

Clinical Activity of Systemic VSV-IFNβ-NIS Oncolytic Virotherapy in Patients with Relapsed Refractory T-cell Lymphoma



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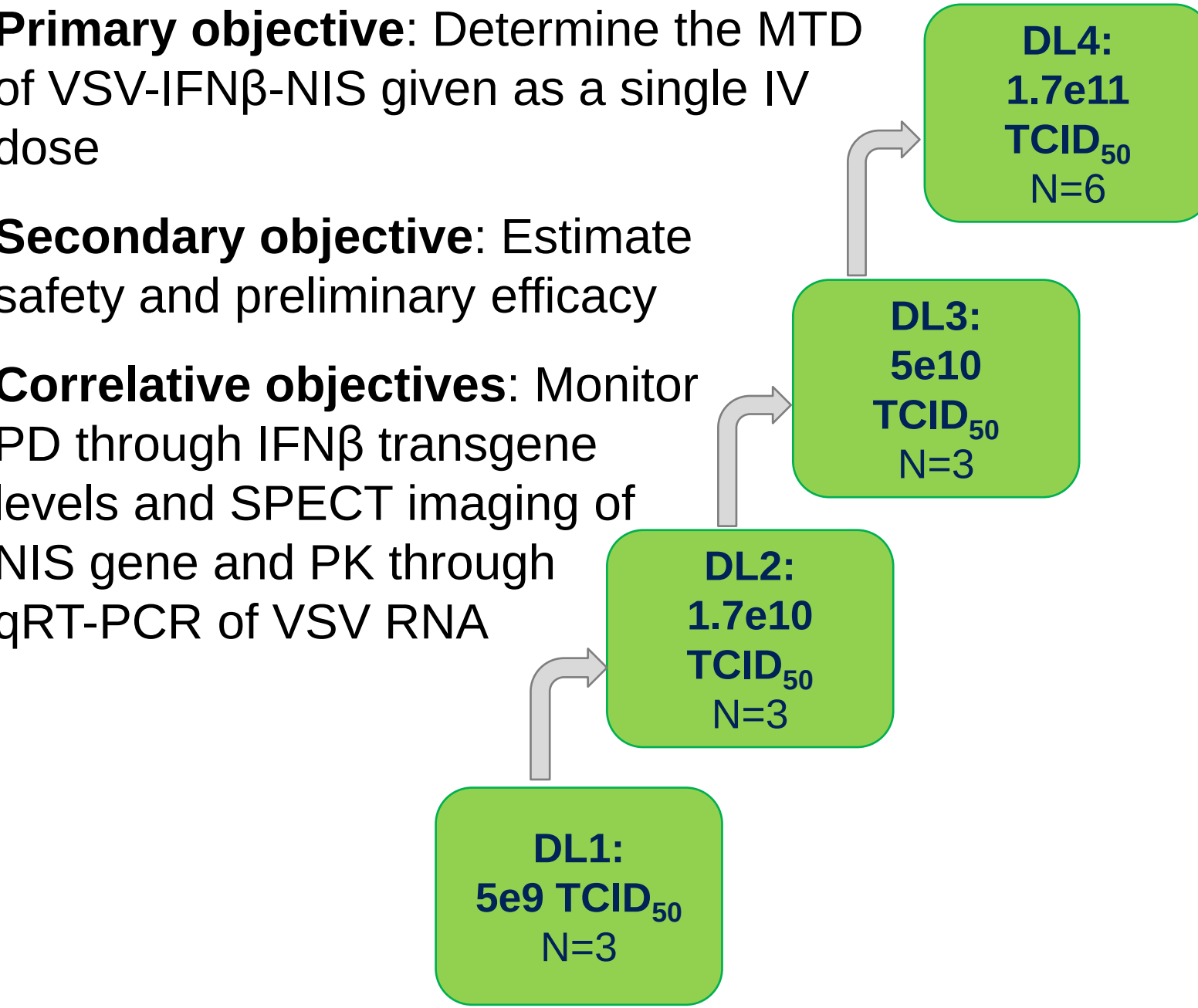


