

Supplemental Data

Title: Cardiovascular toxicity and titin cross-reactivity of affinity enhanced T cells in myeloma and melanoma

Short Title: Cardiovascular toxicity and titin cross-reactivity

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Supplemental Content:

Supplemental Table 1. Calculations of in vivo expansion of MAGE-A3a3a T cells.

Supplemental Figure S1. Original protocol schematics.

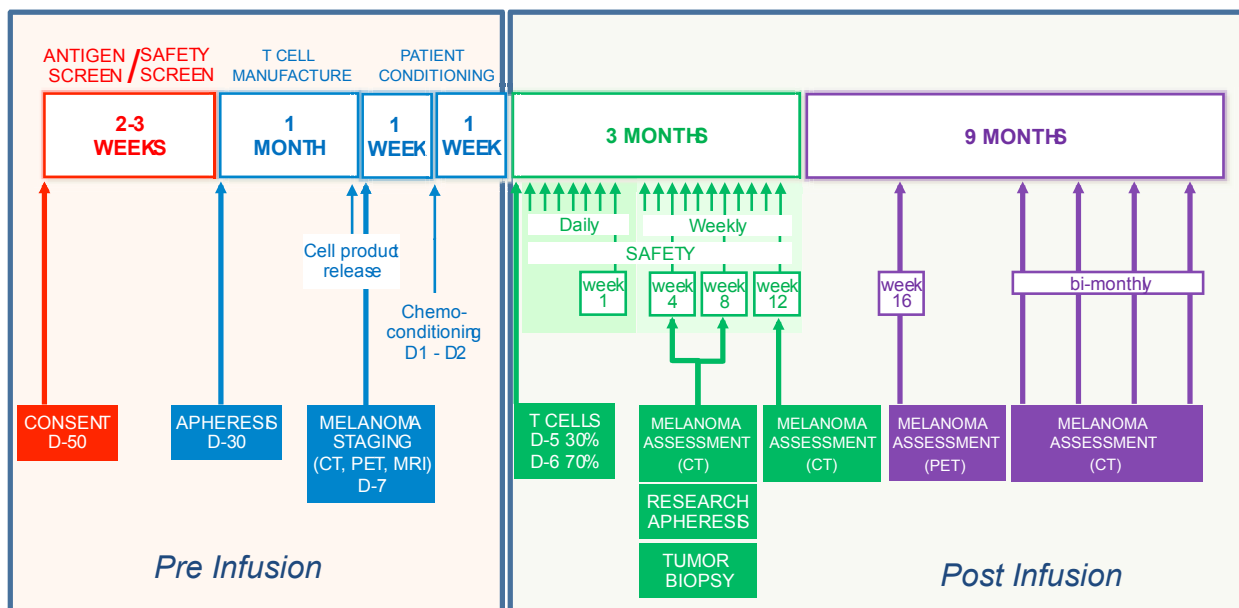
Table S1. Calculations of in vivo expansion of MAGE-A3^{a3a} T cells.

		<u>Day 0</u>	Case 1	Case 2
		Total number of T cells infused	1x10 ¹⁰	5x10 ⁹
		Total number of MAGE-A3^{a3a} T cells infused	5.3x10⁹	2.4x10⁹
<u>Autopsy</u>				
Blood	Total patient weight (kg)		88.2	105
	Total blood volume (ml)		6615	7840
	# MAGE-A3 ^{a3a} cells per ul of blood		100	370
	# MAGE-A3^{a3a} cells in total blood volume		6.61x10⁸	2.90x10⁹
Heart	Weight (gm)		460	542
	# total cells in heart		4.6x10 ¹¹	5.42x10 ¹¹
	# vector copies/ug gDNA in heart		2600	4270
	# MAGE-A3^{a3a} cells		7.70x10⁹	1.49x10¹⁰
Spleen	Weight (gm)		260	250
	# total cells in spleen		2.6x10 ¹¹	
	# vector copies/ug gDNA in spleen		16300	n/a
	# MAGE-A3^{a3a} cells		2.72x10¹⁰	n/a
Bone marrow	Marrow mass at age 65 (gm)		630	630
	# total cells in marrow			6.3x10 ¹¹
	Marrow copies/ug gDNA		n/a	17400
	# MAGE-A3^{a3a} cells		n/a	7.07x10¹⁰
Lungs	Weight (gm)		2280	960
	# total cells in lungs		2.28x10 ¹²	9.60x10 ¹¹
	# vector copies/ug gDNA lung		2050	37500
	# MAGE-A3^{a3a} cells		3.01x10¹⁰	2.32x10¹¹
Liver	Weight (gm)		1750	1630
	# total cells in liver		1.75x10 ¹²	1.63x10 ¹²
	# vector copies/ug gDNA liver		2310	12900
	# MAGE-A3^{a3a} cells		2.60x10¹⁰	1.36x10¹¹
Kidneys	Weight (gm)		380	337
	# total cells in kidney		3.80x10 ¹¹	3.37x10 ¹¹
	# vector copies/ug gDNA kidney		689	2590
	# MAGE-A3^{a3a} cells		1.68x10⁹	5.61x10⁹
Brain	Weight (gm)		1450	1310
	# total cells in brain		1.45x10 ¹²	1.31x10 ¹²
	# vector copies/ug gDNA brain		38.3	441
	# MAGE-A3^{a3a} cells		3.56x10⁸	3.72x10⁹
		Total # MAGE-A3^{a3a} cells at autopsy	9.37x10¹⁰	4.65x10¹¹
		Fold expansion <i>in vivo</i>	17.7	194

