



**The Israel Society
of Surgical Oncology**



Adoptive cell therapy in treating metastatic melanoma The surgeon's perspective

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The Israel Society
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NO DISCLOSURES

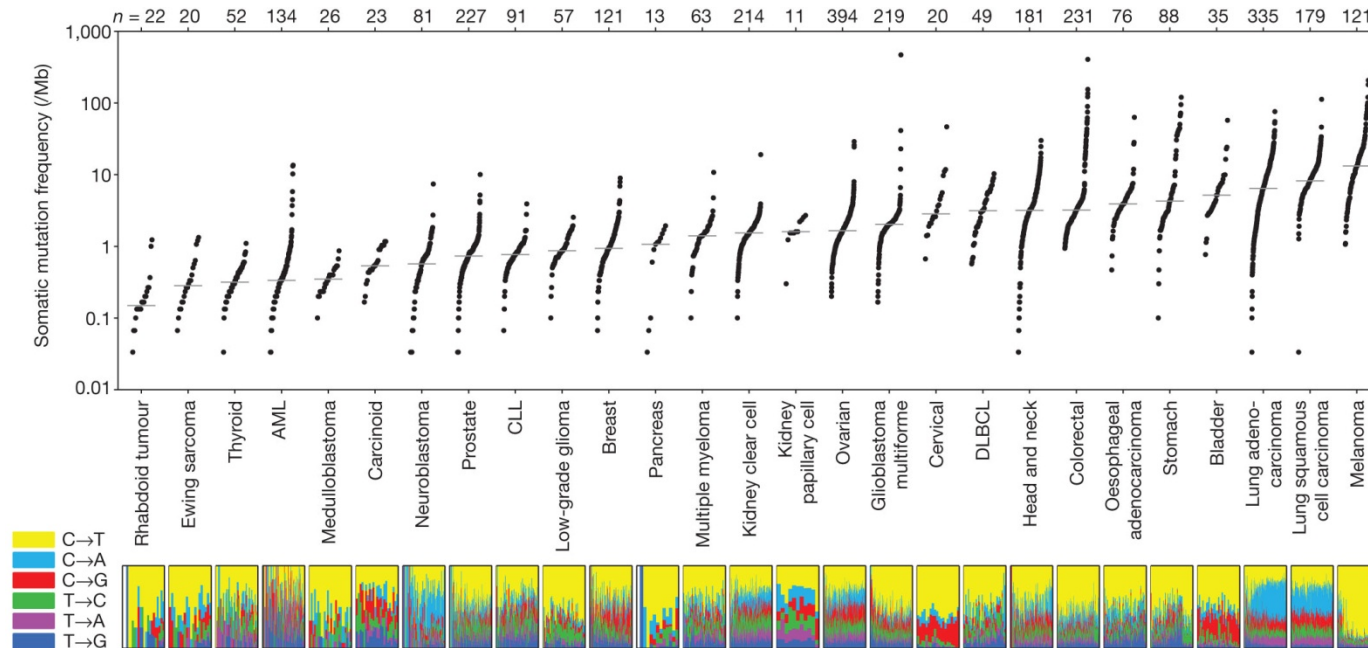
Well, actually I do have one....

I am not an immunologist



“...and all the science I don’t understand. It’s just my job 5 days a week.”

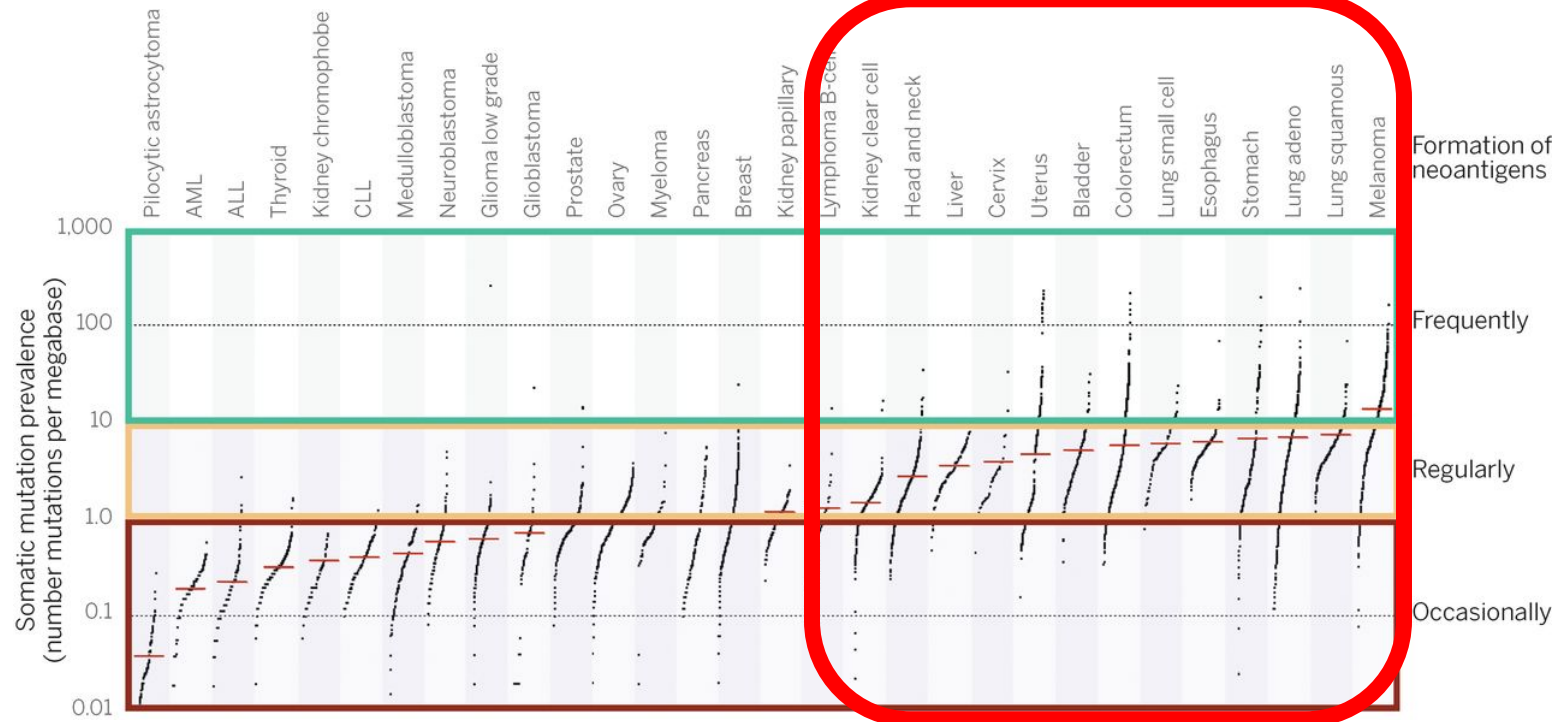
Somatic mutation frequencies observed in exomes from 3,083 tumour–normal pairs.



