

# Plasma proteomics-based models for predicting immunotherapy- and chemotherapy-related toxicity in NSCLC patients

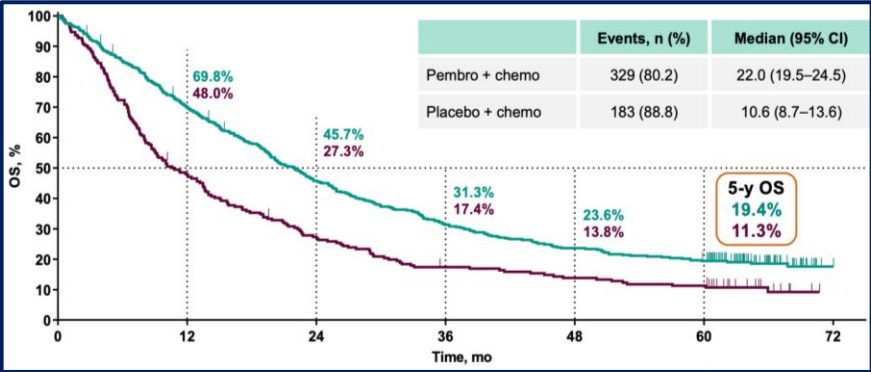
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# Introduction: irAEs from ICI Therapy

