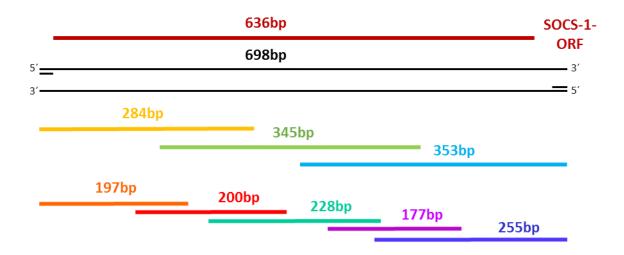
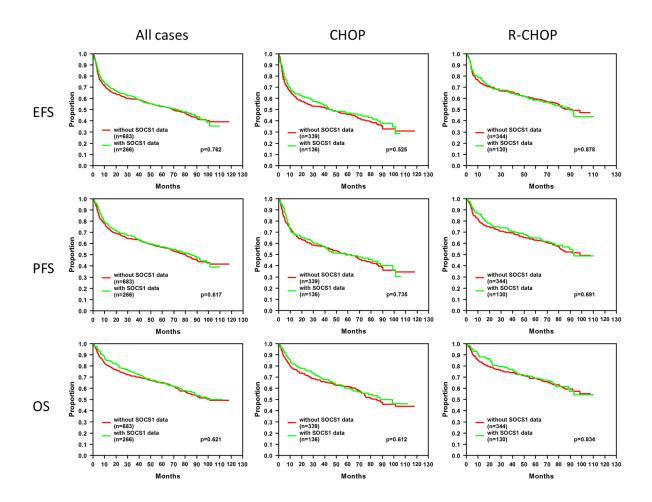
## **Supplementary Data**



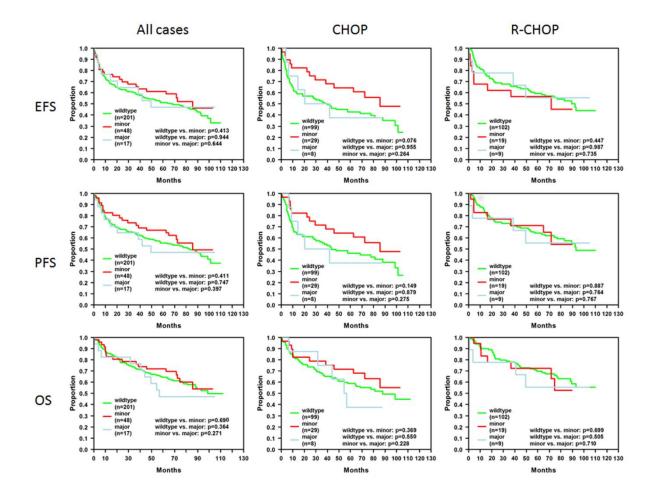
**Supplementary Figure 1:** Schematic position and length of amplicons used to cover the *SOCS1* open reading frame.



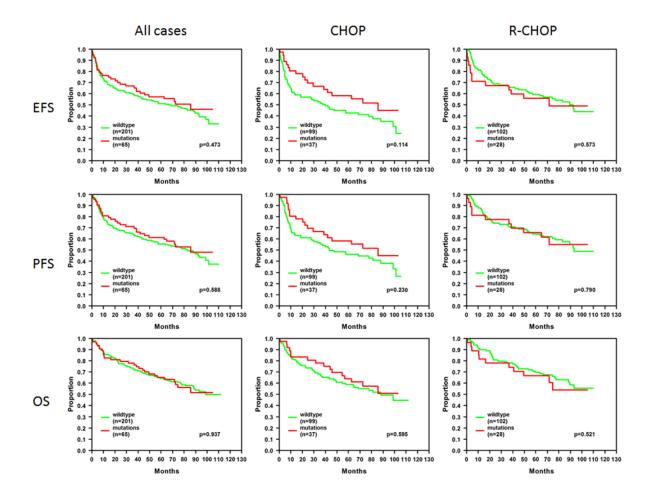
Supplementary Figure 2: The subgroup examined represents the whole RICOVER-60 cohort. The survival time analyses of the patients of the RICOVER-60 trial are shown with (green) or without (red) SOCS1 mutation data with respect to all cases (A) or the patients' treatment (B: CHOP-treated; C: R-CHOP-treated). The analyses were conducted for event-free survival (EFS), progression-free survival (PFS), and overall survival (OS). The corresponding numbers of patients (n) and results of statistical testing for differences (p) are shown. No significant differences were detected.