MS Lawrence *et al. Nature* **000**, 1-5 (2013) doi:10.1038/nature12213

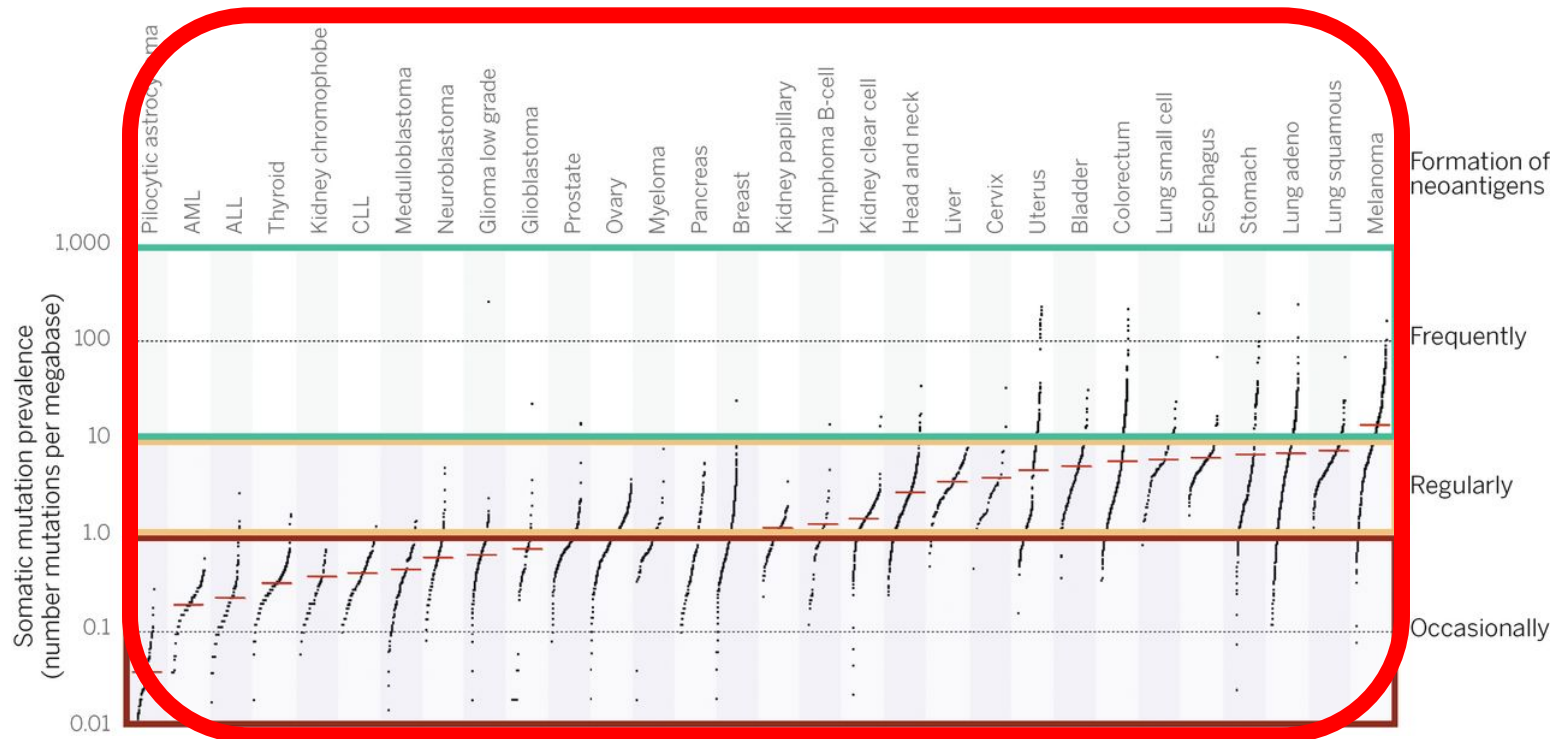
nature

Tumor mutation burden

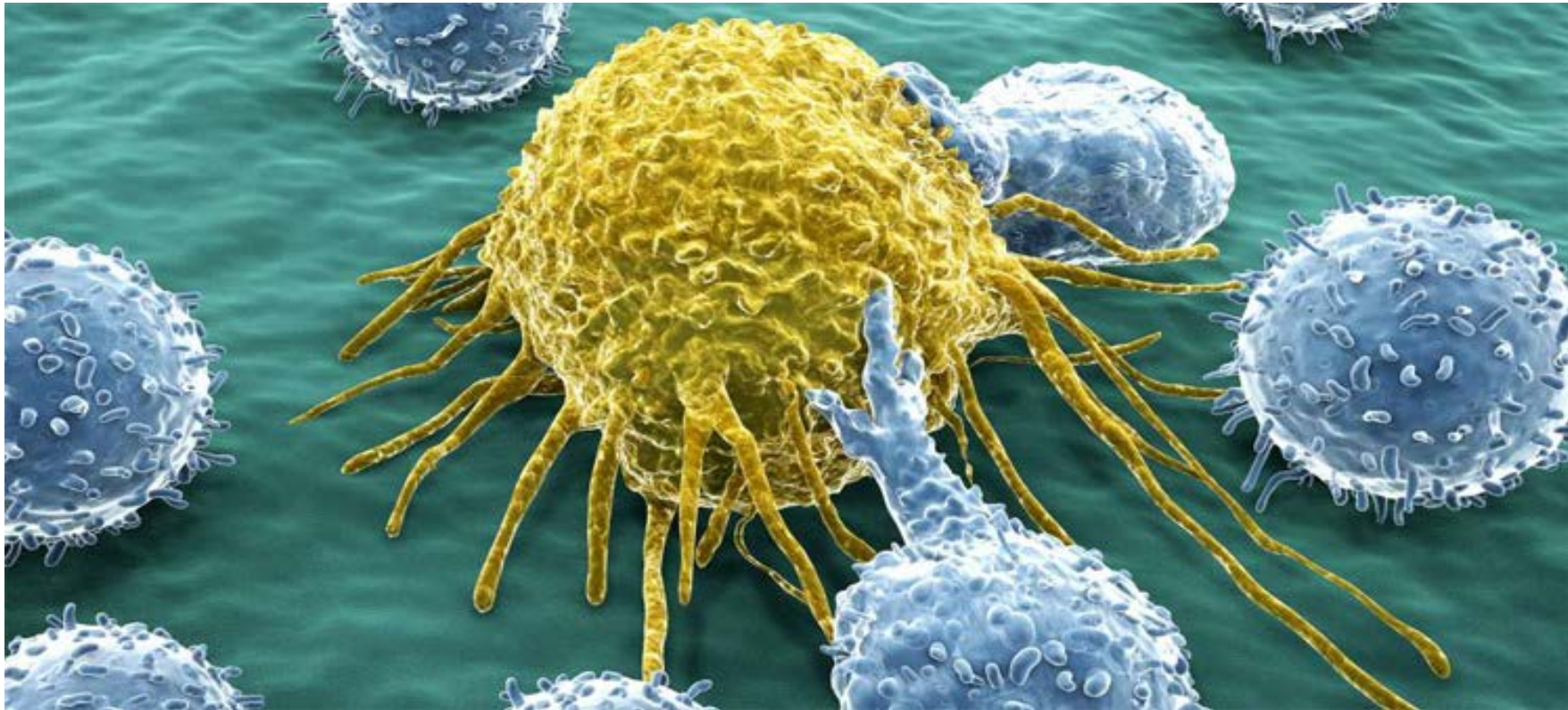


