SGO 2021 VIRTUAL ANNUAL MEETING ON WOMEN'S CANCER®

Society of Gynecologic Oncology

Too much skin in the game? A paradigm shift in our understanding of vulvar and vaginal melanomas as distinct tumor types compared with cutaneous melanomas

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Disclosures

- None

Background

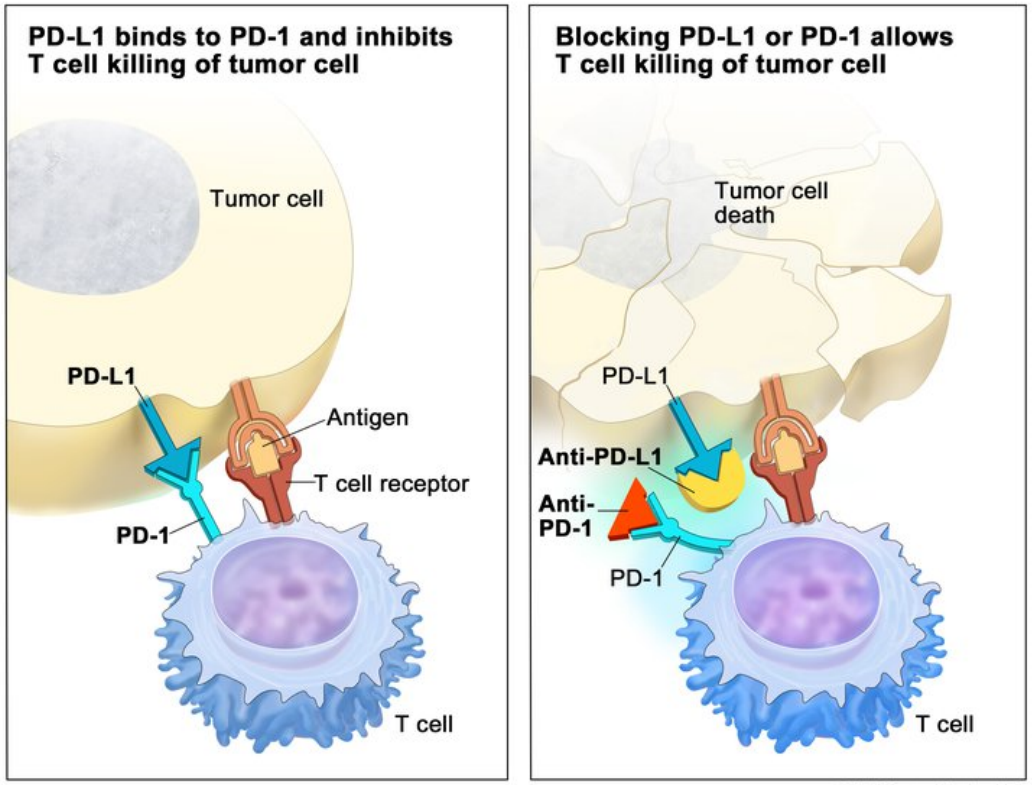
- 5-year survival for VVM is inferior to CM
  - CM – 92%
  - Vulvar – 58%
  - Vaginal 27%

- Current therapeutic strategies for vulvar and vaginal melanoma (VVM) mimic those of cutaneous melanoma (CM)

NCCN guidelines
Surveillance, Epidemiology, and End Results (SEER) data
Sanchez, *Urologic Oncology* 2016

Traditional markers….

