Phase I/II STORM study: Intravenous delivery of a novel oncolytic immunotherapy agent, CAVATAK, in advanced cancer patients

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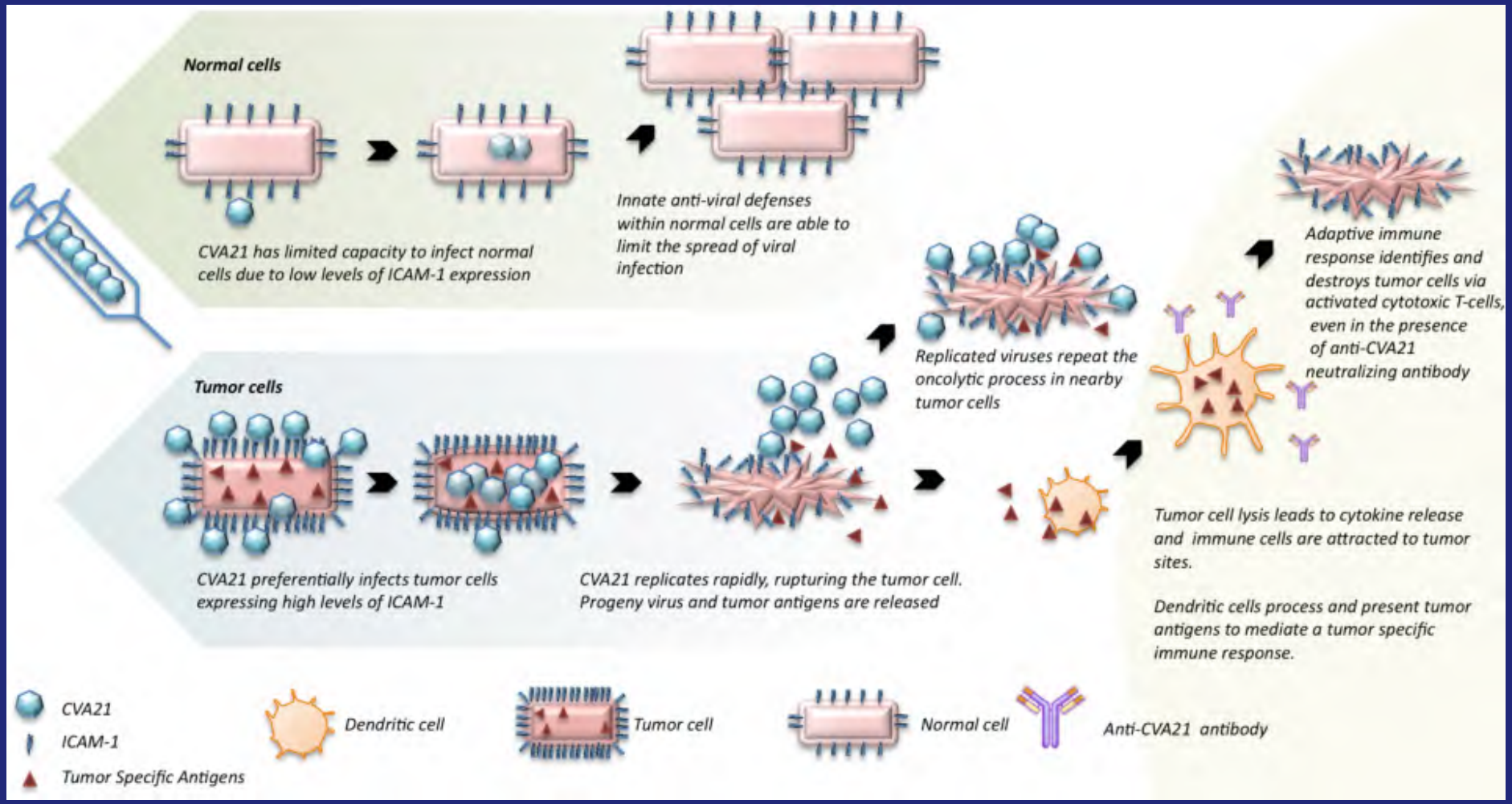
CAVATAK™ (Coxsackievirus A21) an oncolytic immunotherapeutic agent

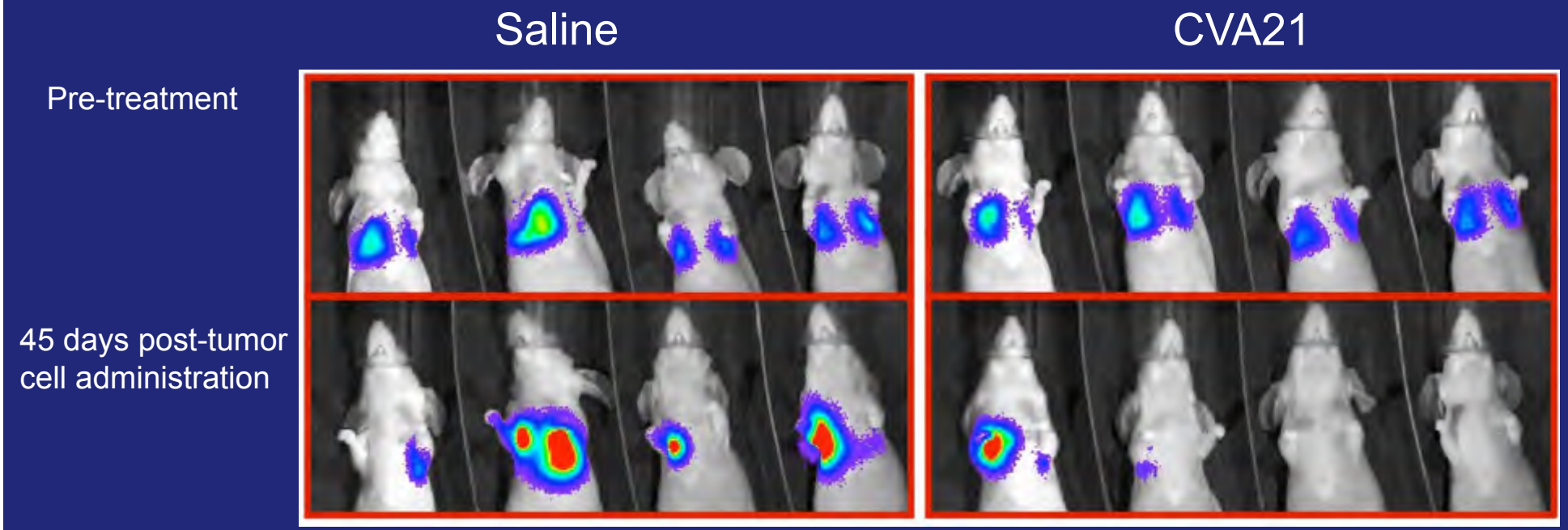
- Proprietary formulation of the oncolytic virus, Coxsackievirus , A 21
- Targeted to specific receptor over expressed on cancer cells (ICAM-1)
- Kills local and metastatic cells by oncolytic and immunotherapeutic activity
- Potential application across a range of cancer types
- Well tolerated in patients with to date no treatment-related grade 3 or 4 adverse events
- Potential intravenous as well as intratumoral and intravesical use
- Potential application as monotherapy or with other new agents
- Manufactured under cGMP at SAFC, California

Coxsackievirus A21(CVA21)

Oncolytic immunotherapeutic modes of action



Pre-clinical anti-tumor activity of mono-therapy intravenous CVA21 in orthotopic mouse model of Non-small cell lung cancer (NCI-H1299-luc^{+} cells)



VLA-004 : Phase I single dose intravenous CAVATAK in subjects bearing ICAM-1 expressing solid tumors

