

#715 Emerging results from the use of an Oncolytic Adenovirus armed with TNFa and IL-2 (TILT-123) in different Phase I Solid Tumor Clinical trials



V. Cervera-Carrascon (1,2), I. M. Svane (3), K. Peltola (4), T. Alanko (5), R. Korpiasaari (5), S. Juteau (6), M. Jaakkola (5), J. Sormunen (5), J. Kononen (5), E. Ellebaek (3), T. Monberg (3), M. Donia (3), A. Khammari (7), B. Dréno (7), J.M. Santos (1,2), S. Sorsa (1,2), R. Havunen (1,2), A. Hemminki (1,2,4).

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Background

- After the first Immune Checkpoint Inhibitor (ICI) was approved (ipilimumab, 2011 for cancer therapy, the list of indications routinely treated with ICIs keeps increasing. In this new era of cancer immunotherapy, the major drawback of the approach is the difficulty in delivering long term benefits to a larger portion of patients.
- Different forms of immunotherapy used in solid tumor cancer patients seem to work better in immunologically hot tumors. To that extent, TILT-123 (an Oncolytic Adenovirus armed with TNFa and IL-2) was designed to stimulate the immune system within the tumor to enable subsequent forms of immunotherapy.
- After discovery and preclinical testing, the therapy was taken into clinical trials in 2020. Two years after, four Phase I clinical trials are ongoing where TILT-123 is being tested to determine its safety as monotherapy (NCT04695327), together with adoptive cell therapy using tumor-infiltrating lymphocytes (NCT04217473), and ICIs (NCT05271318, NCT05222932).

Trial Designs

TILT-T115 (TUNIMO) - NCT04695327

- TILT-123 is being administered through intravenous and intratumoral routes.
- TILT-T115 is currently enrolling at 2 sites in Helsinki, Finland: Docrates Cancer Center and Helsinki University Hospital.
- Trial is an open label phase I clinical trial using a standard 3+3 dose-escalation scheme.
- Treatment is given to participants, who have advanced solid tumors that cannot be treated with curative intent.

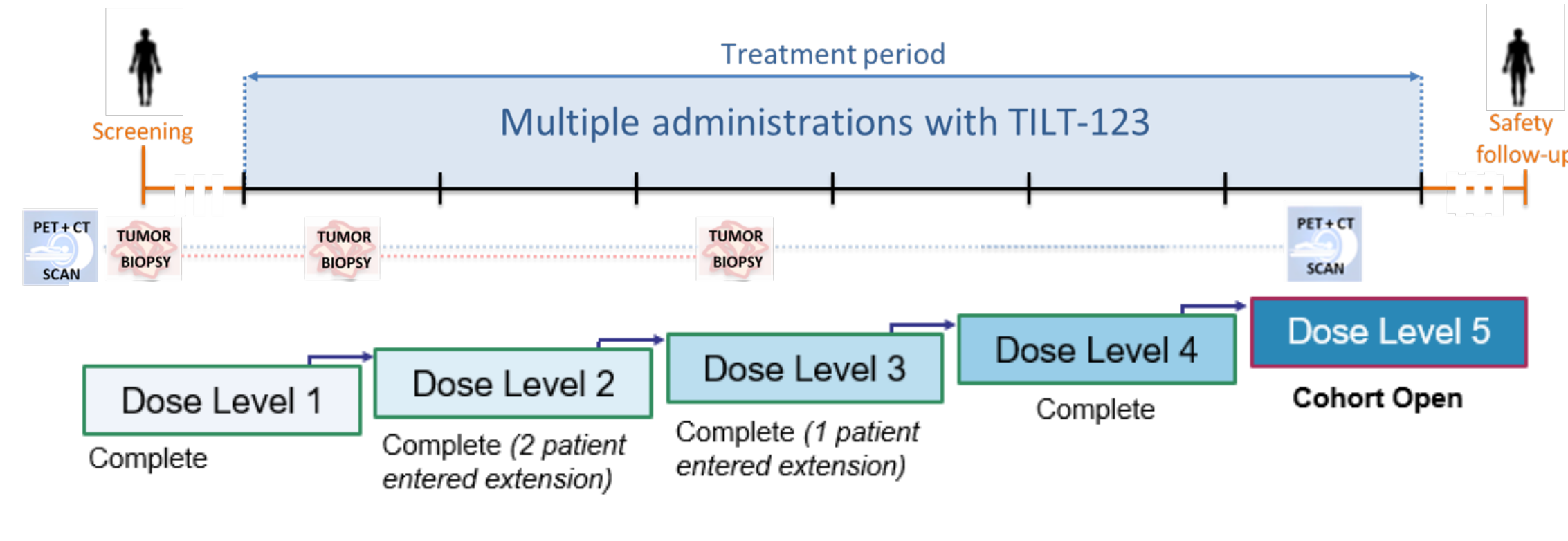


Figure 2 – TILT-T115 Clinical trial design and progress. Progress cut-off 30th August 2022.

TILT-T215 (TUNINTIL) - NCT04217473

- TILT-123 is being administered through intravenous and intratumoral routes.
- TILT-T215 is currently enrolling at 2 sites in Europe: Herlev Hospital, Denmark and at the CHU Nantes, France.
- Trial is an open label phase I clinical trial using a standard 3+3 dose-escalation scheme. TIL Therapy is administered without pre- or post-conditioning.
- Treatment is given to participants, who have metastatic melanoma that cannot be treated with curative intent.

