

**Supplemental Table 1: Comparison of patient characteristics in this study and the main clinical trial cohort.**

	E2496 clinical trial cohort		Patients used in this study		p value
	n	%	n	%	
<b>Total</b>	794		287		
<b>Age</b>					
Median, range	33	16 - 83	32	18 - 79	0.65
<b>Sex</b>					
Male	425	54	161	56	0.28
Female	369	46	126	44	
<b>Performance status*</b>					
0	448	56	172	60	0.21
1	313	39	110	38	
2	23	3	5	2	
Unknown	10	1	0	0	
<b>Disease stage*</b>					
I	32	4	6	2	0.15
II	209	26	72	25	
Ile	40	5	15	5	
III	269	34	112	39	
IIle	32	4	11	4	
IV	203	26	71	25	
Unknown	9	1	0	0	
<b>Histologic subtype*</b>					
Nodular sclerosis	562	71	223	78	0.53
Mixed cellularity	87	11	38	13	
Lymphocyte rich	14	2	8	3	
Lymphocyte depleted	2	0	1	0	
Unclassified	100	13	17	6	
Unknown	29	4	0	0	
<b>IPS *</b>					
0	60	8	20	7	0.37
1	192	24	72	25	
2	260	33	98	34	
3	151	19	58	20	
4	71	9	25	9	
5	39	5	8	3	
6	9	1	5	2	
Unknown	12	2	1	0	
<b>Primary treatment</b>					
ABVD	395	50	144	50	0.92
Stanford V	399	50	143	50	
<b>Outcomes</b>					
Median follow-up		5.3		5.5	
FFS (5 year)		72%		73%	0.90

OS (5 year)	88%	90%	0.78
Total deaths observed	97	32	

*p* values are for comparing patients used in this study (n=287) with those that were not in this study (n=507) in the E2496 clinical trial cohort (n=794).

\*Pearson chi-squared test was performed with unknown and/or unclassified cases excluded.

**Supplemental Table 2: Comparison of patient characteristics and EBER status.**

	EBER <sup>pos</sup>		EBER <sup>neg</sup>		<i>p</i> value
	n	%	n	%	
<b>Total</b>	49		238		
<b>Age (≥45y)</b>					
No	35	71	205	86	0.01
Yes	14	29	33	14	
<b>Sex</b>					
Female	35	71	112	47	0.02
Male	14	29	126	53	
<b>Stage IV disease</b>					
No	35	71	181	76	0.50
Yes	14	29	57	24	
<b>Albumin (&lt;4g/dl)*</b>					
No	14	29	73	31	0.81
Yes	33	67	158	66	
Unknown	2	4	7	3	
<b>Hemoglobin (&lt;10.5g/dl)*</b>					
No	35	71	191	80	0.14
Yes	11	22	34	14	
Unknown	3	6	13	5	
<b>WBC count (≥15,000/mm3)*</b>					
No	44	90	182	76	0.02
Yes	2	4	39	16	
Unknown	3	6	17	7	
<b>Lymphocyte count (&lt;600/mm3 or &lt;8%)*</b>					
No	45	92	206	87	0.41
Yes	2	4	17	7	
Unknown	2	4	15	6	
<b>IPS (≥3)*</b>					
No	26	53	163	68	0.03
Yes	23	47	74	31	
Unknown	0	0	1	0	
<b>Histological subtype*</b>					
Nodular sclerosis	26	53	197	83	<0.01
Mixed cellularity	19	39	19	8	
Lymphocyte rich	2	4	6	3	
Lymphocyte depleted	1	2	0	0	
Unclassified	1	2	16	7	
<b>Treatment received</b>					
ABVD	28	57	116	49	0.28
Stanford V	21	43	122	51	
<b>CD68</b>					
CD68 <sup>low</sup>	15	31	163	68	<0.01

