

**Dossier zur Nutzenbewertung
gemäß § 35a SGB V**

Tisagenlecleucel (Kymriah®)

Novartis Pharma GmbH

Modul 4 A – Separater Anhang 4-H.4

*Refraktäre oder rezidierte
pädiatrische akute lymphatische
B-Zell-Leukämie*

*Quantitativer adjustierter Vergleich von
Tisagenlecleucel mit patientenindividuellen
Versorgungsdaten aus drei Patientenregistern -
Subgruppenanalysen*

Stand: 31.08.2023

1. Full Analysis Set

1.1 Eliana VS. External Control

1.1.1 Overall Remission Rate

Table 1: Eliana VS. External Control: Overall Remission Rate

Subgroup	Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC						
	N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction	
Age	<10 years	32	26 (81,2%)	95	41 (42,9%)	1,89 (1,42 ; 2,52)	5,77 (2,17 ; 15,31)	0,38 (0,22 ; 0,55)	0,0002	0,0002	0,9704
	>= 18 years	14	11 (78,6%)	64	28 (43,5%)	1,82 (1,23 ; 2,69)	4,83 (1,23 ; 19,00)	0,35 (0,11 ; 0,60)	0,0198	0,0198	
	10-18 years	33	29 (87,9%)	101	58 (57,6%)	1,53 (1,24 ; 1,88)	5,33 (1,74 ; 16,30)	0,30 (0,16 ; 0,45)	0,0014	0,0019	
Baseline extramedullary disease presence	No or NA	69	56 (81,2%)	235	111 (47,4%)	1,72 (1,44 ; 2,05)	4,81 (2,50 ; 9,27)	0,34 (0,23 ; 0,45)	0,0000	0,0000	0,1730
	Yes	10	10 (100,0%)	25	16 (62,1%)	1,61 (1,19 ; 2,18)	NaN (NaN ; NaN)	0,38 (0,19 ; 0,57)	0,0345	0,0279	
	NA			75	41 (54,9%)						
Down Syndrom	No	73	61 (83,6%)	180	82 (45,5%)	1,84 (1,52 ; 2,22)	6,10 (3,07 ; 12,09)	0,38 (0,27 ; 0,49)	0,0000	0,0000	0,4646
	Yes	6	5 (83,3%)	5	4 (75,8%)	1,10 (0,60 ; 2,03)	1,60 (0,08 ; 30,98)	0,08 (-0,40 ; 0,55)	1,0000	0,7890	
Gender	Female	34	29 (85,3%)	93	41 (44,5%)	1,92 (1,47 ; 2,50)	7,24 (2,57 ; 20,35)	0,41 (0,25 ; 0,56)	0,0000	0,0001	0,7336

Subgroup	Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC						
	N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction	
Male	45	37 (82,2%)	168	86 (51,2%)	1,61 (1,32 ; 1,97)	4,45 (1,96 ; 10,12)	0,31 (0,18 ; 0,45)	0,0002	0,0009		
Morphologic blast count in bone marrow	high	53	41 (77,4%)	74	45 (60,2%)	1,28 (1,02 ; 1,63)	2,26 (1,02 ; 4,99)	0,17 (0,01 ; 0,33)	0,0555	0,0492	0,0542
	low	26	25 (96,2%)	75	51 (68,7%)	1,40 (1,18 ; 1,66)	11,38 (1,45 ; 89,05)	0,27 (0,15 ; 0,40)	0,0062	0,0083	
	NA			111	31 (27,8%)						
	>=3			66	16 (23,7%)						
Number of previous relapses	0			13	8 (61,9%)						
	1			40	20 (50,8%)						
	2			142	83 (58,7%)						
	NA	79	66 (83,5%)			NA (NA ; NA)	NA (NA ; NA)	NA (NA ; NA)	NA	NA	NA
Previous HSCT	No	31	24 (77,4%)	110	78 (70,3%)	1,11 (0,88 ; 1,39)	1,47 (0,58 ; 3,75)	0,07 (-0,10 ; 0,24)	0,5043	0,4790	0,0011
	Yes	48	42 (87,5%)	150	49 (32,9%)	2,66 (2,07 ; 3,42)	14,27 (5,68 ; 35,83)	0,55 (0,43 ; 0,67)	0,0000	0,0000	
Region	European Union (EU)	27	25 (92,6%)	259	127 (49,0%)	1,89 (1,61 ; 2,23)	13,04 (3,03 ; 56,21)	0,44 (0,32 ; 0,55)	0,0000	0,0028	0,4770
	Rest-of-the-World (ROW)	7	5 (71,4%)			NA (NA ; NA)	NA (NA ; NA)	NA (NA ; NA)	NA	NA	NA
	United States (US)	45	36 (80,0%)	1	0 (0,0%)	3,79 (0,32 ; 44,83)	14,53 (0,59 ; 355,60)	0,58 (0,06 ; 1,11)	0,0585	0,1324	

Subgroup	Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC						
	N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction	
Status of disease	refractory to previous line of therapy	16	11 (68,8%)	58	28 (48,3%)	1,44 (0,94 ; 2,20)	2,40 (0,74 ; 7,77)	0,21 (-0,05 ; 0,47)	0,1642	0,1579	0,0973
	relapsed after previous line of therapy	63	55 (87,3%)	202	99 (48,9%)	1,78 (1,51 ; 2,11)	7,18 (3,25 ; 15,83)	0,38 (0,28 ; 0,49)	0,0000	0,0000	

RR: Risk Ratio; OR: Hazard Ratio; RD: Hazard Ratio; CI: Confidence interval; N: Number of patients; NA: not available/not reached/not estimable; p-value: Fisher, Barnard; p-value interaction: LRT

1.1.2 Overall Survival

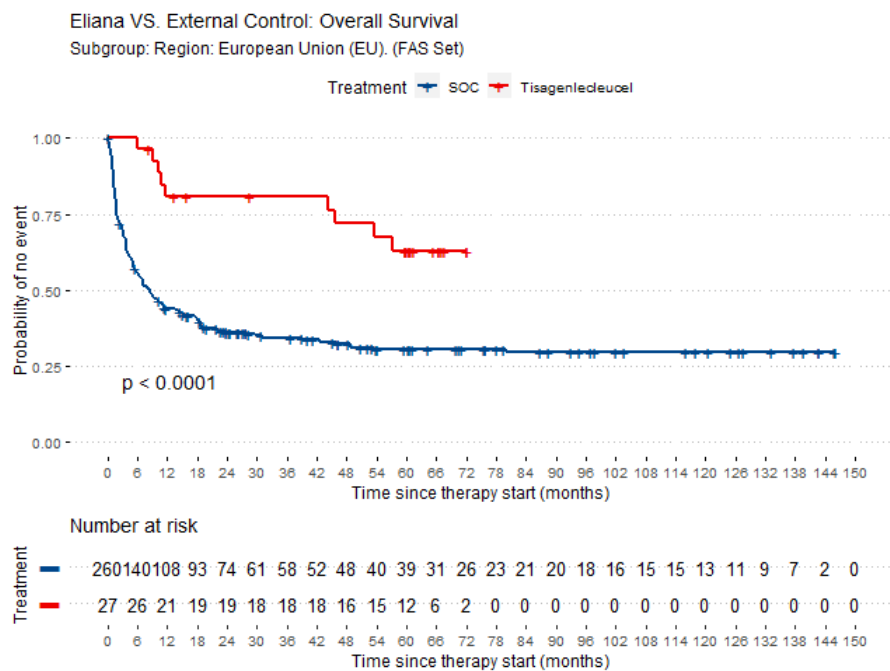
Table 2: Eliana VS. External Control: Overall Survival

Subgroup	Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC			
	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95%-KI)	p-value	p-value interaction	
Age	<10 years	32	17 (53,1%)	45,60 (17,94 ; NA)	95	69 (72,0%)	6,08 (3,88 ; 11,24)	0,44 (0,26 ; 0,75)	0,0022	0,5921
	>= 18 years	14	7 (50,0%)	57,36 (11,79 ; NA)	65	43 (65,9%)	12,45 (5,19 ; 23,72)	0,55 (0,26 ; 1,16)	0,1401	
	10-18 years	33	10 (30,3%)	NA (NA ; NA)	101	60 (58,8%)	11,04 (4,24 ; NA)	0,34 (0,17 ; 0,68)	0,0011	
Baseline extramedullary disease presence	No or NA	69	31 (44,9%)	NA (NA ; NA)	236	161 (68,3%)	7,26 (5,26 ; 12,45)	0,42 (0,29 ; 0,61)	0,0000	0,6846
	Yes	10	3 (30,0%)	NA (NA ; NA)	25	10 (37,9%)	NA (NA ; NA)	0,58 (0,14 ; 2,51)	0,4183	
Down Syndrom	NA				76	46 (60,1%)	NA (NA ; NA)			0,5764
	No	73	31 (42,5%)	NA (NA ; NA)	180	120 (66,6%)	6,93 (4,14 ; 18,79)	0,40 (0,26 ; 0,60)	0,0000	
	Yes	6	3 (50,0%)	32,20 (13,31 ; NA)	5	5 (100,0%)	1,94 (1,94 ; NA)	0,19 (0,04 ; 0,91)	0,0361	
Gender	Female	34	13 (38,2%)	NA (NA ; NA)	93	72 (77,3%)	6,31 (3,12 ; 13,63)	0,26 (0,14 ; 0,47)	0,0000	0,0570
	Male	45	21 (46,7%)	NA (NA ; NA)	168	99 (58,8%)	11,24 (5,42 ; 80,07)	0,56 (0,35 ; 0,88)	0,0138	
	high	53	28 (52,8%)	44,29 (16,62 ; NA)	74	48 (64,3%)	7,23 (3,94 ; 80,07)	0,56 (0,33 ; 0,94)	0,0136	0,1884