Background

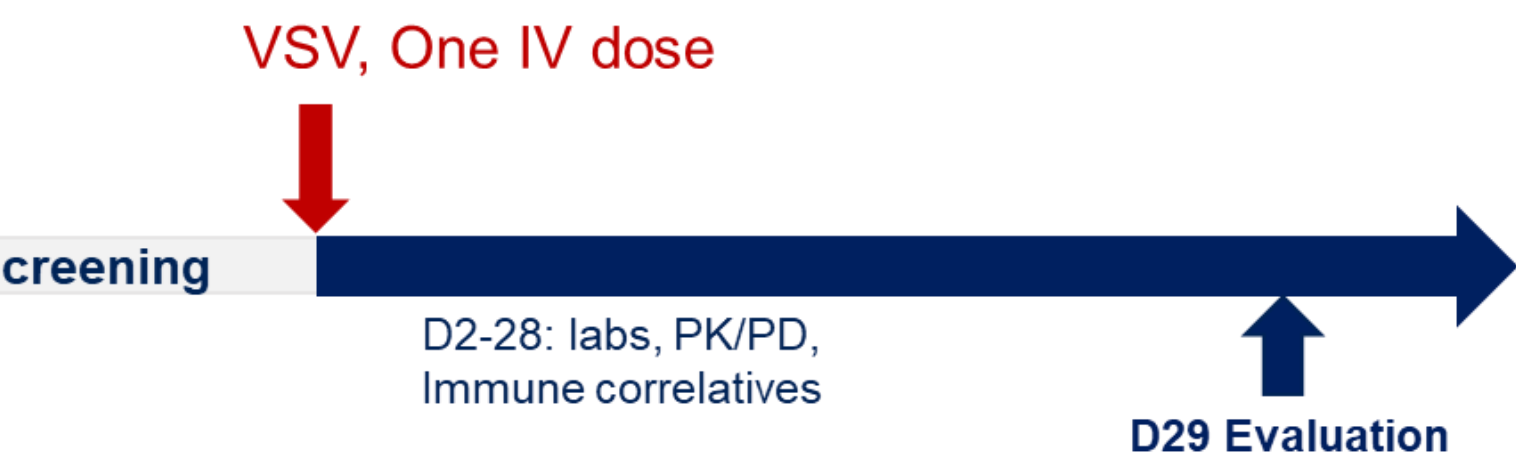
VSV-IFNβ-NIS was engineered to encode IFNβ and sodium iodine symporter (NIS)

N	P	M	IFNβ	G	NIS	L
VSV virus • Low seroprevalence • allows systemic delivery • Rapid replication and tumor cell killing IFNβ • Serves an index of viral proliferation • Enhances host antitumor immunity NIS • Reporter gene to enable monitoring of viral spread by PET/SPECT imaging						

Objectives



Study Schema



Patients

Pt ID	Sex	Age	Cancer Type	# Tx	D L	Viral dose	DLT
1A.1	F	69	MM	10		5 x 10 ⁹	
1A.2	M	59	MM	4	1	TCID ₅₀	No
1A.3	F	49	MM	7			
2A.1	F	66	CTCL	11		1.7 x 10 ¹⁰	
2A.2	M	88	CTCL	5	2	TCID ₅₀	No
2A.3	M	72	AML	6			
3A.1	M	63	MM	7		5 x 10 ¹⁰	
3A.2	F	64	MM	3	3	TCID ₅₀	No
3A.3	M	56	PTCL	3			
4A.1	M	64	MM	7			
4A.2	M	63	MM	4			
4A.3	F	67	PTCL	5		1.7x10 ¹¹	
4A.4	F	56	PTCL	5	4	TCID ₅₀	No
4A.5	M	33	PTCL	7			
4A.6	M	60	PTCL	2			