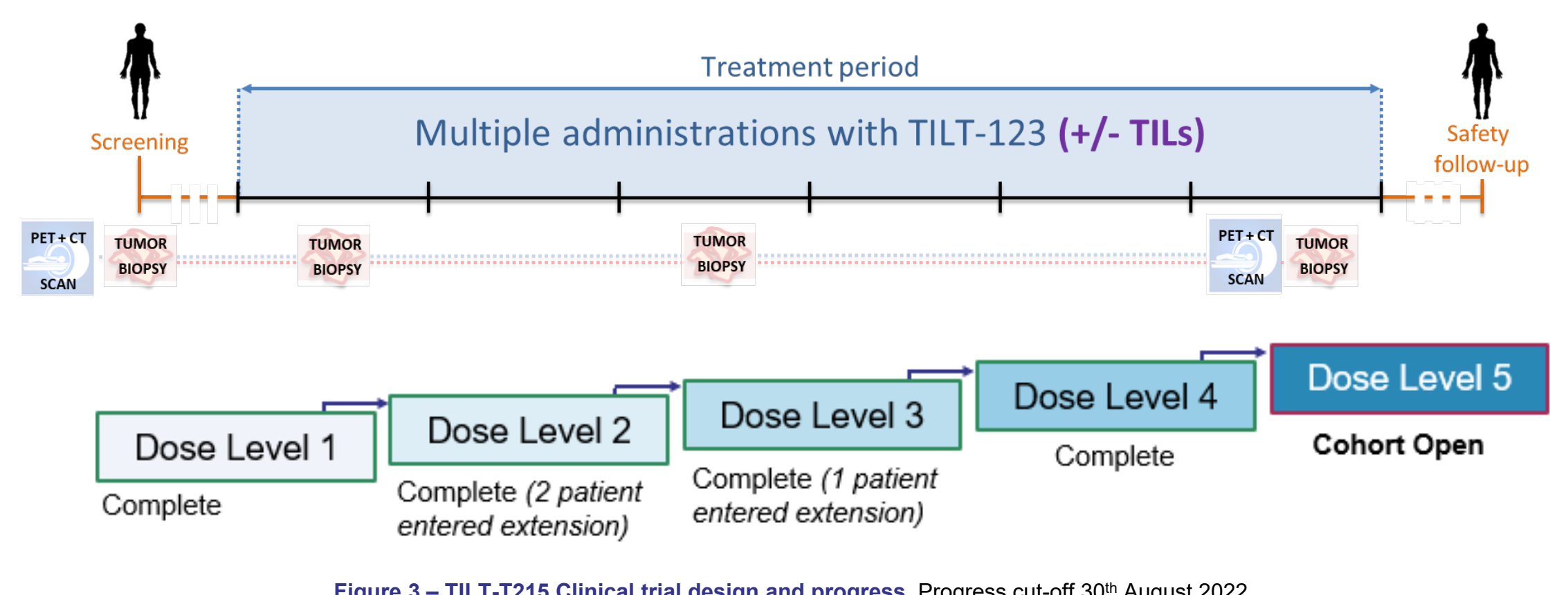


Figure 3 – TILT-T215 Clinical trial design and progress. Progress cut-off 30th August 2022.

1 Demographics and Safety

TILT-T115 (TUNIMO) - NCT04695327

Table 1 – Demographics of dose levels 1-3. Data cut-off 30th of August 2022. The results have not been monitored audited or verified by the quality assurance.

Parameter	Total (n=9 pts)
Sex	
Female	6
Male	3
Age at Enrollment (Years)	Median 60 (range 38-71)
Performance Status	
0	2
1	7
Tumor Type	
Lung	1
Melanoma	2
Sarcoma	2
Ovary	2
Breast	1
Thyroid	1
Prior Cancer therapies	
Median number of previous systemic treatment lines	5
Chemotherapy	35
Targeted Therapy	4
Combinations	4
Radiation Therapy	7
Surgery	8
Immunotherapy	5

Table 2 – TILT-123-related adverse events in dose levels 1-3 as judged by the investigators. Data cut-off 30th of August 2022. Adverse events graded based on the Common Terminology Criteria for Adverse Events (CTCAE). The results have not been monitored audited or verified by the quality assurance.

Preferred Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Cumulative Event Number (any grade)	Event Frequency (any grade per patient)
Chills	3	1	0	0	0	4	22%
Diarrhea	0	1	0	0	0	1	11%
Edema in feet	1	0	0	0	0	1	11%
Fatigue	2	1	0	0	0	3	22%
Fever	6	0	0	0	0	6	33%
Lymphopenia	0	1	0	0	0	1	11%
Neutropenia	0	1	0	0	0	1	11%
Pain in hands and legs	1	0	0	0	0	1	11%
Subfebrile body temperature	1	0	0	0	0	1	11%
Swelling of metastases	1	0	0	0	0	1	11%
Tinnitus	1	0	0	0	0	1	11%
Tiredness	0	1	0	0	0	1	11%
Total	16	6	0	0	0	22	

- Patients enrolled underwent several lines of therapy before enrolling into the trial;
- WHO/ECOG performance status was mostly 1;
- Most common types of cancers in dose levels 1-3 were melanoma, Sarcoma and Ovary cancers;
- The most frequent AEs in dose levels 1-3 observed were fever, chills and fatigue;
- Grade 3-5 AEs **were not seen** in dose levels 1-3;
- Serious AEs **were not seen** in dose levels 1-3;
- Dose-limiting toxicities **were not seen** in dose levels 1-3.

TILT-T215 (TUNINTIL) - NCT04217473

Table 3 – Demographics of dose levels 1-3. Data cut-off 30th of August 2022. The results have not been monitored audited or verified by the quality assurance.