Study Design

10 subjects
advanced melanoma, prostate, breast or colorectal cancer

<1:16 anti-CAVATAK serum antibodies

↓

Single infusion

1 x10^6 $TCID_{50}$ n=3

1 x10^8 $TCID_{50}$ n=4

1 x10^9 $TCID_{50}$ n=2

1 x10^{10} $TCID_{50}$ n=1

Study Endpoints

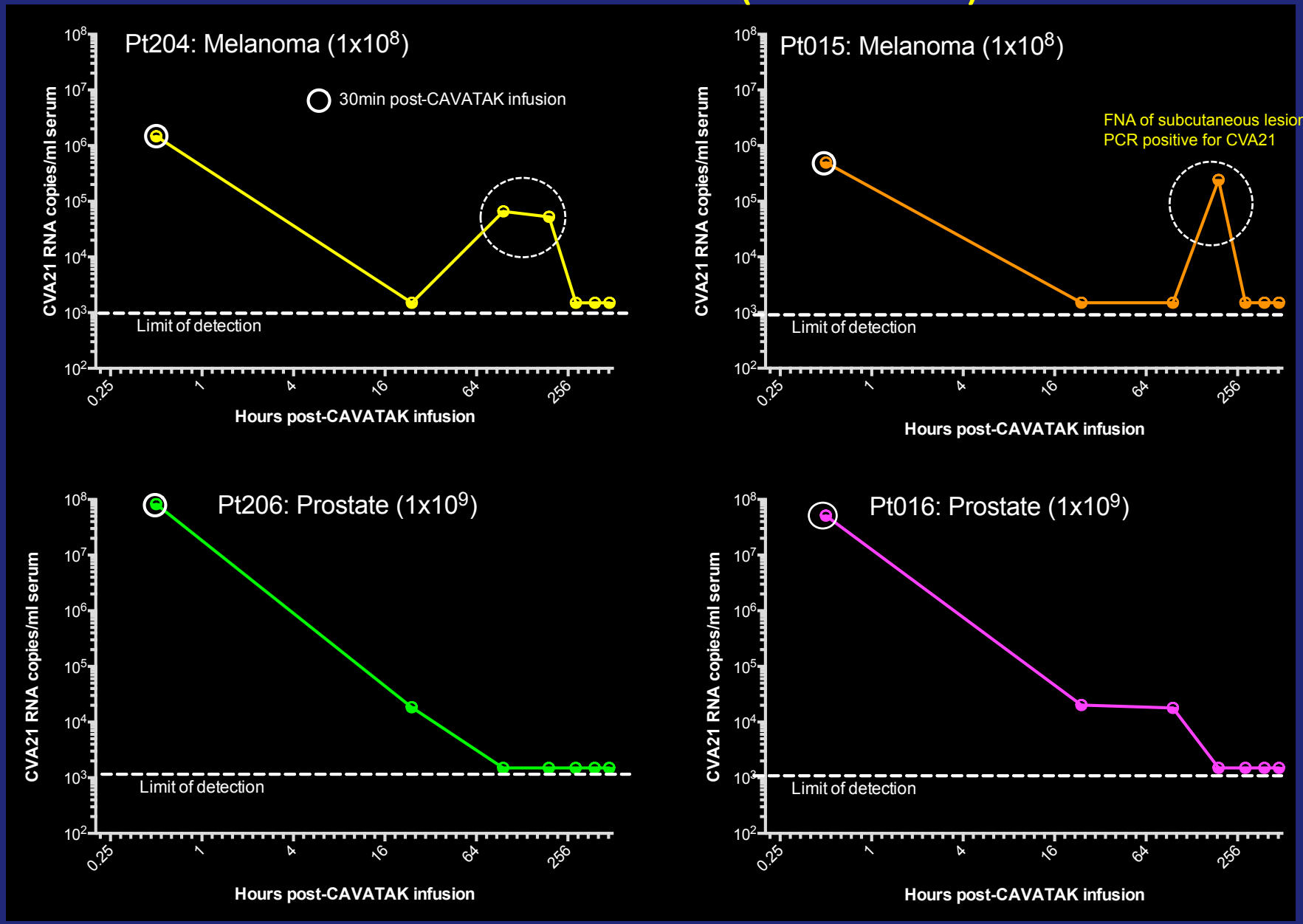
Primary

- Patient tolerability
- Determination of MTD

Secondary

- Pharmacokinetics of serum viral load and anti-CAVATAK antibodies
- Viral excretion

VLA-004 (Single dose IV study): Pharmacokinetics Serum viral load (viral RNA)



VLA-004 conclusions

- CAVATAK IV fusion well tolerated
- No SAE related to CAVATAK
- No MTD reached
- Preliminary evidence of CAVATAK tumour targeting
- Preliminary evidence of secondary CAVATAK replication
- Significant levels of neutralising antibodies
- were detected by Day 5 to Day 12
- CAVATAK detected in some excretion samples day 5-20

VLA-009 (STORM study): Phase I/II multi-dose intravenous CAVATAK in subjects with advanced melanoma, prostate, NSCLC or bladder cancer

VLA-009A (Monotherapy)

27 subjects with advanced melanoma, prostate, NSCLC or bladder cancer with <1:16 anti-CAVATAK serum antibodies

IV infusions of CAVATAK

on Day **1,3,5**,21,43,64,85.106,127,158

Cohort 1
Any cancer
1 x10^8 $TCID_{50}$
n=3

Cohort 2
Any cancer
3 x 10^8 $TCID_{50}$
n=3

Cohort 3
1 x 10^9 $TCID_{50}$
Mandatory lesion biopsy
Melanoma ,NSCLC, Bladder
And Prostate cancer n=3 each

VLA-009B (Chemotherapy combination)

IV infusions of CAVATAK
Day 1,3,5,21,43,64,85.106,127,158 + Docetaxel or Carbo/Pac every 3 weeks

Cohort 1
Selected cancer
1 x10^8 $TCID_{50}$
+ Docetaxel or Carbo/Pac
n=3

Cohort 2
Selected cancer
3 x10^8 $TCID_{50}$
+ Docetaxel or Carbo/Pac
n=3

Cohort 3
Selected cancer
1 x10^9 $TCID_{50}$
+ Docetaxel or Carbo/Pac
n=3

Study Endpoints

Primary
- Patient tolerability
- Determination of MTD

Secondary
- Pharmokinetics of serum viral load and anti-CAVATAK antibodies
- Viral excretion
- Level of viral replication in tumor
- Virus-induced tumor cell infiltrates and immune checkpoint molecules

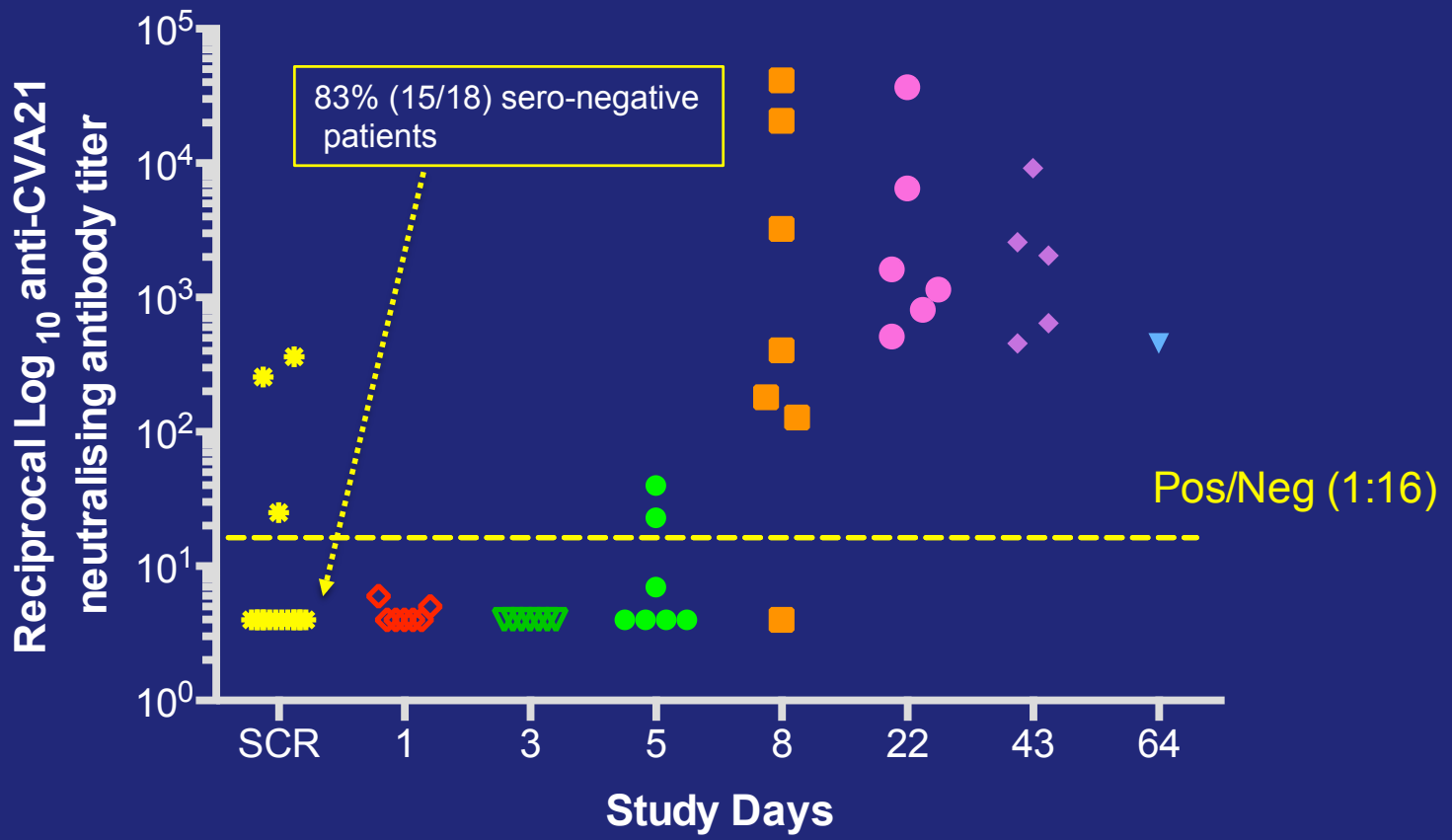
VLA-009 (STORM study): Patient characteristics

