# Anti-PD1 Therapy AFTER allogeneic stem cell transplant

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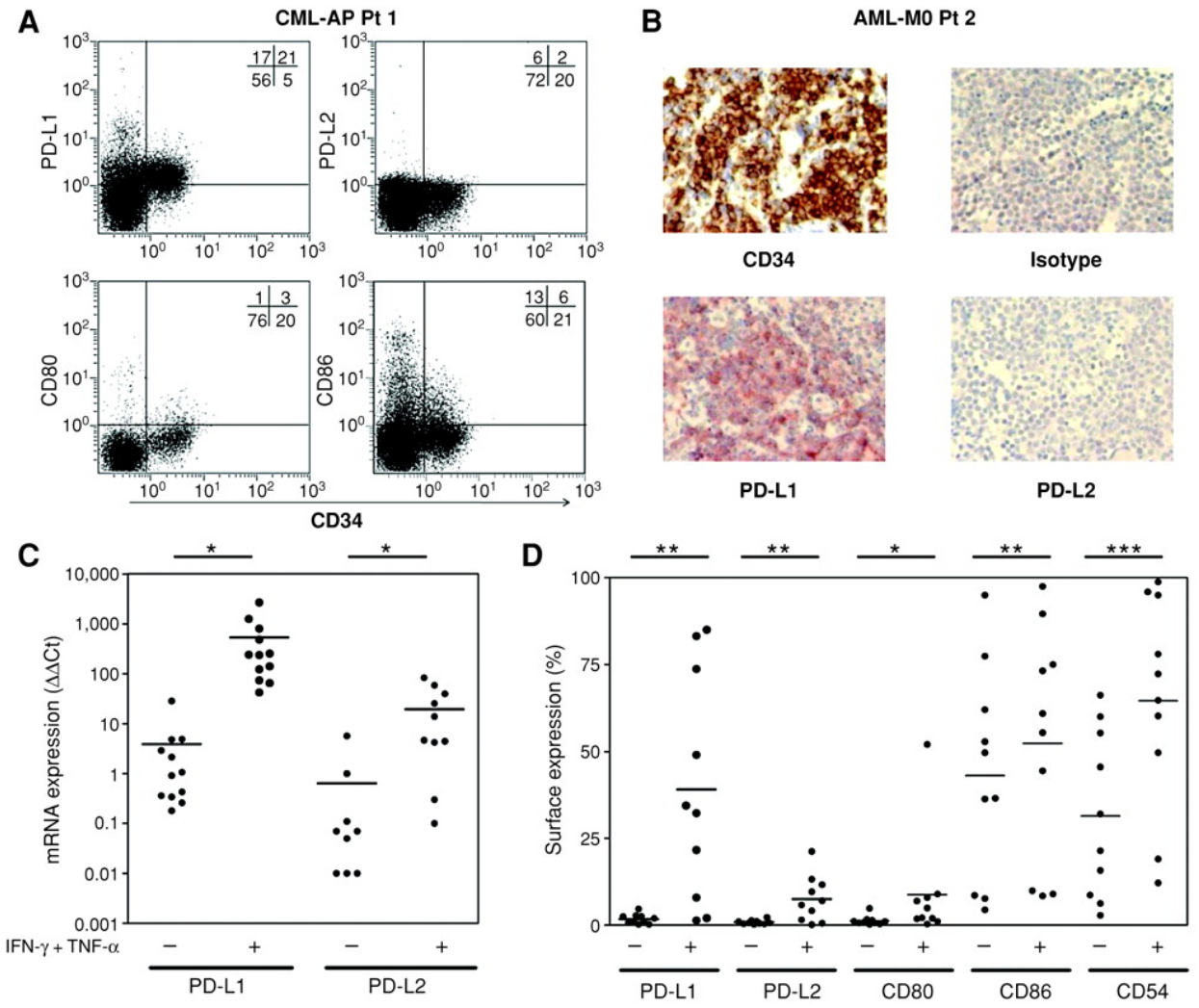
# Conflicts of Interest

