SUPPLEMENTARY APPENDIX

Programmed cell death protein-1 (PD-1)-expression in the microenvironment of classical Hodgkin lymphoma at relapse during anti-PD-1-treatment

Stephanie Sasse,¹ Katharina Reddemann,² Arjan Diepstra,³ Ilske Oschlies,² Antje Schnitter,² Sven Borchmann,^{1,4,5} Andreas Engert,¹ Peter Borchmann¹ and Wolfram Klapper²

¹First Department of Internal Medicine and German Hodgkin Study Group, University Hospital of Cologne, Germany; ²Department of Pathology, Hematopathology Section, University Hospital Schleswig-Holstein, Christian-Albrechts-University, Kiel, Germany; ³Department of Pathology and Medical Biology, University of Groningen, University Medical Centre Groningen, the Netherlands; ⁴Center for Molecular Medicine, University Hospital of Cologne, and ⁵Else Kröner Forschungskolleg Cologne, University of Cologne, Germany

*SS and KR contributed equally to this work.

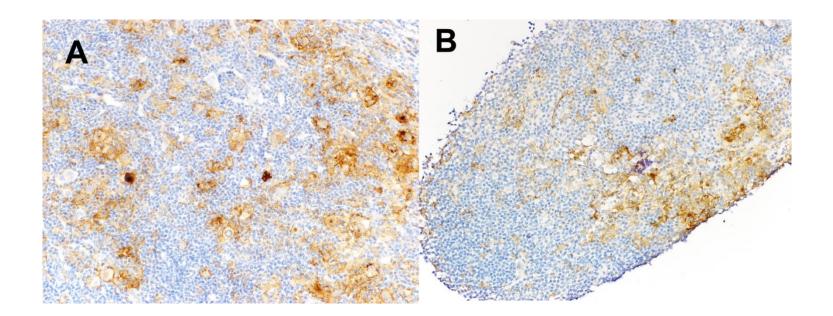
Correspondence: stephanie.sasse@uk-koeln.de doi:10.3324/haematol.2018.196279

Supplemental table 1: Results of immunohistochemical stainings of Hodgkin- and Reed/Sternberg- as well as microenvironmental cells

Patient no.	year	tissue type	cHL subtype	Immu	Immunoprofile of the HRSCs														microenvironment*				
													HLA										
				CD30	CD15	CD20	CD3	PAX5	EBER	PD1L1	PD1	HLA II (DP, DQ, DR)	DM	β2M	HC10	PD1L1	PD1	CD3	CD4	CD8			
1	2011	lymph node	wsub/ns	+	+	-	-	+	ND (LMP negative)	80%	-	ND	ND	ND	ND	12,6	0	116,7	32,3	37,7			
	2015	bone marrow	wsub/ns	+	+	-	-	+	ND (LMP negative)	80%	-	ND	ND	ND	ND	42,7	0	71,7	3,7	60,3			
	2017	lymph node	wsub	+	+	-	NE	+	ND (LMP negative)	100%	-	ND	ND	ND	ND	6,3	4	NE	8,7	62,5			
2	2015	lymph node	lydepl	+	+/-	-	-	+	-	100%	-	-	-	-	-	39,3	0	23,3	3	16,3			
	2017	lymph node	lydepl	+	+	-/+	-	+	-	100%	-	+	-	-	-	12,6	39,7	155	72	15,3			
3	2010	lymph node	ns	+	-	-/+	-	+	-	90%	-	ND	ND	ND	ND	40,3	0	148,3	NE	NE			
	2015	bronchus biopsy	wsub	+	-	-	-	+	-	80%	-	ND	ND	ND	ND	30,3	0	223,3	NE	NE			
4	2015	lymph node	mix	+	+	-	NE	+	-	100%	-	+/-	-	-	-	21,7	2	ND	32,3	51,6			
	2017	lymph node	wsub	+	+	-	-	+	-	50%	1	NE	NE	-	+	25,3	0	123	146	28,6			
5	2007	lymph node	mix	+	+	-	-	ND	-	80%	-	ND	ND	ND	ND	15,3	7,6	221	NE	NE			
	2017	liver	wsub	+	+/-	ND	ND	+	-	NE	NE	-	NE	-	NE	NE	NE	ND	ND	ND			
	2017	liver	wsub	+	ND	-	ND	NE	-	NE	NE	•	NE	NE	NE	NE	NE	NE	NE	NE			
6	2013	lymph node	wsub	+	NE	-	-	+	-	100%	-	ND	ND	ND	ND	11,3	0	84,7	ND	ND			
	2017	bronchus biopsy	wsub	+	+	-	-	+	-	100%	-	ND	ND	ND	ND	NE	0	34	NE	9,3			
7	2014	soft tissue	mix	+	+/-	-	-	+	-	100%	-	ND	ND	ND	ND	50,7	18,7	212	180	51,3			
	2017	lymph node	wsub	+	+	-	-	+	-	100%	-	ND	ND	ND	ND	21,3	67	239	NE	67			
8	2012	lymph node	mix	+	-	-/+	-	+	-	100%	-	ND	ND	ND	ND	NE	0	218,7	219	29,7			
	2014	soft tissue	wsub/ns	+	-	-	-	+/-	-	100%	-	ND	ND	ND	ND	25,3	0	171,3	223,6	29			
	2017	lymph node	lyrich	+	-	-	-	+	-	90%	-	ND	ND	ND	ND	35,3	71,3	124,3	93	31			
9	2016	lymph node	ns	+	-/+	-	-	+	ND (LMP negative)	50%	-	ND	ND	ND	ND	NE	5	91,6	81,6	22			
	2018	bone marrow	wsub	+	-	-	ND	+	ND (LMP negative)	90%	-	ND	ND	ND	ND	NE	22	ND	53	20			

cHL: classic Hodgkin lymphoma; wsub: without subtyping; wsub/ns: without subtyping due to small size of biopsy but with severe sclerosis; ns: nodular sclerosis cHL; lydepl: Lymphocyte depleted cHL; mix: mixed-cellularitiy cHL; lyrich: Lymphocyte-rich cHL; +: all cells positive; +/-: most cells positive; -/+: few cells positive, -: all cells negative; NE: not evaluable; ND: not done; EBER: Epstein-Barr virus encoding RNA (detection by in situ-hybridisation), LMP: Epstein-Barr virus latent membrane protein 1; HLA: human leucocyte antigene; β2M: Beta-2-microglobulin; HC10: heavy chain 10 (HLA I); *total number of PD1, PD1L1, CD3, CD8 and CD4 positive microenvironmental cells was counted in three high-power fields (HPF, 1000-fold magnification using oil immersion), given here is the average value which was used for further analysis. HPF was chosen with at least one HRSC in the center in order to analyze

Supplemental Figure 1



Supplemental figure 1:

PD-L1 staining in patient 4 who appeared to have a slight reduction in PD-L1 staining of the HRSC between pre- (A) and post-treatment biopsy (Original magnification 200x)