## irAEs are common in NSCLC



### KN189: Pembro-Chemo

All grade irAE: 27.9%

G3+ irAE: 12.3%

### KN024: Pembro mono

All grade irAE: 18%

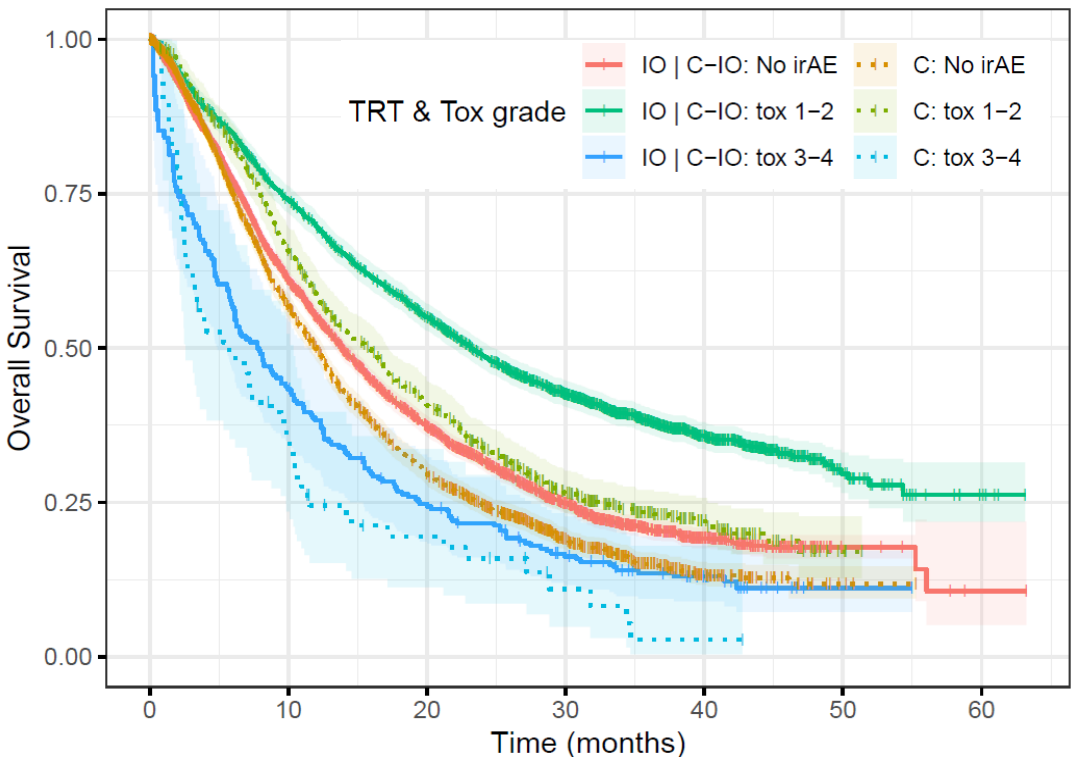
G3+ irAE: 9%

### CM227: Ipi/Nivo

All grade irAE: 38%

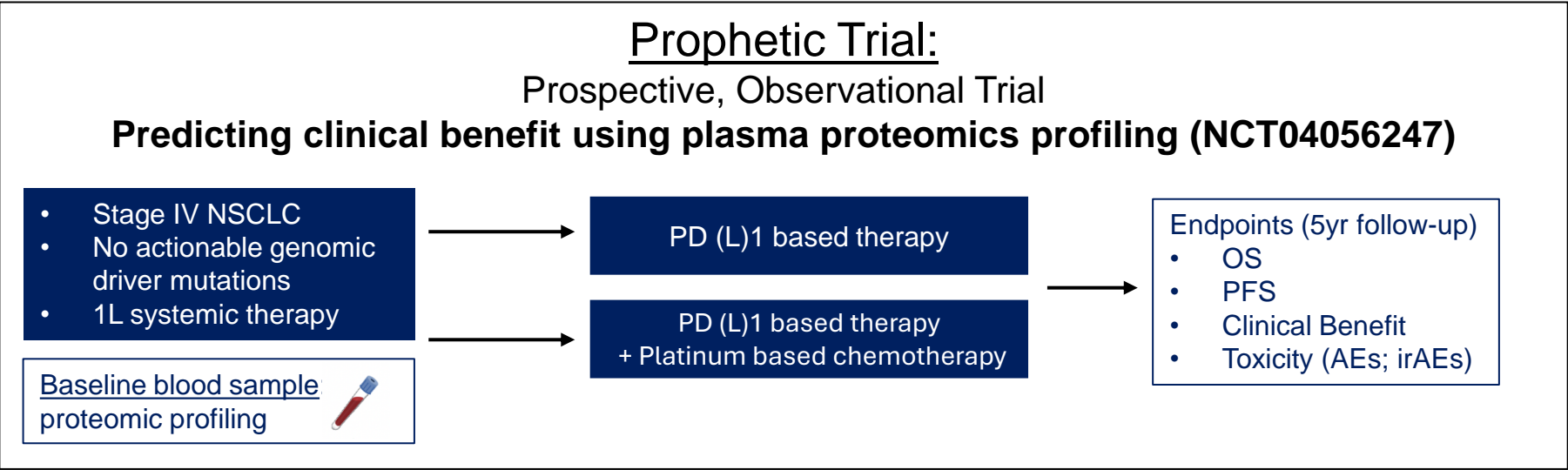
G3+ irAE: 19%

## High-grade irAEs are associated with poor OS



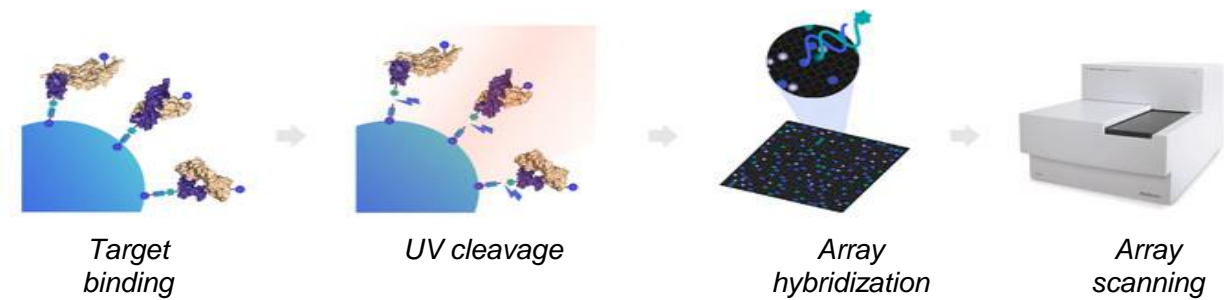
There are no validated biomarkers for irAEs, an area of increasing clinical relevance