- Research Funding from –
  - Bristol Myers Squibb
  - Celldex Therapeutics
  - Seattle Genetics

# PD-1 Blockade after Allo Transplant

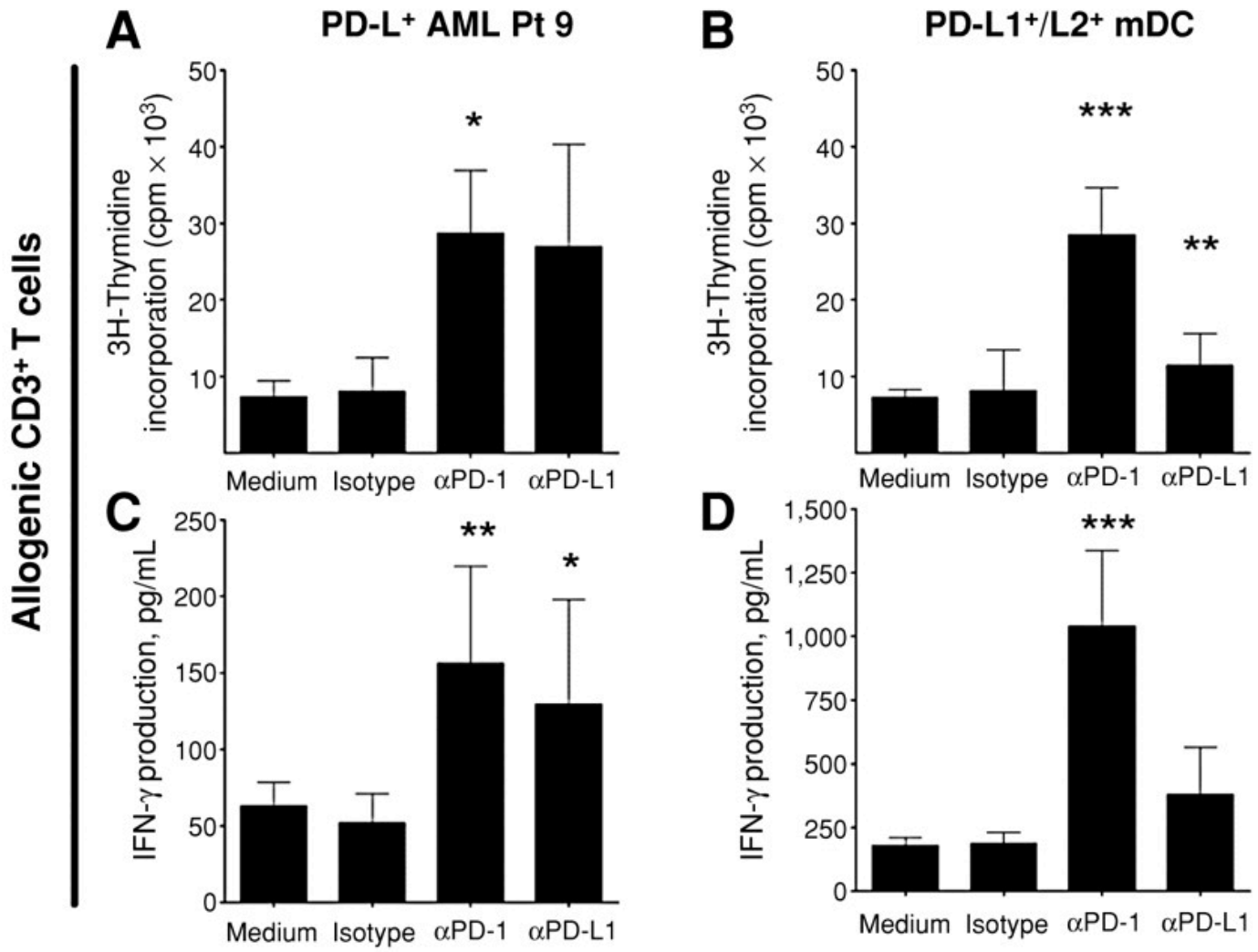
- Preclinical data regarding the role of PD-1/PD-L1 interactions in allo patients
  - Some data suggests benefit
  - Some data suggests risk
- Clinical data with anti-PD-1 antibodies post allogeneic transplant.