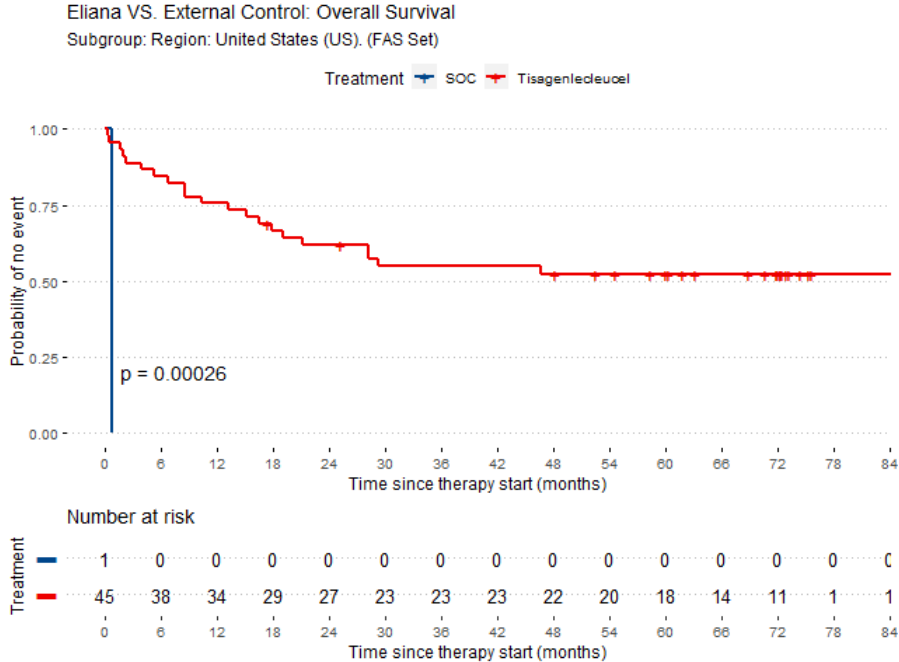
Subgroup	Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC		
	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95%-KI)	p-value	p-value interaction
Morphologic blast count in bone marrow	low	26	6 (23,1%)	75	42 (56,3%)	22,01 (14,59 ; NA)	0,27 (0,12 ; 0,65)	0,0016	
	NA			112	81 (72,2%)	NA (NA ; NA)			
	>=3			66	51 (76,9%)	NA (NA ; NA)			
Number of previous relapses	0			13	7 (54,4%)	NA (NA ; NA)			
	1			40	27 (69,1%)	NA (NA ; NA)			
	2			142	85 (60,0%)	NA (NA ; NA)			
	NA	79	34 (43,0%)				NA (NA ; NA)	NA	NA
Previous HSCT	No	31	13 (41,9%)	111	60 (54,3%)	18,79 (11,33 ; NA)	0,65 (0,35 ; 1,21)	0,1524	0,0566
	Yes	48	21 (43,8%)	150	110 (73,6%)	4,99 (3,78 ; 8,28)	0,29 (0,18 ; 0,47)	0,0000	
Region	European Union (EU)	27	9 (33,3%)	260	169 (65,2%)	8,54 (5,39 ; 17,71)	0,31 (0,17 ; 0,57)	0,0003	0,0480
	Rest-of-the-World (ROW)	7	4 (57,1%)				NA (NA ; NA)	NA	NA
	United States (US)	45	21 (46,7%)	1	1 (100,0%)	0,76 (NA ; NA)	0,05 (0,01 ; 0,18)	0,0001	0,0480

Subgroup		Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC		
		N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95%-KI)	p-value	p-value interaction
Status of disease	refractory to previous line of therapy	16	7 (43,8%)	NA (NA ; NA)	59	40 (67,6%)	7,10 (4,14 ; 19,58)	0,49 (0,22 ; 1,11)	0,0779	0,7780
	relapsed after previous line of therapy	63	27 (42,9%)	NA (NA ; NA)	202	131 (64,7%)	8,51 (5,26 ; 18,79)	0,41 (0,27 ; 0,63)	0,0000	

HR: Hazard Ratio; CI: Confidence interval; N: Number of patients; NA: not available/not reached/not estimable; p-value: Scoretest; p-value interaction: LRT



1.1.2.1 Figure 1: Eliana VS. External Control: Overall Survival - Subgroup: Region: European Union (EU). (FAS Set)



1.1.2.2 Figure 2: Eliana VS. External Control: Overall Survival - Subgroup: Region: United States (US). (FAS Set)

1.2 Pooled Data VS. External Control

1.2.1 Overall Remission Rate

Table 3: Pooled Data VS. External Control: Overall Remission Rate

Subgroup	Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC						
	N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction	
Age	<10 years	80	62 (77,5%)	96	52 (54,6%)	1,42 (1,14 ; 1,76)	2,86 (1,48 ; 5,54)	0,23 (0,09 ; 0,36)	0,0024	0,0017	0,9506
	>= 18 years	39	29 (74,4%)	64	28 (44,1%)	1,74 (1,24 ; 2,42)	3,87 (1,62 ; 9,22)	0,32 (0,13 ; 0,50)	0,0022	0,0018	
	10-18 years	83	69 (83,1%)	111	65 (58,3%)	1,43 (1,19 ; 1,72)	3,53 (1,77 ; 7,01)	0,25 (0,13 ; 0,37)	0,0003	0,0002	
Baseline extramedullary disease presence	No or NA	181	140 (77,3%)	239	121 (50,6%)	1,54 (1,33 ; 1,79)	3,38 (2,20 ; 5,20)	0,27 (0,18 ; 0,36)	0,0000	0,0000	0,6735
	Yes	21	20 (95,2%)	33	25 (75,6%)	1,26 (1,01 ; 1,57)	6,47 (0,75 ; 56,20)	0,20 (0,02 ; 0,37)	0,0749	0,0999	
BCR-ABL	negative or NA	194	152 (78,4%)	263	140 (53,4%)	1,48 (1,29 ; 1,69)	3,21 (2,11 ; 4,87)	0,25 (0,17 ; 0,34)	0,0000	0,0000	0,0947
	positive	8	8 (100,0%)	9	5 (60,4%)	1,65 (0,96 ; 2,84)	NaN (NaN ; NaN)	0,40 (0,07 ; 0,72)	0,2000	0,0822	
Down Syndrom	NA			82	49 (59,8%)						
	No	188	148 (78,7%)	184	92 (50,3%)	1,57 (1,33 ; 1,84)	3,66 (2,33 ; 5,76)	0,28 (0,19 ; 0,38)	0,0000	0,0000	0,8488
	Yes	14	12 (85,7%)	5	4 (75,9%)	1,13 (0,65 ; 1,95)	1,90 (0,15 ; 24,71)	0,10 (-0,32 ; 0,52)	1,0000	0,8273	

Subgroup	Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC						
	N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction	
Gender	Female	92	69 (75,0%)	88	44 (50,4%)	1,50 (1,18 ; 1,90)	3,00 (1,60 ; 5,62)	0,25 (0,11 ; 0,39)	0,0007	0,0005	0,4599
	Male	110	91 (82,7%)	183	101 (55,2%)	1,51 (1,29 ; 1,76)	3,95 (2,23 ; 7,00)	0,28 (0,18 ; 0,38)	0,0000	0,0000	
MLL Rearrangement	No or NA	197	156 (79,2%)	262	139 (53,1%)	1,50 (1,31 ; 1,72)	3,42 (2,24 ; 5,20)	0,27 (0,18 ; 0,35)	0,0000	0,0000	0,7254
	Yes	5	4 (80,0%)	9	6 (69,5%)	1,15 (0,62 ; 2,12)	1,75 (0,13 ; 23,61)	0,10 (-0,35 ; 0,56)	1,0000	0,9208	
Morphologic blast count in bone marrow	high	131	96 (73,3%)	77	56 (72,8%)	1,01 (0,85 ; 1,20)	1,03 (0,54 ; 1,94)	0,01 (-0,12 ; 0,13)	1,0000	1,0000	0,0063
	low	68	61 (89,7%)	72	47 (65,2%)	1,38 (1,14 ; 1,66)	4,65 (1,85 ; 11,68)	0,25 (0,11 ; 0,38)	0,0006	0,0005	
	NA	3	3 (100,0%)	122	43 (34,8%)	NA (NA ; NA)	NA (NA ; NA)	NA (NA ; NA)	NA	NA	NA
Number of previous relapses	>=3			58	16 (27,3%)						
	0			19	10 (54,4%)						
	1			53	26 (50,0%)						
	2			141	93 (65,8%)						
	NA	202	160 (79,2%)			NA (NA ; NA)	NA (NA ; NA)	NA (NA ; NA)	NA	NA	NA
Previous HSCT	No	88	66 (75,0%)	123	92 (75,0%)	1,01 (0,86 ; 1,18)	1,02 (0,54 ; 1,92)	0,00 (-0,11 ; 0,12)	1,0000	0,9650	0,0000
	Yes	114	94 (82,5%)	149	53 (36,0%)	2,31 (1,83 ; 2,91)	8,47 (4,71 ; 15,23)	0,47 (0,36 ; 0,57)	0,0000	0,0000	