Schumacher and Schreiber, Science 2015

Tumor mutation burden



Adoptive cell transfer therapy

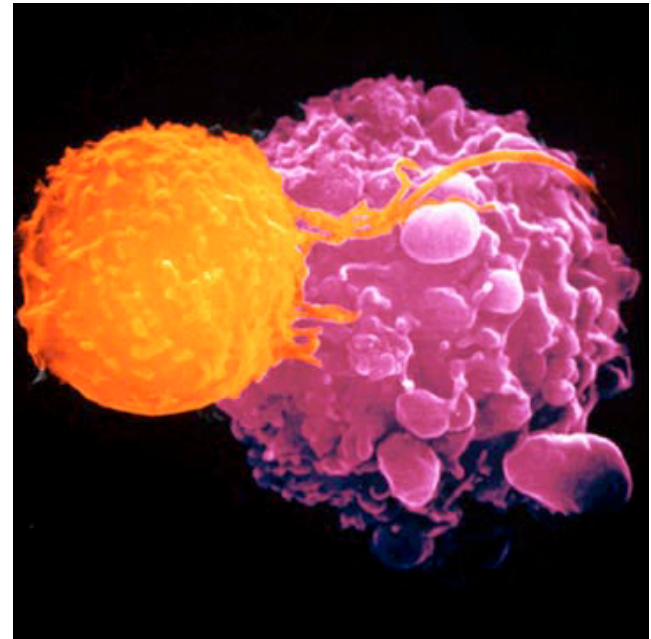


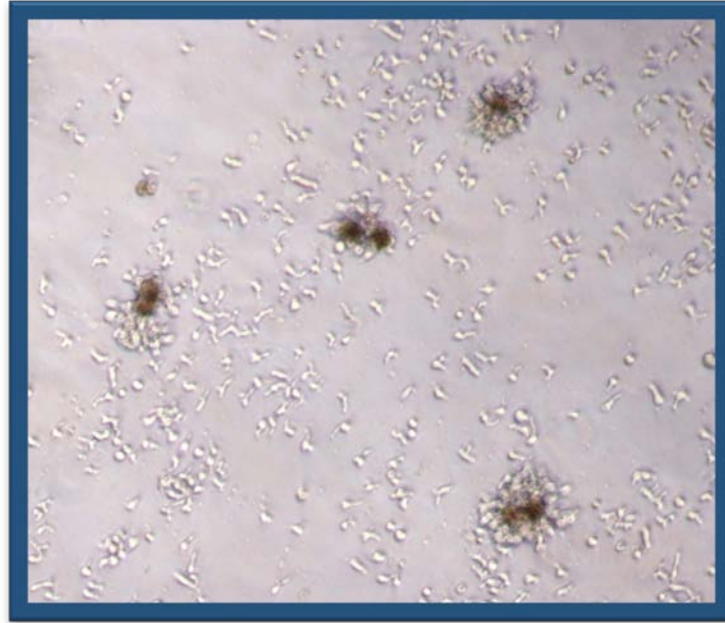
Tumor Infiltrating Lymphocytes (TILs)