Parameter	Total (n=9 pts)
Sex	
Female	2
Male	7
Age at Enrollment (Years)	Median 48 (range 25-68)
Performance Status	
0	8
1	1
Melanoma Type	
Cutaneous	4
Ocular	2
Mucosal	2
Other	1
Prior Cancer therapies	
Median number of previous systemic treatment lines	3
Chemotherapy	4
Targeted Therapy	4
Radiation Therapy	2
Surgery	10
Immunotherapy	28

Preferred Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Cumulative Event Number (any grade)	Event Frequency (any grade per patient)
Allopexia	1	0	0	0	0	1	11%
Anorexia	0	1	0	0	0	1	11%
Anthrax	1	0	0	0	0	1	11%
Arthralgia	1	0	0	0	0	1	11%
Chills	1	0	0	0	0	1	11%
Diarrhea	4	0	0	0	0	4	22%
Dizziness	1	0	0	0	0	1	11%
Edema in left eye	1	0	0	0	0	1	11%
Fatigue	0	0	0	0	0	0	0%
Fever	2	2	0	0	0	4	44%
Flushing	2	0	0	0	0	2	22%
Headache	3	0	0	0	0	3	33%
Itching at injection sites	1	0	0	0	0	1	11%
Lymphopenia	1	0	0	0	0	1	11%
Memory impairment	0	0	0	0	0	0	0%
Nausea	3	0	0	0	0	3	33%
Nutrition	2	0	0	0	0	2	22%
Pain	1	0	0	0	0	1	11%
Pain from injection	3	0	0	0	0	3	33%
Pain in liver from injection	0	0	0	0	0	0	0%
Pain, left knee	1	0	0	0	0	1	11%
Severe myelodysplasia at rest	1	0	0	0	0	1	11%
TSH decreased	1	0	0	0	0	1	11%
Vitiligo	1	0	0	0	0	1	11%
Weighting	1	0	0	0	0	1	11%
Worsening of Headache	0	3	0	0	0	3	33%
Total	41	9	3	0	0	53	

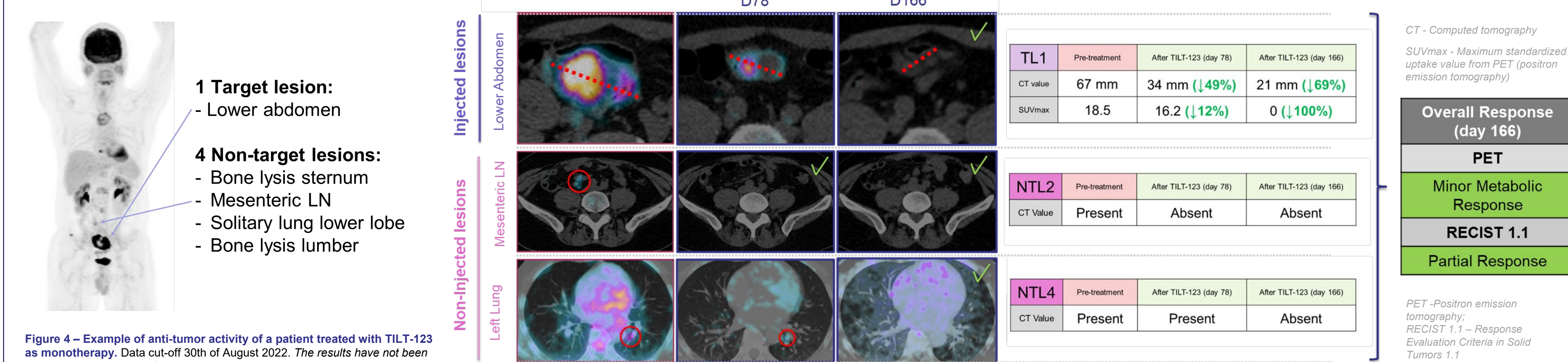
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2 Anti-tumor Activity

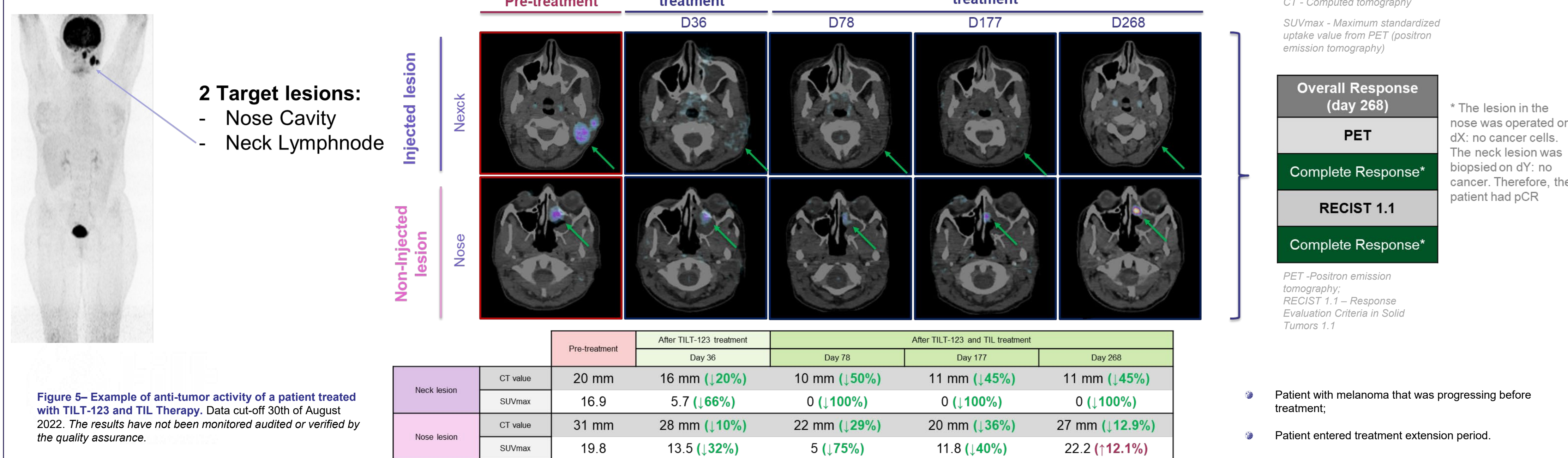
TILT-T115 (TUNIMO) - NCT04695327

Example #1 - Patient with Thyroid Cancer



TILT-T215 (TUNINTIL) - NCT04217473

Example #2 - Patient with Melanoma (Dose Level 3)