Subgroup	Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC						
	N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction	
Region	European Union (EU)	68	60 (88,2%)	270	145 (53,8%)	1,65 (1,43 ; 1,90)	6,54 (3,01 ; 14,19)	0,35 (0,25 ; 0,44)	0,0000	0,0000	0,4173
	Rest-of-the-World (ROW)	10	7 (70,0%)			NA (NA ; NA)	NA (NA ; NA)	NA (NA ; NA)	NA	NA	
	United States (US)	124	93 (75,0%)	1	0 (0,0%)	2,84 (0,26 ; 30,78)	8,32 (0,32 ; 215,34)	0,48 (-0,15 ; 1,12)	0,2598	0,1864	
Status of disease	refractory to previous line of therapy	40	27 (67,5%)	55	30 (53,7%)	1,27 (0,92 ; 1,77)	1,84 (0,79 ; 4,29)	0,14 (-0,05 ; 0,34)	0,2084	0,1661	0,0675
	relapsed after previous line of therapy	162	133 (82,1%)	216	116 (53,6%)	1,54 (1,33 ; 1,78)	4,02 (2,48 ; 6,50)	0,29 (0,20 ; 0,38)	0,0000	0,0000	

RR: Risk Ratio; OR: Hazard Ratio; RD: Hazard Ratio; CI: Confidence interval; N: Number of patients; NA: not available/not reached/not estimable; p-value: Fisher, Barnard; p-value interaction: LRT

1.2.2 Overall Survival

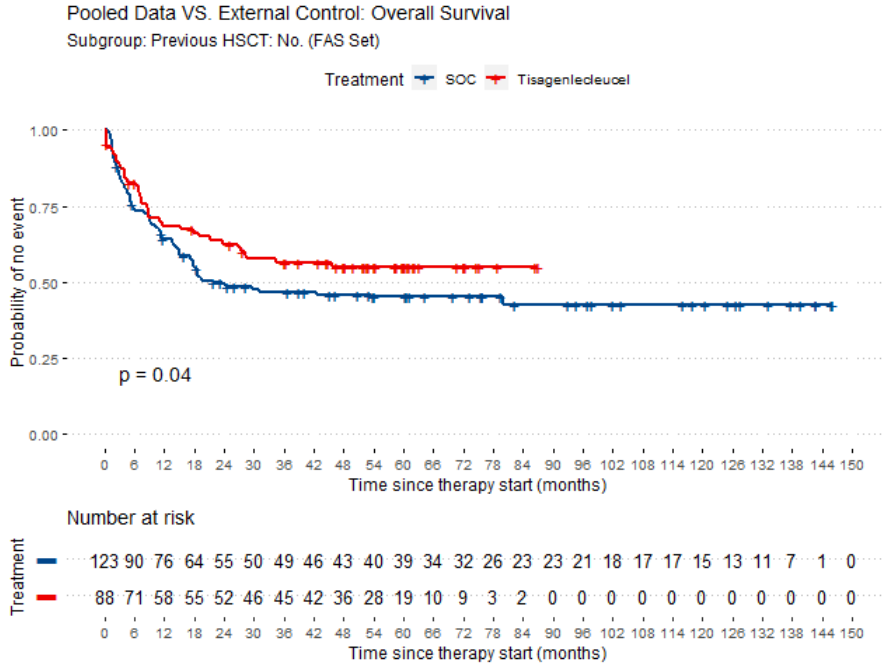
Table 4: Pooled Data VS. External Control: Overall Survival

Subgroup	Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC		
	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95%-KI)	p-value	p-value interaction
Age	<10 years	80	37 (46,2%)	96	61 (63,8%)	8,61 (5,62 ; NA)	0,53 (0,33 ; 0,85)	0,0019	0,4886
	>= 18 years	39	20 (51,3%)	66	45 (68,3%)	11,33 (5,42 ; 22,01)	0,61 (0,37 ; 1,00)	0,0606	
	10-18 years	83	33 (39,8%)	NA (NA ; NA)	111	71 (63,8%)	11,50 (5,09 ; 45,86)	0,43 (0,27 ; 0,67)	
Baseline extramedullary disease presence	No or NA	181	80 (44,2%)	240	165 (68,7%)	8,77 (6,08 ; 14,00)	0,45 (0,34 ; 0,59)	0,0000	0,0402
	Yes	21	10 (47,6%)	33	12 (36,3%)	NA (NA ; NA)	1,11 (0,34 ; 3,64)	0,8124	
BCR-ABL	negative or NA	194	88 (45,4%)	264	172 (64,9%)	10,55 (7,03 ; 18,79)	0,50 (0,38 ; 0,67)	0,0000	0,4680
	positive	8	2 (25,0%)	9	6 (65,5%)	17,25 (8,28 ; NA)	0,26 (0,06 ; 1,07)	0,0781	
Down Syndrom	NA			84	53 (63,2%)	NA (NA ; NA)			0,0969
	No	188	85 (45,2%)	184	119 (64,7%)	8,61 (5,26 ; 23,52)	0,49 (0,36 ; 0,68)	0,0000	
	Yes	14	5 (35,7%)	5	5 (100,0%)	6,05 (1,94 ; NA)	0,11 (0,03 ; 0,39)	0,0006	
Gender	Female	92	44 (47,8%)	89	69 (78,1%)	7,23 (5,19 ; 14,00)	0,39 (0,27 ; 0,57)	0,0000	0,3022

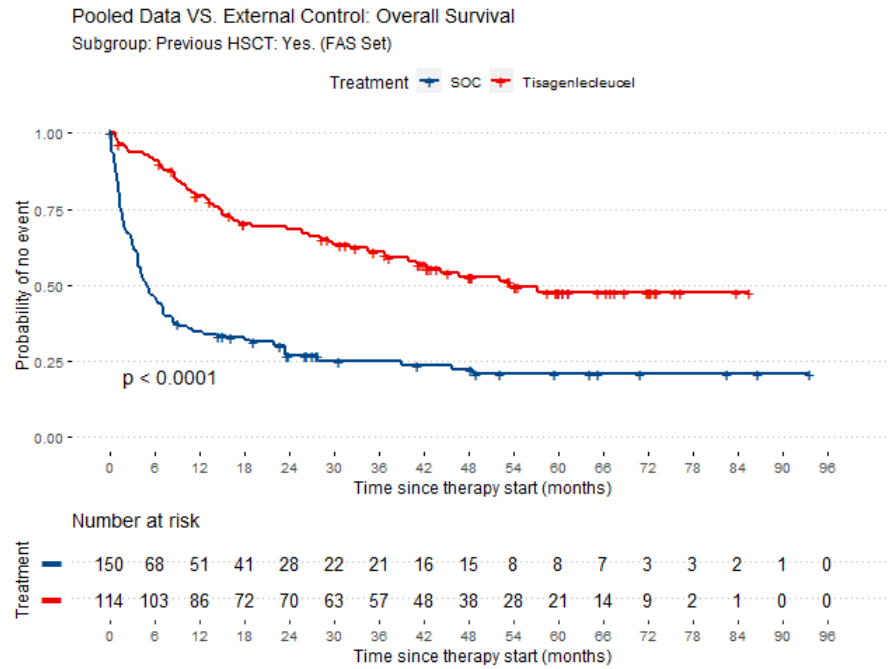
Subgroup	Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC		
	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95%-KI)	p-value	p-value interaction
Male	110	46 (41,8%)	NA (NA ; NA)	184	108 (58,5%)	14,92 (8,77 ; 80,07)	0,52 (0,36 ; 0,76)	0,0002	
MLL Rearrangement	No or NA	197	87 (44,2%)	264	170 (64,6%)	10,35 (7,03 ; 17,84)	0,49 (0,37 ; 0,64)	0,0000	0,4534
	Yes	5	3 (60,0%)	9	7 (72,1%)	23,52 (3,94 ; NA)	0,94 (0,25 ; 3,48)	0,9311	
Morphologic blast count in bone marrow	high	131	65 (49,6%)	77	46 (59,9%)	13,63 (7,23 ; NA)	0,73 (0,47 ; 1,14)	0,0999	0,0593
	low	68	24 (35,3%)	72	45 (61,9%)	18,00 (8,54 ; 48,66)	0,37 (0,22 ; 0,62)	0,0001	
	NA	3	1 (33,3%)	124	86 (69,7%)	NA (NA ; NA)	NA (NA ; NA)	NA	
Number of previous relapses	>=3			58	49 (83,9%)	NA (NA ; NA)			
	0			20	12 (58,9%)	NA (NA ; NA)			
	1			54	37 (69,6%)	NA (NA ; NA)			
	2			141	79 (56,1%)	NA (NA ; NA)			
	NA	202	90 (44,6%)	NA (NA ; NA)			NA (NA ; NA)	NA	NA
Previous HSCT	No	88	38 (43,2%)	123	67 (54,0%)	21,78 (14,92 ; NA)	0,75 (0,49 ; 1,15)	0,1620	0,0023
	Yes	114	52 (45,6%)	150	111 (73,8%)	4,99 (3,81 ; 8,61)	0,33 (0,22 ; 0,49)	0,0000	