- Anti-PD1 monotherapy
- Anti-PD1/ipilimumab combo
- BRAF/MEK inhibitor combo

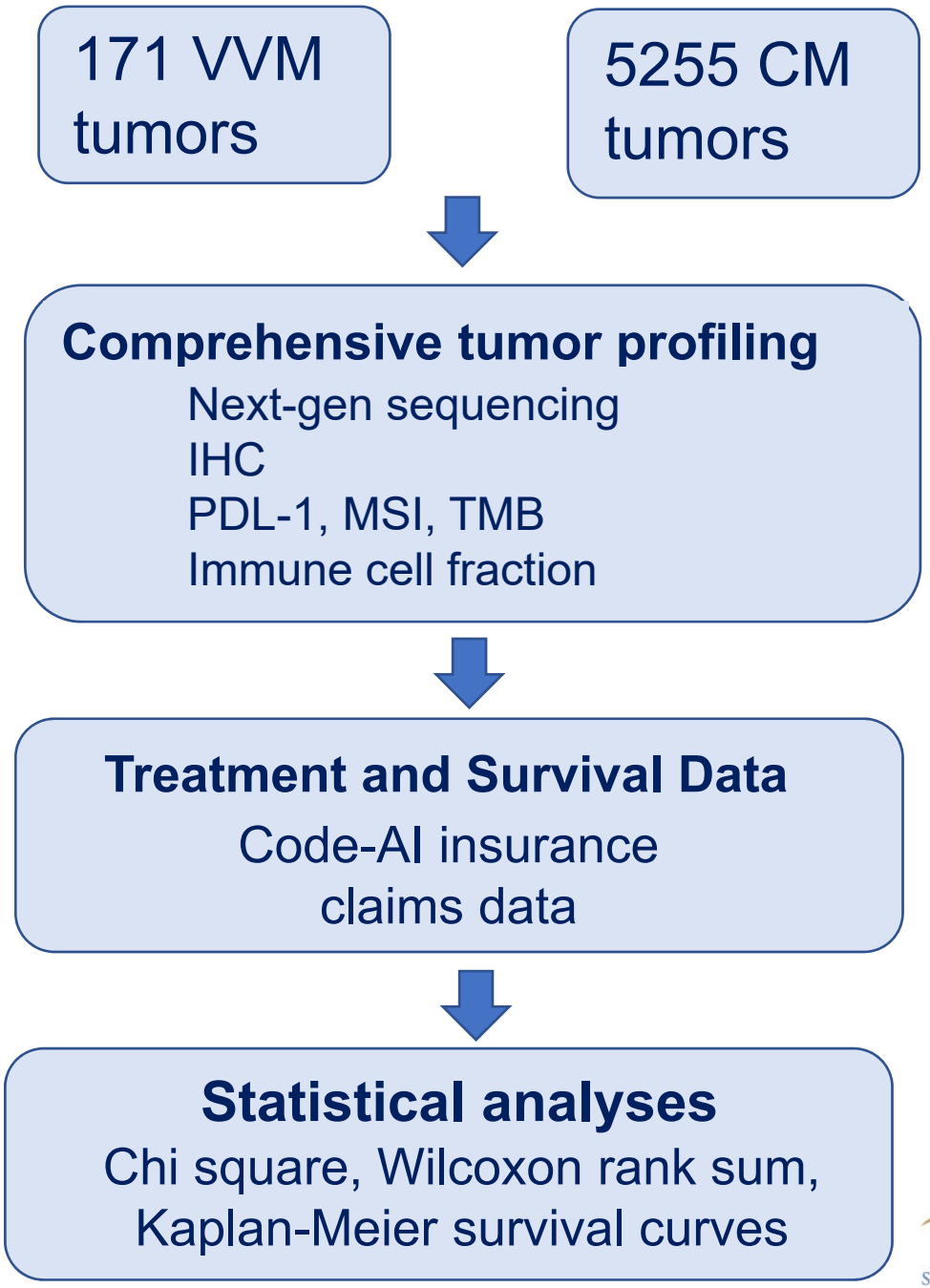


Honey *AACR blogs* 2019