# Methods: Study Schema

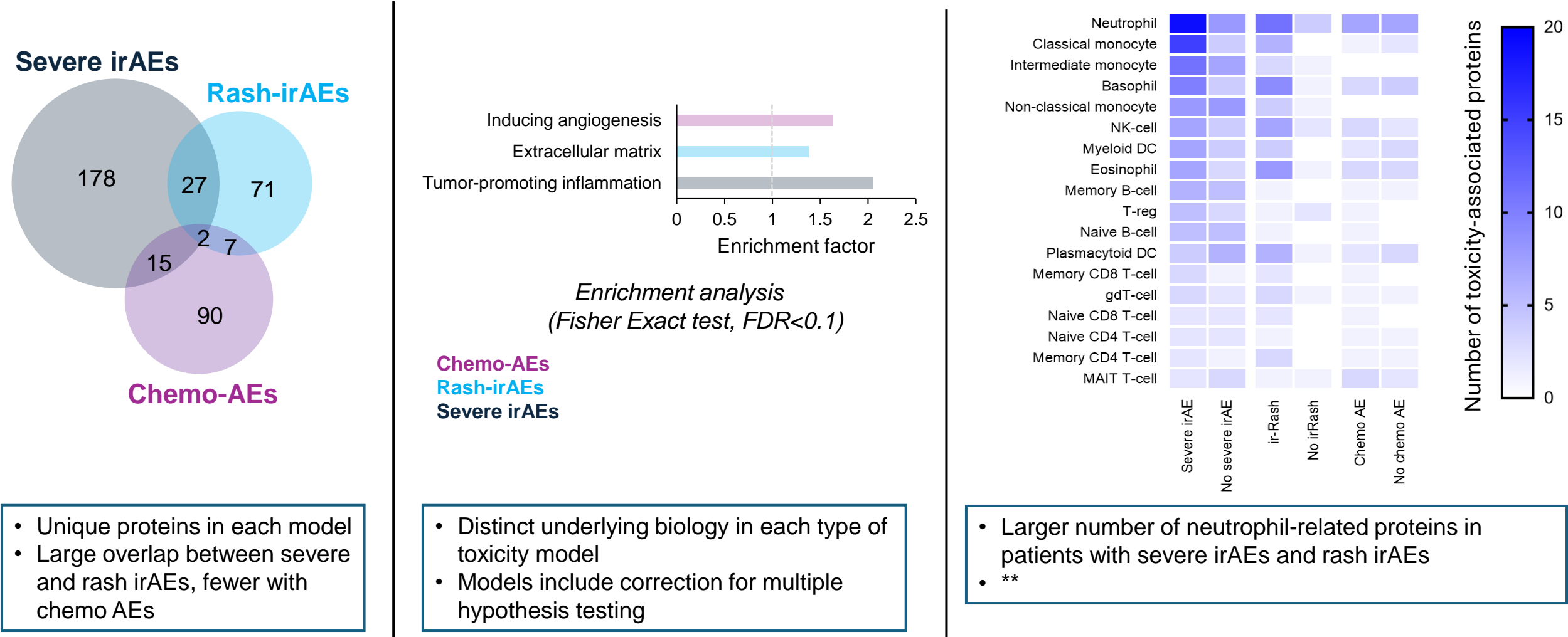


## Proteomics profiling

- SomaScan technology (Aptamer-based)
- Examines protein expression levels
- >7000 proteins/sample



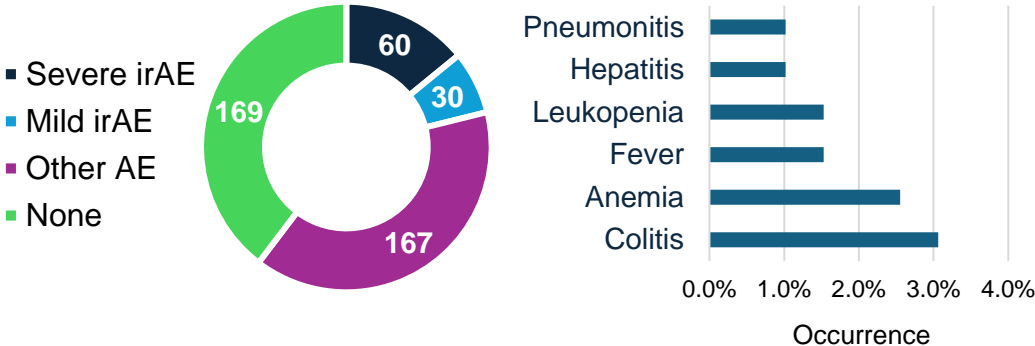
# Results: The 3 models differ in the proteomic signatures