# Benefit? Relapsed Myeloid leukemia cells post allogeneic transplant express PD-L1




Wieger J. Norde et al. Cancer Res 2011;71:5111-5122

# Benefit? Blocking PD1 post allogeneic transplant restores T-cell function

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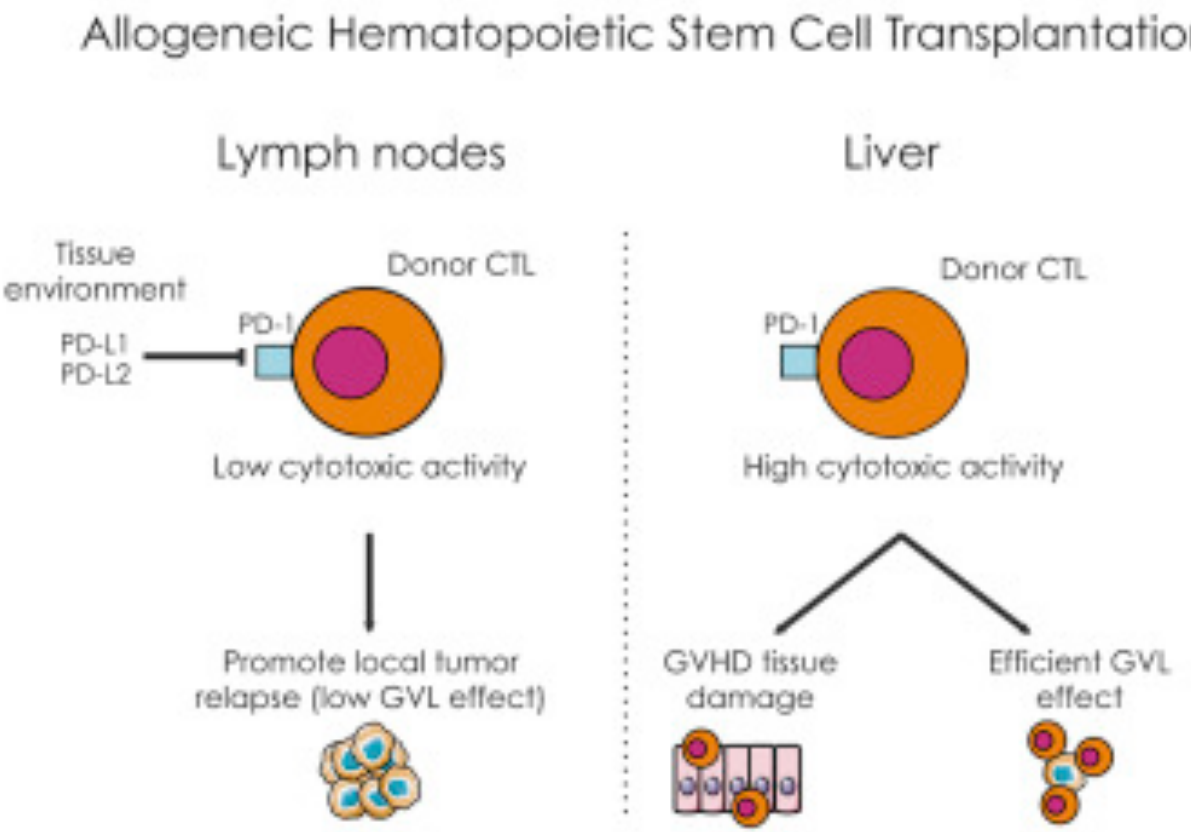
# Risk? The PD-1 Axis Creates Tumor Niches after Allogeneic Hematopoietic Stem Cell Transplantation.