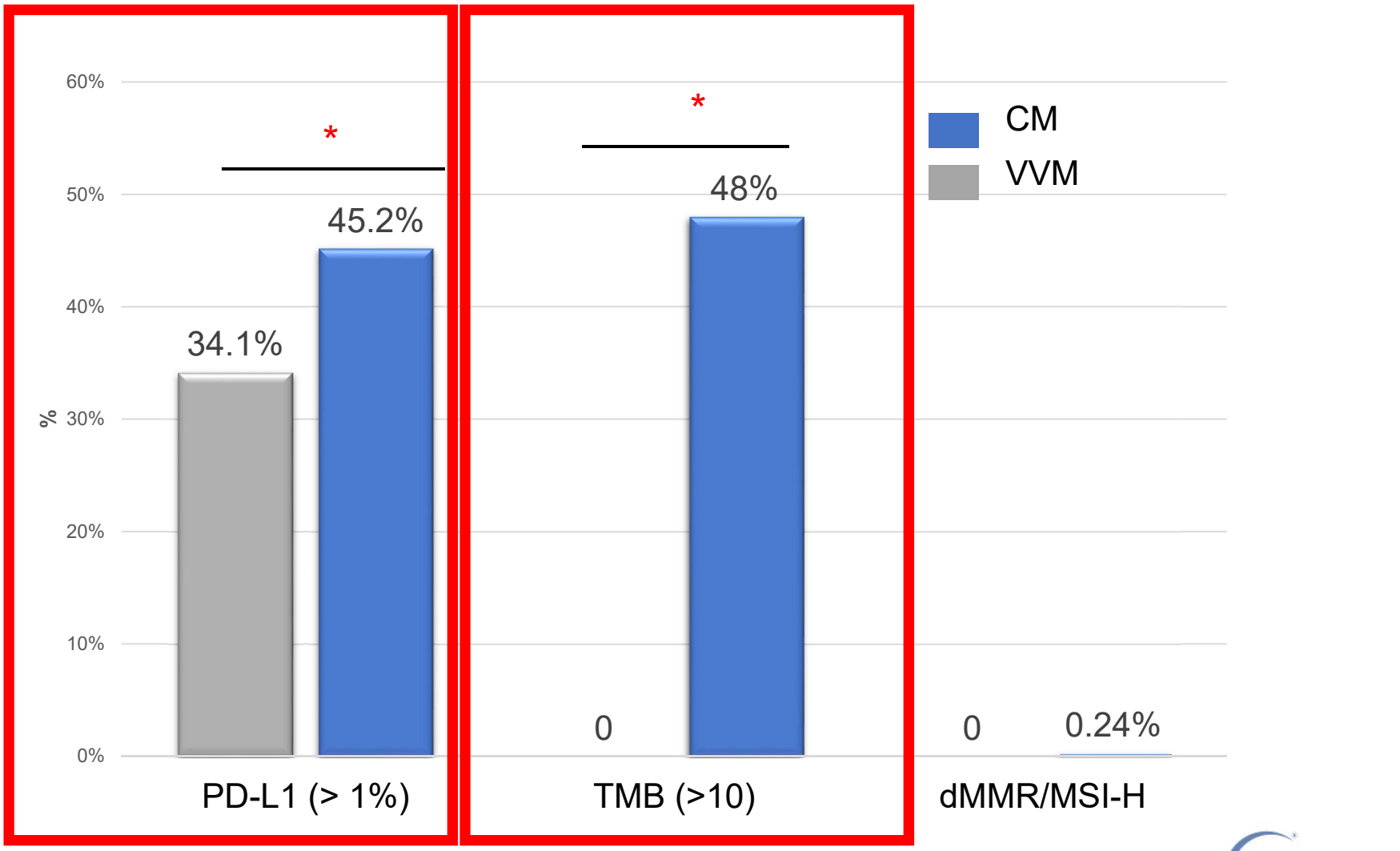
Objectives

- Compare molecular profiles of VVM with CM
- Explore the significance of Immune-Oncology (IO) agents on survival for VVM