T Cells which are naturally present within the tumor

Specificity against tumor antigens

Potential to kill tumor cells



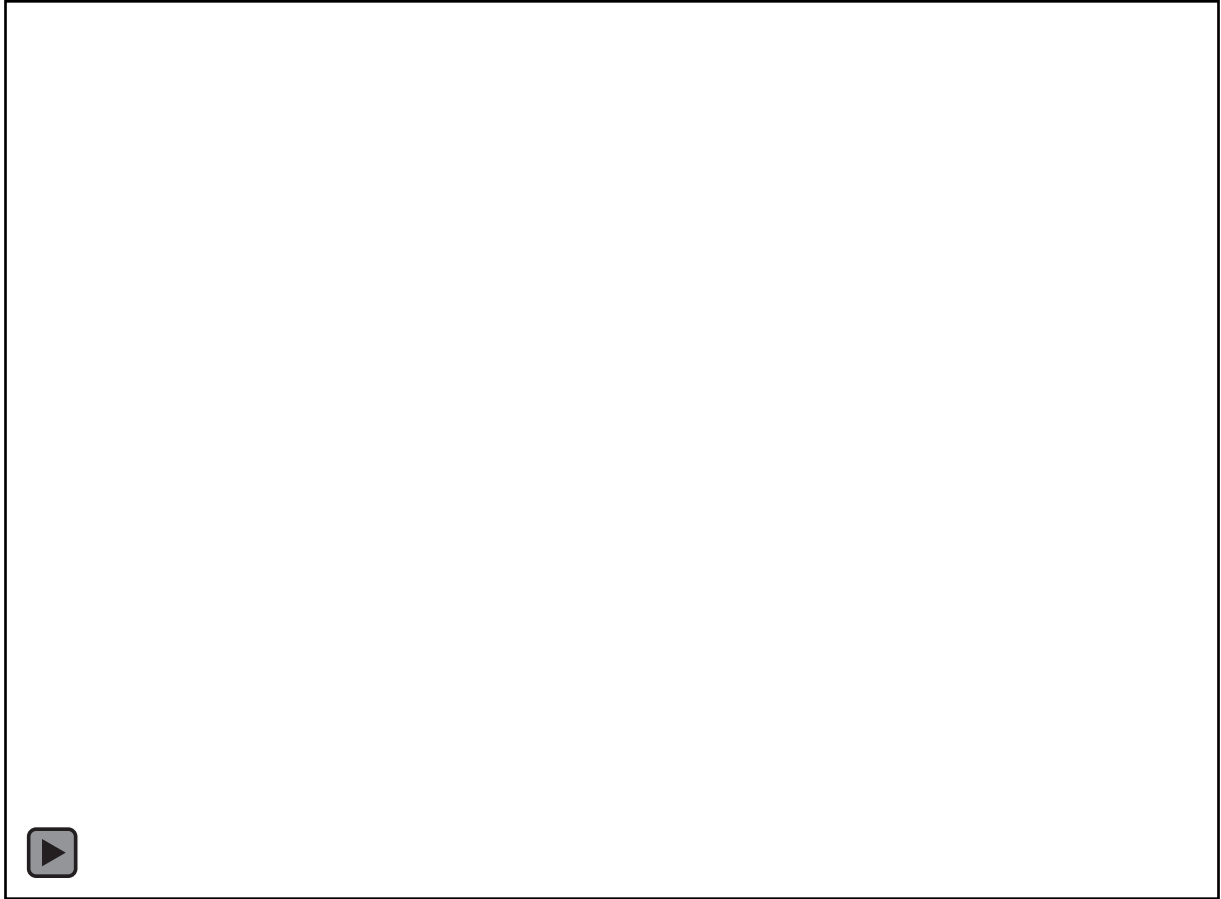


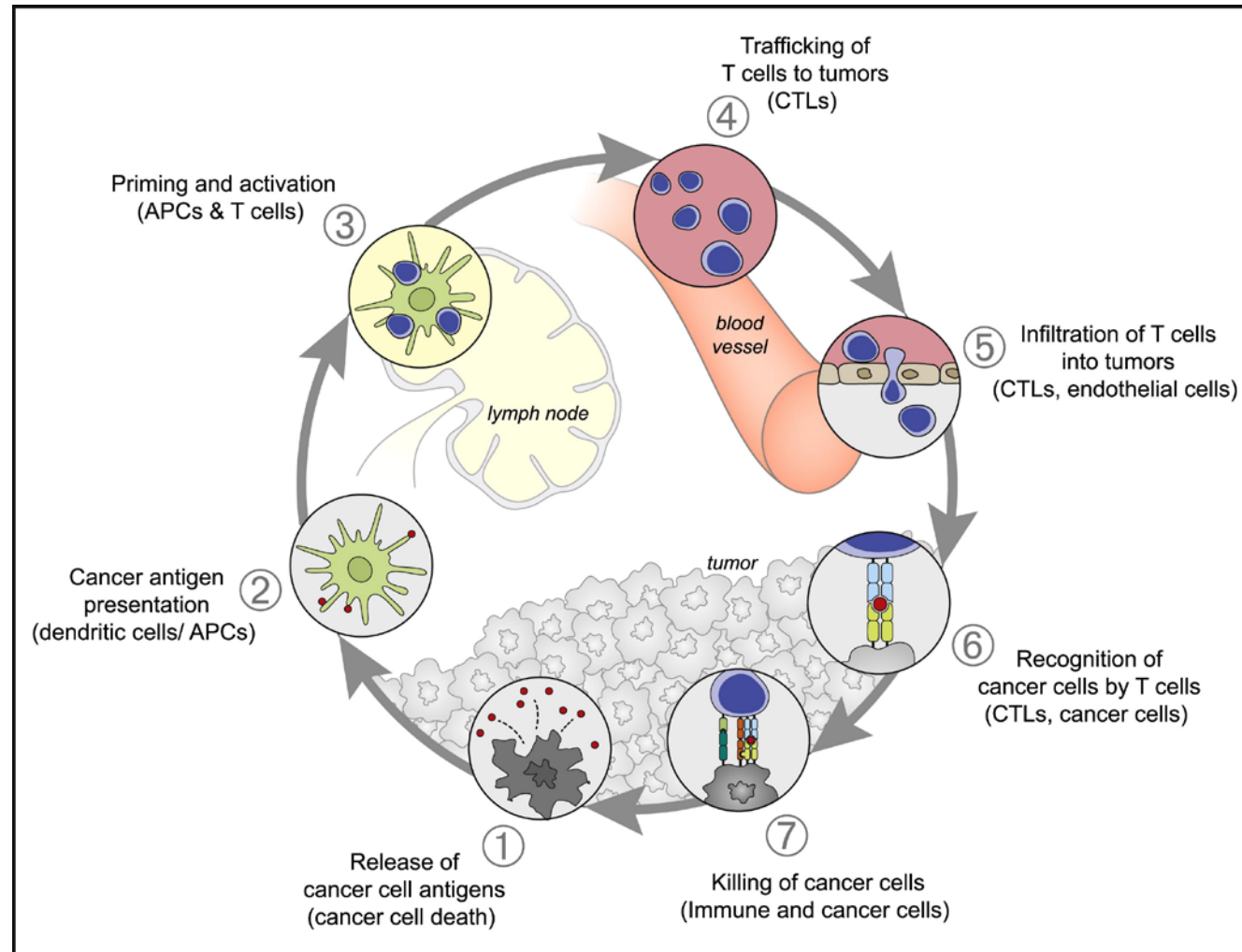
At least 80×10^6 TIL

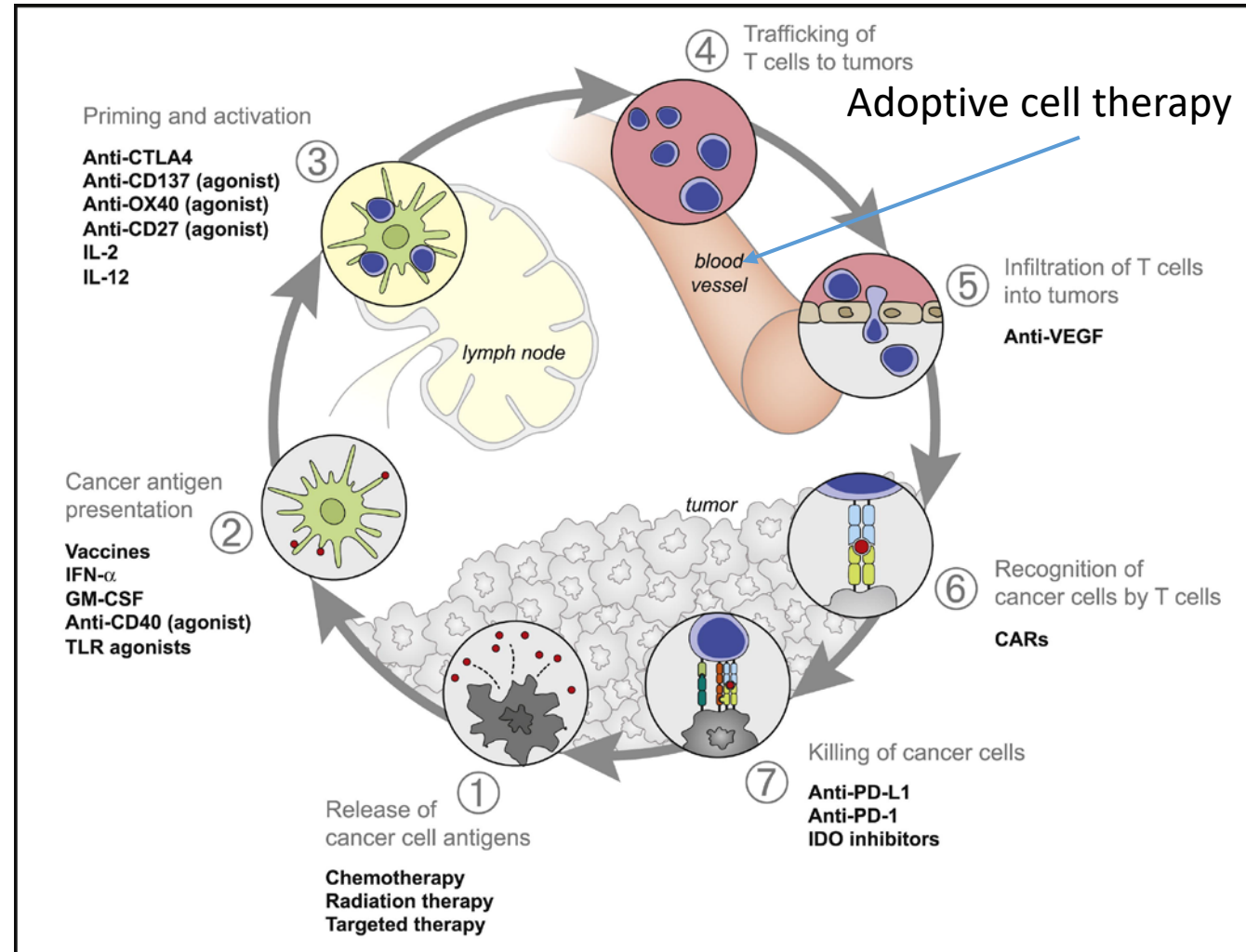
No melanoma cells

In minimal time (8-18 days)

TIL attacking melanoma cells in vitro

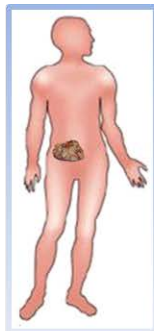




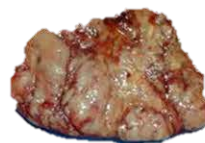




שיבא - מרכז רפואי אקדמי מצטיין



Surgery

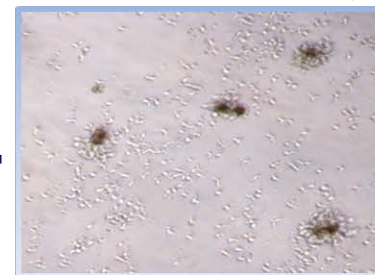


Transfer to
Clean Lab

Pheresis (feeders)

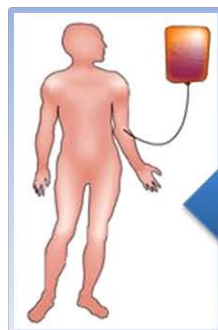


Establishment of
TIL cultures ($\geq 5 \times 10^7$ TIL)



Activation and Rapid
Expansion to app. 5×10^{10} TIL
within 14 days

EIM GMP lab
Microbiology



**Lympho
depletion:**
Eliminate
suppressor
cells

Recovery
(Oncology)

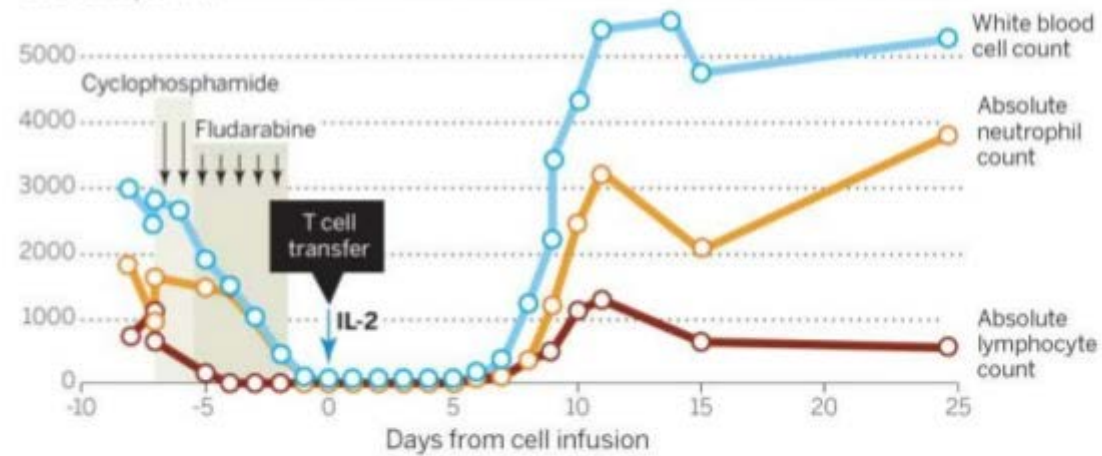
HD CTx (BMT)
IL-2+TIL (EIM)

Lympho-Depletion Prior to Adoptive T Cell Therapy

Lymphodepletion prior to T cell transfer is followed by immune reconstitution

Peripheral blood cell count

6000 cells per mm^3



Current Surgical data

- 196 patients-121 male 75 female. Median age 53
- 242 harvests
- 66% GA 33% LA
- Numerous tumor sites



Current Surgical data

196 patients, 242 tumor specimens

• Tissue Source	Number (%)
-----------------	------------

• Subcutaneous	93 (38.4)
• Lymph node	58 (24)
• Lung	47 (19.4)
• Visceral	32 (13.2)
• CNS	5 (2.1)
• Muscle	4 (1.7)
• Bone	2 (0.8)
• Breast	1 (0.4)

Current Surgical data

Visceral organ harvest sites:

- Liver,
- Spleen,
- Gall bladder,
- Adrenal,
- Small bowel and Colon



Current Surgical data

- Serious complications causing delay of treatment: wound dehiscence, pancreatic leak, persistent pleural effusion
- Mortality: 3 mortalities (chemotherapy related), no surgery related mortality

Oncologic response

- Objective clinical response (per RECIST criteria v1.1) rate : 28%
- CR 8% PR 20%
- Clinical benefit-44%
- Median OS 10 months
- Responders-median OS 58 months vs non responders OS 6 months
- Median PFS 3 months
- Responders PFS 23 months vs non responders 2.5 months