**Supplementary Figure 3:** Comparison of positional accumulation of variants across *SOCS1* using publicly available databases across different cancer types. A. cBioportal, B. COSMIC.



Supplementary Figure 4: Survival curves of DLBCL patients related to SOCS1 mutation subtypes. The survival time analyses of the patients of the RICOVER 60 trial are shown with wildtype (green), minor mutated (red), or major mutated (light blue) SOCS1 with respect to all cases (A) or patient treatments (B: CHOP-treated; C: R-CHOP-treated). The analyses were conducted for event-free survival (EFS), progression-free survival (PFS), and overall survival (OS). The corresponding numbers of patients (n) and results of statistical testing for differences (p) are shown. No significant differences were detected.



Supplementary Figure 5: Survival of DLBCL patients related to overall SOCS1 mutations. The survival time analyses of the patients of the RICOVER 60 trial are shown with wildtype (green) or mutated (red) SOCS-1 with respect to all cases (A) or patient treatments (B: CHOP-treated; C: R-CHOP-treated). The analyses were calculated for event-free survival (EFS), progression-free survival (PFS), and overall survival (OS). The corresponding numbers of patients (n) and results of statistical testing for differences (p) are shown. No significant differences were detected

**Supplementary Table 1:** Primer sequences of PCR primers used to cover the *SOCS1* open reading frame. Either 3 longer (L) or 5 shorter amplicons (S) were used. Primers were named as follows: numbers indicate the amplicon counted from 3' to 5'. L or S indicates a long or a short amplicon. f= forward primer, r= reverse revers primer.

Primer	Sequence 5'-3'
1Lf = 1Sf	GGCTGGCCCCTTCTGTAG
1Lr = 2Sr	CCCCGTGCACGCTCA
2Lf = 3Sf	GCACTTCCGCACATTCCGTT
2Lr = 4Sr	TGGCGCAGCGGGGCCCCCAGCAT
3Lf = 4Sf	GAACTGCTTTTTCGCCCTTA
3Lr = 5Sr	ACGGCATCCCAGTTAATGCT
1Sr	AACGGAATGTGCGGAAGTGC
2Sf	TTCCTCCTCTTCCTCCT
3Sr	GAAGAGGCAGTCGAAGCTCT
5Sf	AGAGCTTCGACTGCCTCTTC

## Supplementary Table 2: A: Summary of patient characteristics,

immunohistochemistry and fluorescence in situ hybridization data. Grouping of the patients with respect to the *SOCS1* mutation status, three different classifiers and the treatment with or without rituximab. No significant differences were found. B: Immunohistochemical detection of characteristic markers in DLBCL and FISH analyses. Patients were grouped into patients with neutral and patients with pathogenic *SOCS1* mutations. Grouping of the patients with respect to the *SOCS1* mutation status, three different classifiers and the treatment with or without rituximab. Significant differences were detected in the expressions of HLADR independently from the specific *SOCS1* mutation classifier. No further differences could be detected.