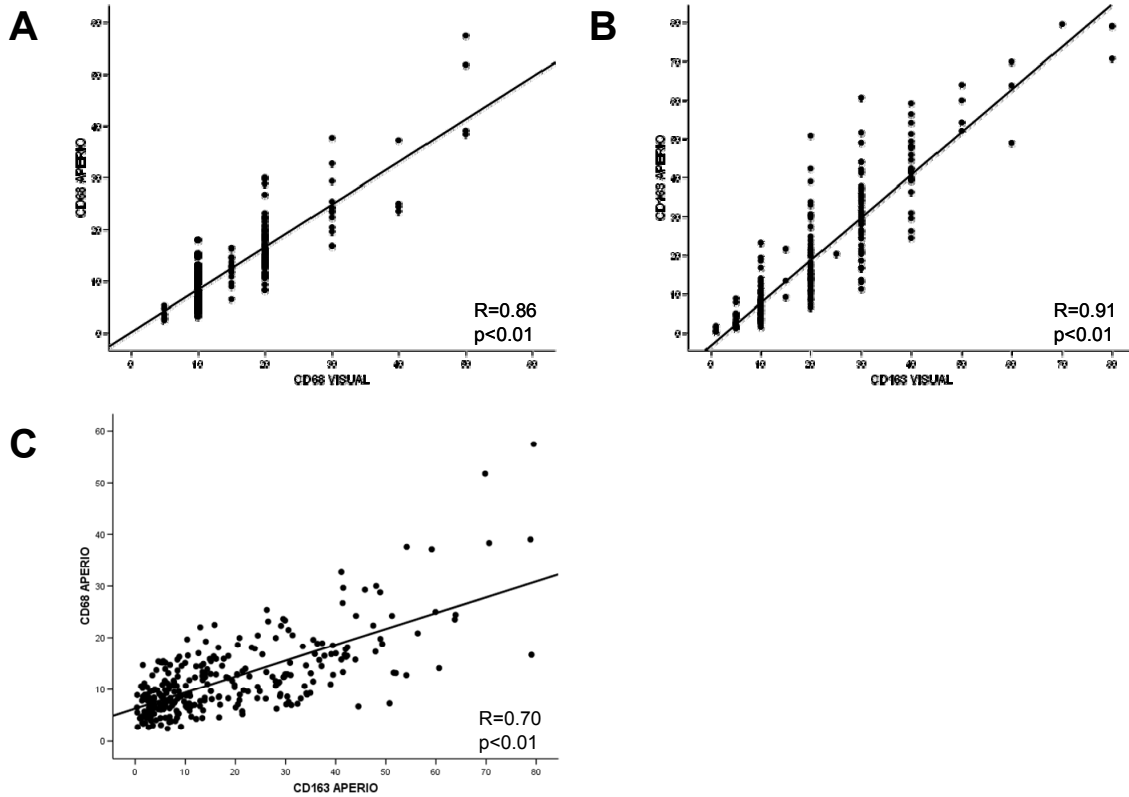
<b>CD163</b>	CD68 <sup>high</sup>	34	69	75	32	
	CD163 <sup>low</sup>	20	41	148	62	<i>&lt;0.01</i>
	CD163 <sup>high</sup>	29	59	90	38	

*p* values are for comparing between EBER-positive and negative cases.

\*Pearson chi-squared test was performed with unknown or unclassified cases excluded.