Subgroup		Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC		
		N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95%-KI)	p-value	p-value interaction
Region	European Union (EU)	68	24 (35,3%)	NA (NA ; NA)	272	176 (64,8%)	11,04 (7,23 ; 18,79)	0,38 (0,25 ; 0,57)	0,0000	0,1019
	Rest-of-the-World (ROW)	10	5 (50,0%)	NA (NA ; NA)				NA (NA ; NA)	NA	
	United States (US)	124	61 (49,2%)	42,38 (27,50 ; NA)	1	1 (100,0%)	0,76 (NA ; NA)	0,03 (0,01 ; 0,09)	0,0000	
Status of disease	refractory to previous line of therapy	40	18 (45,0%)	NA (NA ; NA)	56	36 (64,8%)	11,37 (5,88 ; 24,38)	0,57 (0,32 ; 1,00)	0,0496	0,6043
	relapsed after previous line of therapy	162	72 (44,4%)	NA (NA ; NA)	217	141 (64,9%)	10,35 (6,31 ; 18,79)	0,48 (0,35 ; 0,65)	0,0000	

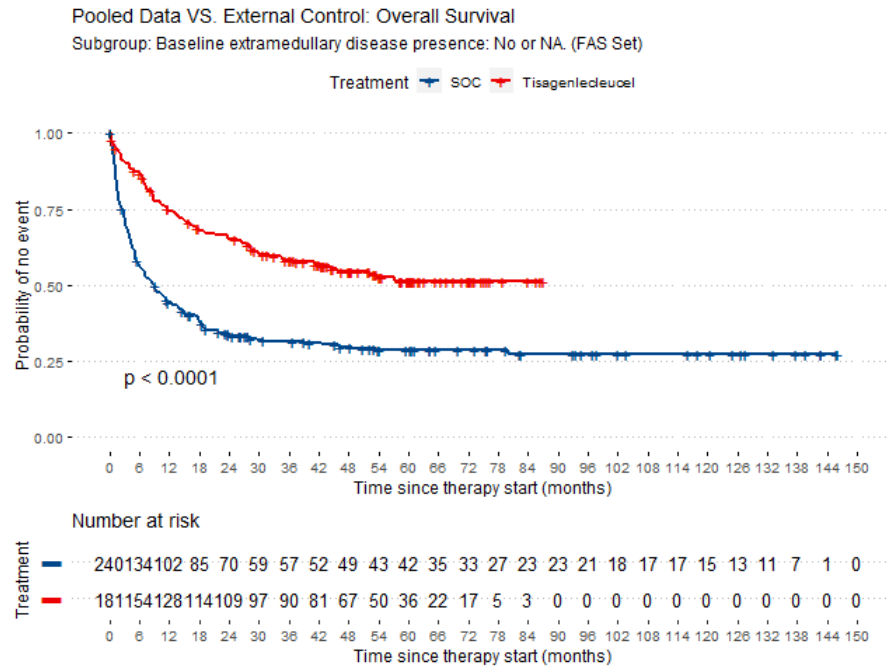
HR: Hazard Ratio; CI: Confidence interval; N: Number of patients; NA: not available/not reached/not estimable; p-value: Scoretest; p-value interaction: LRT



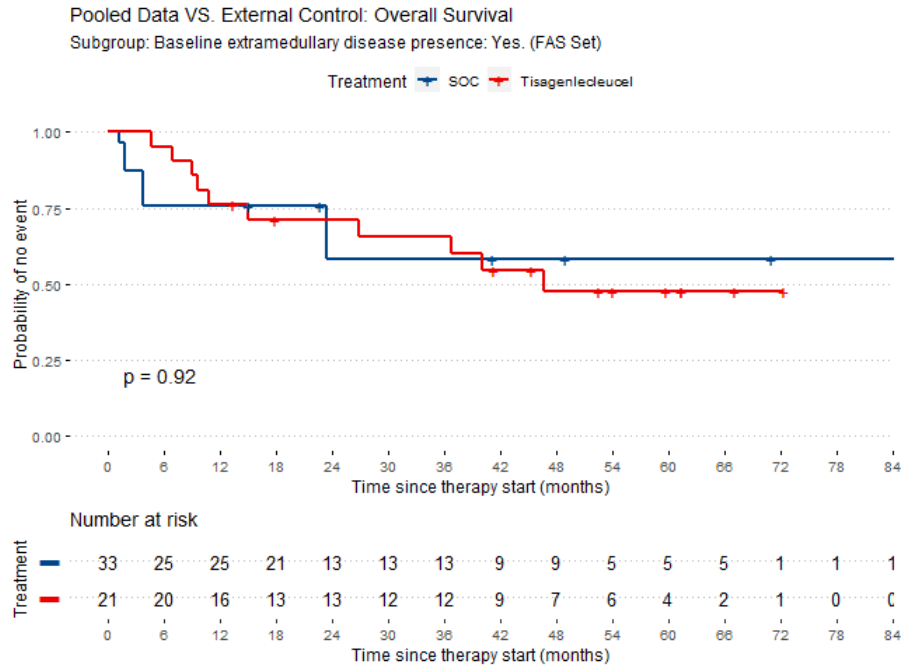
1.2.2.1 Figure 3: Pooled Data VS. External Control: Overall Survival - Subgroup: Previous HSCT: No. (FAS Set)



1.2.2.2 Figure 4: Pooled Data VS. External Control: Overall Survival - Subgroup: Previous HSCT: Yes. (FAS Set)



1.2.2.3 Figure 5: Pooled Data VS. External Control: Overall Survival - Subgroup: Baseline extramedullary disease presence: No or NA. (FAS Set)



1.2.2.4 Figure 6: Pooled Data VS. External Control: Overall Survival - Subgroup: Baseline extramedullary disease presence: Yes. (FAS Set)

2. Intent-To-Treat Set

2.1 Eliana VS. External Control

2.1.1 Overall Remission Rate

Table 5: Eliana VS. External Control: Overall Remission Rate

Subgroup	Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC						
	N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction	
Age	<10 years	39	25 (64,1%)	94	42 (45,1%)	1,42 (1,03 ; 1,96)	2,17 (1,01 ; 4,69)	0,19 (0,01 ; 0,37)	0,0572	0,0507	0,9649
	>= 18 years	17	11 (64,7%)	67	29 (43,7%)	1,50 (0,96 ; 2,33)	2,40 (0,80 ; 7,26)	0,21 (-0,04 ; 0,47)	0,1735	0,1195	
	10-18 years	40	29 (72,5%)	114	67 (58,8%)	1,23 (0,96 ; 1,57)	1,84 (0,84 ; 4,06)	0,14 (-0,03 ; 0,30)	0,1341	0,1528	
Baseline extramedullary disease presence	No or NA	86	55 (64,0%)	243	116 (48,0%)	1,34 (1,09 ; 1,64)	1,93 (1,16 ; 3,21)	0,16 (0,04 ; 0,28)	0,0119	0,0107	0,0607
	Yes	10	10 (100,0%)	32	22 (69,2%)	1,45 (1,15 ; 1,82)	NaN (NaN ; NaN)	0,31 (0,15 ; 0,47)	0,0839	0,0543	
	NA			82	46 (55,3%)						
Down Syndrom	No	89	60 (67,4%)	187	90 (47,9%)	1,41 (1,14 ; 1,73)	2,25 (1,33 ; 3,82)	0,20 (0,07 ; 0,32)	0,0029	0,0023	0,5806
	Yes	7	5 (71,4%)	5	3 (68,9%)	1,04 (0,48 ; 2,23)	1,13 (0,09 ; 14,37)	0,02 (-0,51 ; 0,56)	1,0000	0,9990	
Gender	Female	42	28 (66,7%)	91	42 (45,9%)	1,45 (1,07 ; 1,98)	2,35 (1,10 ; 5,05)	0,21 (0,03 ; 0,38)	0,0394	0,0278	0,7571