A		patients with DLBCL with SOCS1 data	wildtype	minor mutations	major mutation s	p-value	wildtype	mutations	p-value	putative normal	putative defect	p-value
		(n=266)	(n=201)	(n=48)	(n=17)		(n=201)	(n=65)		(n=228)	(n=38)	
	Gender: male	143 (54%)	103 (51%)	28 (58%)	12 (71%)	0.240	103 (51%)	40 (62%)	0.148	119 (52%)	24 (63%)	0.209
	female	123 (46%)	98 (49%)	20 (42%)	5 (29%)		98 (49%)	25 (39%)		109 (48%)	14 (37%)	
	Age: median (range)	68	69	68	67	0.455	69	67	0.342	69	67	0.233
		(61, 80)	(61, 80)	(61, 77)	(62, 75)		(61, 80)	(61, 77)		(61, 80)	(61, 77)	
	IP I factors:	255 (4200)	204 (4000)	40 (4000)	47 (4 000)		204 (4000)	CE (40.00()		220 (4000)	20 (4 0 00)	
	age>60	266 (100%)	201 (100%)	48 (100%)	17 (100%)	- 0.754	201 (100%)	65 (100%)	- 0.700	228 (100%)	38 (100%)	- 0.242
	LDH>UNV	110 (41%)	84 (42%)	18 (38%)	8 (47%)	0.764	84 (42%) 21 (10%)	26 (40%)	0.799	91 (40%)	19 (50%)	0.242
	ECOG>1	29 (11%)	21 (10%)	5 (10%)	3 (18%)	0.631	()	8 (12%)	0.676	24 (11%)	5 (13%)	0.581
	stage III/IV extranodal disease>1	115 (43%)	85 (42%)	19 (40%)	11 (65%)	0.171	85 (42%)	30 (46%)		97 (43%)	18 (47%)	0.578
	IP1:	40 (15%)	31 (15%)	4 (8%)	5 (29%)	0.111	31 (15%)	9 (14%)	0.757	33 (15%)	7 (18%)	0.529
	IPI.	104 (39%)	78 (39%)	20 (42%)	6 (35%)		78 (39%)	26 (40%)		91 (40%)	13 (34%)	
	1			15 (31%)								
	2	66 (25%) 66 (25%)	49 (24%) 54 (27%)	8 (17%)	2 (12%) 4 (24%)	0.222	49 (24%) 54 (27%)	17 (26%) 12 (19%)	0.429	55 (24%) 60 (26%)	11 (29%) 6 (16%)	0.133
	4.5	30 (11%)	20 (10%)	5 (10%)	5 (29%)		20 (10%)	10 (15%)		22 (10%)	8 (21%)	
	Bulky disease	86 (32%)	61 (30%)	20 (42%)	5 (29%)	0.310	61 (30%)	25 (39%)	0.224	70 (31%)	16 (42%)	0.164
	B-symptoms	75 (28%)	57 (28%)	13 (27%)	5 (29%)	1.000	57 (28%)	18 (28%)	0.224	66 (29%)	9 (24%)	0.104
	E-involvement	136 (51%)	99 (49%)	25 (52%)	12 (71%)	0.237	99 (49%)	37 (57%)	0.282	111 (49%)	25 (66%)	0.051
	Bone marrow involvement	8 (3%)	8 (4%)	0 (0%)	0 (0%)	0.501	8 (496)	0 (0%)	0.206	8 (4%)	0 (0%)	0.606
	Centroblastic	177 (67%)	137 (68%)	30 (63%)	10 (59%)	0.301	137 (68%)	40 (62%)	0.200	150 (66%)	27 (71%)	0.000
	Immunoblastic	19 (7%)	16 (8%)	2 (4%)	1 (6%)		16 (8%)	3 (5%)		18 (8%)	1 (3%)	
	P lasmoblastic	1 (0.4%)	1 (1%)	0 (0%)	0 (0%)		1 (1%)	0 (0%)		1 (0%)	0 (0%)	
	Anaplastic large cell (ALC)	4 (2%)	2 (1%)	2 (4%)	0 (0%)		2 (1%)	2 (3%)		4 (2%)	0 (0%)	
	T-cell-rich B-Cell-Lymphom	4 (2%) 7 (3%)	4 (2%)	2 (4%)	1 (6%)		4 (2%)	3 (5%)		5 (2%)	2 (5%)	