3 Neutralizing antibodies, biosafety and T-cell Infiltration

TILT-T215 (TUNINTIL) - NCT04217473

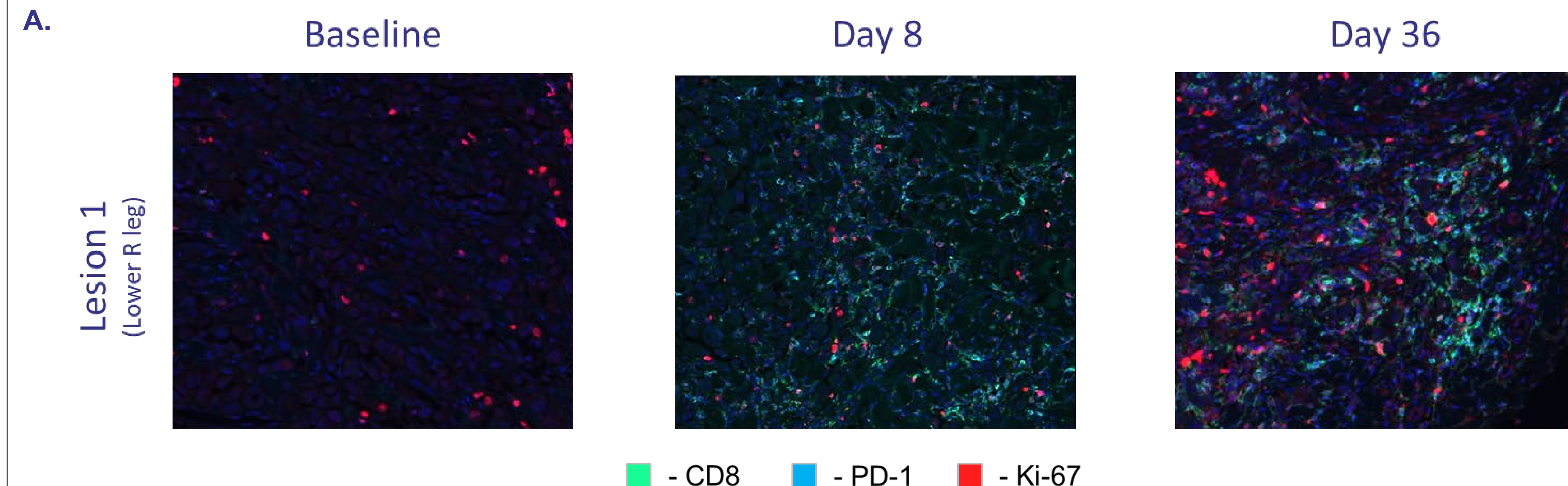
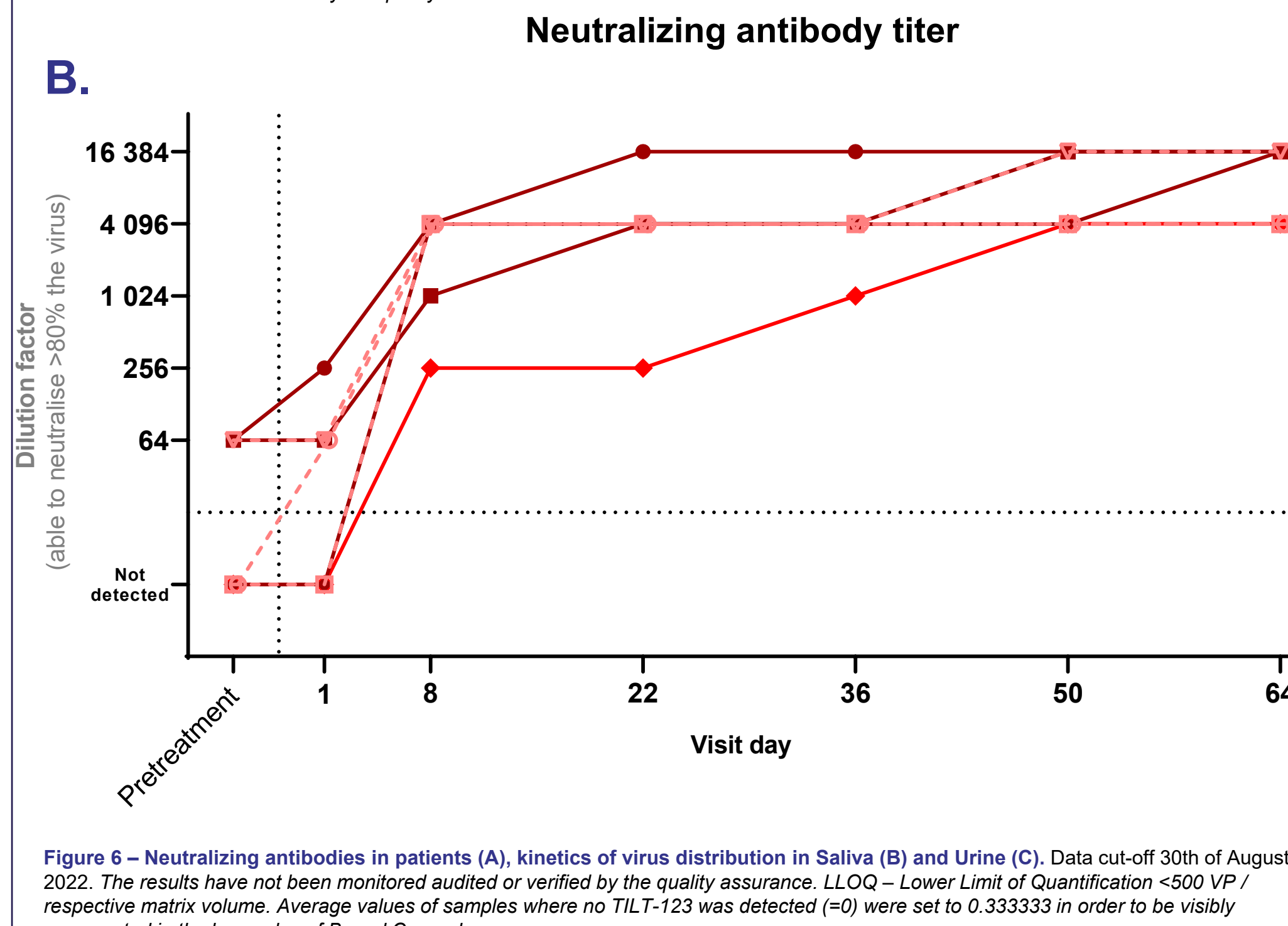


