Cancer (NSCLC) develop brain metastases
- Median survival of less than one year from brain metastases diagnosis



Divergence in survival between patients who develop brain metastases within 2 years and those who do not in our cohort

- Brain metastases are not easily predicted
 - Unmet need in the care of NSCLC patients
- Problem Statement
 - Predict the probability of developing brain metastases
 - Exclude patients who have brain metastases at diagnoses

Data

- AACR Project GENIE BPC Dataset
 - 956 Stage II-IV NSCLC patients from 4 institutions
 - NGS sequencing between 2015-2017
- Covariates: Demographics, Anticancer therapies, mutations and copy number alterations (restricted to oncogenic using OncoKB)

TP53 and *EGFR* Mutations associated with *increased* risk of brain metastases.

Nivolumab and *Alectinib* associated with *decreased* risk of brain metastases.

Our statistical model *predicts* brain metastases with an AUC of *.71 (+/- .07)*.

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Methods

- Univariate analysis with Fisher's test
- Comparison of 5 machine learning algorithms for prediction of brain metastases:
 - Random Forest (RF), Support Vector Machine (SVM), Lasso and Ridge regression, Ensemble (avg. of ridge, SVM, RF)
- Evaluate with area under the curve (AUC)
 - Measures the model's discrimination

Results

Univariate Associations

Increased Risk	Decreased Risk
EGFR, TP53 Mutations	KRAS, NOTCH1 Mutations
Etoposide	Nivolumab, Alectinib,
EGFR, ERBB2 Amplification	Atezolizumab,
CDKN2A, CDKN2B, RB1 Deletion	Pembrolizumab, Gemcitabine, Vinorelbine

Model Comparison

Model	Cross-validation on Train Set	Test AUC
RF	0.69 (0.63-0.75)	.72
SVM	0.68 (0.62-0.74)	.66
Lasso	0.7 (0.63-0.77)	.71
Ridge	0.68 (0.62-0.74)	.68
Ensemble	0.71 (0.64-0.78)	.72

Future Directions

- Study associated genetic alterations
- Account for competing risk of death with landmark analysis