	NOS	7 (3%) 54 (20%)	39 (19%)	12 (25%)	3 (18%)		39 (19%)	15 (23%)		48 (21%)	6 (16%)	
	Prim. mediast. B-cell lymphoma	4 (2%)	2(1%)	0 (0%)	2 (12%)		2 (1%)	2 (3%)		2 (1%)	2 (5%)	
	FTIIII. IIIEdiasi. b-ceii iyilipiloilia	4(2/0)	2(1/0)	0 (0/0)	2 (12/0)		2 (1/0)	2 (3/8)		2 (1/6)	2 (3/0)	
		(n=136)	(n=99)	(n=29)	(n=8)		(n=99)	(n=37)		(n=115)	(n=21)	
СНОР	Gender: male	73 (54%)	51 (52%)	18 (62%)	4 (50%)	0.621	51 (52%)	22 (60%)	0.408	61 (53%)	12 (57%)	0.729
	female	63 (46%)	48 (49%)	11 (38%)	4 (50%)		48 (49%)	15 (41%)		54 (47%)	9 (43%)	
	Age: median (range)		69 (61, 79)	68 (61, 77)	64 (62, 75)	0.365	69 (61, 79)	68 (61, 77)	0.259	69 (61, 79)	66 (61, 76)	0.070
	IP I factors:									. , ,		
	age>60	136 (100%)	99 (100%)	29 (100%)	8 (100%)	-	99 (100%)	37 (100%)	-	115 (100%)	21 (100%)	-
	LDH>UNV	53 (39%)	39 (39%)	11 (38%)	3 (38%)	1.000	39 (39%)	14 (38%)	0.868	44 (38%)	9 (43%)	0.691
	ECOG>1	17 (12%)	12 (12%)	4 (14%)	1 (13%)	0.902	12 (12%)	5 (14%)	0.779	15 (13%)	2 (10%)	1.000
	stage III/IV	58 (43%)	42 (42%)	10 (35%)	6 (75%)	0.125	42 (42%)	16 (43%)	0.932	48 (42%)	10 (48%)	0.616
	extranodal disease>1	19 (14%)	16 (16%)	1 (3%)	2 (25%)	0.109	16 (16%)	3 (8%)	0.228	16 (14%)	3 (14%)	1.000
	IPI:	54 (40%)	38 (38%)	14 (48%)	2 (25%)		38 (38%)	16 (43%)		46 (40%)	8 (38%)	
	1	36 (26%)	26 (26%)	8 (28%)	2 (25%)		26 (26%)	10 (45%)		30 (26%)	6 (29%)	
	2	30 (22%)	25 (25%)	3 (10%)	2 (25%)	0.473	25 (25%)	5 (14%)	0.423	27 (24%)	3 (14%)	0.590
	4,5	16 (12%)	10 (10%)	4 (14%)	2 (25%)		10 (10%)	6 (16%)		12 (10%)	4 (19%)	
	Bulky disease	40 (29%)	27 (27%)	12 (41%)	1 (13%)	0.217	27 (27%)	13 (35%)	0.371	33 (29%)	7 (33%)	0.668
	B-symptoms	39 (29%)	28 (28%)	9 (31%)	2 (25%)	0.943	28 (28%)	11 (30%)	0.868	34 (30%)	5 (24%)	0.592
	E-involvement	72 (53%)	51 (52%)	15 (52%)	6 (75%)	0.487	51 (52%)	21 (57%)	0.586	59 (51%)	13 (62%)	0.371
	Bone marrow involvement	3 (2%)	3 (3%)	0 (0%)	0 (0%)	1.000	3 (3%)	0 (0%)	0.562	3 (3%)	0 (0%)	1.000
	Centroblastic	92 (68%)	69 (70%)	18 (62%)	5 (63%)	2.000	69 (70%)	23 (62%)	0.502	77 (67%)	15 (71%)	2.000
	Immunoblastic	10 (7%)	8 (8%)	2 (7%)	0 (0%)		8 (8%)	2 (5%)		10 (9%)	0 (0%)	
	P lasmoblastic	0 (0%)	0 (0%)	0 (0%)	0 (0%)		0 (0%)	0 (0%)		0 (0%)	0 (0%)	
	Anaplastic large cell (ALC)	0 (0%)	0 (0%)	0 (0%)	0 (0%)		0 (0%)	0 (0%)		0 (0%)	0 (0%)	
	T-cell-rich B-Cell-Lymphom	5 (4%)	2 (2%)	2 (7%)	1(13%)		2 (2%)	3 (8%)		3 (3%)	2 (10%)	
	NOS	26 (19%)	18 (18%)	7 (24%)	1(13%)		18 (18%)	8 (22%)		23 (20%)	3 (14%)	