Figure 7 – Example of immune cell infiltration in a tumor from a patient treated in the TILT-T215 demonstrated by multiplex immunohistochemistry. Data cut-off 30th of August 2022. Upper row shows an uninjected tumor, lower row shows an injected tumor. The results have not been monitored audited or verified by the quality assurance.



Conclusions

- So far, phase I studies indicate that TILT-123 is safe in humans in dose levels 1-3, both as monotherapy and in combination with TIL therapy;
- The safety profile seen in the abovementioned dose levels, is consistent with other virus-based immunotherapies, with the most common AE being fever in both trials;
- Treatment with TILT-123 enabled anti-tumor response as monotherapy. When coupled with another immunotherapy, such as TIL Therapy, it can lead to deepened responses;
- Responses can be observed in lesions in which TILT-123 was not injected;
- Shedding of TILT-123 genomes in saliva and urine samples were detected in some patients treated in the TILT-T215 trial, as expected, however, the presence of functional virus remains to be determined;
- Administration of TILT-123 can enrich the tumor microenvironment with T-cells in melanoma patients from TILT-T215.

For more information contact:
Victor Cervera (victor@tilt.bio.com)



We thank the patients and staff at:



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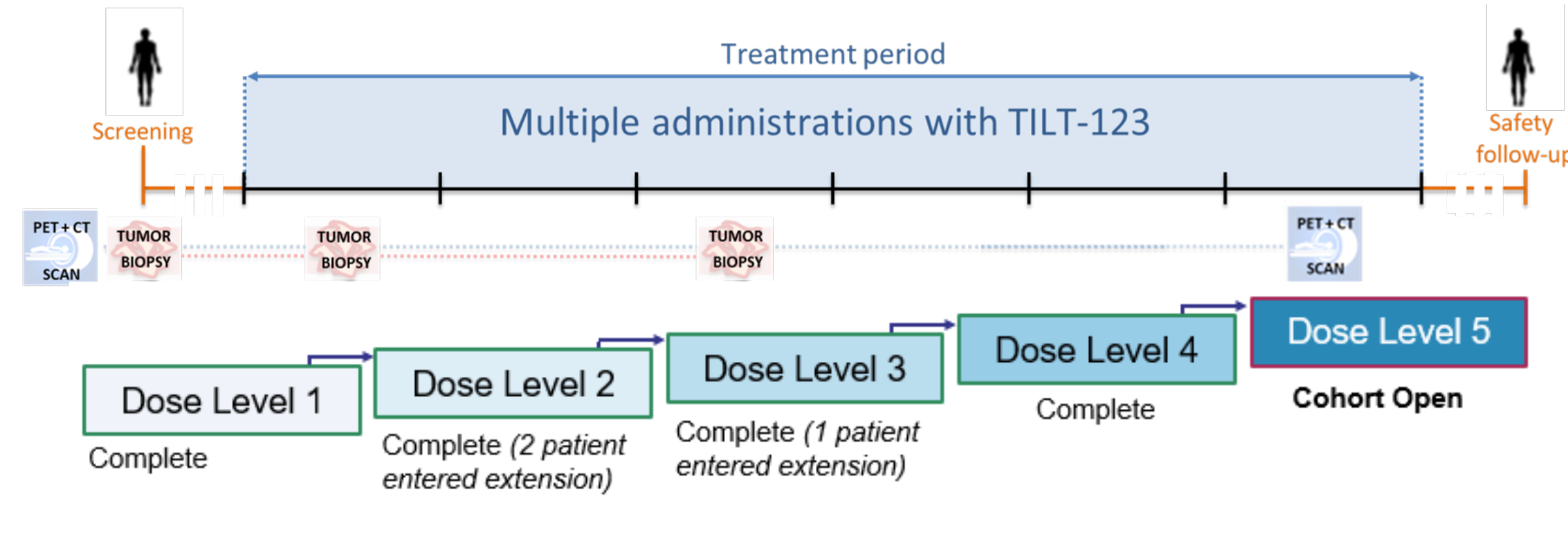


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TILT-T215 (TUNINTIL) - NCT04217473

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- Treatment is given to participants, who have metastatic melanoma that cannot be treated with curative intent.