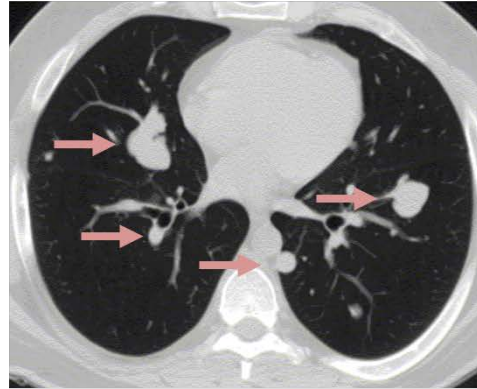
Pre-treatment (Jul-09)



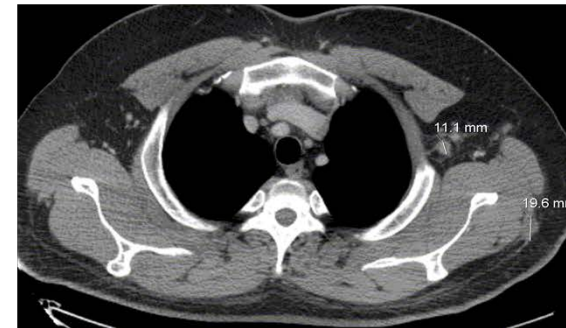
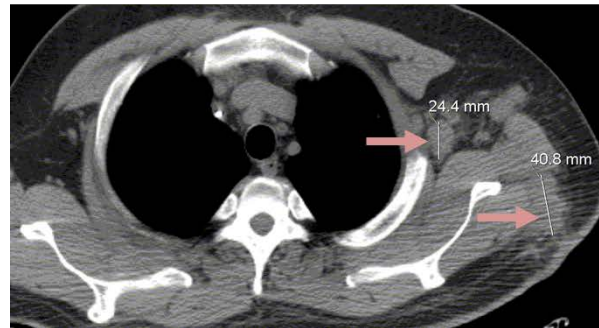
Post-treatment (Dec-10)



Pre-treatment (Mar-08)

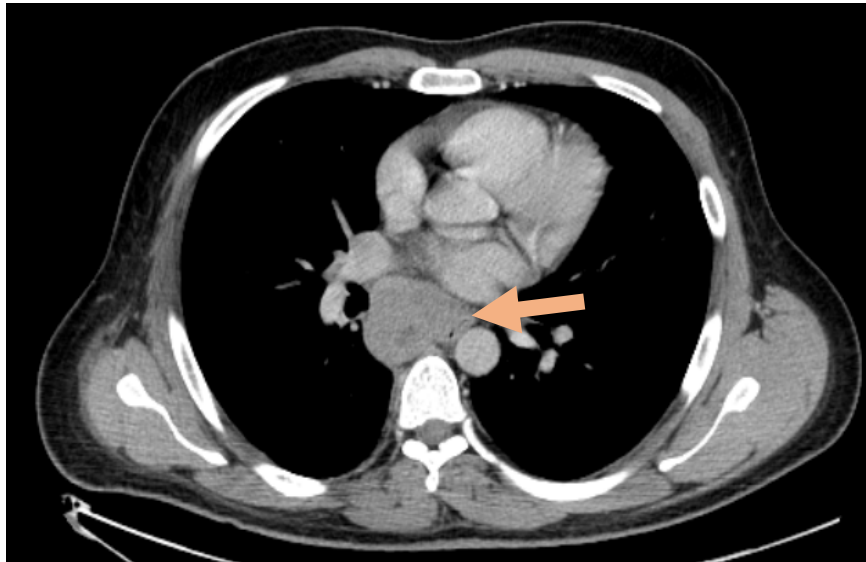


Post-treatment (Jun-08)

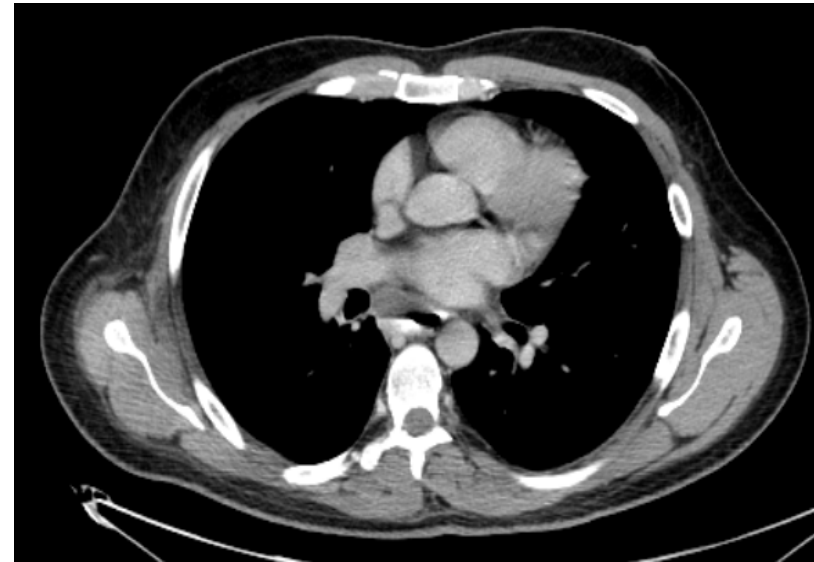


Patient Y31

Pre-treatment (May-10)

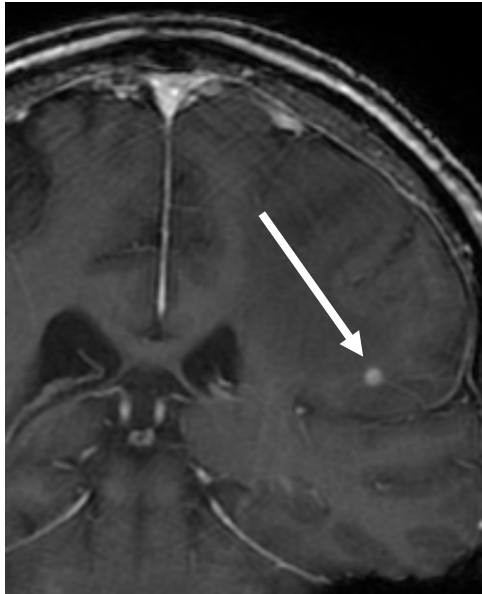


Post-treatment (Sep-10)