	Patient Identification Code	Gender	Cancer Indication	Previous Lines of Treatment	Duration of Treatment (cycles)
Cohort 1	03-001	Male	NSCLC	Chemotherapy x3, clinical trial (AZD4547), lobectomy (RUL, RML)	3
	03-002	Male	Melanoma	Chemotherapy x2, resection	2
	02-001	Male	Bladder	Chemotherapy x3, radiotherapy	8
Cohort 2	02-002	Male	Bladder	immunotherapy, chemotherapy, TUR x 2	4
	01-001	Male	Prostate	hormonal therapy x6, clinical trial (ONY-P-1), radiotherapy, chemotherapy	8
	02-003	Male	NSCLC	Chemotherapy x3, radiotherapy	2
Cohort 3	01-005	Male	Prostate	Hormonal therapy x2, radiotherapy, immunotherapy	3
	01-006	Male	Prostate	Hormonal therapy x4, radiotherapy	6
	03-005	Male	Prostate	Radiotherapy, hormone therapy, chemotherapy x2	1
	02-005	Female	Melanoma	Vem, pembro	3
	03-006	Male	Melanoma	Ipi, chemo, RT	2

VLA-009 (STORM study): Product-related Adverse events

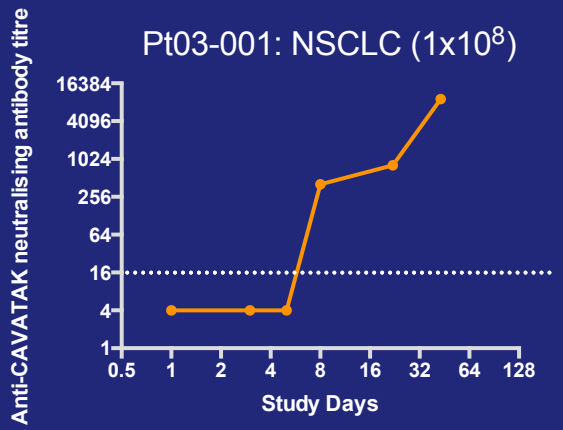
AE Terminology	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Pyrexia	2 (18%)	-	-	-	-
Fatigue	2 (18%)	1 (9%)	-	-	-
Flu-like symptoms	2 (18%)	-	-	-	-
Dry skin	1 (9%)	-	-	-	-
Bloating	1 (9%)	-	-	-	-
Diarrhoea	1 (9%)	-	-	-	-
Lethargy	1 (9%)	-	-	-	-

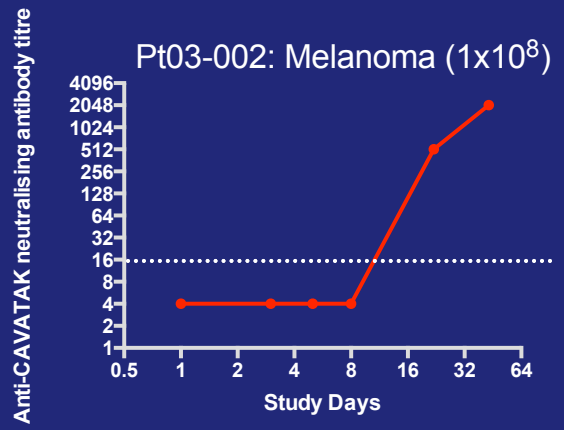
VLA-009 (STORM study): Patient anti-viral immune response: Serum neutralizing antibody levels