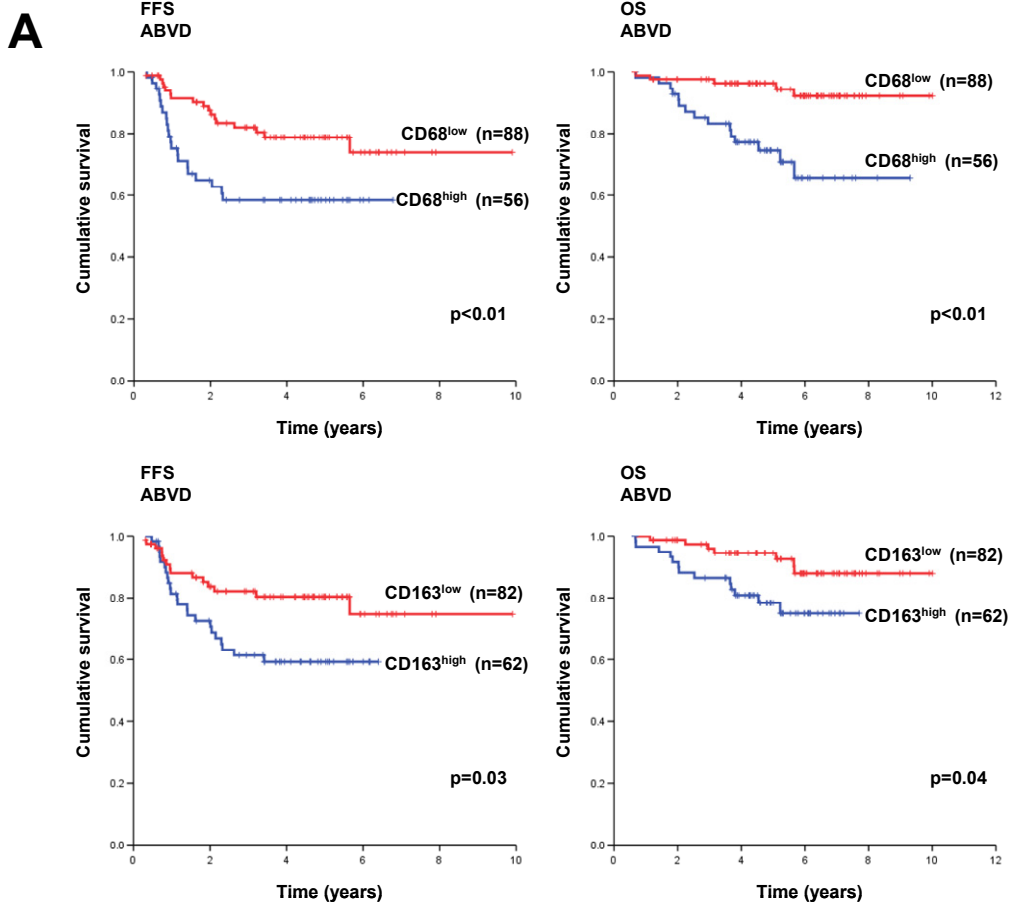
**Supplemental Figure 1. Correlation between Aperio and visual scores for CD68 and CD163 IHC expression.**

a) CD68 Aperio vs. visual scores, b) CD163 Aperio vs. visual scores, c) CD68 vs. CD163 Aperio scores.

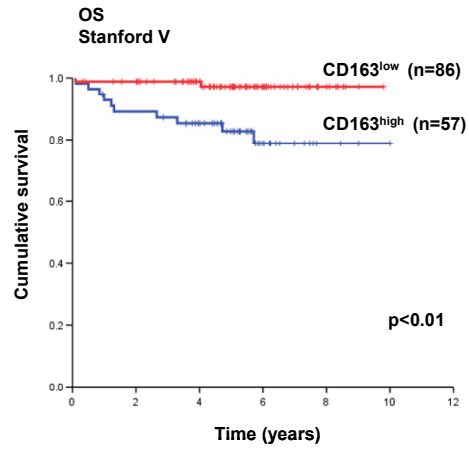
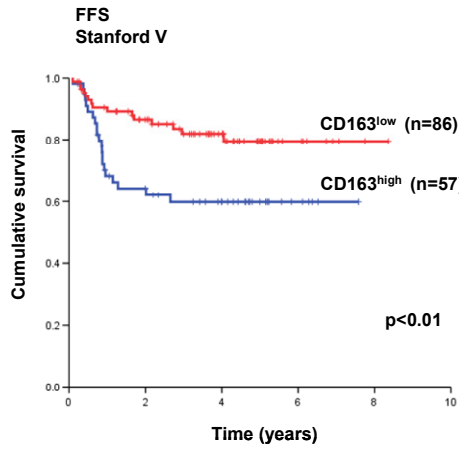
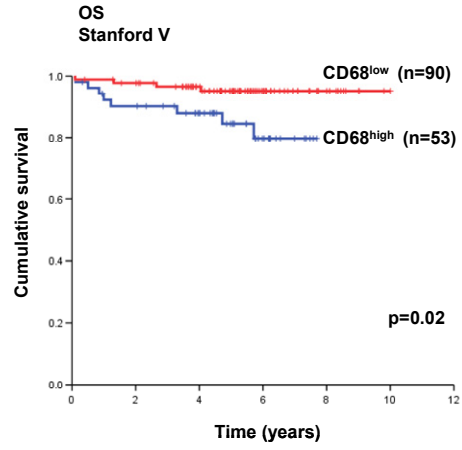
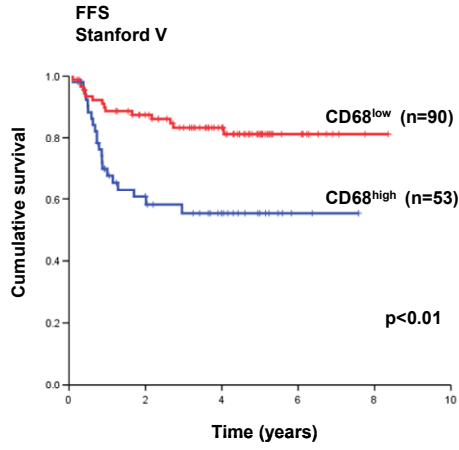


