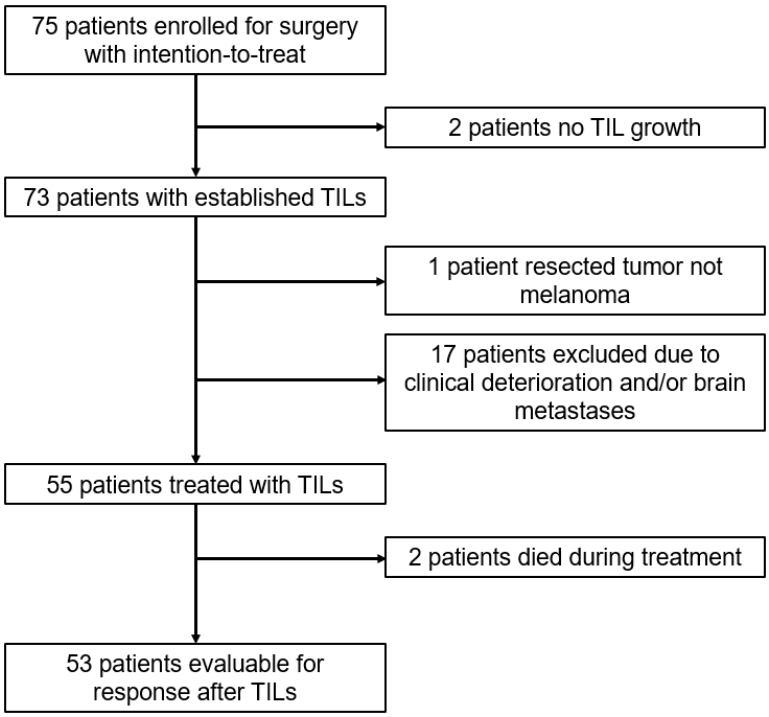
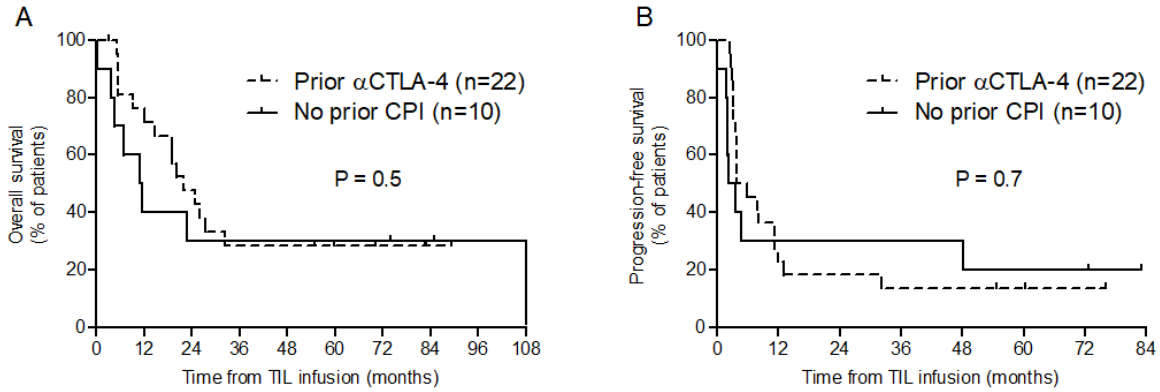
Supplementary file for

"A future role for adoptive T cell therapy in checkpoint inhibitor resistant metastatic melanoma"