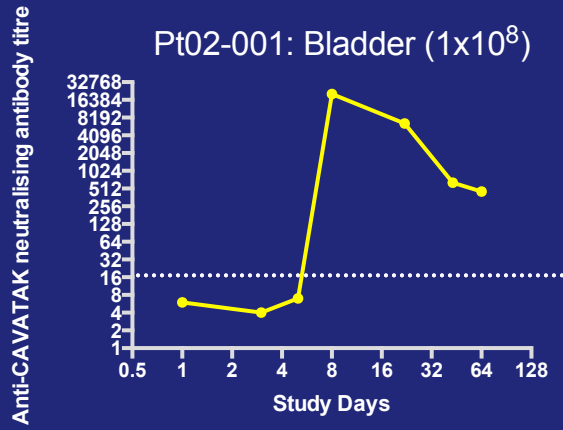


VLA-009 (STORM study): Individual patient anti-CAVATAK immune response

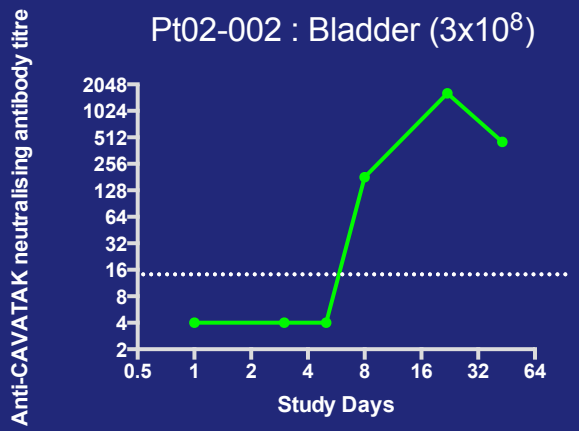
Cohort 1

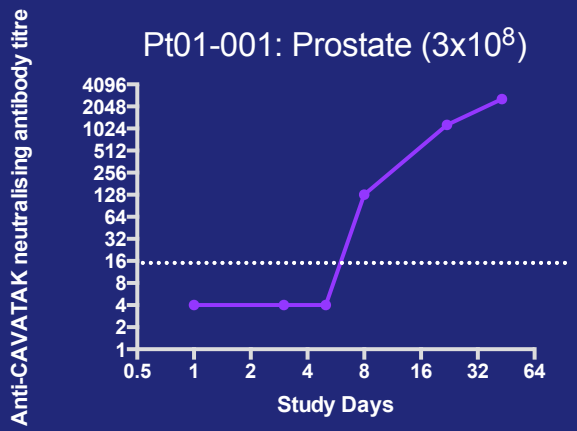


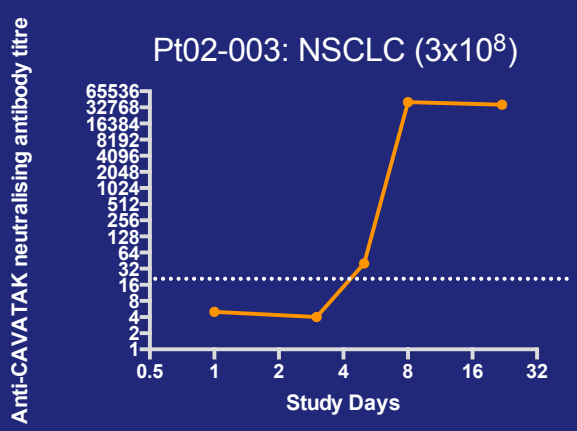




Cohort 2

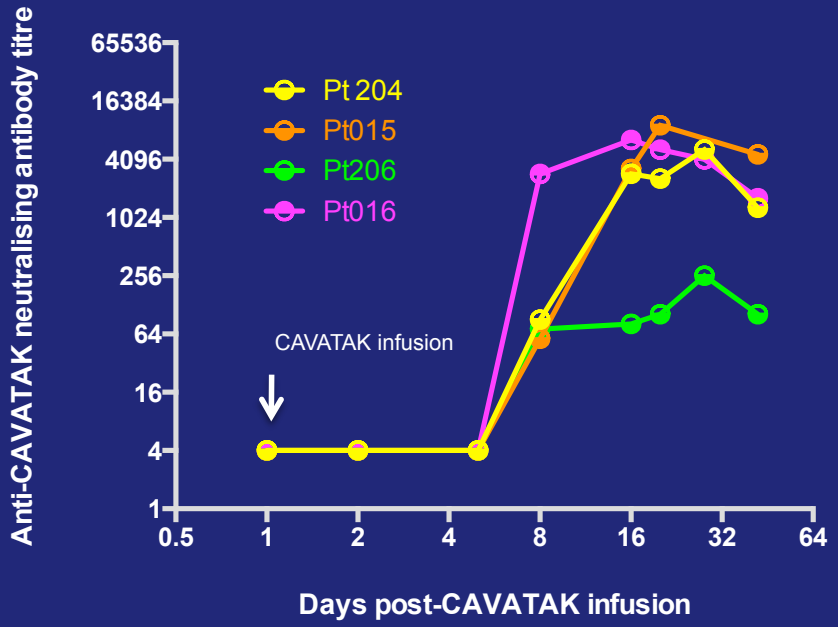




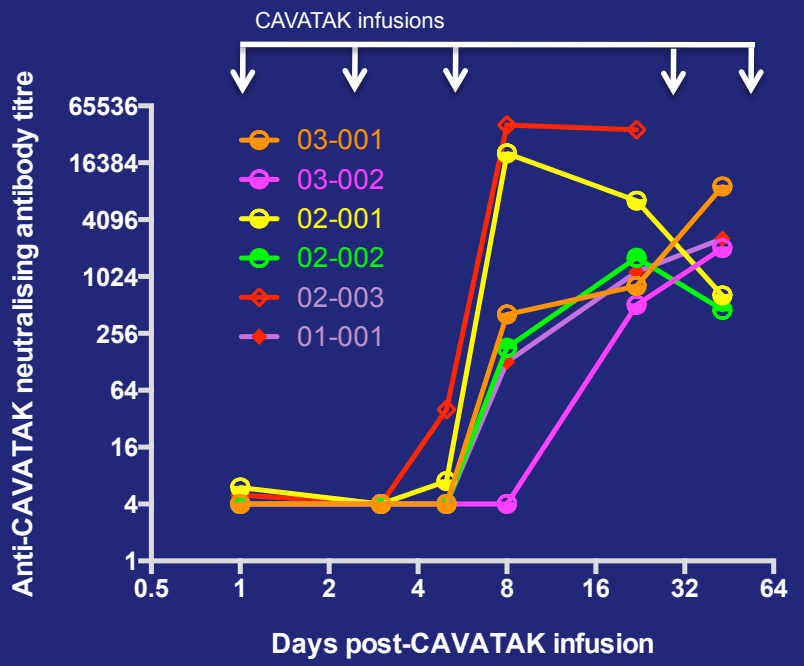


VLA-004 (single-dose) and VLA-009 (multi-dose): Pharmacokinetics Serum anti-CAVATAK neutralising antibody development

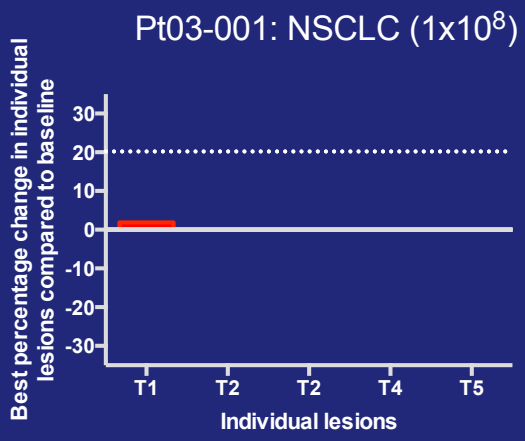
VLA-004 single IV dose

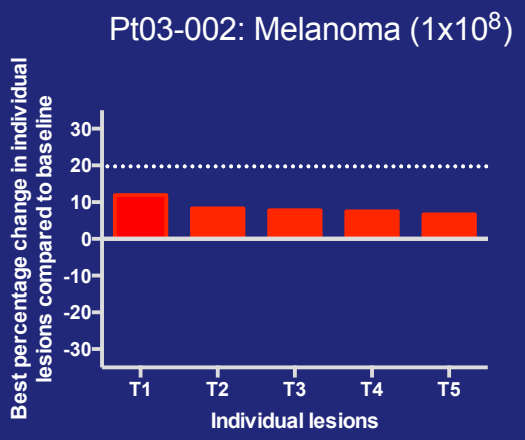


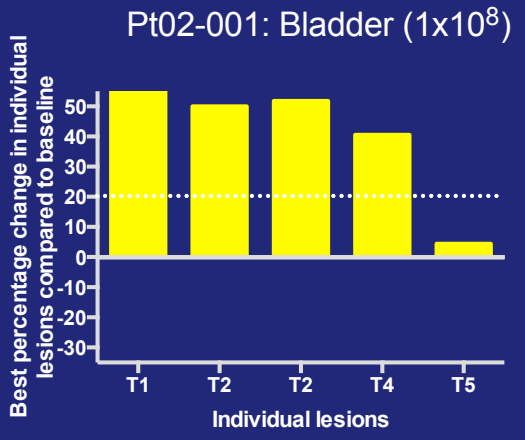
VLA-009 multi IV dose

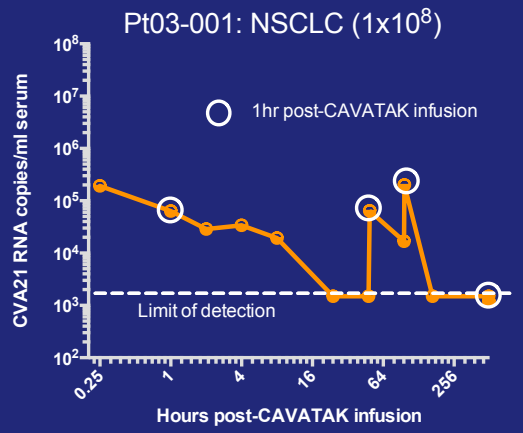


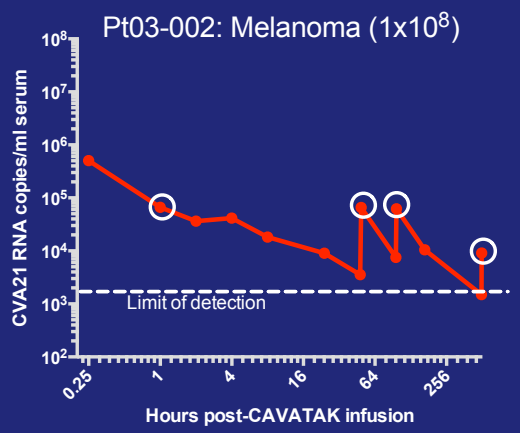
VLA-009 (STORM study): Individual lesion response and Pharmacokinetics of serum viral load (viral RNA): Cohort 1