	Prim. mediast. B-cell lymphoma	3 (2%)	2 (2%)	0 (0%)	1(13%)		2 (2%)	1 (3%)		2 (2%)	1 (5%)	
	FTIIII. HIEdiasi. b-ceii iyilipiloilia	3 (2/0)	2 (2/0)	0 (0/0)	1 (13/0)		2 (2/0)	1 (3/0)		2 (2/6)	1 (3/0)	
		(n=130)	(n=102)	(n=19)	(n=9)		(n=102)	(n=28)		(n=113)	(n=17)	
R-CHOP	Gender: male	70 (54%)	52 (51%)	10 (53%)	8 (89%)	0.084	52 (51%)	18 (64%)	0.211	58 (51%)	12 (71%)	0.137
	female	60 (46%)	50 (49%)	9 (47%)	1 (11%)		50 (49%)	10 (36%)		55 (49%)	5 (29%)	
	Age: median (range)		68	67	67	0.953	68	67	0.854	68	67	0.830
			(61, 80)	(62, 77)	(62, 74)		(61, 80)	(62, 77)		(61, 80)	(62, 77)	
	IP I factors:											
	age>60	130 (100%)	102 (100%)		9 (100%)	-	102 (100%)	28 (100%)	-	113 (100%)	17 (100%)	-
	LDH>UNV	57 (44%)	45 (44%)	7 (37%)	5 (56%)	0.651	45 (44%)	12 (43%)	0.905	47 (42%)	10 (59%)	0.182
	ECOG>1	12 (9%)	9 (9%)	1 (5%)	2 (22%)	0.308	9 (9%)	3 (11%)	0.721	9 (8%)	3 (18%)	0.193
	stage III/IV	57 (44%)	43 (42%)	9 (47%)	5 (56%)	0.725	43 (42%)	14 (50%)	0.459	49 (43%)	8 (47%)	0.775
	extranodal disease>1 IPI:	21 (16%)	15 (15%)	3 (16%)	3 (33%)	0.303	15 (15%)	6 (21%)	0.394	17 (15%)	4 (24%)	0.477
	1	50 (38%)	40 (39%)	6 (32%)	4 (44%)		40 (39%)	10 (36%)		45 (40%)	5 (29%)	
	2	30 (23%)	23 (23%)	7 (37%)	0 (0%)	0.215	23 (23%)	7 (25%)	0.847	25 (22%)	5 (29%)	0.217
	3	36 (28%)	29 (28%)	5 (26%)	2 (22%)	0.215	29 (28%)	7 (25%)	0.64/	33 (29%)	3 (18%)	0.217
	4, 5	14 (11%)	10 (10%)	1 (5%)	3 (33%)		10 (10%)	4 (14%)		10 (9%)	4 (24%)	
	Bulky disease	46 (35%)	34 (33%)	8 (42%)	4 (44%)	0.592	34 (33%)	12 (43%)	0.351	37 (33%)	9 (53%)	0.104
	B-symptoms	36 (28%)	29 (28%)	4 (21%)	3 (33%)	0.717	29 (28%)	7 (25%)	0.719	32 (28%)	4 (24%)	0.779
	E-involvement	64 (49%)	48 (47%)	10 (53%)	6 (67%)	0.558	48 (47%)	16 (57%)	0.344	52 (46%)	12 (71%)	0.059
	Bone marrow involvement	5 (4%)	5 (5%)	0 (0%)	0 (0%)	1.000	5 (5%)	0 (0%)	0.584	5 (4%)	0 (0%)	1.000
	Centroblastic	85 (65%)	68 (67%)	12 (63%)	5 (56%)		68 (67%)	17 (61%)		73 (65%)	12 (71%)	
	Immunoblastic	9 (7%)	8 (8%)	0 (0%)	1 (11%)		8 (8%)	1 (4%)		8 (7%)	1 (6%)	
	P lasmoblastic	1 (1%)	1 (1%)	0 (0%)	0 (0%)		1 (1%)	0 (0%)		1 (1%)	0 (0%)	
	Anaplastic large cell (ALC)	4 (3%)	2 (2%)	2 (11%)	0 (0%)		2 (2%)	2 (7%)		4 (4%)	0 (0%)	
	T-cell-rich B-Cell-Lymphom	2 (2%)	2 (2%)	0 (0%)	0 (0%)		2 (2%)	0 (0%)		2 (2%)	0 (0%)	
	NOS	28 (22%)	21 (21%)	5 (26%)	2 (22%)		21 (21%)	7 (25%)		25 (22%)	3 (18%)	
		20 (22/0)	0 (0%)	0 (0%)	1(11%)		0 (0%)	1 (4%)		0 (0%)	3 (20/0)	