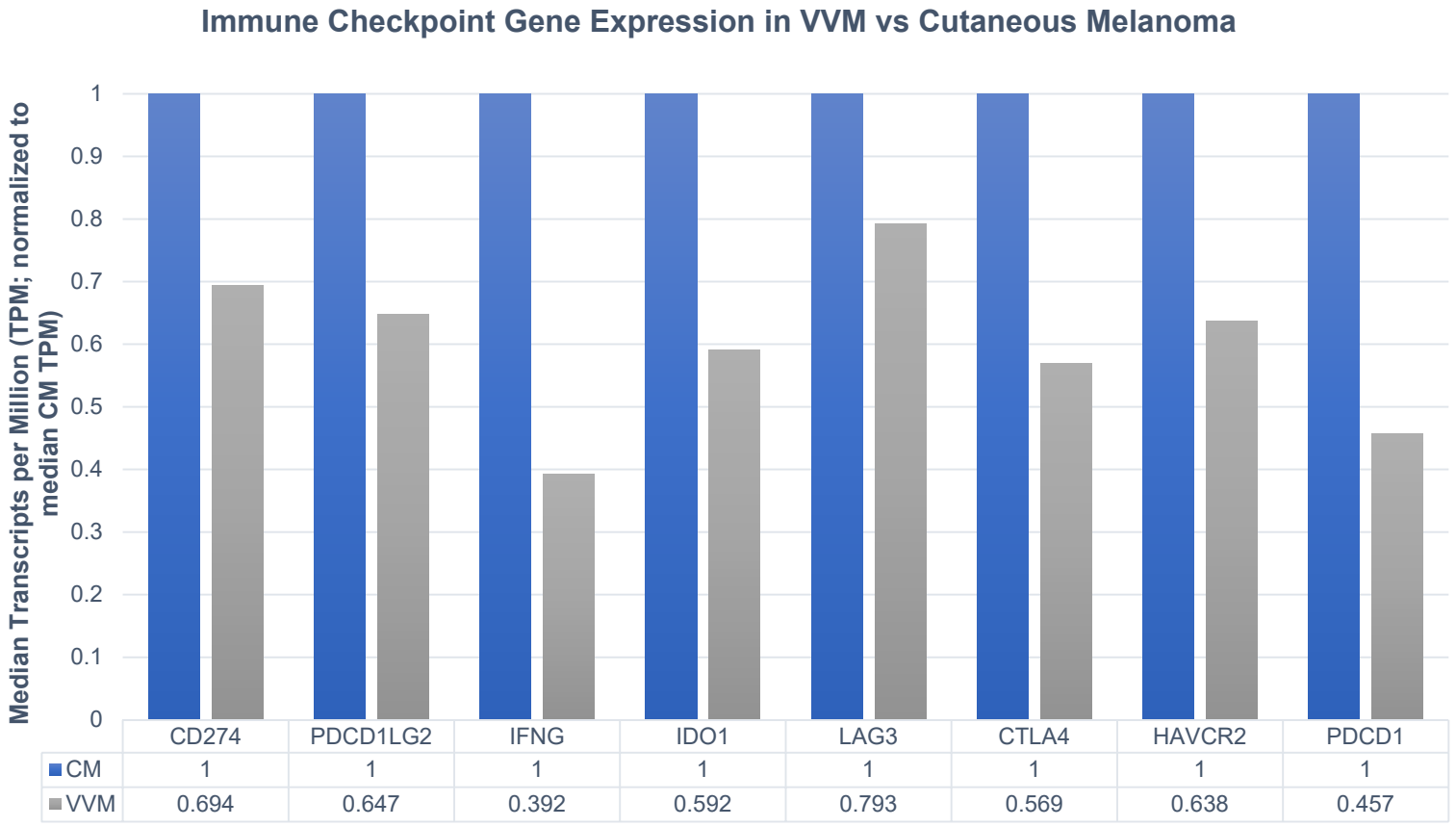
Methods


171 VVM tumors
5255 CM tumors
Comprehensive tumor profiling
Next-gen sequencing
IHC
PDL-1, MSI, TMB
Immune cell fraction
Treatment and Survival Data
Code-AI insurance claims data
Statistical analyses
Chi square, Wilcoxon rank sum, Kaplan-Meier survival curves