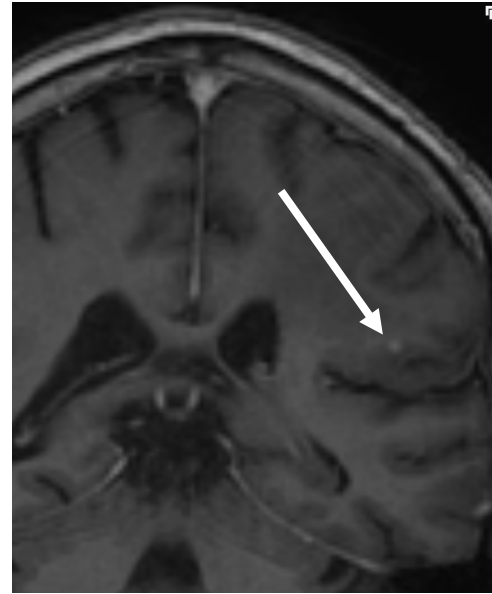


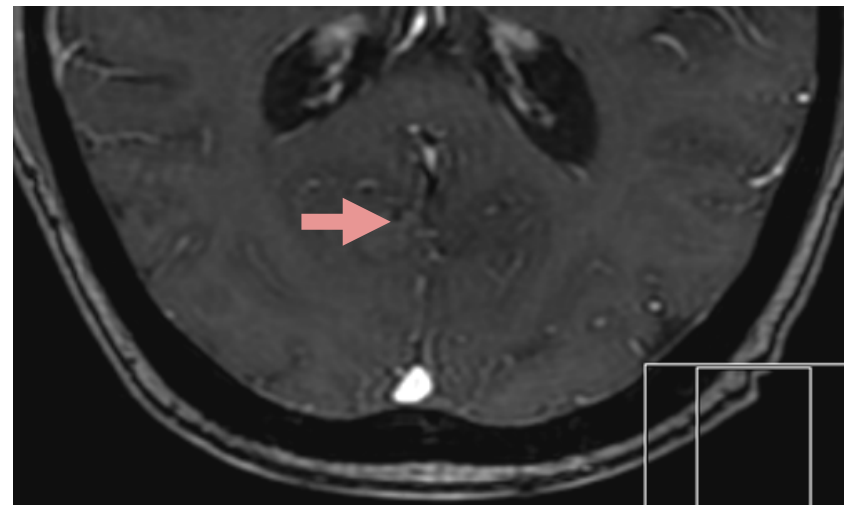
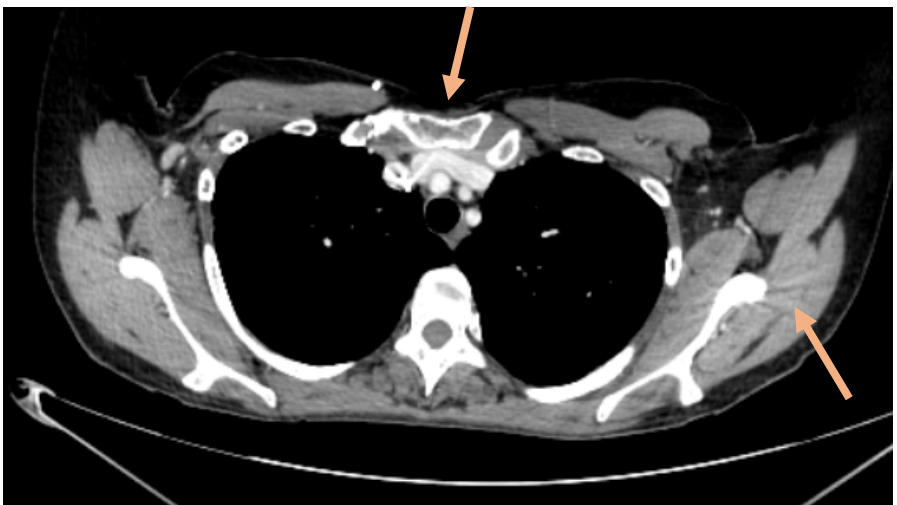
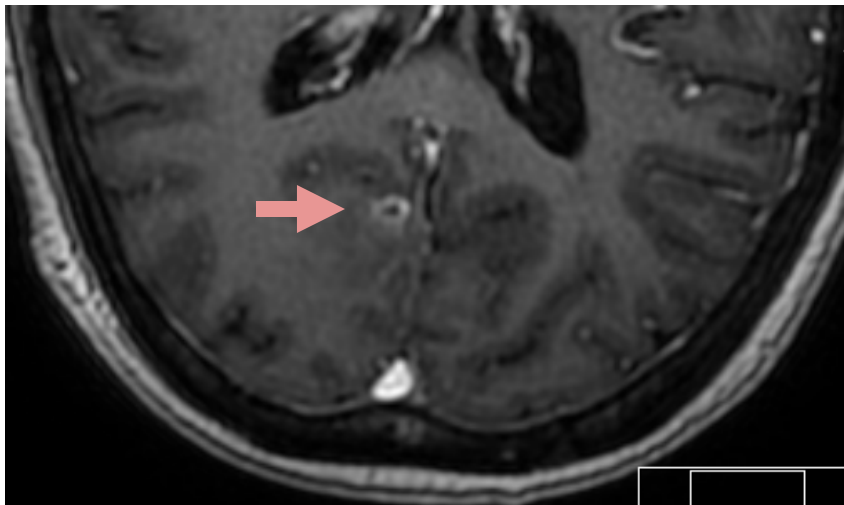
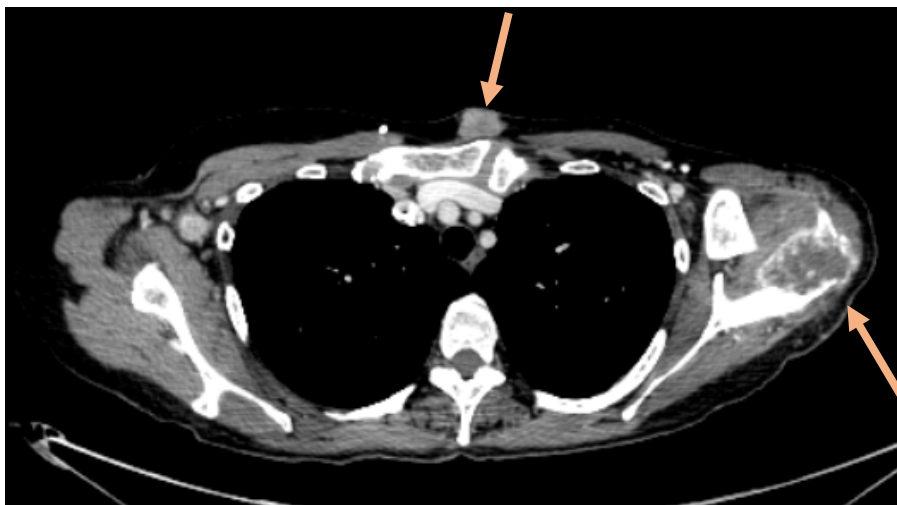
Patient Y38

Pre-treatment (Nov-10)