D	wildtype	minor	major	p-value	wildtype	mutations	p-value	putative neutral	putative defect	p-value
D	(n=163)	(n=37)	(n=14)		(n=163)	(n=51)		(n=184)	(n=30)	
Morphology:										
Immunoblastic	15 (12%)	1 (4%)	0 (0%)	0.508	15 (12%)	1(3%)	0.196	16 (12%)	0 (0%)	0.131
Centroblastic	113 (88%)	24 (96%)	9 (100%)		113 (88%)	33 (97%)		123 (89%)	23 (100%)	
IHC:										
BCL2 (51-100%)	102/152 (67%)	23/34 (68%)	7/14 (50%)	0.445	102/152 (67%)	30/48 (63%)	0.557	114/173 (66%)	18/27 (67%)	0.937
BCL6 (26-100%)	109/138 (79%)	28/33 (85%)	13/13 (100%	0.153	109/138 (79%)	41/46 (89%)	0.125	124/156 (80%)	26/28 (93%)	0.093
MYC (41-100%)	32/123 (26%)	10/29 (35%)	3/10 (30%)	0.629	32/123 (26%)	13/39 (33%)	0.374	35/139 (25%)	10/23 (44%)	0.070
CD5 (1-100%)	10/145 (7%)	2/34 (6%)	1/14 (7%)	1.000	10/145 (7%)	3/48 (6%)	1.000	11/166 (7%)	2/27 (7%)	1.000
CD10 (1-100%)	51/149 (34%)	11/34 (32%)	3/14 (21%)	0.693	51/149 (34%)	14/48 (29%)		55/169 (33%)	10/28 (36%)	0.741
HLADR (1-100%)	135/151 (89%)			0.015	135/151 (89%)	34/47 (72%)	0.004	150/171 (88%)	19/27 (70%)	0.035
MUM1 (5-100%)	123/146 (84%)	29/34 (85%)	10/12 (83%)	1.000	123/146 (84%)	39/46 (85%)	0.930	141/167 (84%)	21/25 (84%)	1.000
Ki 67 (76-100%)	101/142 (71%)				101/142 (71%)			117/163 (72%)	15/25 (60%)	0.230
MYC+/BCL2+	24/106 (23%)				24/106 (23%)			26/119 (22%)	8/20 (40%)	0.095
FISH:										
BCL2 positive	18/149 (12%)	7/33 (21%)	2/12 (17%)	0.276	18/149 (12%)	9/45 (20%)	0.179	21/169 (12%)	6/25 (24%)	0.127
BCL6 positive	52/152 (34%)	9/34 (27%)	4/12 (33%)	0.700	52/152 (34%)	13/46 (28%)	0.452	57/172 (33%)	8/26 (31%)	0.810
MYC positive	12/150 (8%)	2/34 (6%)	1/13 (8%)	1.000	12/150 (8%)	3/47 (6%)	1.000	13/171 (8%)	2/26 (8%)	1.000
IGH positive	37/90 (41%)	6/12 (50%)	2/8 (25%)	0.606	37/90 (41%)	8/20 (40%)	0.927	41/97 (42%)	4/13 (31%)	0.428
MYC+/BCL2+	2/116 (2%)	2/23 (9%)	0/8 (0%)	0.196	2/116 (2%)	2/31 (7%)	0.196	3/130 (2%)	1/17 (6%)	0.392
MYC+/BCL6+	1/115 (1%)	0/25 (0%)	0/8 (0%)	1.000	1/115 (1%)	0/33(0%)	1.000	1/129 (1%)	0/19 (0%)	1.000