Subgroup	Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC						
	N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction	
Male	54	37 (68,5%)	184	97 (52,7%)	1,30 (1,04 ; 1,64)	1,97 (1,03 ; 3,74)	0,16 (0,02 ; 0,30)	0,0429	0,0374		
Morphologic blast count in bone marrow	high	68	40 (58,8%)	79	52 (65,2%)	0,90 (0,70 ; 1,17)	0,76 (0,39 ; 1,49)	-0,06 (-0,22 ; 0,09)	0,4978	0,5315	0,0107
	low	28	25 (89,3%)	73	48 (65,9%)	1,35 (1,10 ; 1,67)	4,30 (1,18 ; 15,65)	0,23 (0,08 ; 0,39)	0,0242	0,0181	
	NA			122	38 (31,5%)						
Number of previous relapses	>=3			68	18 (26,8%)						
	0			14	8 (59,9%)						
	1			47	22 (46,9%)						
	2			146	90 (61,8%)						
	NA	96	65 (67,7%)			NA (NA ; NA)	NA (NA ; NA)	NA (NA ; NA)	NA	NA	NA
Previous HSCT	No	39	24 (61,5%)	119	87 (72,9%)	0,85 (0,65 ; 1,11)	0,61 (0,28 ; 1,30)	-0,11 (-0,28 ; 0,06)	0,2296	0,1940	0,0000
	Yes	57	41 (71,9%)	155	52 (33,3%)	2,16 (1,64 ; 2,85)	5,14 (2,64 ; 10,01)	0,39 (0,25 ; 0,52)	0,0000	0,0000	
Region	European Union (EU)	30	24 (80,0%)	273	138 (50,7%)	1,58 (1,28 ; 1,96)	3,91 (1,55 ; 9,86)	0,29 (0,14 ; 0,45)	0,0020	0,0105	0,4283
	Rest-of-the-World (ROW)	9	5 (55,6%)			NA (NA ; NA)	NA (NA ; NA)	NA (NA ; NA)	NA	NA	NA
	United States (US)	57	36 (63,2%)	1	0 (0,0%)	2,76 (0,24 ; 31,79)	5,75 (0,23 ; 140,96)	0,40 (-0,17 ; 0,97)	0,1559	0,2690	

Subgroup	Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC						
	N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction	
Status of disease	refractory to previous line of therapy	19	11 (57,9%)	56	29 (51,0%)	1,15 (0,72 ; 1,82)	1,35 (0,47 ; 3,84)	0,07 (-0,18 ; 0,33)	0,7913	0,5891	0,2873
	relapsed after previous line of therapy	77	54 (70,1%)	218	110 (50,3%)	1,39 (1,15 ; 1,70)	2,32 (1,33 ; 4,04)	0,20 (0,08 ; 0,32)	0,0033	0,0029	

RR: Risk Ratio; OR: Hazard Ratio; RD: Hazard Ratio; CI: Confidence interval; N: Number of patients; NA: not available/not reached/not estimable; p-value: Fisher, Barnard; p-value interaction: LRT

2.1.2 Overall Survival

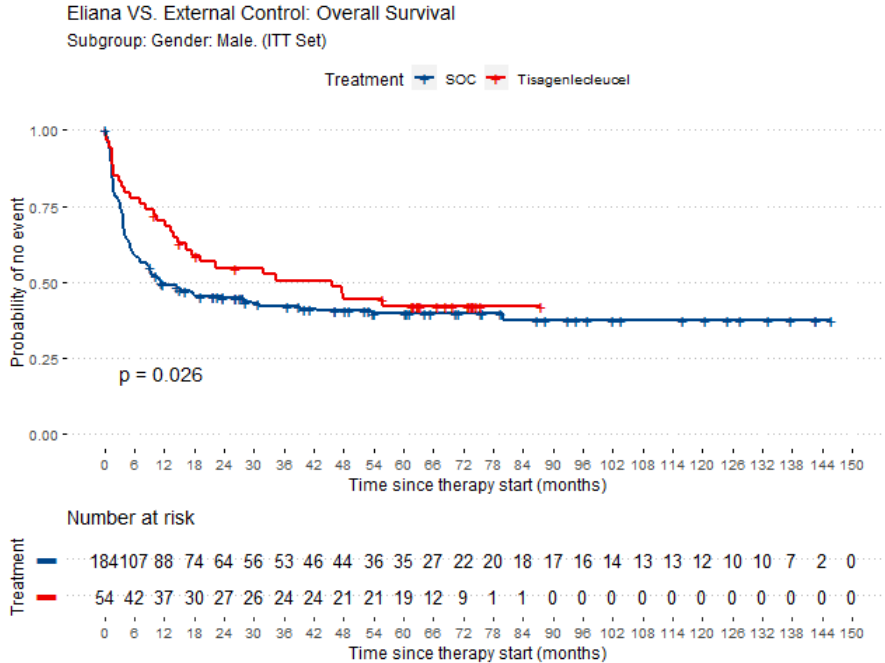
Table 6: Eliana VS. External Control: Overall Survival

Subgroup	Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC			
	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95%-KI)	p-value	p-value interaction	
Age	<10 years	39	25 (64,1%)	19,35 (11,50 ; NA)	94	63 (67,7%)	7,03 (4,96 ; 17,71)	0,69 (0,42 ; 1,15)	0,1161	0,6597
	>= 18 years	17	9 (52,9%)	59,37 (12,12 ; NA)	67	46 (68,3%)	12,45 (5,39 ; 22,01)	0,64 (0,32 ; 1,27)	0,2174	
	10-18 years	40	16 (40,0%)	NA (NA ; NA)	114	67 (58,5%)	11,04 (5,09 ; NA)	0,53 (0,29 ; 0,95)	0,0195	
Baseline extramedullary disease presence	No or NA	86	47 (54,7%)	31,84 (16,56 ; NA)	243	166 (68,4%)	8,51 (5,85 ; 12,45)	0,60 (0,43 ; 0,83)	0,0016	0,7469
	Yes	10	3 (30,0%)	NA (NA ; NA)	32	10 (30,8%)	NA (NA ; NA)	0,79 (0,17 ; 3,63)	0,7260	
Down Syndrom	NA				83	50 (60,4%)	NA (NA ; NA)			0,4810
	No	89	46 (51,7%)	47,61 (20,07 ; NA)	187	121 (64,7%)	7,23 (5,09 ; 18,79)	0,59 (0,41 ; 0,86)	0,0024	
	Yes	7	4 (57,1%)	34,40 (3,09 ; NA)	5	5 (100,0%)	6,05 (1,94 ; NA)	0,28 (0,08 ; 0,98)	0,0712	
Gender	Female	42	20 (47,6%)	59,37 (16,56 ; NA)	91	70 (76,8%)	7,20 (4,99 ; 13,63)	0,38 (0,23 ; 0,63)	0,0001	0,0415
	Male	54	30 (55,6%)	45,73 (16,49 ; NA)	184	107 (57,8%)	11,50 (6,08 ; NA)	0,78 (0,51 ; 1,21)	0,2411	
	high	68	43 (63,2%)	16,56 (11,50 ; 59,37)	79	48 (60,5%)	10,35 (5,26 ; NA)	0,92 (0,57 ; 1,49)	0,7056	0,0066

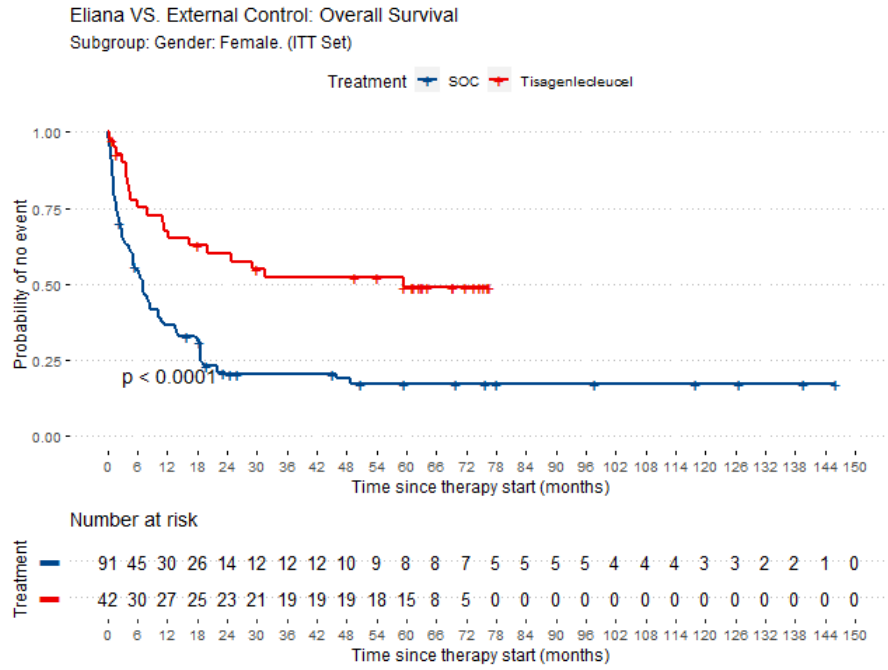
Subgroup	Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC		
	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95%-KI)	p-value	p-value interaction
Morphologic blast count in bone marrow	low	28	7 (25,0%)	73	44 (60,5%)	18,79 (9,13 ; NA)	0,27 (0,12 ; 0,59)	0,0006	
	NA			122	84 (68,4%)	NA (NA ; NA)			
	>=3			68	52 (75,9%)	NA (NA ; NA)			
Number of previous relapses	0			14	8 (57,9%)	NA (NA ; NA)			
	1			47	33 (71,1%)	NA (NA ; NA)			
	2			146	83 (56,8%)	NA (NA ; NA)			
	NA	96	50 (52,1%)				NA (NA ; NA)	NA	NA
Previous HSCT	No	39	21 (53,8%)	120	63 (53,0%)	19,22 (13,63 ; NA)	0,99 (0,58 ; 1,70)	0,9830	0,0090
	Yes	57	29 (50,9%)	155	113 (72,5%)	5,26 (3,81 ; 8,54)	0,41 (0,26 ; 0,64)	0,0000	
Region	European Union (EU)	30	13 (43,3%)	274	175 (63,9%)	9,36 (6,31 ; 18,17)	0,47 (0,27 ; 0,79)	0,0067	0,0541
	Rest-of-the-World (ROW)	9	5 (55,6%)				NA (NA ; NA)	NA	NA
	United States (US)	57	32 (56,1%)	24,87 (14,78 ; NA)	1	1 (100,0%)	0,76 (NA ; NA)	0,04 (0,01 ; 0,14)	0,0000