Michonneau et al. Immunity. 2016 Jan 19;44(1):143-54.

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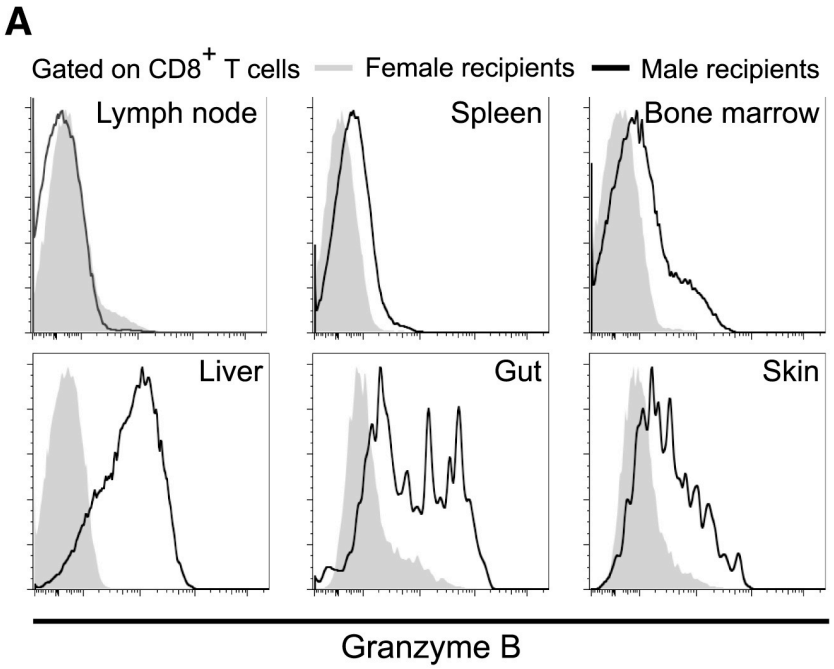