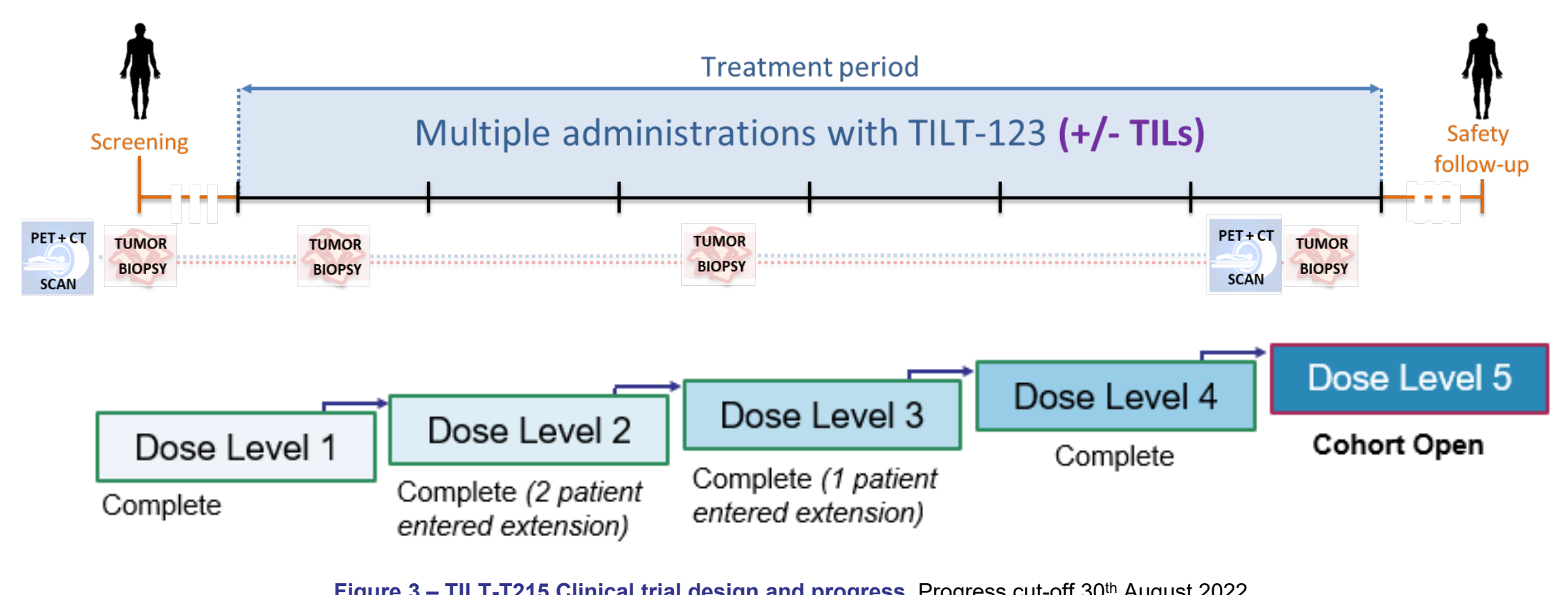


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Melanoma	2
Sarcoma	2
Ovary	2
Breast	1
Thyroid	1
Prior Cancer therapies	
Median number of previous systemic treatment lines	5
Chemotherapy	35
Targeted Therapy	4
Combinations	4
Radiation Therapy	7
Surgery	8
Immunotherapy	5

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Diarrhea	0	1	0	0	0	1	11%
Edema in feet	1	0	0	0	0	1	11%
Fatigue	2	1	0	0	0	3	22%
Fever	6	0	0	0	0	6	33%
Lymphopenia	0	1	0	0	0	1	11%
Neutropenia	0	1	0	0	0	1	11%
Pain in hands and legs	1	0	0	0	0	1	11%
Subfebrile body temperature	1	0	0	0	0	1	11%
Swelling of metastases	1	0	0	0	0	1	11%
Tinnitus	1	0	0	0	0	1	11%
Tiredness	0	1	0	0	0	1	11%
Total	16	6	0	0	0	22	

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- WHO/ECOG performance status was mostly 1;
- Most common types of cancers in dose levels 1-3 were melanoma, Sarcoma and Ovary cancers;
- The most frequent AEs in dose levels 1-3 observed were fever, chills and fatigue;
- Grade 3-5 AEs **were not seen** in dose levels 1-3;
- Serious AEs **were not seen** in dose levels 1-3;
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TILT-T215 (TUNINTIL) - NCT04217473