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Supplemental Figure 2. CD68 and CD163 expression and survival in A) patients treated with ABVD, and B) patients treated with Stanford V chemotherapy.



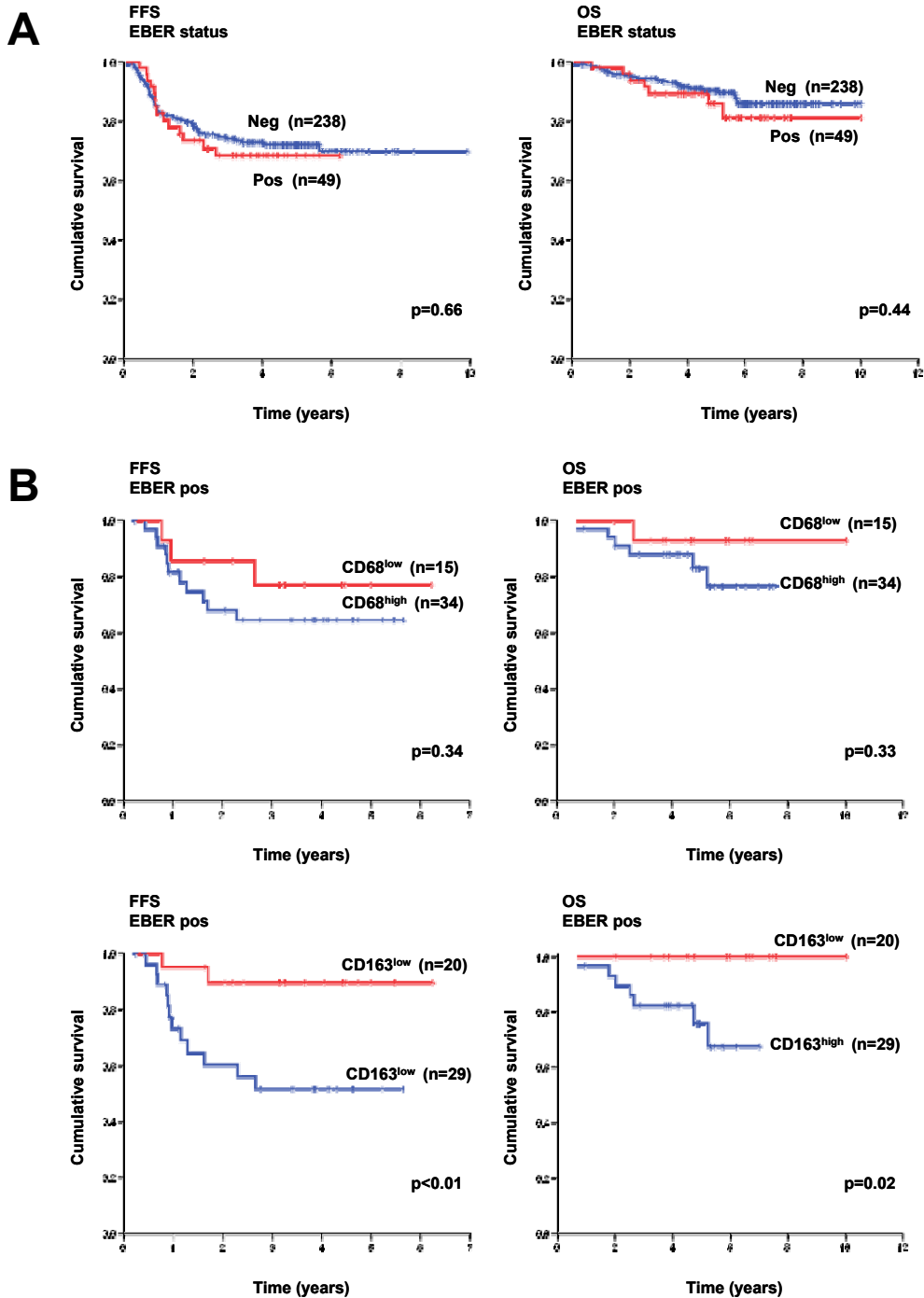
**B**



Supplemental Figure 3. EBER status and survival.

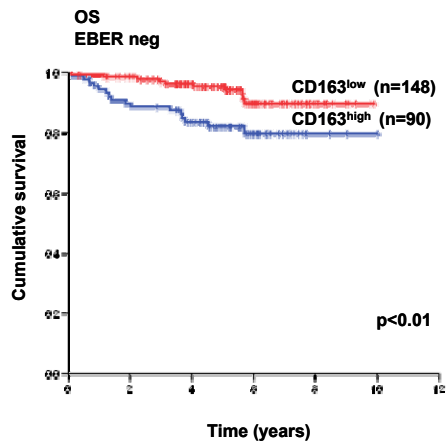