Markers of IO Therapy Response

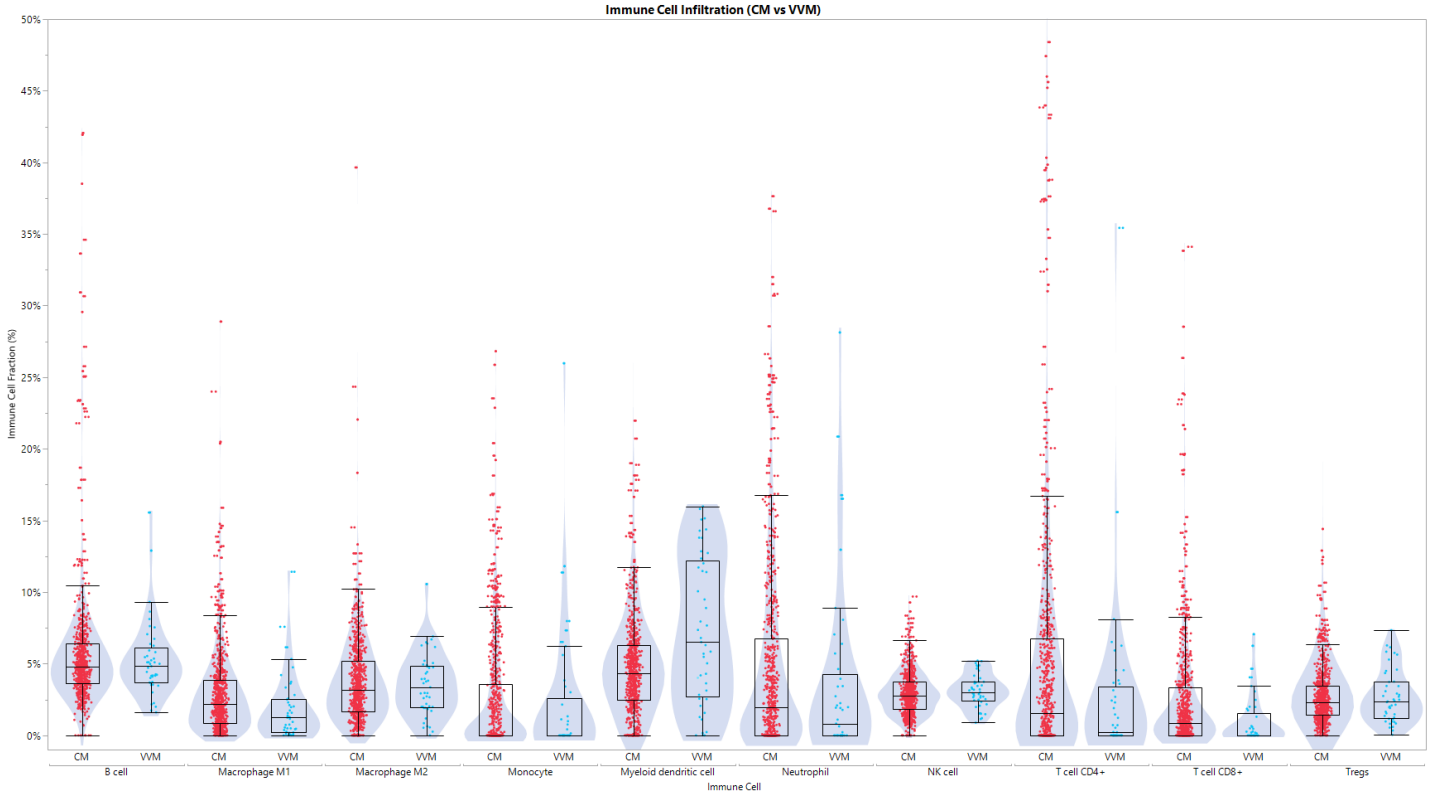


Immune Checkpoint Gene Expression in VVM vs Cutaneous Melanoma



	CD274	PDCD1LG2	IFNG	IDO1	LAG3	CTLA4	HAVCR2	PDCD1
CM	1	1	1	1	1	1	1	1
VVM	0.694	0.647	0.392	0.592	0.793	0.569	0.638	0.457

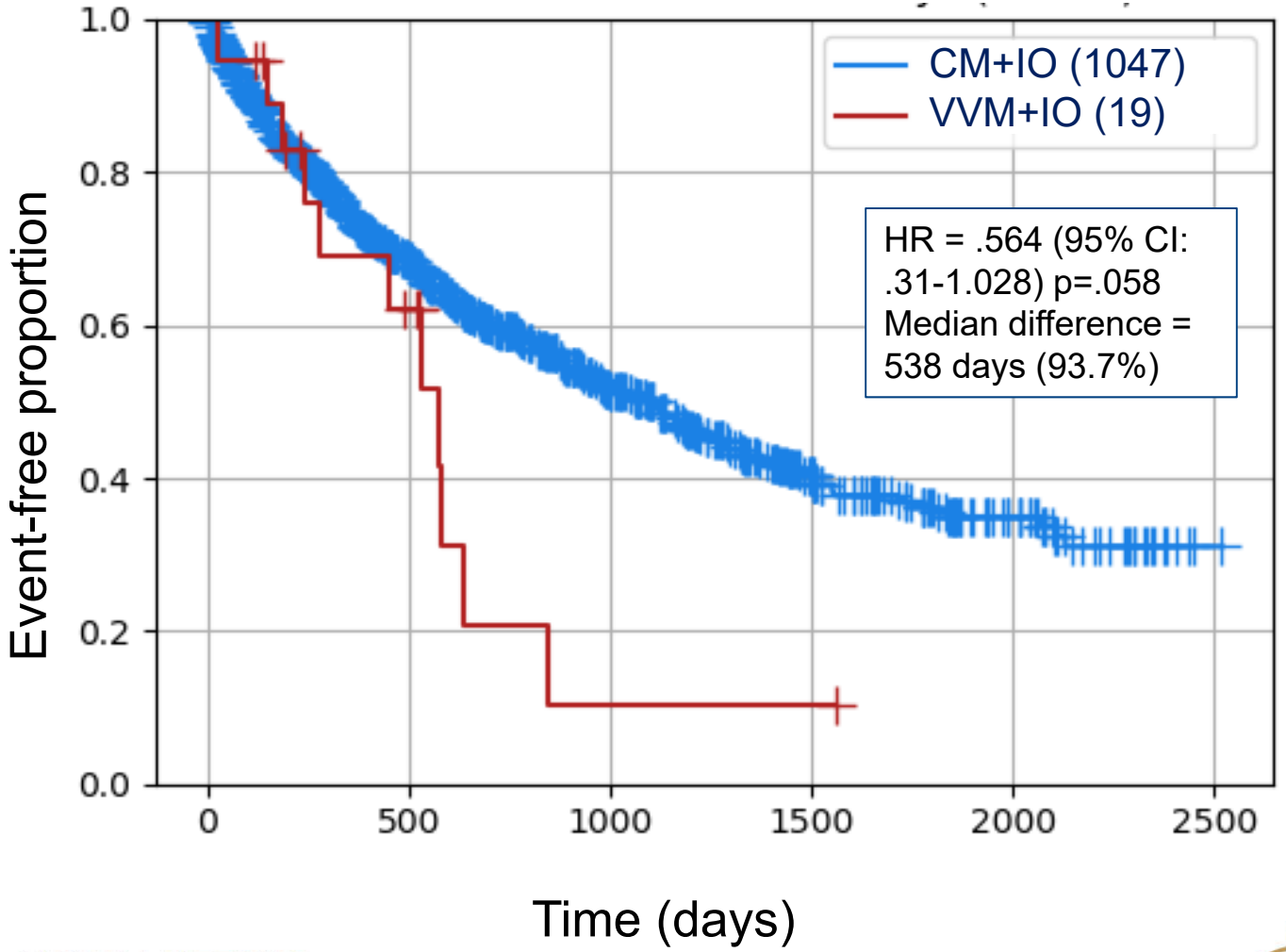
Tumor Immuno-environment



Immune Cell	Median %		P-value
	CM	*VVM*	
B Cells	4.80%	4.83%	0.9362
Macrophages M1	**2.21%**	**1.24%**	**0.0023**
Macrophages M2	3.19%	3.36%	0.9096
Monocytes	0.00%	0.00%	0.4611
Neutrophils	1.96%	0.82%	0.1324
NK Cells	2.78%	3.01%	0.1768
CD4+ T Cells	**1.54%**	**0.22%**	**0.0373**
CD8+ T Cells	**0.87%**	**0.00%**	**0.0007**
Regulatory T Cells	2.29%	2.37%	0.9706
Myeloid Dendritic Cells	**4.33%**	**6.51%**	**0.0016**

Effect of IO on Overall Survival

VVM + IO Therapy vs CM + IO Therapy



Significantly altered biomarkers and pathways – VVM and CM

	Molecular Alteration	VVM	CM	P-value
Gene	CNA-KIT	14.7%	1.5%	< 0.0001
	NGS-KIT	13.2%	2.8%	< 0.0001
	NGS-ATRX	28.4%	3.8%	< 0.0001
	NGS-SF3B1	27.8%	1.6%	< 0.0001