# Results: Severe-irAE Prediction

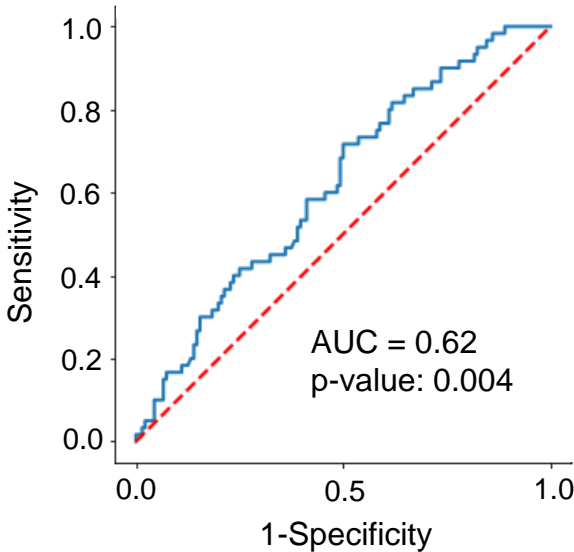
Prophet Trial: irAE Cohort (n= 426)

Category	Parameter	irAE cohort
Sex	Male	249
	Female	177
ECOG	0	136
	1	240
	2	47
	Unknown	3
Histology	Non-squamous	312
	Squamous	97
	Unknown	17
Treatment type	ICI+Chemo	151
	ICI monotherapy	275

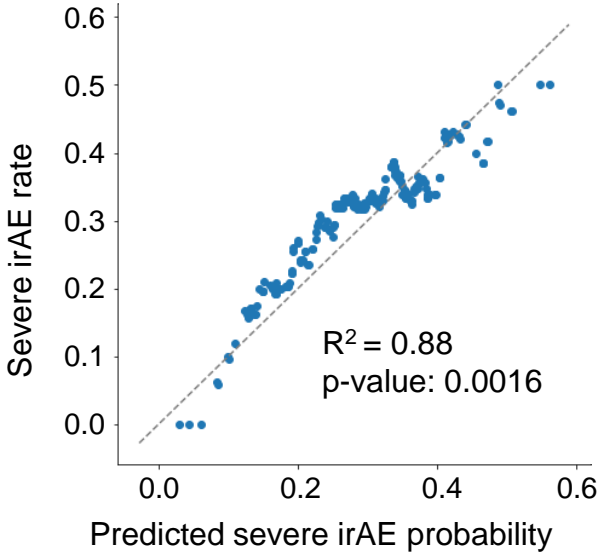


**Definition:**

- Severe irAE: grade  $\geq 3$  irAEs within the first 100 days that leading to treatment discontinuation



irAE model demonstrated statistically significant predictive capabilities

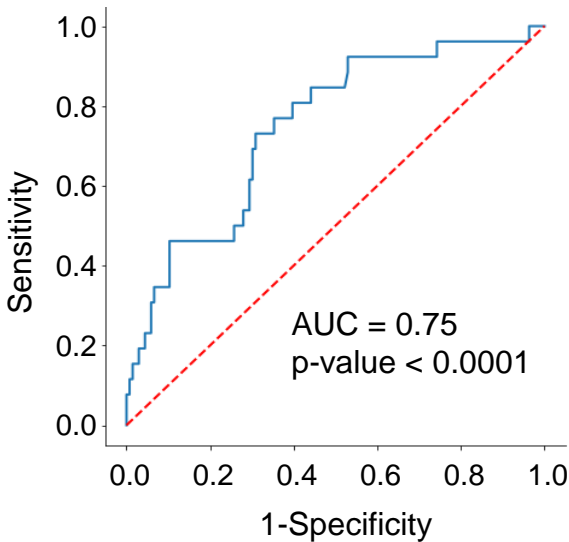
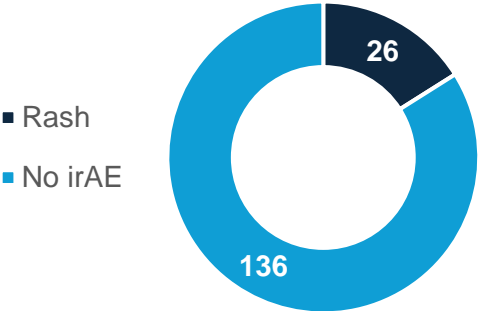


High correlation between predicted severe irAE probability and the observed severe irAE rate