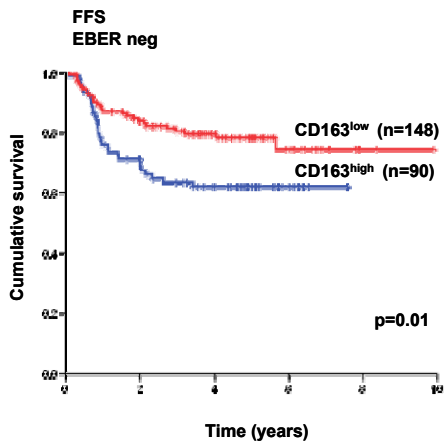
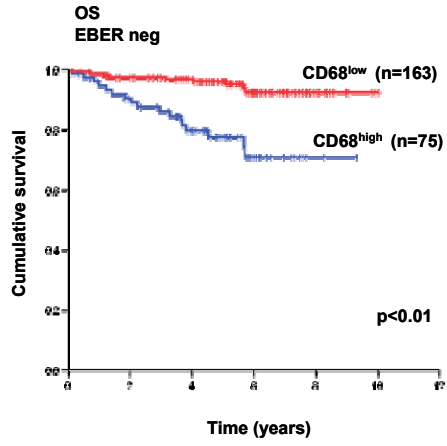
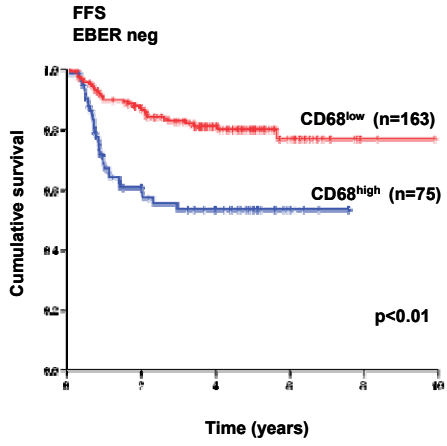
A) EBER status and survival. CD68 and CD163 IHC expression and survival

in B) EBER-positive cases, and C) EBER-negative cases.





**C**



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