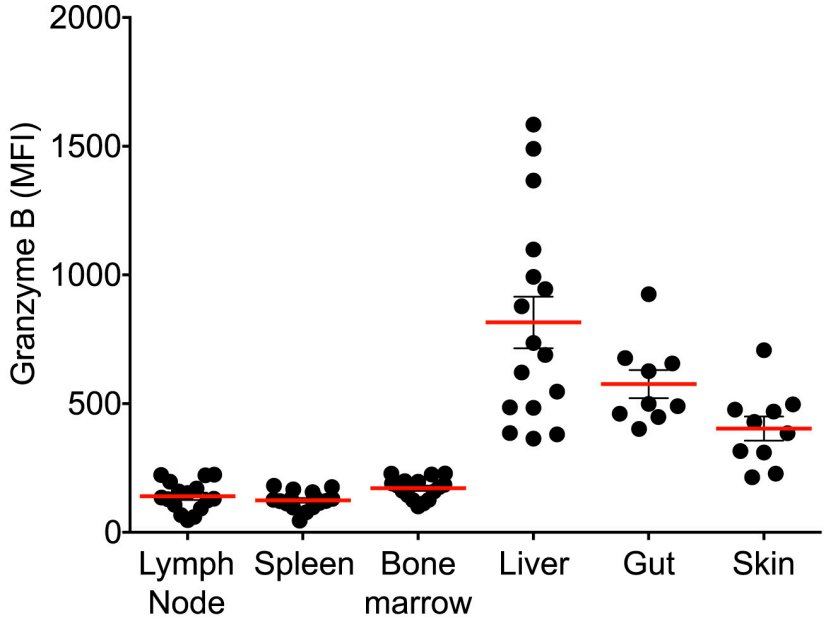


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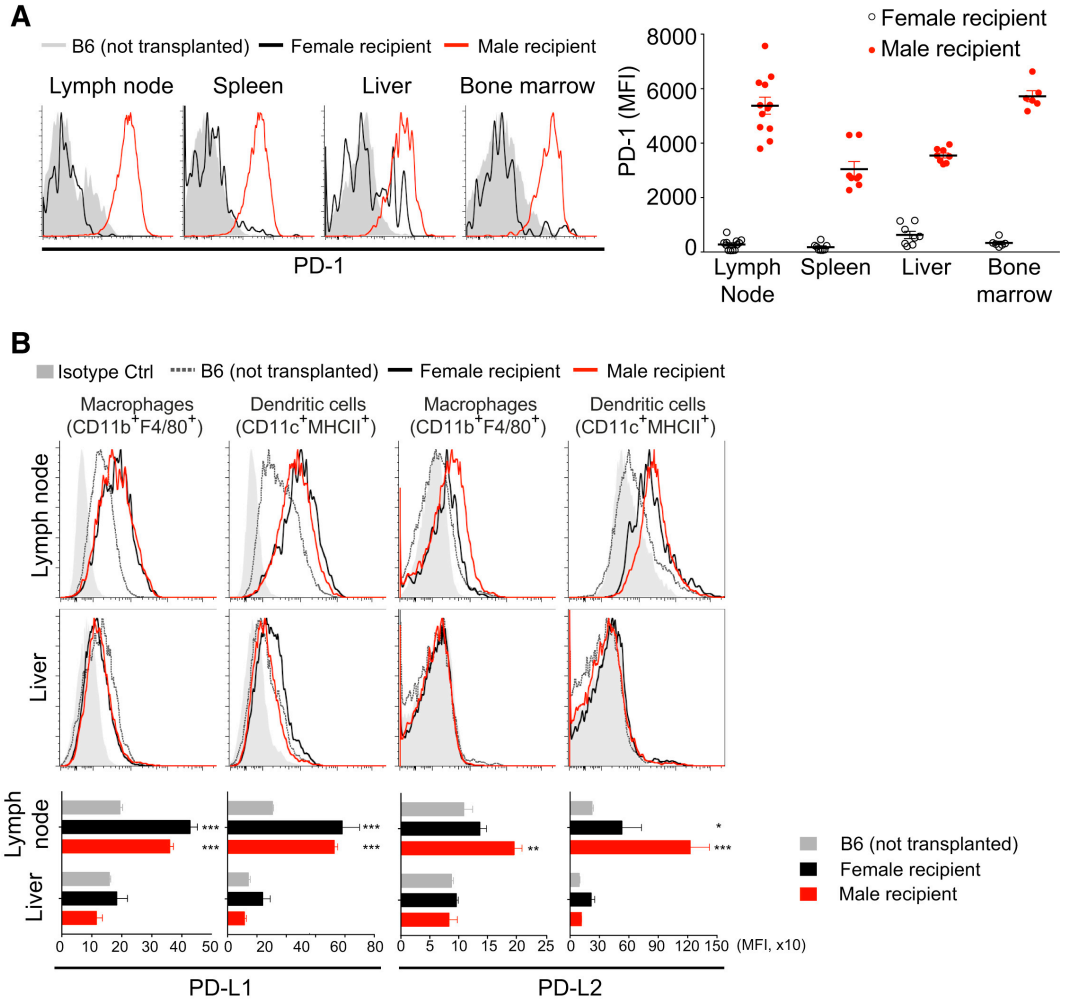