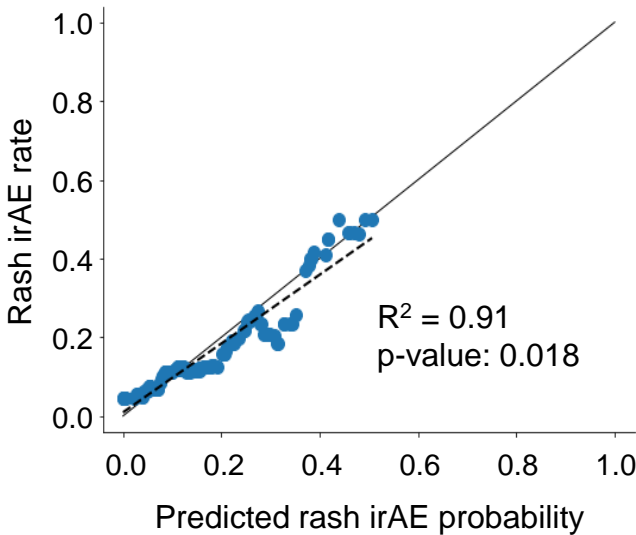
# Results: Specific-irAE Prediction (Test Case: Rash)

Prophet Trial: Rash Cohort (n= 162)

Category	Parameter	Rash cohort
Sex	Male	96
	Female	66
ECOG	0	55
	1	96
	2	11
Histology	Non-squamous	120
	Squamous	38
	Unknown	4
Treatment type	ICI+Chemo	50
	ICI monotherapy	109
	Ipi Nivo	3



Rash model demonstrated statistically significant predictive capabilities



High correlation between predicted rash probability and the observed rash rate

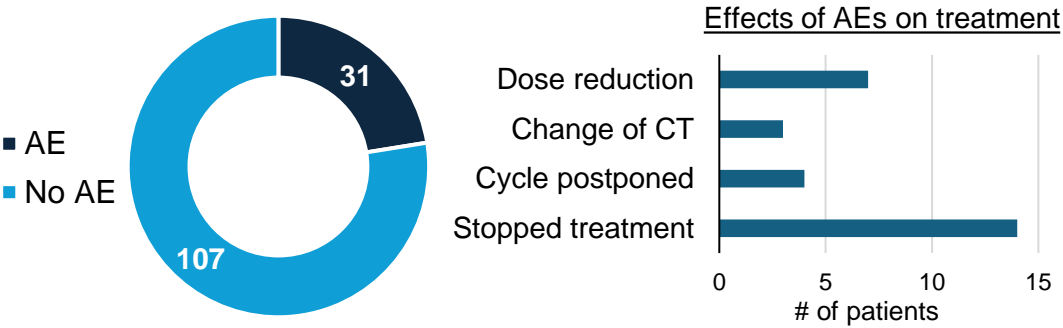


# Results: Chemo-Associated AE Prediction

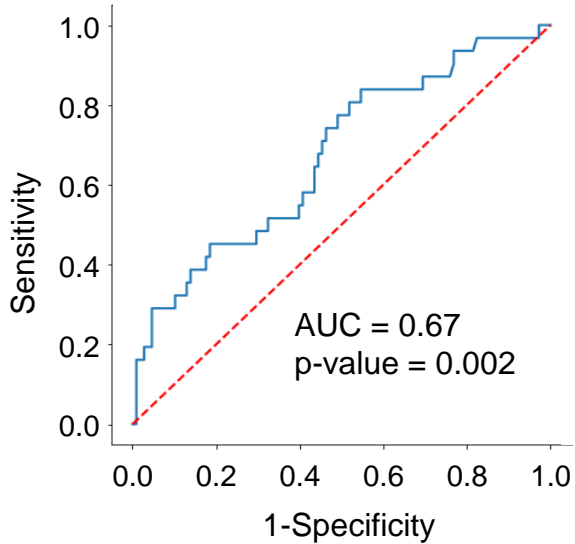
Prophet Trial: Chemo Cohort (n= 138)\*

Category	Parameter	Chemo cohort
Sex	Male	96
	Female	42
ECOG	0	68
	1	68
	2	1
	Unknown	1
Histology	Non-squamous	92
	Squamous	45
	Unknown	1
Treatment	Platinum doublet	138

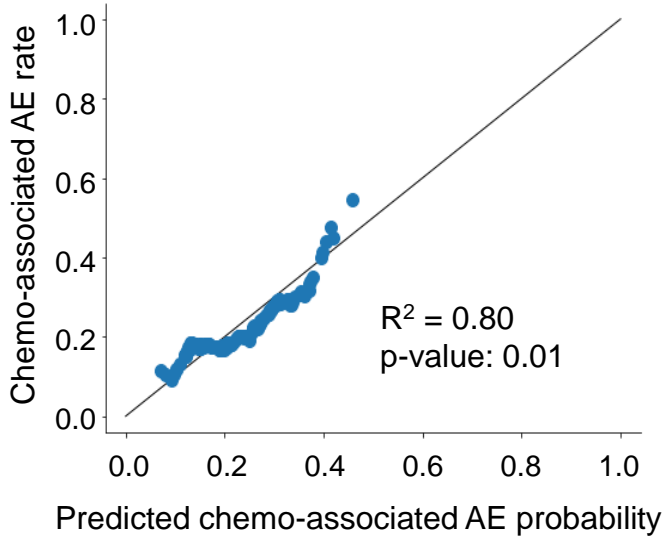
\* Historic 1L cohort



23 patients (74% of those who experienced chemo AEs) modified / stopped treatment due to AE