Subgroup		Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC		
		N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95%-KI)	p-value	p-value interaction
Status of disease	refractory to previous line of therapy	19	10 (52,6%)	47,61 (5,16 ; NA)	57	39 (67,9%)	10,12 (5,26 ; 19,22)	0,62 (0,31 ; 1,23)	0,1710	0,9479
	relapsed after previous line of therapy	77	40 (51,9%)	45,73 (17,58 ; NA)	218	137 (63,0%)	9,13 (6,08 ; 18,79)	0,62 (0,42 ; 0,90)	0,0068	

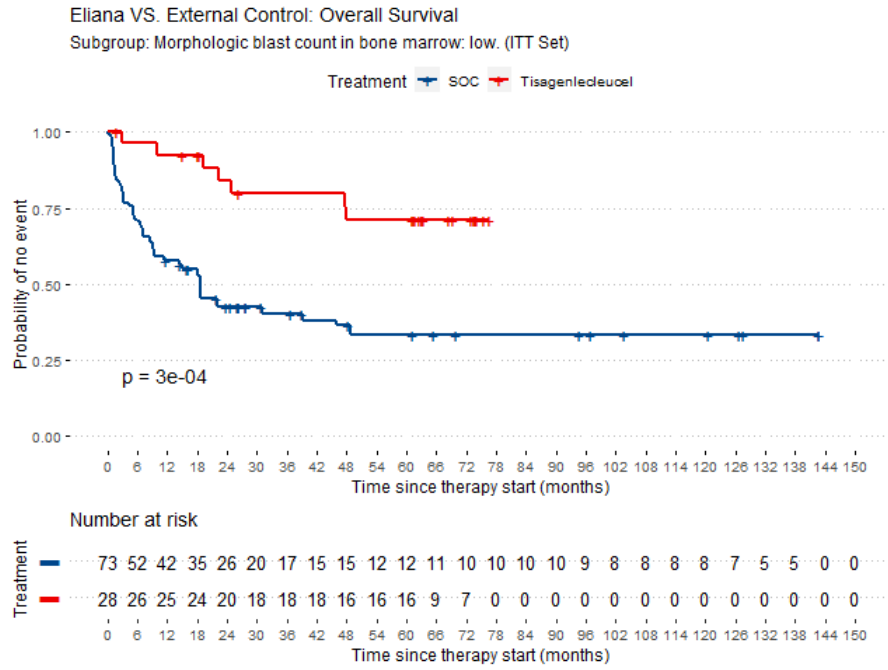
HR: Hazard Ratio; CI: Confidence interval; N: Number of patients; NA: not available/not reached/not estimable; p-value: Scoretest; p-value interaction: LRT



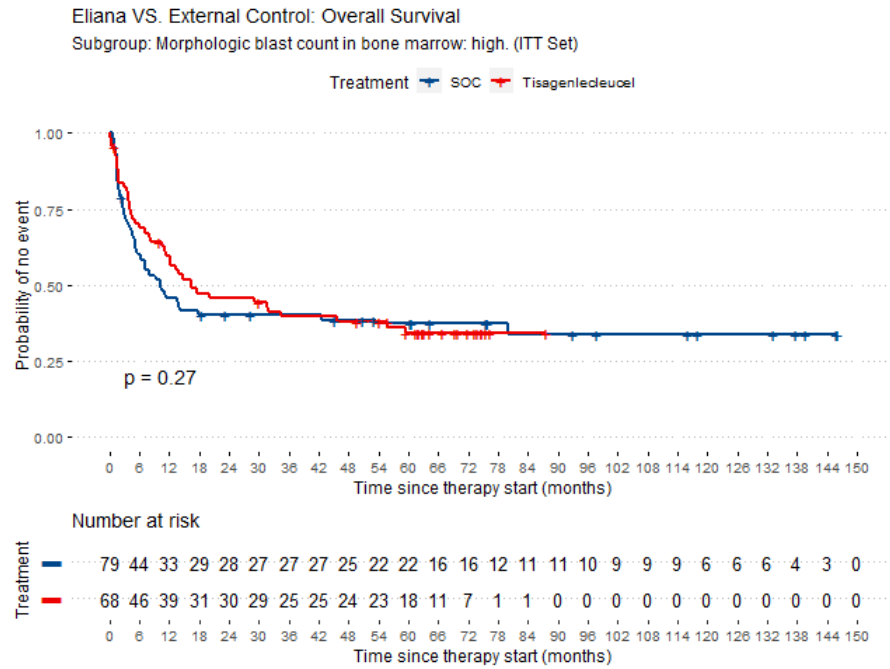
2.1.2.1 Figure 7: Eliana VS. External Control: Overall Survival - Subgroup: Gender: Male. (ITT Set)



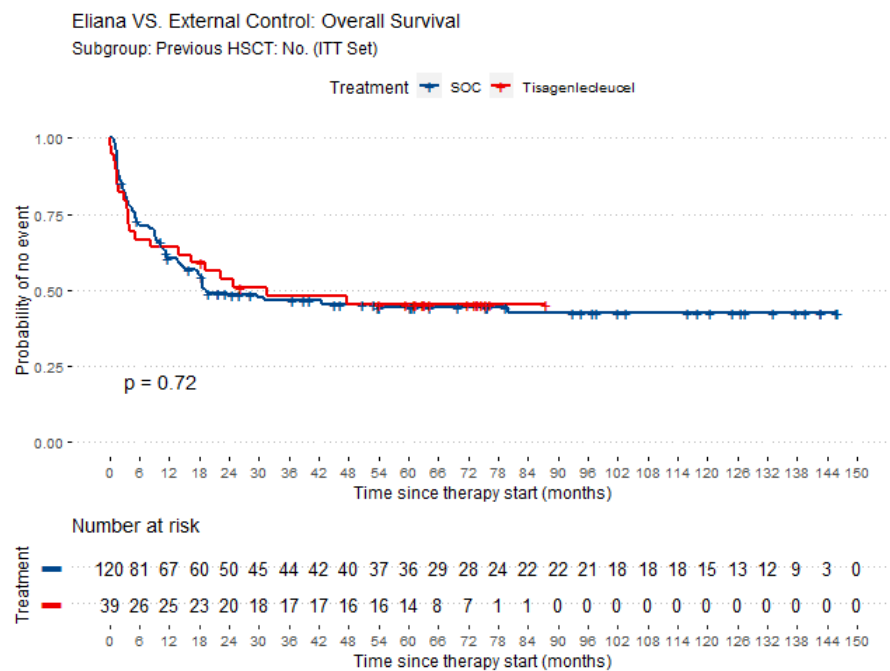
2.1.2.2 Figure 8: Eliana VS. External Control: Overall Survival - Subgroup: Gender: Female. (ITT Set)