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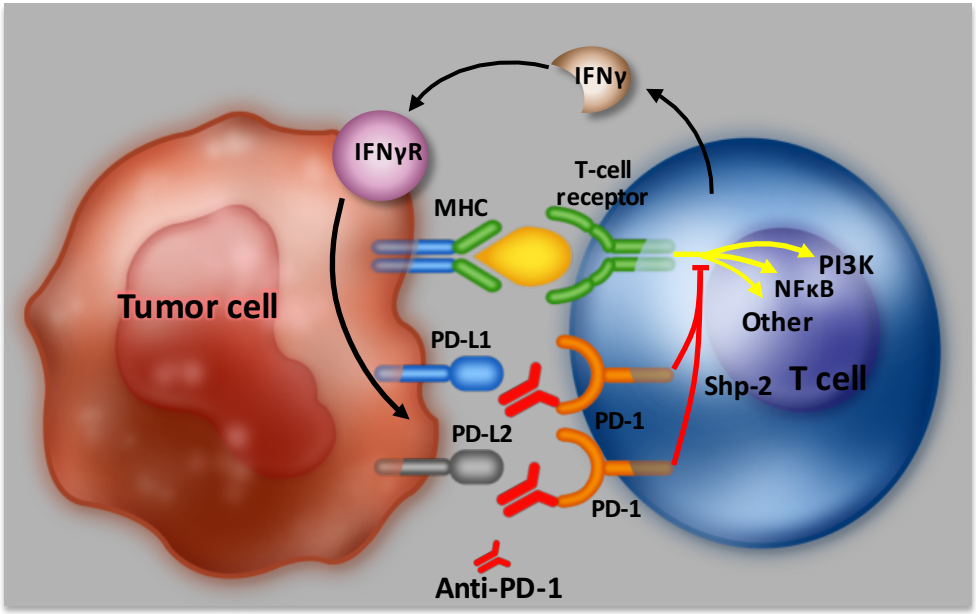
# PD-1 Blockade

- PD-1 ligands are overexpressed in inflammatory environments and attenuate the immune response via PD-1 on immune effector cells.[1]
- PD-L1 expressed on malignant cells and/or in the tumor