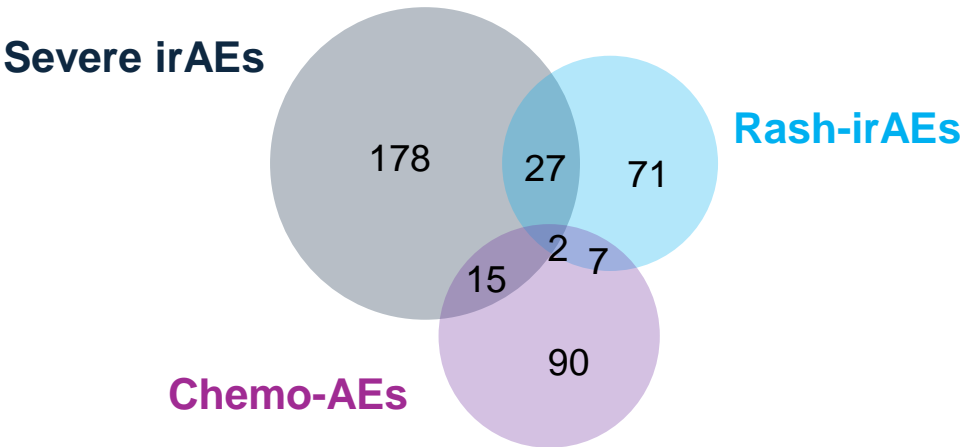
Chemo-AE model demonstrated statistically significant predictive capabilities



High correlation between predicted chemo-AE probability and the observed chemo-AE rate

# Summary

- Three novel proteomic models for predicting AEs based on baseline plasma sample
- The model for specific irAE (Rash) shows the potential to develop a model for additional specific irAEs
- The three models differ in the proteins and the underlying biology
- The signatures may enable targeting potential AEs in high-risk patients





# Colleagues and Collaborators

**Beaumont RCSI Cancer Centre**

- Christopher Cluxton, MD PhD
- Catriona Dowling, PhD

**MGH**

- Ryan J. Sullivan, MD PhD

**Northwestern University**

- Young Kwang Chae, MD

**UC Davis**

- David Gandara

**Roswell Park Comprehensive Cancer Center**

- Igor Puzanov

**Ohio State University**

- David Carbone

**Mayo Clinic, Jacksonville**

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**Heidelberg University**

- Petros Christopoulos

**Shamir Medical Center**

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- Carmel Fink

**OncoHost**

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- Coren Lahav
- Yehonatan Elon
- Michal Harel

**Thomas Jefferson University**

- Adam P. Dicker

- Jair Bar, **Sheba Medical Center**
- Niels Reinmuth, **Asklepios Kliniken GmbH**
- Mor Moskovitz, **Rabin Medical Center**
- Alona Zer, **Rambam Medical Center**
- Michal Lotem, **Hadassah Medical Center**
- David Farrugia, **Cheltenham General Hospital**
- Rivka Katzenelson, **Kaplan Medical Center**
- Gillian Price, **Aberdeen Royal Infirmary Grampian NHS**
- Abed Agbarya, **Bnai-Zion Medical Center**
- Helen Cheley, **Swansea Bay UHB**
- Adam Hassani, **South Tyneside and Sunderland NHS Foundation Trust**
- Mahmoud Abu-Amna, **Haemek Medical Center**
- Tom Geldart, **Royal Bournemouth Hospital**
- Anirban Chatterjee, **The Shrewsbury and Telford Hospital**
- Andreas Polychronis, **Mount Vernon Cancer Centre and Lister Hospital**
- Maya Gottfried, **Meir Medical Center**
- Tatiana Harkovsky, **Barzilai Medical Center**
- Alison Brewster, **Withybush Hospital Hawel Dda UHB**
- Ido Wolf, **Sourasky Medical Center**
- Ella Tepper, **Assuta Medical Center**

All the patients who participated in this study