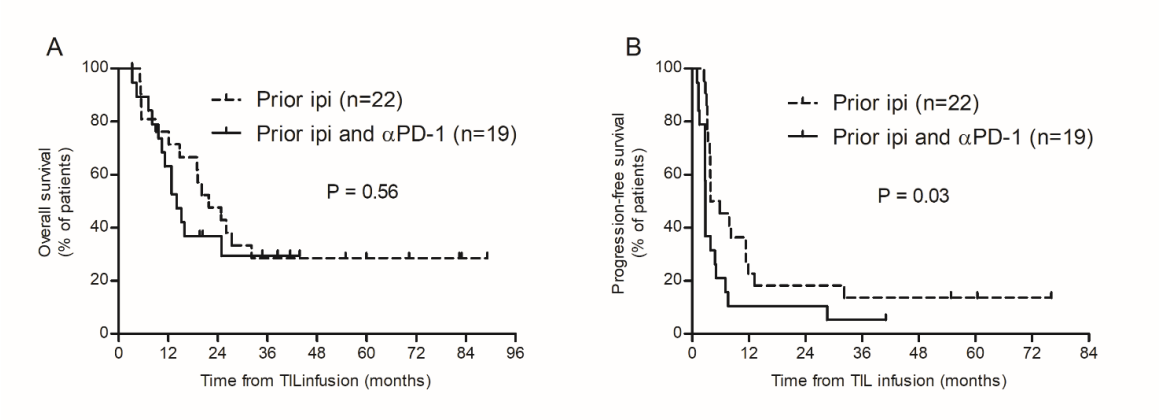


Supplementary figure 1. Outline of patient enrolment and number of dropouts. TIL; tumor-infiltrating lymphocyte.

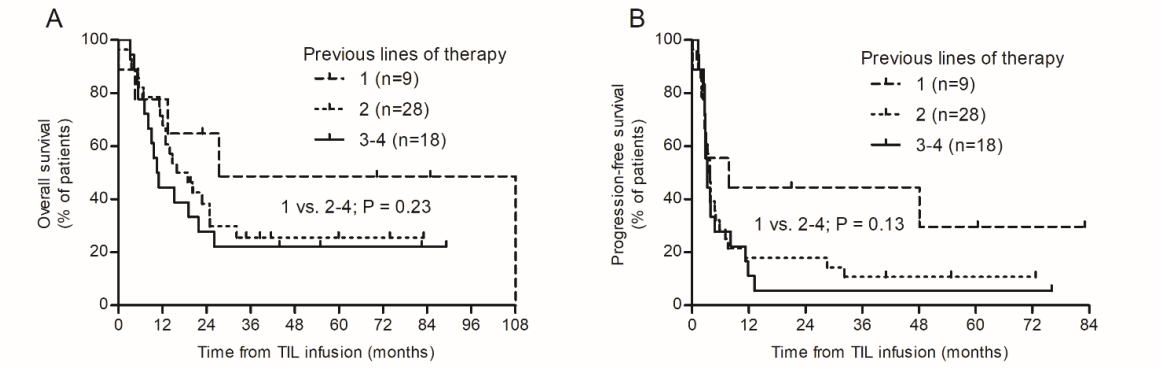


Supplementary figure S2. Kaplan-Meier curves showing overall (A) and progression-free survival (B) in patients previously treated with anti-CTLA-4 blockade (n = 22) or not previously treated with checkpoint inhibitors (n = 10).

Borch TH, *et al. J Immunother Cancer* 2020; 8:e000668. doi: 10.1136/jitc-2020-000668



Supplementary figure S3. Kaplan-Meier curves showing overall (A) and progression-free survival (B) in patients previously treated with anti-CTLA-4 blockade (n = 22) or previously treated with both anti-PD-1 and anti-CTLA-4 (n = 19).



Supplementary figure S4. Kaplan-Meier curves showing overall (A) and progression-free survival (B) in patients previously treated with one line of systemic therapy (n = 9), two lines (n = 28) or three or more lines (n = 18).

Borch TH, *et al. J Immunother Cancer* 2020; 8:e000668. doi: 10.1136/jitc-2020-000668

Treatment characteristics, median (range)			
Days in hospital[a]			19 (15; 37)
Units RBC transfusion			4 (0; 25)
Units PLT transfusion			6 (0; 17)
Days with neutrophils < 0.5 x 10^9/L			8 (4; 14)
Treatment-emergent adverse events	**Grade 1-2**	**Grade 3-4**	**Grade 5**
Neutrophil count decreased		55	
Febrile neutropenia		54	
Infections, verified[b]		18	
Fatigue	18	36	
Dyspnoea	31	16	
Nausea	33	6	
Vomiting	23	2	
Diarrhea	42	3	
Dermatitis[c]	31	3	
Atrial fibrillation	2	1	
Delirium	7	5	
Mortality[d]			2
Vitiligo	3		
Uveitis	2		

Supplementary Table T1. Treatment characteristics and select treatment-emergent adverse events. In addition to listed adverse events, all patients experienced bone marrow suppression (i.e. anemia, low platelet count and temporary complete depletion of leukocytes in the blood) and electrolyte derangements (i.e. low sodium and potassium levels). [a] The two patients who died during admission are not included in the median of admission days. [b] Infections were managed according to local clinical practice and were treatable with antibiotics and/or supportive measures. [c] Dermatitis includes dry skin and/or maculopapular rash. [d] See main text for description. RBC, red blood cell. PLT, platelet.