microenvironment suppresses tumor infiltrating lymphocyte activity and interferes with host antitumor immunity.[2]




[1]Francisco LM et al. J Exp Med 2009;206:3015-29.
[2]Andorsky DJ et al. Clin Cancer Res 2011;17:4232-44

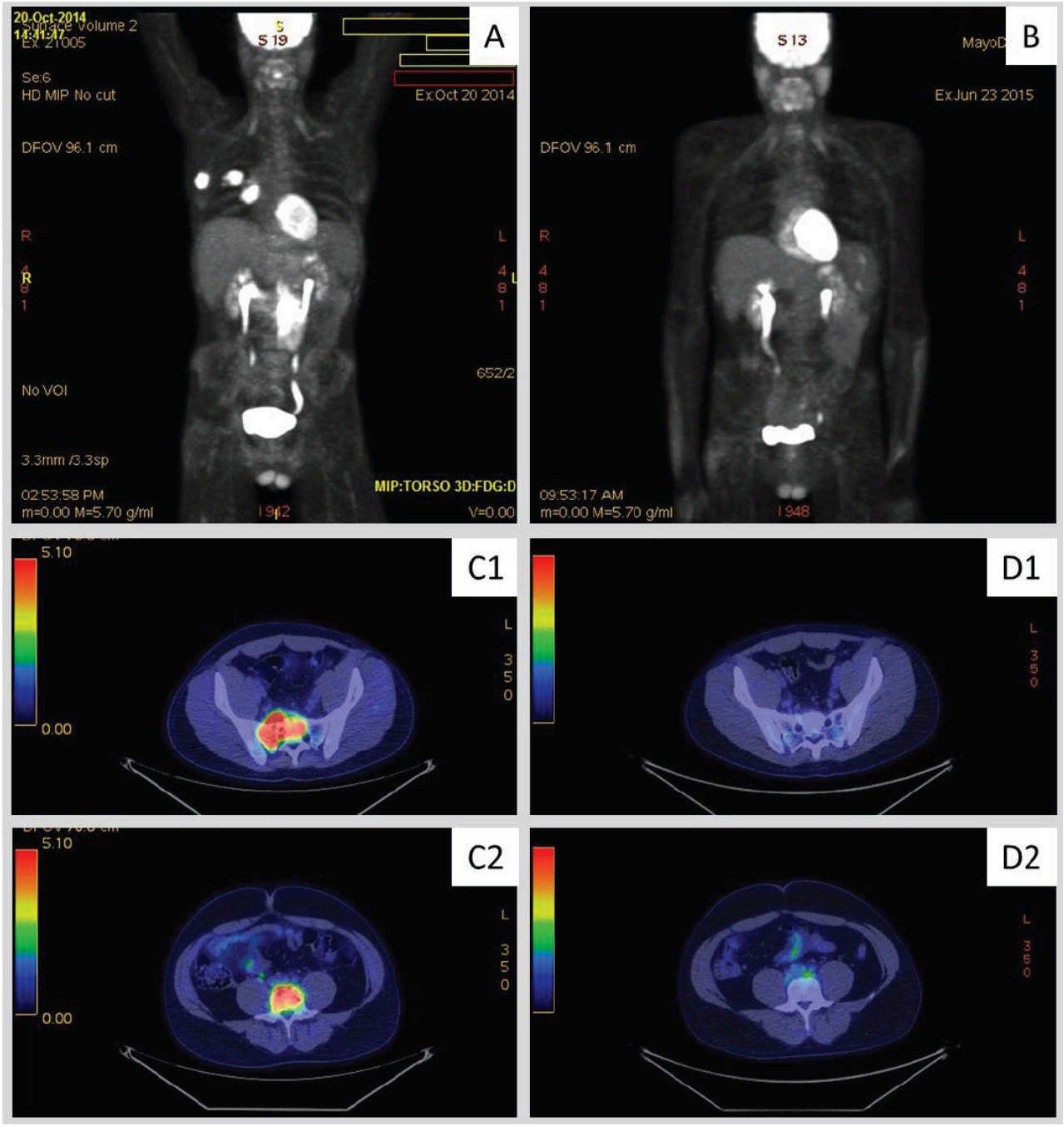
# Clinical Results with PD-1 Blockade post Allo