BCL2+/BCL6+	4/115 (4%)	1/24 (4%)	0/7 (0%)	1.000	4/115 (4%)	1/31 (3%)	1.000	4/128 (3%)	1/18 (6%)	0.487
MYC+/BCL2+/BCL6+	0/110 (0%)	0/22 (0%)	0/7 (0%)	-	0/110 (0%)	0/29 (0%)	-	0/123 (0%)	0/16 (0%)	-
Hans dassifier: ABC	70/426 (F7n/)	47/22 (F2n/)	7/44 (C40/)	0.024	30/406 (F3n/)	24/42 (500)	0.050	00 (454 (500))	42/25/400/\	0.220
	78/136 (57%)	17/32 (53%)		0.824	78/136 (57%)	24/43 (56%)		90/154 (58%)	12/25 (48%)	0.328
GCB	58/136 (43%)	15/32 (47%)	4/11 (36%)		58/136 (43%)	19/43 (44%)		64/154 (42%)	13/25 (52%)	
Lymph 2Cx***:	C# (4.40 (40×1)	4.4/0.4/44.4/	= (40 (=00))	0.000	C= (4.40 (4.00()	40 (44 (40=4)	0 =04	=4 (4 = 0 ( 4 = e/)	40/05/00=/)	
ABC	65/140 (46%)	14/34 (41%)			65/140 (46%)	19/44 (43%)		74/158 (47%)	10/26 (39%)	0.527
GCB	59/140 (42%)	15/34 (44%)		(global)	59/140 (42%)	18/44 (41%)		66/158 (42%)	11/26 (42%)	(global)
intermediate/unclassified	16/140 (11%)	5/34 (15%)	2/10 (20%)		16/140 (11%)	7/44 (16%)		18/158 (11%)	5/26 (19%)	0.654
				(ABC vs. GCB)			(ABC vs. GCB)			(ABC vs. GCB)
IHC-score**:	(440 (50-1)		0/40/00-1		/ / / / -	00/0=/00-/1		24/422/424/	101001==()	
0, 1	75/119 (63%)	14/27 (52%)		0.287	75/119 (63%)	22/37 (60%)		84/133 (63%)	13/23 (57%)	0.545
2, 3	44/119 (37%)	13/27 (48%)	2/10 (20%)		44/119 (37%)	15/37 (41%)		49/133 (37%)	10/23 (44%)	
FISH/IHC-score**:			- 4- 4							
0, 1	68/113 (60%)	12/24 (50%)		0.130	68/113 (60%)	20/33 (61%)		76/127 (60%)	12/19 (63%)	0.783
2, 3, 4	45/113 (40%)	12/24 (50%)	1/9 (11%)		45/113 (40%)	13/33 (39%)		51/127 (40%)	7/19 (37%)	
P53 (26-100%)										
P53 mutated	26/146 (18%)	5/36 (14%)	0/12 (0%)		26/146 (18%)	5/48 (10%)		27/166 (16%)	4/28 (14%)	1.000
	28/109 (26%)	5/18 (28%)	2/8 (25%)	1.000	28/109 (26%)	7/26 (27%)	0.897	30/120 (25%)	5/15 (33%)	0.535

<sup>\*</sup> sample according to Horn et al. Blood 2013 with SOCS1 data

\*\* Horn et al. Blood 2013

\*\*\* sample according to Staiger et al. JCO 2017 submitted/review with SOCS1 data