Response rate among evaluable patients			
	N	n	RR (%)
All patients[a]	53	20	38
Stage			
≤ M1a	6	3	50
M1b	6	3	50
M1c	41	14	34
LDH > 2 x ULN	6	1	17
Disease sites			
CNS	10	2	20
Liver	10	2	20
Prior CPI			
Anti-CTLA-4	22	10	45
Anti-PD-1	3	1	33
Both as monotherapy	19	6	32
No CPI	9	3	33
No. previous lines of therapy			
1	8	5	63
2	27	9	33
3	14	5	36
4	4	1	25
IL-2 dose			
Low-dose s.c.	6	2	33
Decrescendo	47	18	38

Supplementary table T2. Response rate according to baseline or treatment characteristics in evaluable patients. [a]In total treated 55 patients; two were not evaluable. N; number of patients in the group. n; number of responding patients according to RECIST.

Baseline characteristics of PD-1 näive patients vs. PD-1 progressors

		No prior αPD-1		**Prior αPD-1 +/- αCTLA-4**	
		n = 32	%	n = 23	%
ECOG PS	0	21	66	13	57
	1	9	28	9	39
	≥ 2	2	6	1	4
Stage	IIIB	0	-	2	9
	M1a	2	6	2	9
	M1b	4	13	2	9
	M1c	26	81	17	74
LDH	Normal LDH	11	34	9	39
	LDH > ULN < 2 x ULN	15	47	12	52
	LDH ≥ 2 x ULN	5	16	2	9
	Unknown	1	3	0	0
No. metastatic sites (median, range)		4	(1-7)	4	(1-8)
History of CNS mets	Yes	8	25	3	13
	No	24	75	20	87
Liver mets	Yes	4	13	7	30
	No	28	88	16	70
Lines of prior therapy	1	5	16	4	17
	2	15	47	12	52
	≥ 3	12	38	7	30

Supplementary table T3. Patient characteristics in subgroups either not previously treated with anti-PD-1 blockade or previously treated with anti-PD-1 blockade with or without sequential anti-CTLA-4 blockade.

Median overall and progression-free survival and duration of response related to lines of prior therapies in the metastatic setting				
	Prior lines of therapy			
	1	**2**	**3**	**4**
	n = 9	n = 28	n = 14	n = 4
Response rate (%)	62.5[a]	33.3[a]	35.7	25
Median OS (months)	27.4	17.4	13.1	6.3
Median PFS (months)	7.8	3.8	3.2	2.2
DOR both CR and PR, median (months)	48.1[b]	25.6	11.6[c]	
# Complete response	3	2	1	0
DOR, median (months)	60.4+	47.9+	13.2	-
DOR, min (months)	48.1	41+	13.2	-
DOR, max (months)	83.1+	54.8+	13.2	-
DOR, range (months)	(48.1-83.1+)	(41+-54.8+)	(13.2)	-
# Partial response	2	7	4	1
DOR, median (months)	14.4+	11.3	9.8	76.1+
DOR, min (months)	7.8	2.7	3.9	76.1+
DOR, max (months)	21+	72.7+	11.9	76.1+
DOR, range (months)	(7.8-21+)	(2.7-72.7+)	(3.9-11.9)	(76.1+)
# Ongoing responses (CR/PR)	3 (2/1)	3 (2/1)	0	1 (0/1)

Supplementary table T4. Median overall survival, progression-free survival and duration of response related to lines of prior therapies in the metastatic setting. [a]One patient in each group was not evaluable for response. [b]Median DOR not reached. [c]Median DOR for 3 and 4 prior lines of therapy. +Ongoing response.