Baseline

Day 23: lesions cleared

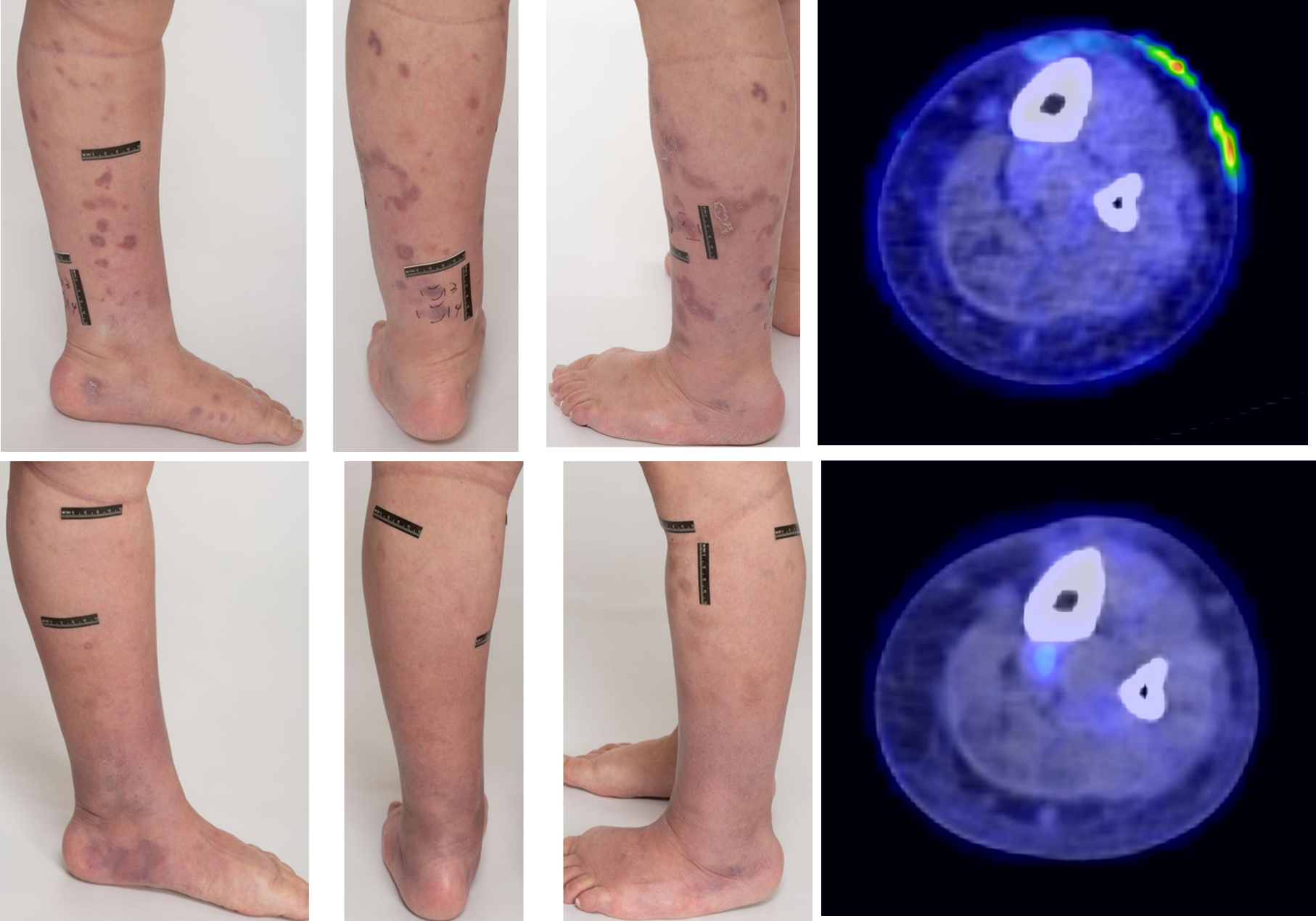
Day 101, 4Gy

Day 110

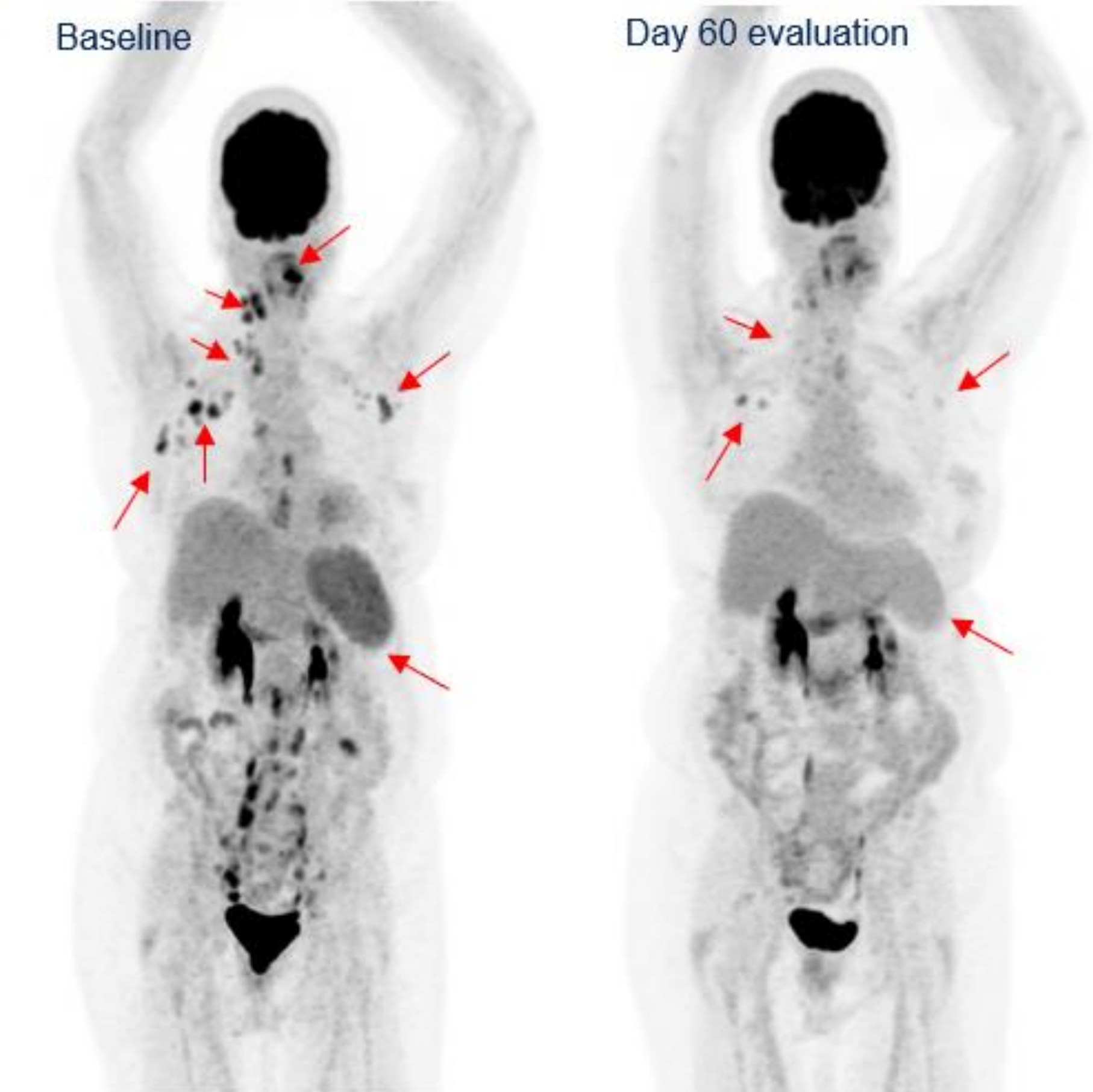
Pt 2A.1: PR 3 months, DL2 CD30+ CTCL

After RT, response on relapsed non target lesions. Abscopal response?