Legend to Supplemental Table 1. Weights of organs were measured at autopsy in both patients.

Copies of vector were measured per microgram of genomic DNA in various organs as indicated. We made the following assumptions: for total blood volume, we assumed that total blood volume was a function of weight (75 ml blood/kg). For solid organs, we assumed that 1 kg contained 1×10^{12} cells. The current estimate for human male diploid genome nuclei of cells in G1 phase of the cell cycle is 6.436 pg of genomic DNA per cell. Therefore, we estimated that the number of MAGE-A3^{a3a} T cells in an organ was (# of total cells in organ * 0.000006436 microgram of genomic DNA/cell * measured copies of vector/microgram genomic DNA). The total number of MAGE-A3^{a3a} T cells was calculated by adding the total number of MAGE-A3^{a3a} T cells in total blood volume and in each organ (i.e. total blood volume + heart + spleen or bone marrow + lungs + liver + kidneys + brain). We did not include pericardial fluid from Case 2, which contained a large number of cell markings by PCR, because we did not have a cell count on the fluid; similarly, we did not have complete data for skeletal muscle or the GI tract; these could all result in an underestimate. However, we also recognize that there may be an overestimation factor based on vascularization of tissues (double counting of marked cells in blood and in the vascular portion of the tissue, especially lung).

Melanoma protocol schema (Case 1)



Myeloma protocol schema (Case 2)

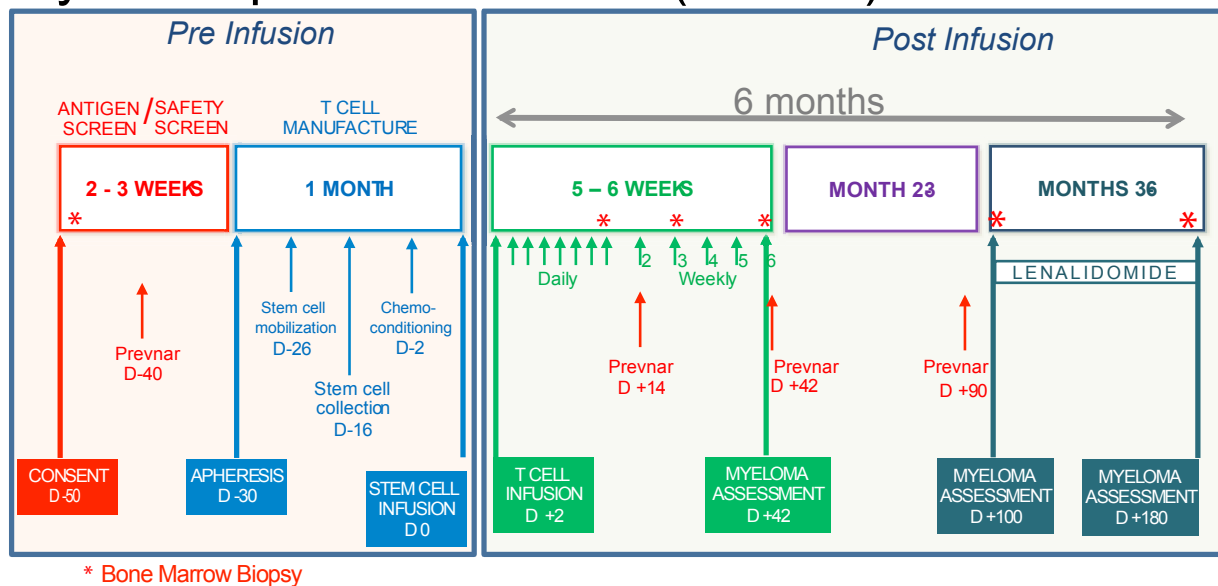


Figure S1. Original protocol schematics. Top panel: Melanoma study UPCC1611 (Case1).

Bottom panel: Myeloma study UPCC1411 (Case 2).