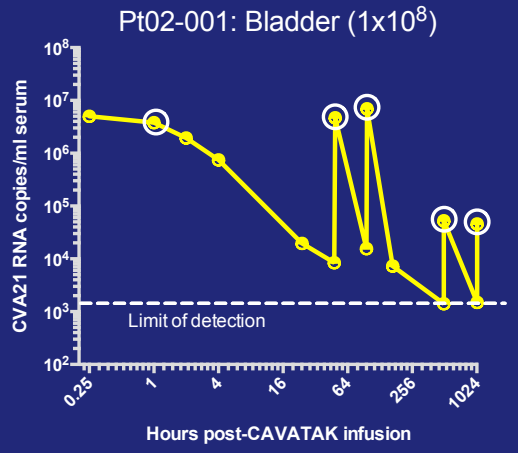




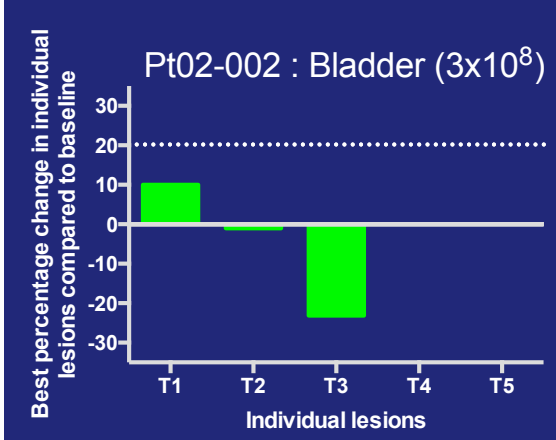


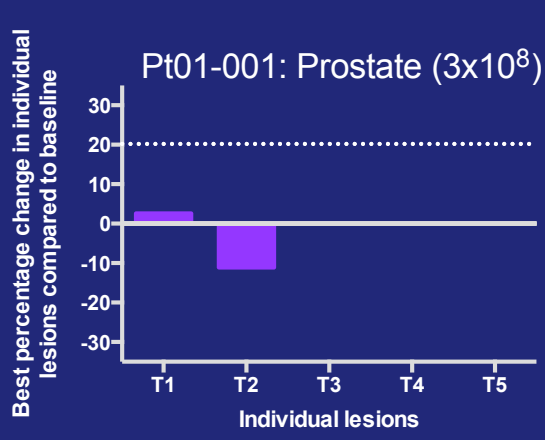


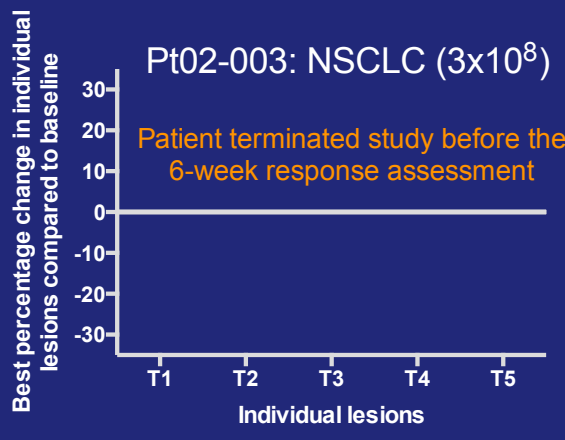


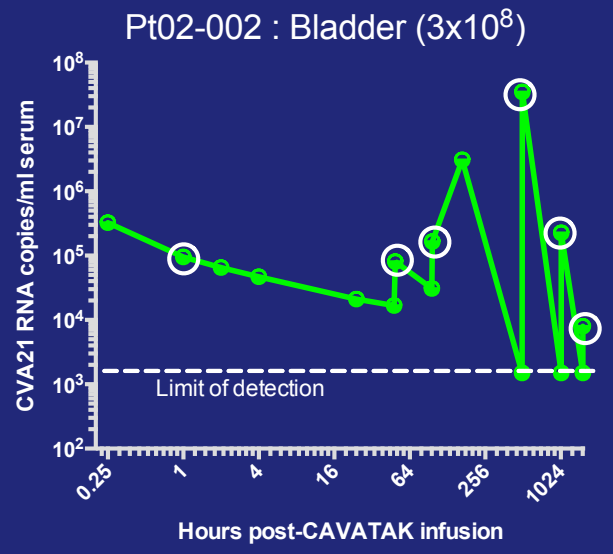


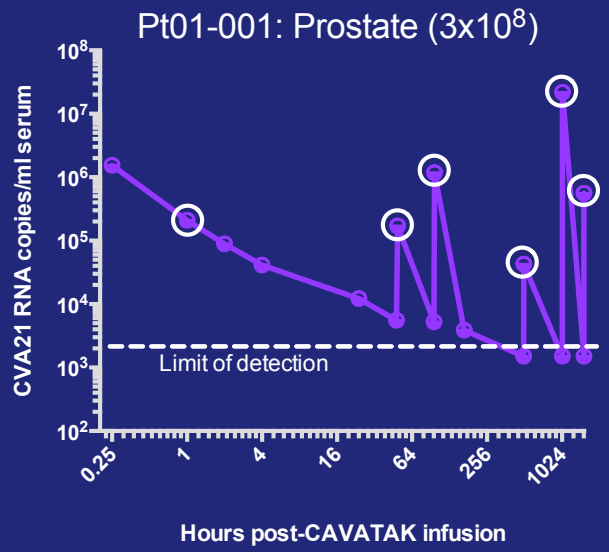
VLA-009 (STORM study): Individual lesion response and Pharmacokinetics of serum viral load (viral RNA): Cohort 2