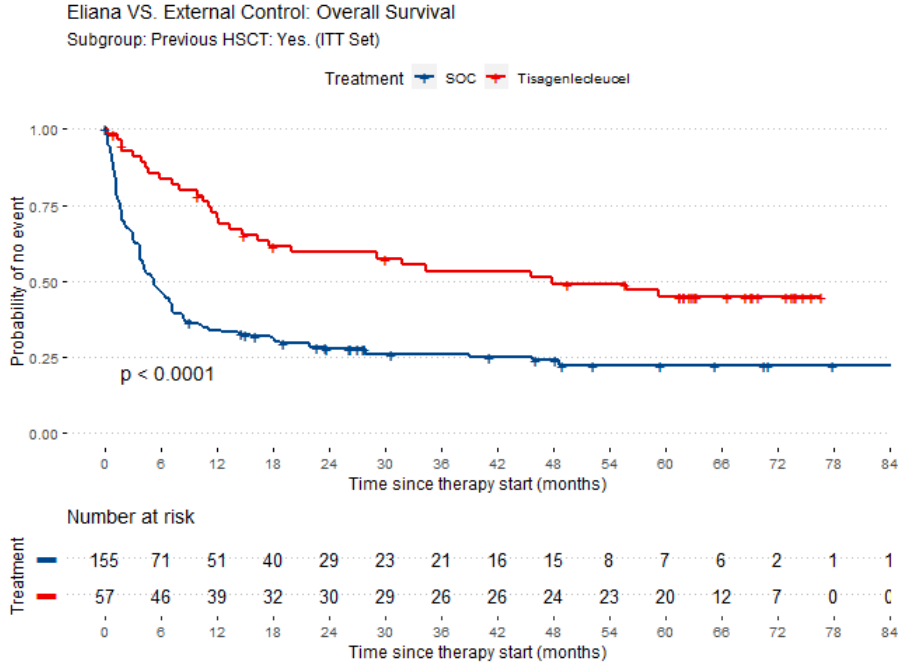
2.1.2.3 Figure 9: Eliana VS. External Control: Overall Survival - Subgroup: Morphologic blast count in bone marrow: low. (ITT Set)



2.1.2.4 Figure 10: Eliana VS. External Control: Overall Survival - Subgroup: Morphologic blast count in bone marrow: high. (ITT Set)



2.1.2.5 Figure 11: Eliana VS. External Control: Overall Survival - Subgroup: Previous HSCT: No. (ITT Set)



2.1.2.6 Figure 12: Eliana VS. External Control: Overall Survival - Subgroup: Previous HSCT: Yes. (ITT Set)

2.2 Pooled Data VS. External Control

2.2.1 Overall Survival

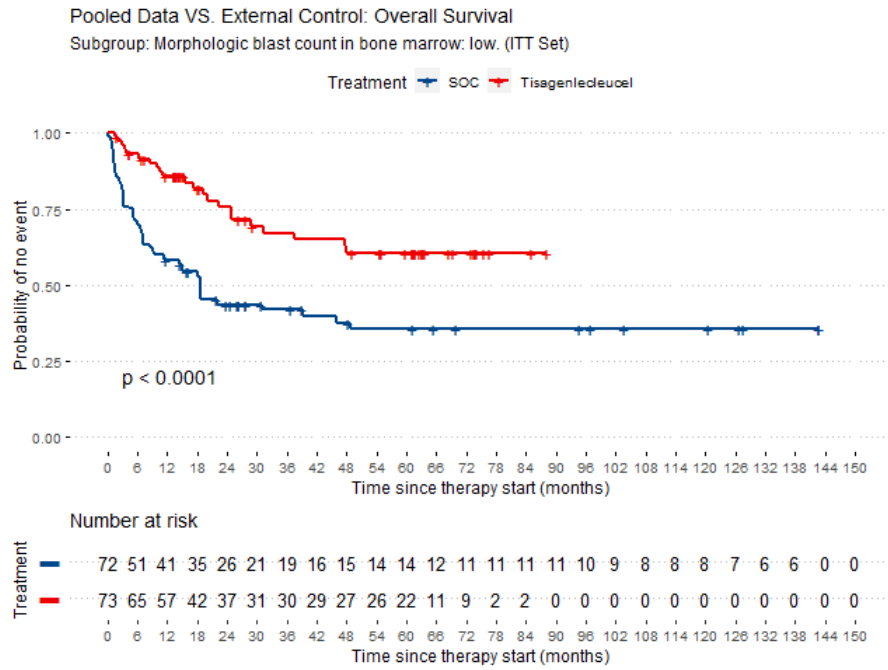
Table 7: Pooled Data VS. External Control: Overall Survival

Subgroup	Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC			
	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95%-KI)	p-value	p-value interaction	
Age	<10 years	92	41 (44,6%)	37,65 (19,35 ; NA)	91	60 (65,5%)	8,15 (5,26 ; 48,66)	0,56 (0,36 ; 0,89)	0,0042	0,6815
	>= 18 years	48	24 (50,0%)	16,56 (13,40 ; NA)	74	52 (70,3%)	10,74 (5,19 ; 19,58)	0,70 (0,44 ; 1,13)	0,1545	
	10-18 years	96	38 (39,6%)	NA (NA ; NA)	116	69 (59,8%)	11,50 (5,09 ; NA)	0,53 (0,33 ; 0,85)	0,0016	
Baseline extramedullary disease presence	No or NA	212	95 (44,8%)	35,78 (25,92 ; NA)	247	167 (67,7%)	8,61 (5,88 ; 14,00)	0,54 (0,41 ; 0,70)	0,0000	0,4051
	Yes	24	8 (33,3%)	NA (NA ; NA)	34	14 (40,5%)	NA (NA ; NA)	0,82 (0,24 ; 2,75)	0,6542	
BCR-ABL	negative or NA	228	102 (44,7%)	35,78 (27,30 ; NA)	273	176 (64,5%)	10,35 (6,21 ; 18,79)	0,58 (0,44 ; 0,76)	0,0000	0,2217
	positive	8	1 (12,5%)	NA (NA ; NA)	8	5 (61,3%)	17,25 (8,28 ; NA)	0,17 (0,02 ; 1,21)	0,0733	
Down Syndrom	NA				95	57 (60,1%)	NA (NA ; NA)			0,0745
	No	220	98 (44,5%)	37,65 (27,30 ; NA)	180	118 (65,6%)	8,54 (5,09 ; 22,01)	0,56 (0,40 ; 0,77)	0,0000	
	Yes	16	5 (31,2%)	NA (NA ; NA)	5	5 (100,0%)	6,05 (1,94 ; NA)	0,16 (0,05 ; 0,47)	0,0015	

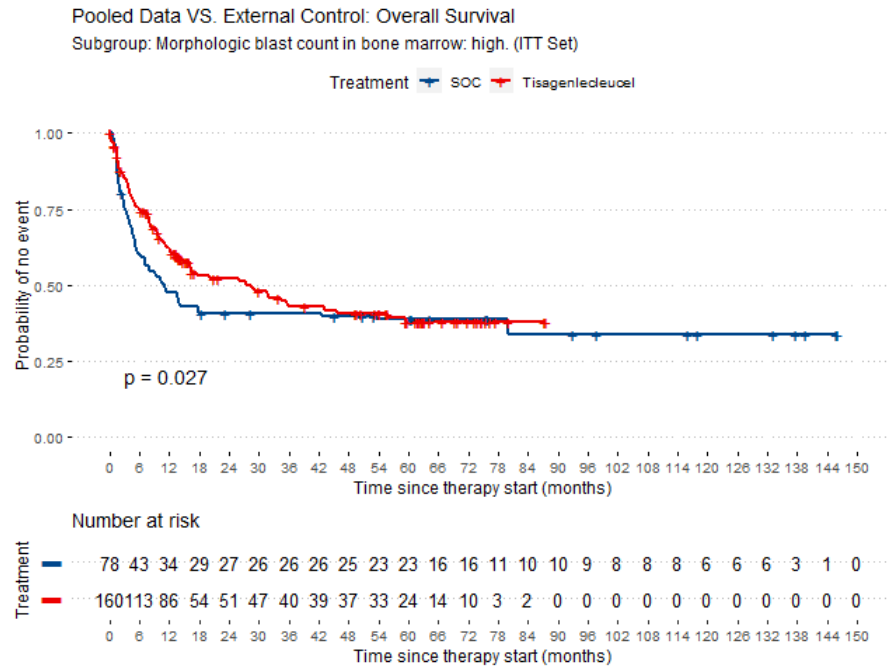
Subgroup	Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC			
	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95%-KI)	p-value	p-value interaction	
Gender	Female	104	47 (45,2%)	31,74 (20,17 ; NA)	93	70 (75,0%)	7,39 (5,26 ; 18,79)	0,43 (0,30 ; 0,62)	0,0000	0,1403
	Male	132	56 (42,4%)	47,61 (28,81 ; NA)	188	111 (59,2%)	12,45 (6,05 ; 80,07)	0,64 (0,44 ; 0,92)	0,0057	
MLL Rearrangement	No or NA	231	100 (43,3%)	43,20 (28,81 ; NA)	272	174 (64,1%)	9,43 (6,21 ; 18,17)	0,56 (0,42 ; 0,74)	0,0000	0,5703
	Yes	5	3 (60,0%)	11,50 (9,33 ; NA)	9	7 (73,3%)	23,52 (3,29 ; NA)	1,14 (0,29 ; 4,54)	0,8581	
Morphologic blast count in bone marrow	high	160	81 (50,6%)	28,48 (16,10 ; 55,89)	78	46 (59,5%)	11,04 (5,59 ; NA)	0,82 (0,52 ; 1,30)	0,2975	0,0252
	low	73	22 (30,1%)	NA (NA ; NA)	72	43 (59,8%)	18,79 (9,13 ; NA)	0,40 (0,23 ; 0,69)	0,0003	
	NA	3	0 (0,0%)	NA (NA ; NA)	131	92 (69,8%)	NA (NA ; NA)	NA (NA ; NA)	NA	
Number of previous relapses	>=3				68	52 (76,4%)	NA (NA ; NA)			
	0				21	13 (60,5%)	NA (NA ; NA)			
	1				58	40 (69,4%)	NA (NA ; NA)			
	2				135	77 (56,9%)	NA (NA ; NA)			
	NA	236	103 (43,6%)	NA (NA ; NA)				NA (NA ; NA)	NA	NA
Previous HSCT	No	105	47 (44,8%)	35,65 (20,17 ; NA)	129	68 (52,8%)	21,78 (14,92 ; NA)	0,91 (0,60 ; 1,37)	0,6150	0,0004