	NGS-BRAF	8.5%	35.8%	< 0.0001
Pathway	mRNA Splicing	28.9%	2.8%	< 0.0001
	DNA Damage Sensors	16.4%	5.2%	< 0.0001
	Cell Cycle	7.2%	18.8%	0.001
	Chromatin Remodeling	6.3%	21.4%	< 0.0001
	Wnt	0.8%	6.8%	0.008

Significantly altered biomarkers and pathways – KIT mutated sub-analysis

KIT mutated VVM vs KIT mutated CM

Molecular Alteration	KIT mut VVM	KIT mut CM	P-value
RTK RAS	100%	100%	1
mRNA Splicing	69%	9%	<0.0001
DNA Damage Sensors	13%	3%	0.1374
VEGF Signaling Pathway	13%	20%	0.7331
Cell Cycle	6%	23%	0.1877
Chromatin Remodeling	0%	31%	0.0057
TP53 Pathway	0%	27%	0.0118

KIT mutated vs KIT wild type VVM

Molecular Alteration	KIT mut VVM	KIT wt VVM	P-value
CNA-KIT	56.3%	6.3%	<0.0001
RTK RAS	100%	51%	0.0002
mRNA Splicing	69%	21%	0.0003

Conclusions

- VVM has distinct molecular profile
  - Less favorable immune phenotype
  - Lower rate of BRAF mutations
  - Higher rate KIT mutations/amplifications
- Worse survival when treated to IO therapy

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Thank You

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