Responses



Pt 4A.3 Ongoing 16-month CR at DL4 CD30+ Multisite anaplastic large cell TCL

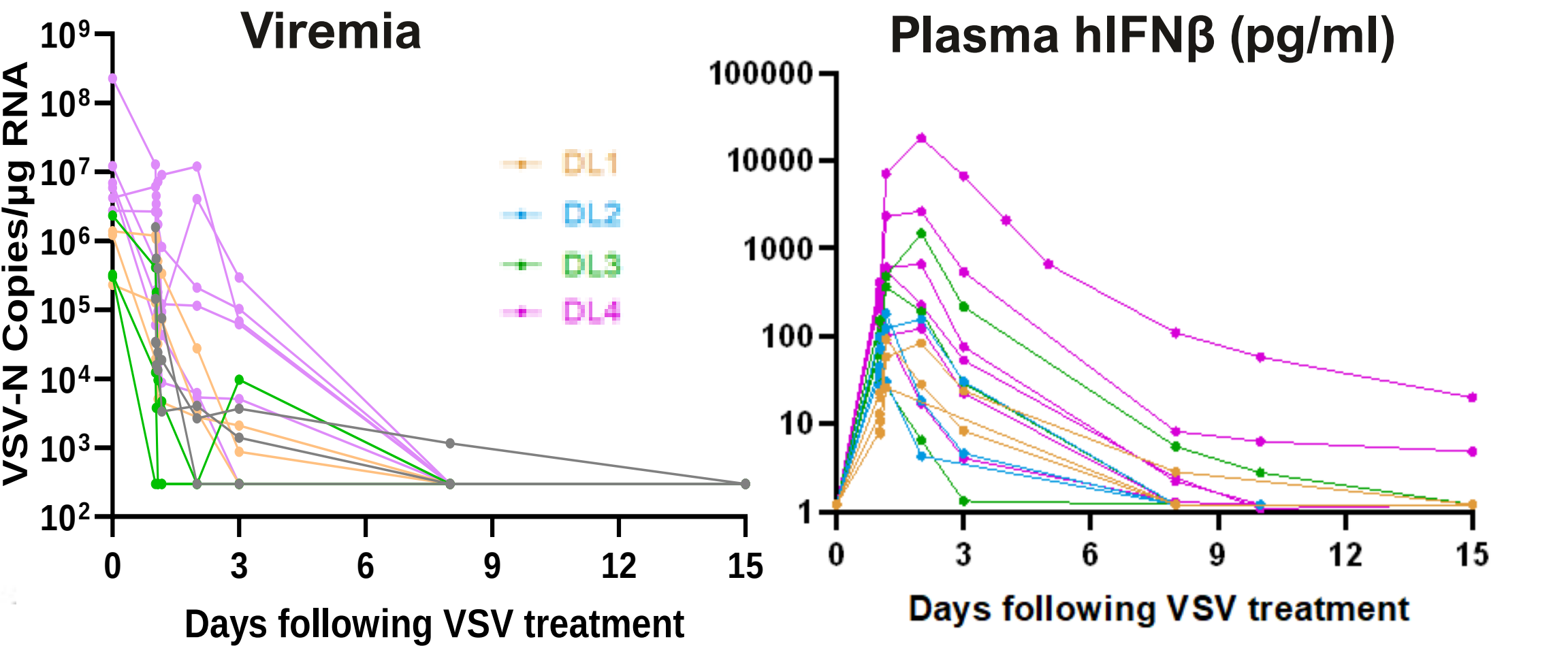


Pt 4A.4 Partial Response DL4 CD30+ PTCL

Safety

Dose VSV-IFNβ-NIS	TCID 5 x 10 ⁹			TCID 1.7 x 10 ¹⁰			TCID 5 x 10 ¹⁰			TCID 1.7 x 10 ¹¹					
	1A.1 MM	1A.2 MM	1A.3 MM	2A.1 TCL	2A.2 TCL	2A.3 AML	3A.1 MM	3A.2 MM	3A.3 TCL	4A.1 MM	4A.2 MM	4A.3 TCL	4A.4 TCL	4A.5 TCL	4A.6 TCL
Hem AE															
anemia															
Lymph ↓															
platelet ↓															
neut ↓															
WBC ↓															
fever															
anorexia															
headache															
↓Ca															
pain															
diarrhea															
nausea															
CRS															
dizziness															
chills															
vomiting															
fatigue															
tachycardia															
ALT ↑															
anxiety															
Cr ↑															
tremor															
ALP ↑															

Pharmacokinetics



Conclusion

A single IV dose of VSV-IFNβ-NIS up to 1.7 x 10¹¹ TCID₅₀ is safe in pts with R/R hematologic malignancies

no DLT, no CRS> Grade 2

R/R T-Cell Lymphoma pts demonstrate efficacy signal to single agent VSV-IFNβ-NIS

- overall heavily pretreated refractory cohort
- 50% response at DL4
- responses with a single dose

Insertion of transgenes useful for noninvasive assessment

- IFNβ a biomarker of intratumoral amplification