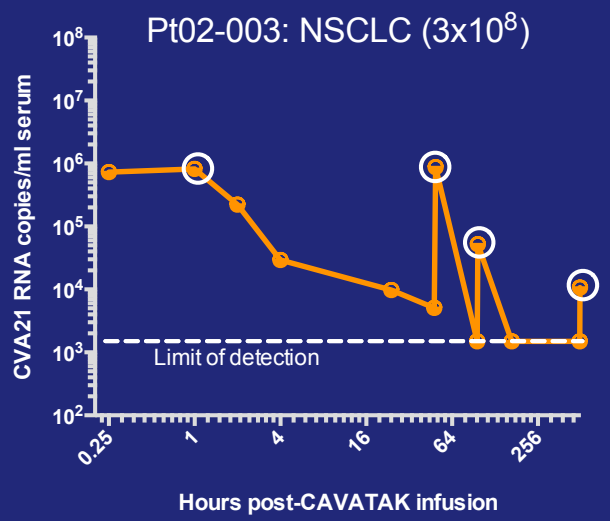












VLA-009 (STORM study): Target lesion response: Patient 02-002 - Cohort 2

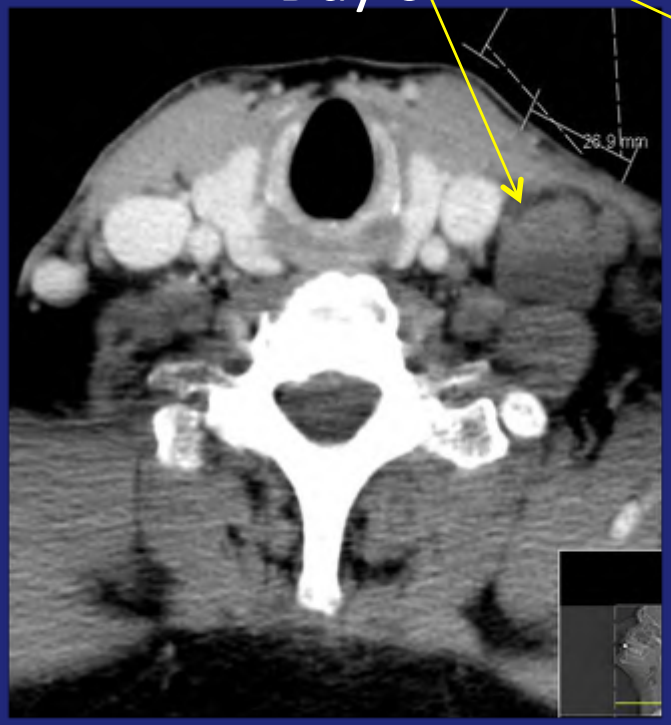
Pt 02-002: Cohort 2

Male with metastatic bladder cancer

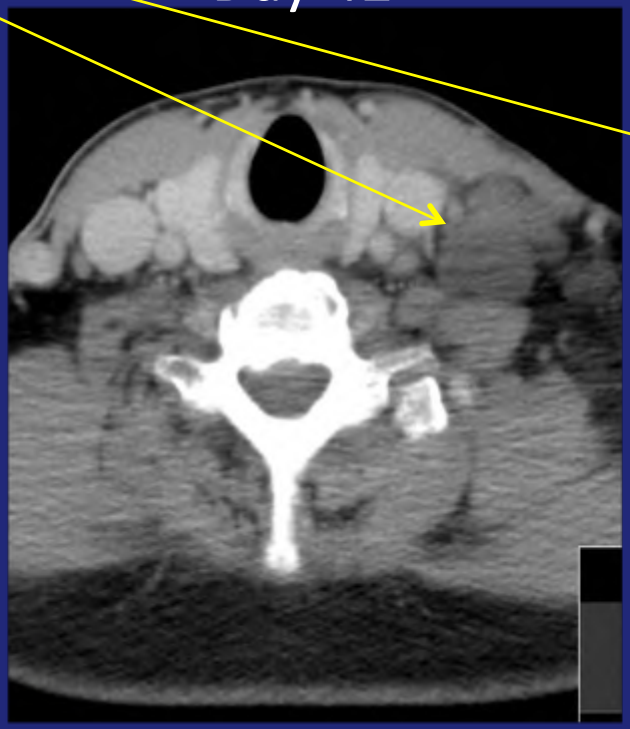
Left level III/IV Lymph Node

23% reduction

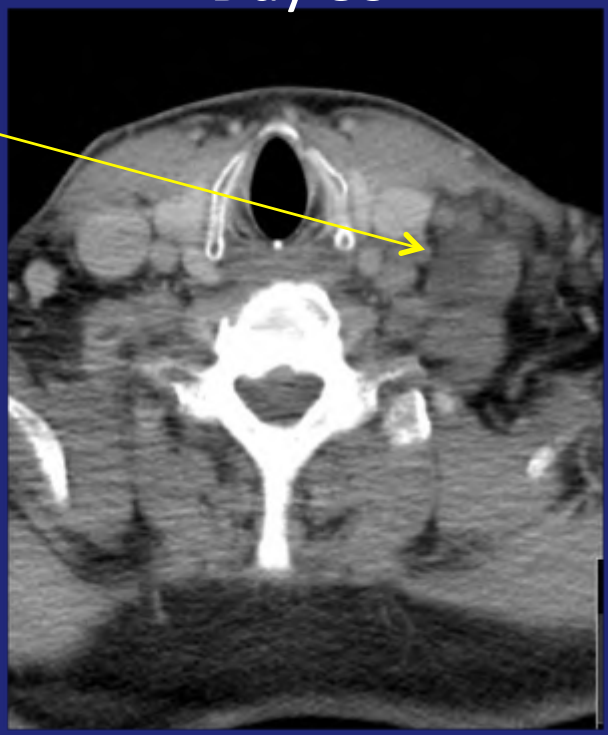
Day 0



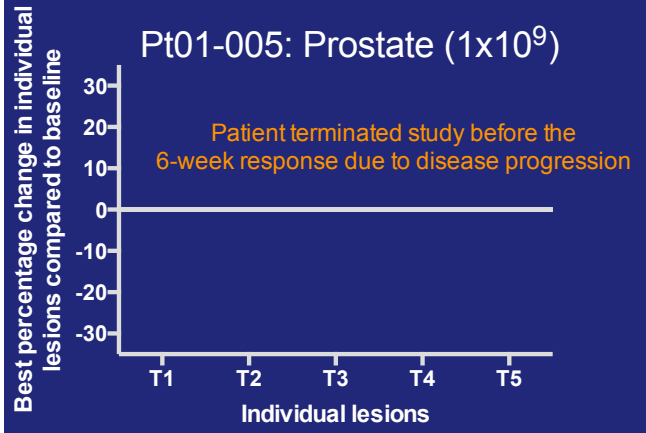
Day 42

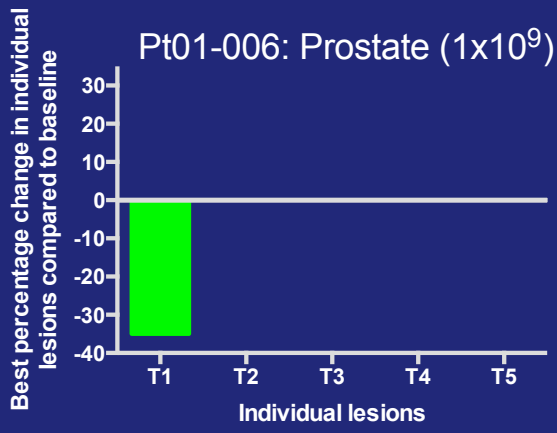


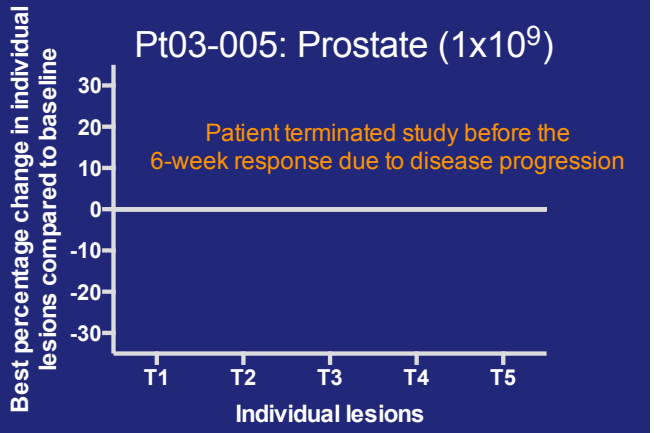
Day 83

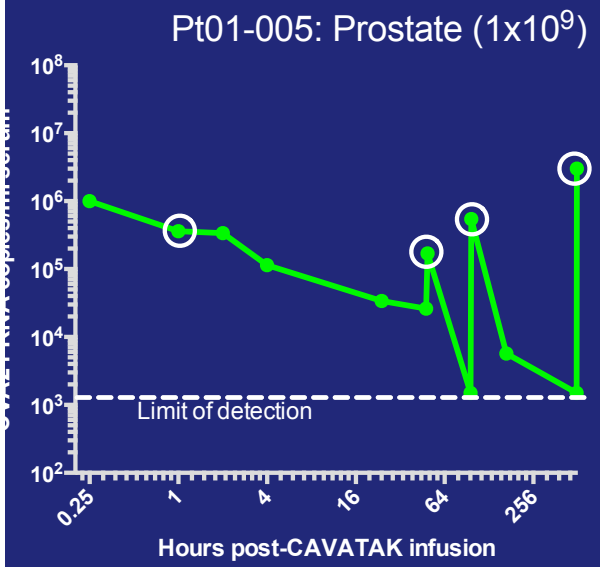


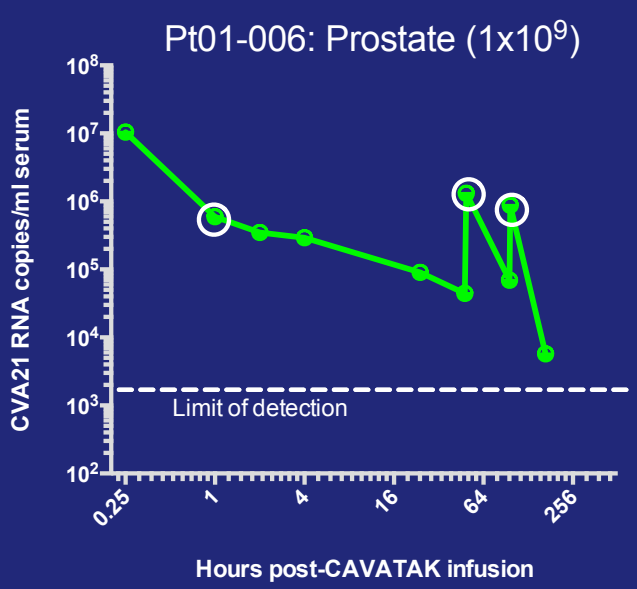
VLA-009 (STORM study): Individual lesion response and Pharmacokinetics of serum viral load (viral RNA): Cohort 3 - Prostate

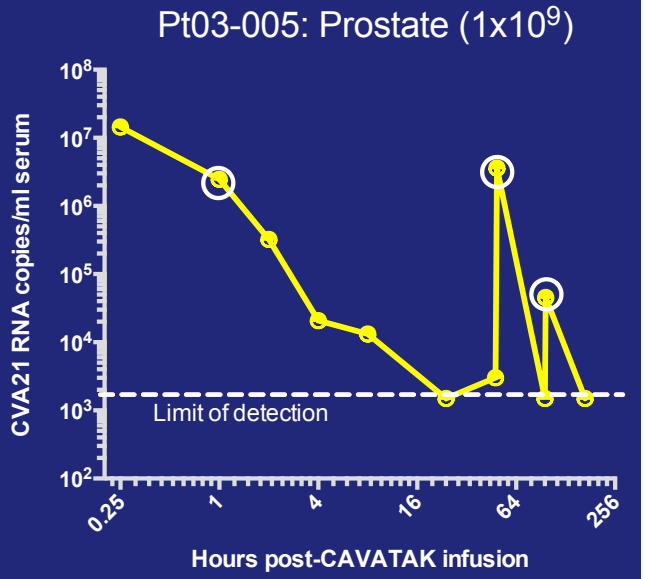












VLA-009 (STORM study): Target lesion response: Patient 01-006 – Cohort 3:Prostate cancer