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Cutaneous	4
Ocular	2
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Other	1
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Chemotherapy	4
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Radiation Therapy	10
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Anthrax	1	0	0	0	0	1	11%
Arthralgia	1	0	0	0	0	1	11%
Chills	1	0	0	0	0	1	11%
Diarrhea	4	0	0	0	0	4	22%
Discomfort	1	0	0	0	0	1	11%
Edema, by left eye	1	0	0	0	0	1	11%
Fatigue	3	2	0	0	0	5	22%
Fever	2	2	0	0	0	4	22%
Headache	3	0	0	0	0	3	22%
Itching at injection sites	1	0	0	0	0	1	11%
Lymphopenia	1	0	0	0	0	1	11%
Memory impairment	1	0	0	0	0	1	11%
Nausea	3	0	0	0	0	3	22%
Nutrition	2	2	0	0	0	4	22%
Pain	1	0	0	0	0	1	11%
Pain from injection	3	0	0	0	0	3	22%
Pain in knee from injection	0	0	1	0	0	1	11%
Pain, left knee	1	0	0	0	0	1	11%
Severe myelodysplasia at rest	1	0	0	0	0	1	11%
TSH decreased	1	0	0	0	0	1	11%
Vitiligo	1	0	0	0	0	1	11%
Weighting	1	0	0	0	0	1	11%
Worsening of Headache	0	3	0	0	0	3	22%
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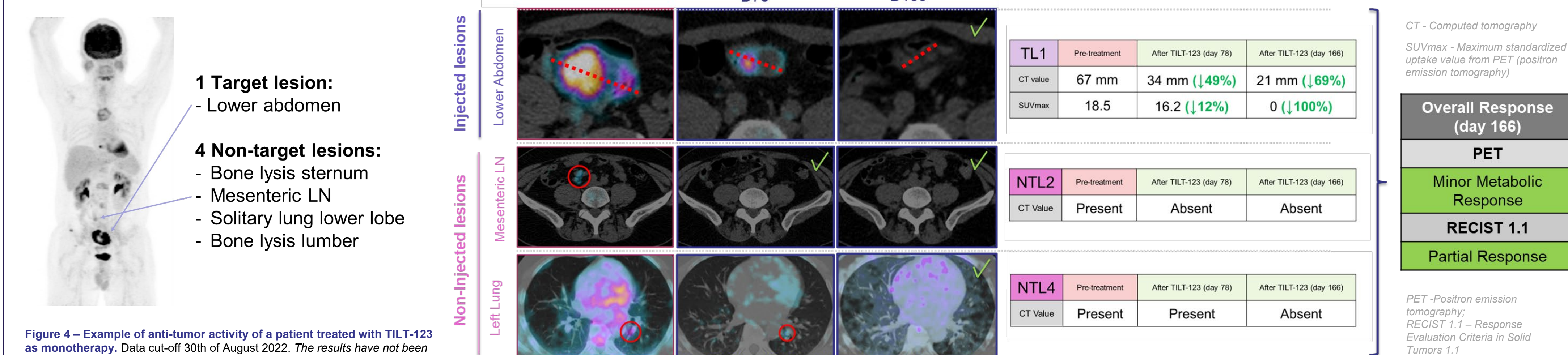
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2 Anti-tumor Activity

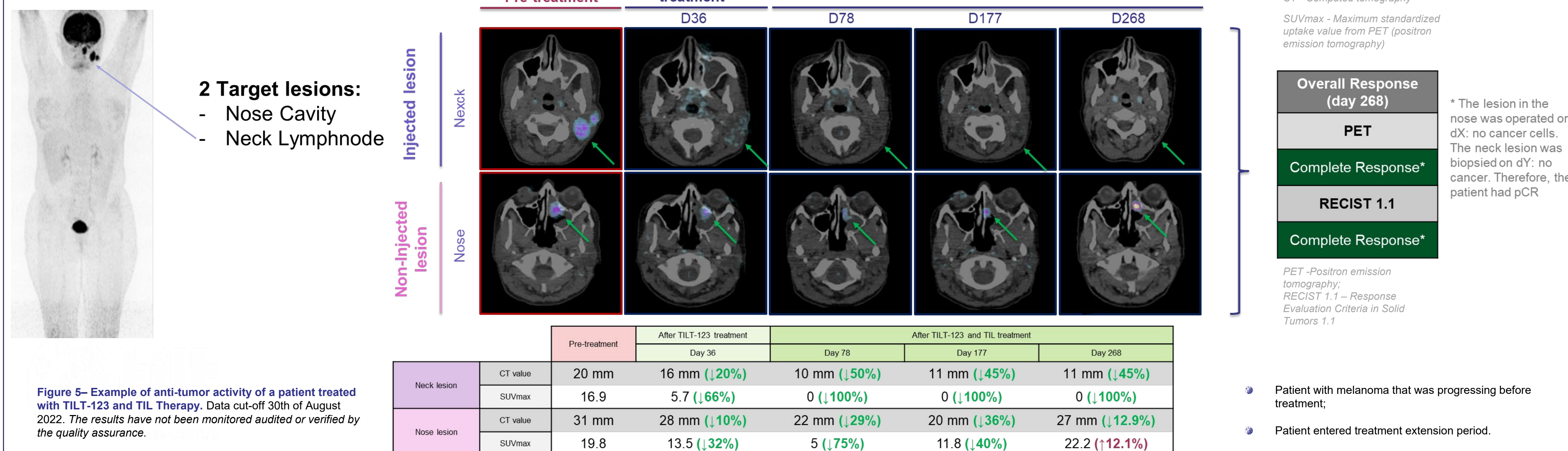
TILT-T115 (TUNIMO) - NCT04695327

Example #1 - Patient with Thyroid Cancer



TILT-T215 (TUNINTIL) - NCT04217473

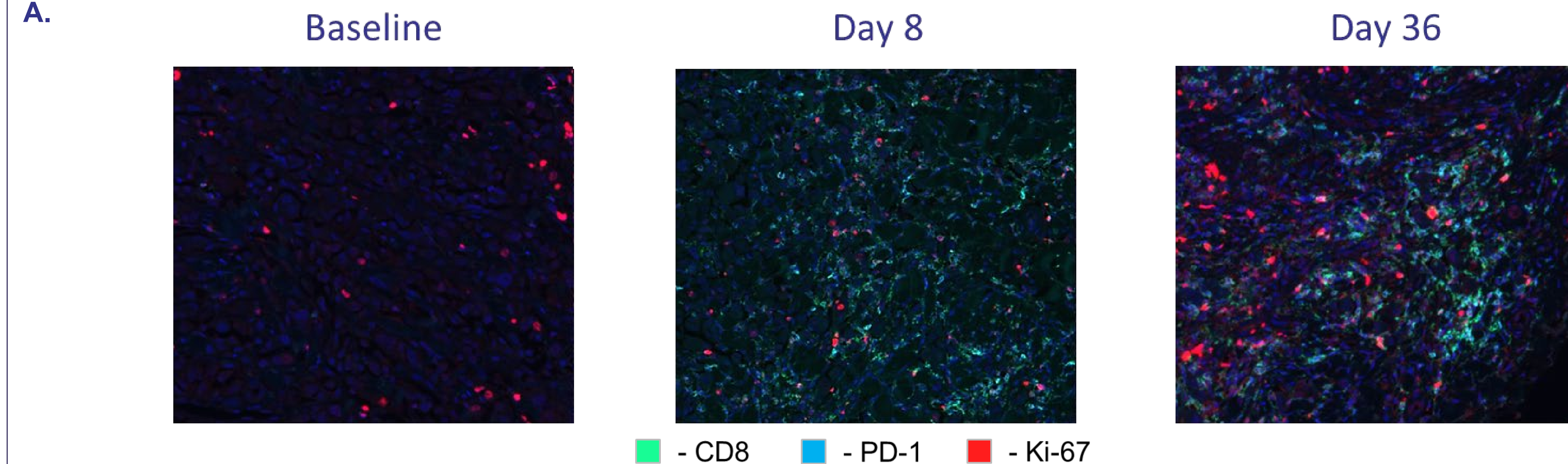
Example #2 - Patient with Melanoma (Dose Level 3)