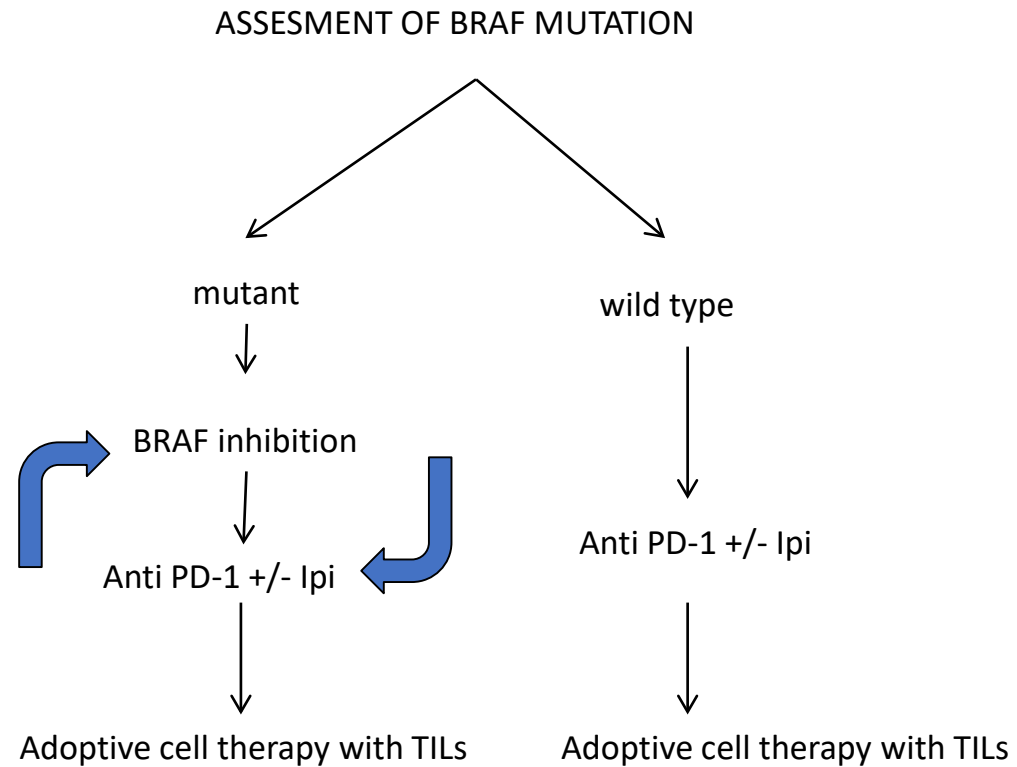


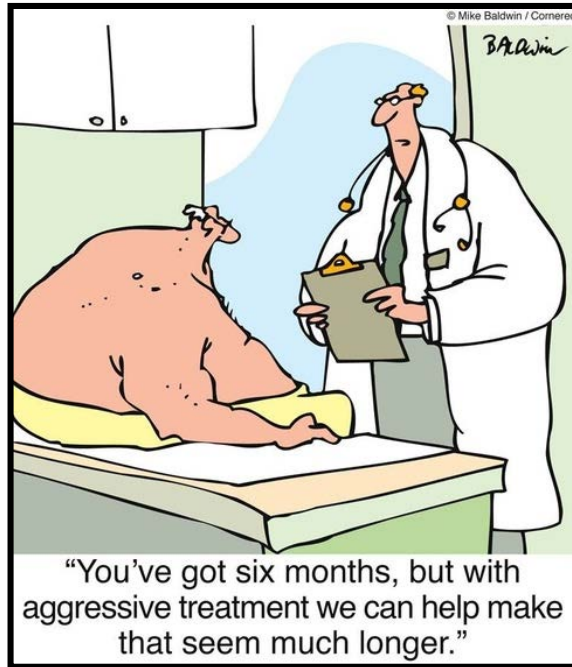
Post-treatment (Jan-11)





CURRENT TREATMENT ALGORITHM 2019





"You've got six months, but with aggressive treatment we can help make that seem much longer."

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Showing: 1-21 of 21 studies 25 studies per page

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Recruiting	Adoptive Cell Therapy Following a Non-myeloablative, Lymphodepleting Induction Regimen in Metastatic Melanoma Patients	Malignant Melanoma Stage IV	- Drug: Fludarabine - Drug: Cyclophosphamide - Biological: TIL - Drug: IL-2	Sheba Medical Center Ramat Gan, Israel
2	☐	Recruiting	A Prospective Randomized and Phase 2 Trial for Metastatic Melanoma Using Adoptive Cell Therapy With Tumor Infiltrating Lymphocytes Plus IL-2 Either Alone or Following the Administration of Pembrolizumab	Melanoma	- Drug: Cyclophosphamide - Drug: Fludarabine - Drug: Aldeslaukin (and 2 more...)	National Institutes of Health Clinical Center, 9000 Rockville Pike Bethesda, Maryland, United States
3	☐	Recruiting	The ACTIVATE (Adoptive Cell Therapy InVigorated to Augment Tumor Eradication) Trial	- Advanced Ovarian Cancer - Malignant Melanoma	- Drug: Cyclophosphamide - Drug: Fludarabine - Procedure: Pembrolizumab (and 2 more...)	Princess Margaret Cancer Centre Toronto, Ontario, Canada
4	☐	Recruiting	TIL-ACT After NMA Chemo With IL-2 and Nivo Rescue in Metastatic Melanoma (mMEL)	Metastatic Melanoma	- Other: TIL - Drug: Cyclophosphamide - Drug: Fludarabine (and 2 more...)	CHUV Oncology Department Lausanne, Vaud, Switzerland
5	☐	Recruiting	Study of Lifileucel (LN-144), Autologous Tumor Infiltrating Lymphocytes, in the Treatment of Patients With Metastatic Melanoma	Metastatic Melanoma	Biological: Lifileucel	- University of California San Diego Moores Cancer Center La Jolla, California, United States - The Angeles Clinic and Research Institute Los Angeles, California, United States - California Pacific Medical Center San Francisco, California, United States (and 50 more...)
6	☐	Recruiting	Immunotherapy Using Tumor Infiltrating Lymphocytes for Patients With Metastatic Melanoma	Metastatic Melanoma	- Drug: Aldesleukin - Drug: Fludarabine - Drug: Cyclophosphamide (and 2 more...)	National Institutes of Health Clinical Center, 9000 Rockville Pike Bethesda, Maryland, United States
7	☐	Recruiting	Combined Therapy of Nivolumab and Adoptive T Cell Therapy in Metastatic Melanoma Patients	Melanoma	Drug: TIL + IL-2 + Nivolumab	Nantes University Hospital Nantes, France

Thank you!

Clinical Team

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Gal Markel (Oncology)

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