Pt 01-006: Cohort 3

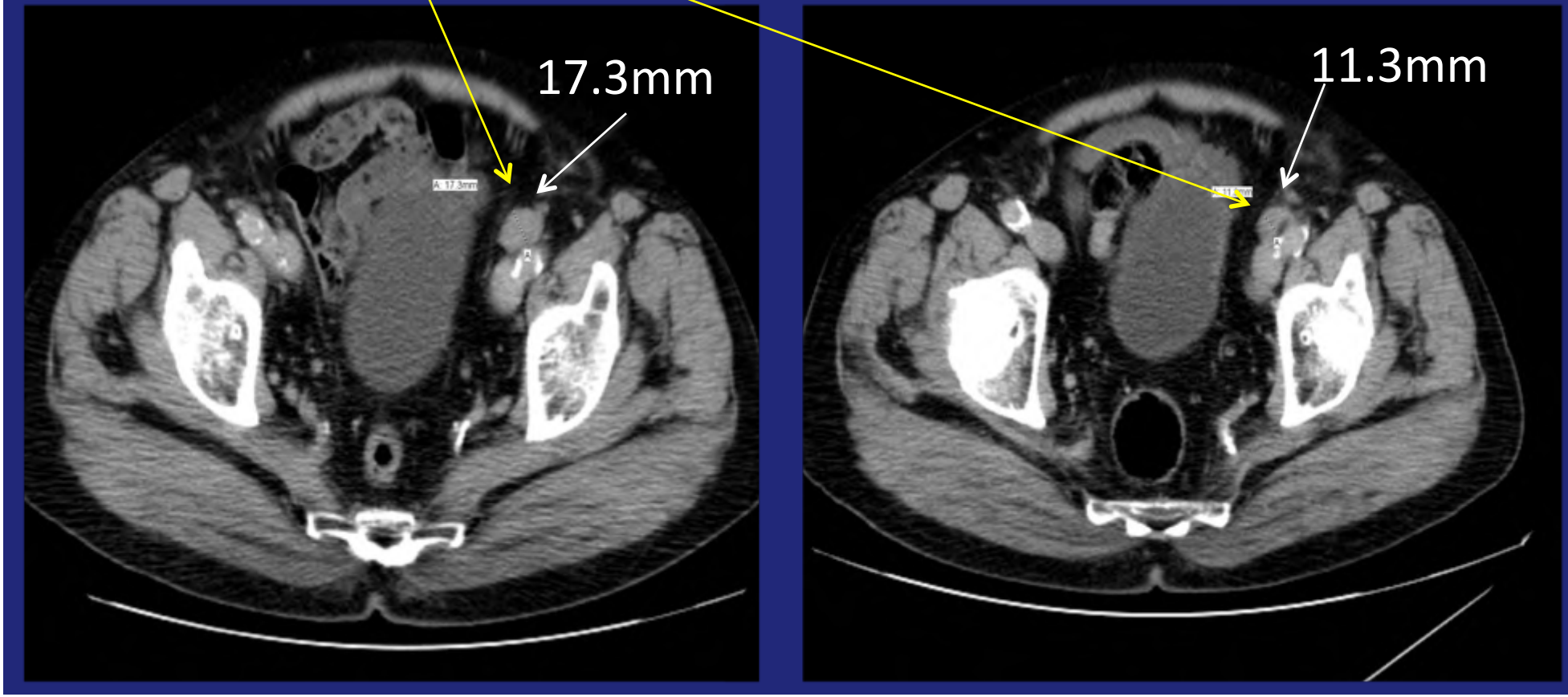
Male with castrate resistant prostate cancer

External ILIAC Lymph Node

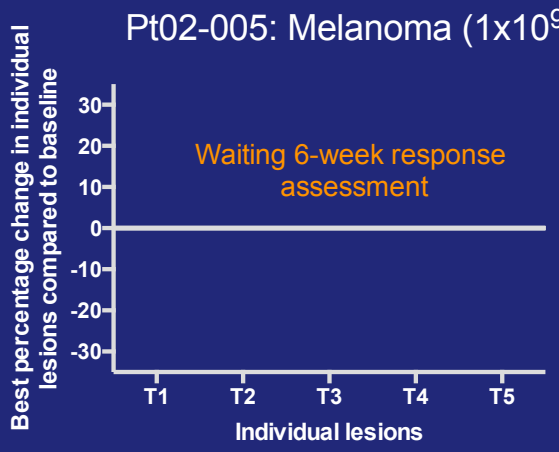
Day 0

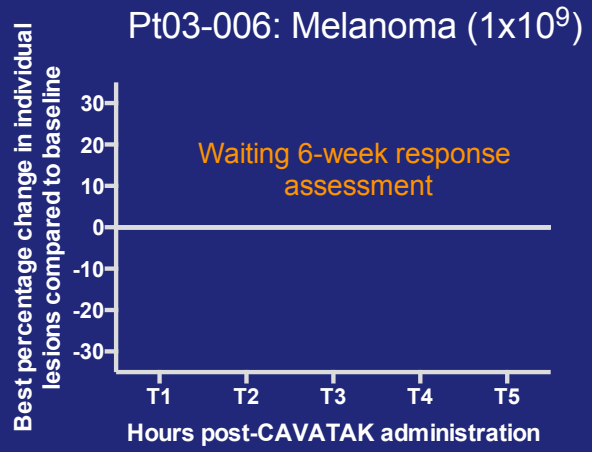
Day 42

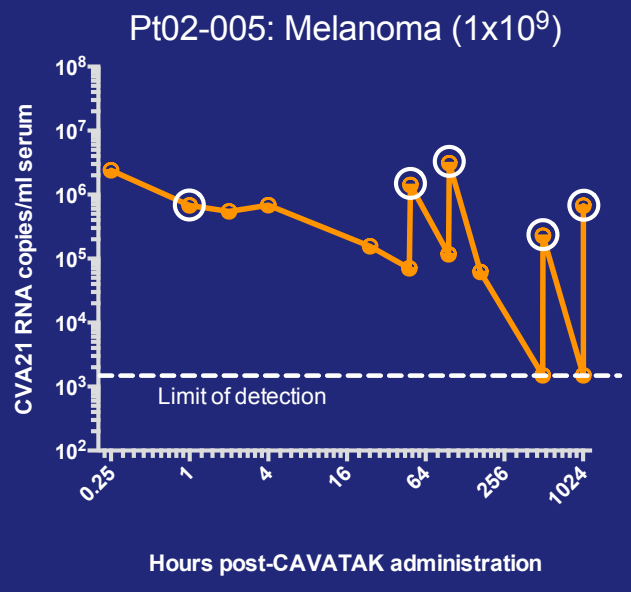
35% reduction

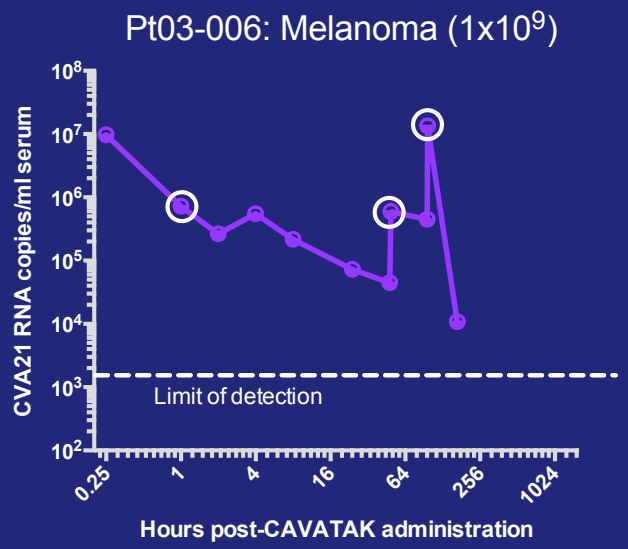


VLA-009 (STORM study): Individual lesion response and Pharmacokinetics of serum viral load (viral RNA): Cohort 3 - Melanoma