**Table 1: Clinical characteristics of the two patients with advanced cHL and history of allogeneic stem cell transplant treated with pembrolizumab**

| PRE-TREATMENT | PATIENT 1 | PATIENT 2 |
|---|---|---|
| Age (years) | 30 | 30 |
| Gender | Male | Male |
| Year of diagnosis | 2007 | 2008 |
| Autologous SCT | March 2008 | April 2009 |
| Allogeneic SCT | January 2009 | January 2014 |
| Number of other prior systemic therapies | 11 | 8 |
| Previous brentuximab vedotin | Yes | Yes |
| Chronic GVHD (location; stage)* | Liver (score 1) | None |
| Prednisone dosage | 2.5 mg daily | 2.5 mg daily |
| Date of first pembrolizumab infusion | October 21, 2014 | July 7, 2015 |

| POST-TREATMENT | PATIENT 1 | PATIENT 2 |
|---|---|---|
| Best overall response | Complete response | Partial Response |
| Chronic GVHD (location; stage)* | Liver (score 1) | None |
| Date of last infusion | October 26, 2015 | October 27, 2015 |
| Number of total infusions | 16 | 7 |
| Date of last radiological assessment | June 23, 2015 | October 5, 2015 |
| Treatment status | Ongoing | Ongoing |

Villasboas et al. Oncotarget 2016

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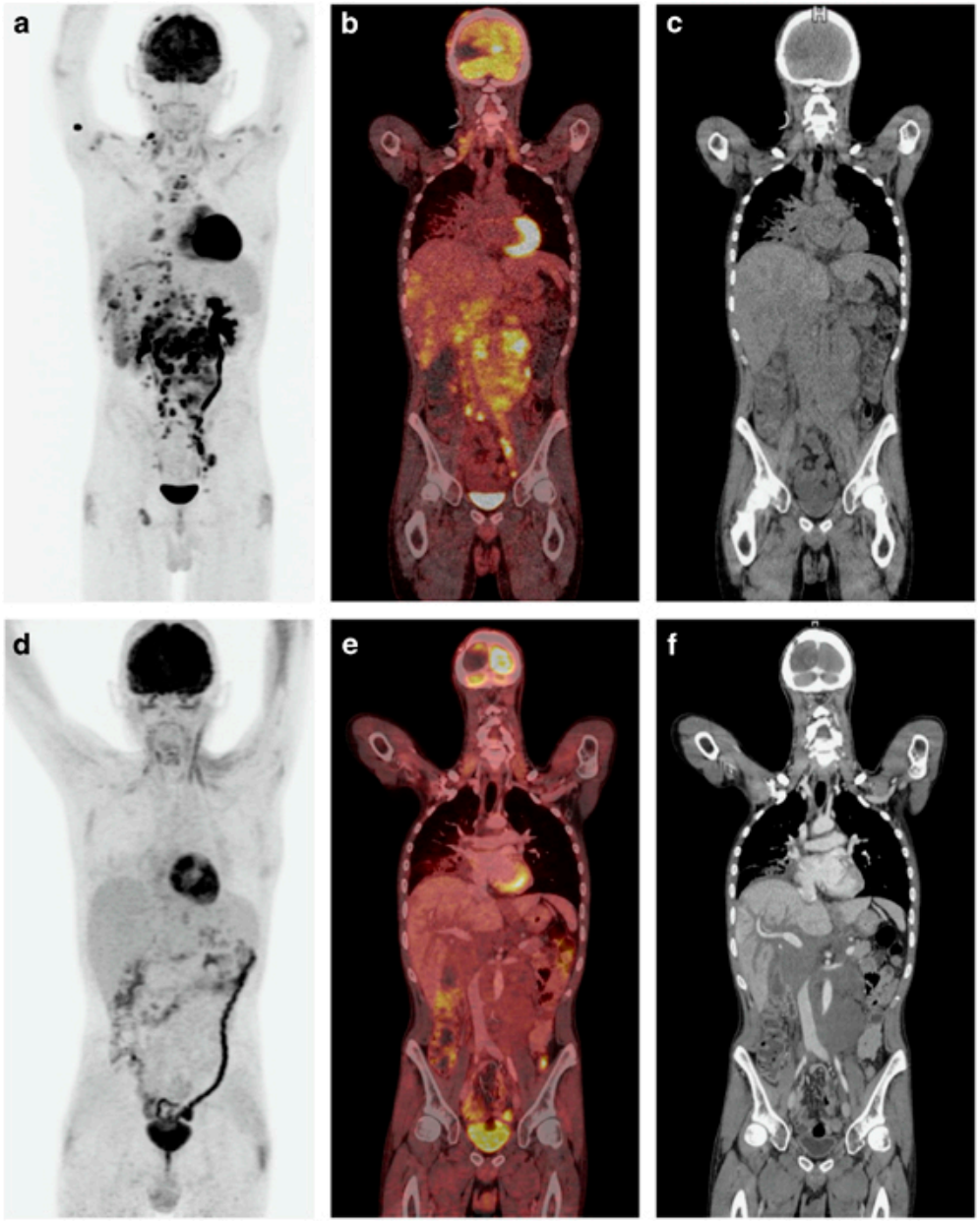


Angenendt et al. Bone Marrow Transplantation (2016) 51, 443–445

# **Cautionary note –**

# Fatal graft vs host disease induced by PD-1 inhibitor pembrolizumab in a patient with Hodgkin's lymphoma

Case report – post allogeneic transplant for Hodgkin lymphoma

**Singh et al. Bone Marrow Transplant 2016**

# Ipilimumab (CTLA-4 blockade) after allogeneic hematopoietic cell transplantation

- 29 patients with relapsed hematologic disease.
- Three patients with lymphoid malignancy developed objective disease responses following ipilimumab:
  - CR in 2 patients with Hodgkin disease
  - PR in a patient with refractory mantle cell lymphoma.
- Ipilimumab did not induce or exacerbate clinical GVHD

**Bashey et al. Blood. 2009;113(7):1581-8.**

# Conclusions

- PD-1 blockade can be given safely post allogeneic transplant
- However, severe toxicity with PD-1 blockade post allogeneic transplant has also been described.
- Cautious if active GVHD present?
- Needs a clinical trial