3 Neutralizing antibodies, biosafety and T-cell Infiltration

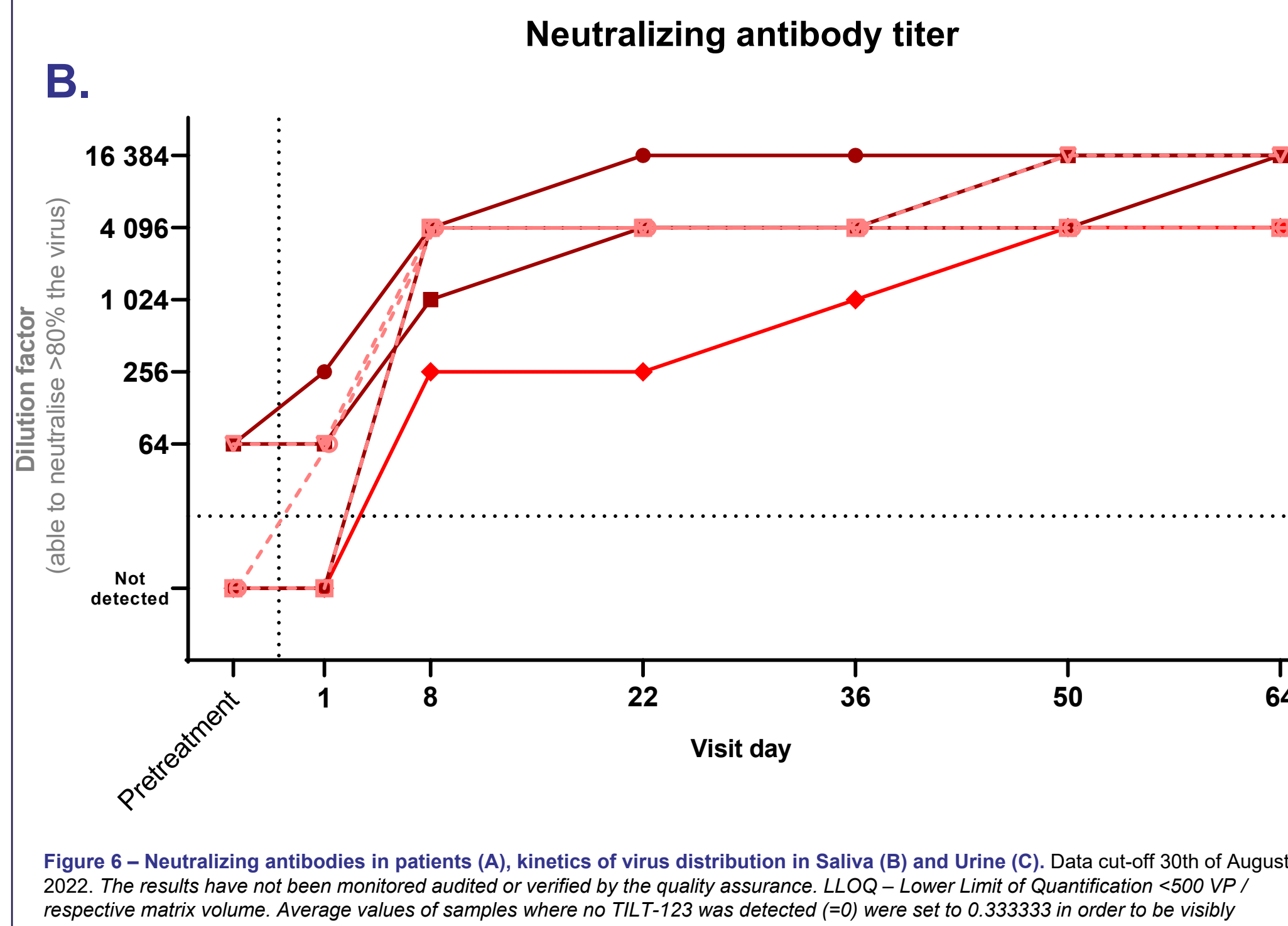
TILT-T215 (TUNINTIL) - NCT04217473

A.



Example of immune cell infiltration in a tumor from a patient treated with TILT-123 (day 1) demonstrated by multiplex immunohistochemistry.

B.



Conclusions

- So far, phase I studies indicate that TILT-123 is safe in humans in dose levels 1-3, both as monotherapy and in combination with TIL therapy;
- The safety profile seen in the abovementioned dose levels, is consistent with other virus-based immunotherapies, with the most common AE being fever in both trials;
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