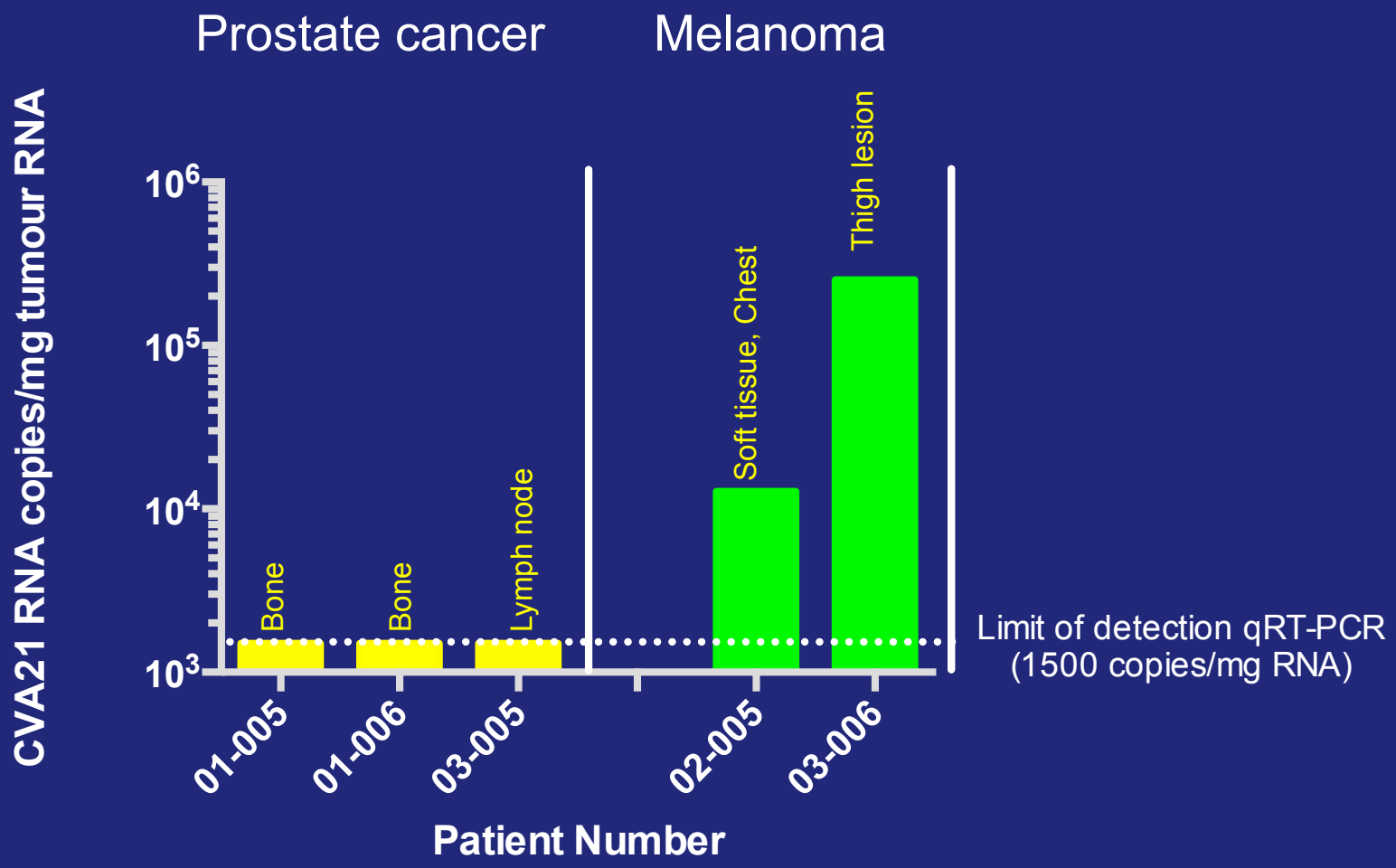




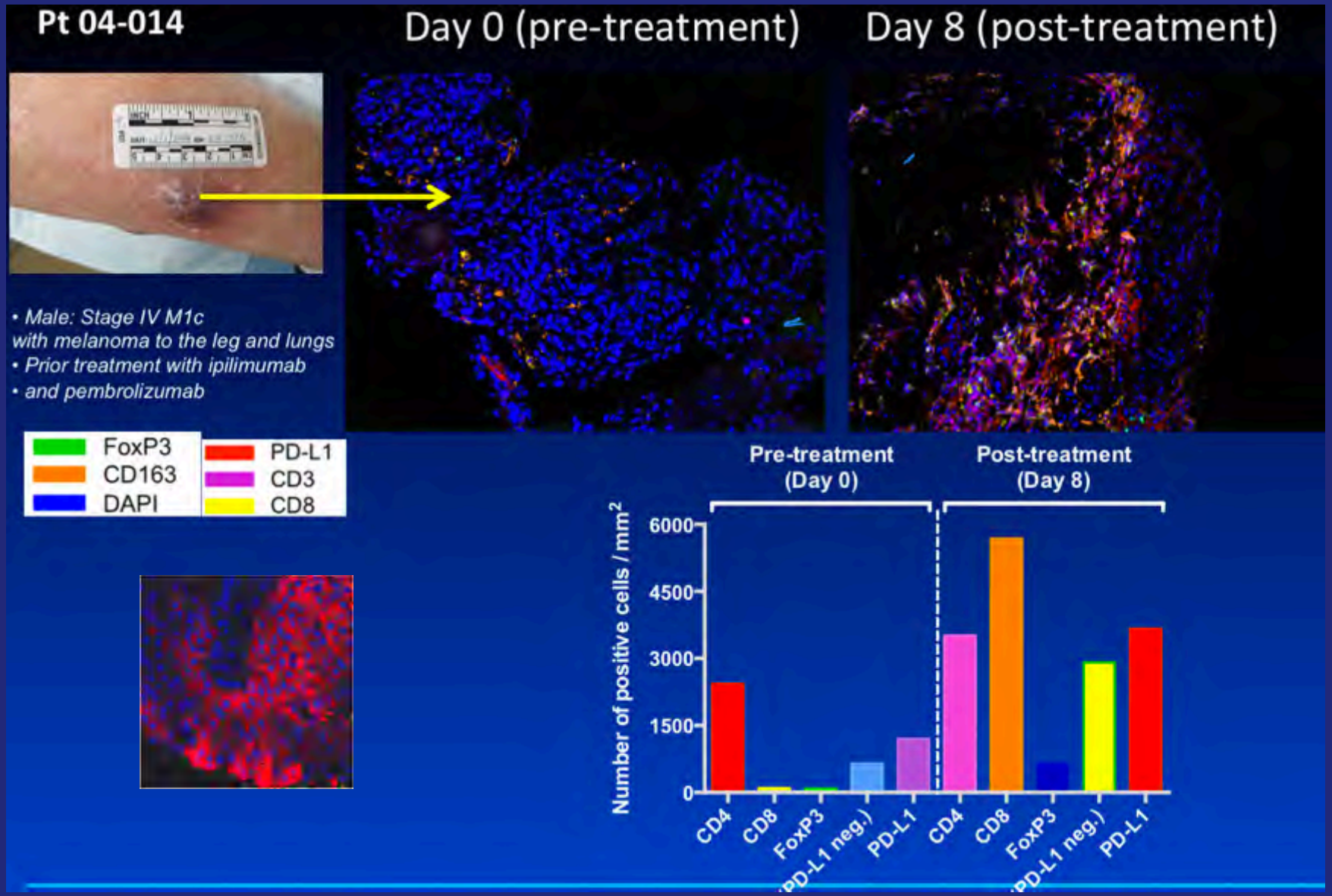




VLA-009 (STORM study): CAVATAK tumor targeting: Biopsy Viral RNA levels : Cohort 3: $1.0x10^9$ $TCID_{50}$ – Prostate and Melanoma



Planned biopsy tissue assessment from Cohort 3 patients: $1.0x10^9$ $TCID_{50}$ for immune cell infiltrate and NanoString immune profiling



VLA-009 (STORM Study): Conclusions

- Multi-dose intravenous administration to patients in Cohorts 1,2 and 3 was well tolerated, with no Grade 3 or 4 product-related AE's
- A number of patients have exhibited signs of possible tumor specific secondary viral replication
- Evidence of CVA21 tumor targeting with 2 of 2 melanoma patients in Cohort 3 displaying CVA21 RNA in tumor biopsies
- Interim data highlight a robust "multi-dosing-window" in the absence of significant levels of nAb for approximately 7 days post initial viral infusion
- Further clinical evaluation of intravenous delivered CVA21 in combination with immune checkpoint inhibitor strategies

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The STORM study patients and families

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