Subgroup	Tisagenlecleucel			SOC			Tisagenlecleucel vs. SOC			
	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	N valid	Patients with event n (%)	Median time to event in Monaten (95 %-KI)	HR (95 %-KI)	p-value	p-value interaction	
Yes	131	56 (42,7%)	43,20 (29,24 ; NA)	152	113 (74,2%)	4,99 (3,81 ; 8,54)	0,37 (0,25 ; 0,54)	0,0000		
Region	European Union (EU)	77	23 (29,9%)	NA (NA ; NA)	280	180 (64,3%)	10,35 (6,97 ; 18,79)	0,40 (0,26 ; 0,62)	0,0000	
	Rest-of-the-World (ROW)	12	6 (50,0%)	NA (NA ; NA)				NA (NA ; NA)	NA	0,1330
	United States (US)	147	74 (50,3%)	31,24 (20,17 ; NA)	1	1 (100,0%)	0,76 (NA ; NA)	0,02 (0,01 ; 0,06)	0,0000	
Status of disease	refractory to previous line of therapy	48	23 (47,9%)	31,74 (9,33 ; NA)	61	39 (64,5%)	11,37 (5,59 ; 24,38)	0,69 (0,42 ; 1,15)	0,1647	0,3552
	relapsed after previous line of therapy	188	80 (42,6%)	43,20 (28,48 ; NA)	220	142 (64,4%)	9,26 (5,85 ; 18,79)	0,54 (0,39 ; 0,74)	0,0000	

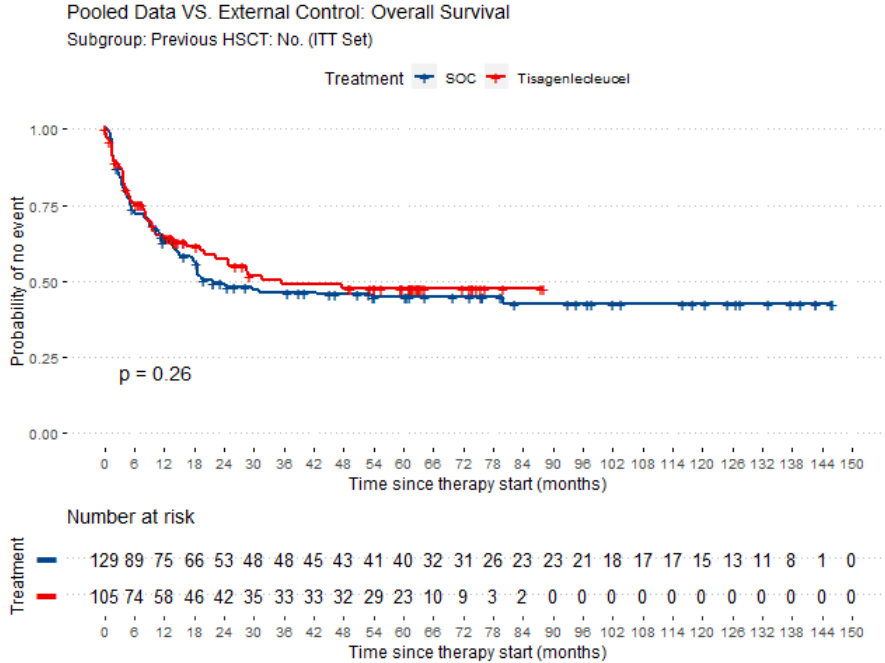
HR: Hazard Ratio; CI: Confidence interval; N: Number of patients; NA: not available/not reached/not estimable; p-value: Scoretest; p-value interaction: LRT



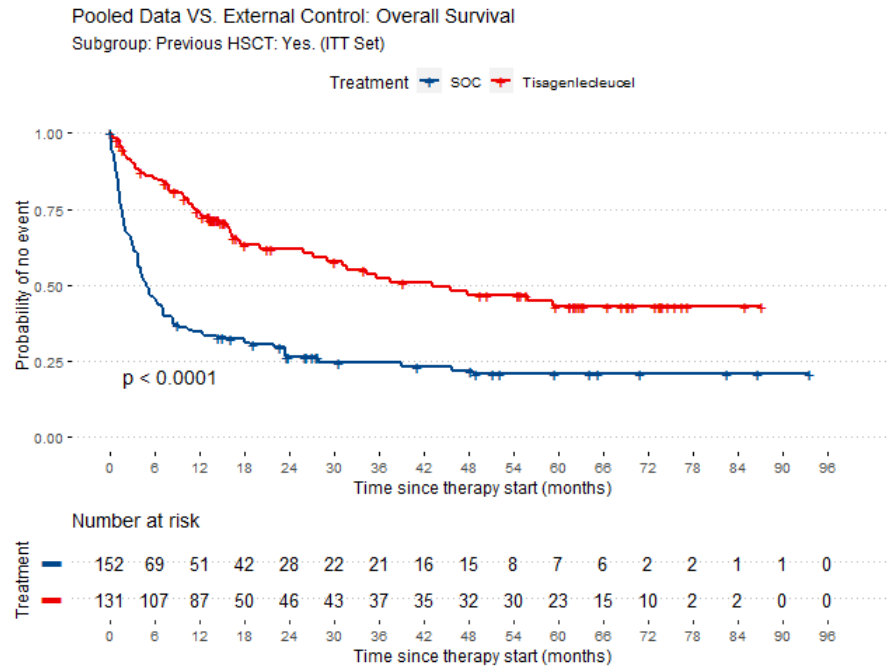
2.2.1.1 Figure 13: Pooled Data VS. External Control: Overall Survival - Subgroup: Morphologic blast count in bone marrow: low. (ITT Set)



2.2.1.2 Figure 14: Pooled Data VS. External Control: Overall Survival - Subgroup: Morphologic blast count in bone marrow: high. (ITT Set)



2.2.1.3 Figure 15: Pooled Data VS. External Control: Overall Survival - Subgroup: Previous HSCT: No. (ITT Set)



2.2.1.4 Figure 16: Pooled Data VS. External Control: Overall Survival - Subgroup: Previous HSCT: Yes. (ITT Set)

2.2.2 Overall Remission Rate

Table 8: Pooled Data VS. External Control: Overall Remission Rate

Subgroup	Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC						
	N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction	
Age	<10 years	92	62 (67,4%)	91	48 (52,4%)	1,29 (1,01 ; 1,64)	1,88 (1,03 ; 3,42)	0,15 (0,01 ; 0,29)	0,0503	0,0382	0,9560
	>= 18 years	48	30 (62,5%)	73	32 (43,7%)	1,47 (1,04 ; 2,07)	2,25 (1,07 ; 4,73)	0,20 (0,02 ; 0,38)	0,0420	0,0314	
	10-18 years	96	69 (71,9%)	116	66 (56,7%)	1,27 (1,03 ; 1,55)	1,95 (1,09 ; 3,47)	0,15 (0,02 ; 0,28)	0,0312	0,0260	
Baseline extramedullary disease presence	No or NA	212	140 (66,0%)	245	121 (49,3%)	1,35 (1,15 ; 1,58)	2,03 (1,39 ; 2,97)	0,17 (0,08 ; 0,26)	0,0003	0,0002	0,9342
	Yes	24	21 (87,5%)	34	24 (71,0%)	1,23 (0,95 ; 1,60)	2,85 (0,69 ; 11,79)	0,16 (-0,04 ; 0,37)	0,2019	0,1936	
BCR-ABL	negative or NA	228	153 (67,1%)	271	140 (51,7%)	1,31 (1,13 ; 1,51)	1,94 (1,35 ; 2,79)	0,16 (0,07 ; 0,24)	0,0004	0,0003	0,0396
	positive	8	8 (100,0%)	8	5 (61,3%)	1,63 (0,93 ; 2,86)	NaN (NaN ; NaN)	0,39 (0,04 ; 0,73)	0,2000	0,0803	
Down Syndrom	NA			93	52 (55,5%)						
	No	220	148 (67,3%)	180	89 (49,4%)	1,36 (1,14 ; 1,62)	2,10 (1,40 ; 3,15)	0,18 (0,08 ; 0,27)	0,0003	0,0003	0,8683
	Yes	16	13 (81,2%)	5	4 (73,9%)	1,10 (0,63 ; 1,91)	1,53 (0,16 ; 15,05)	0,07 (-0,34 ; 0,49)	1,0000	1,0000	
Gender	Female	104	69 (66,3%)	93	46 (49,7%)	1,34 (1,05 ; 1,72)	2,02 (1,14 ; 3,59)	0,17 (0,03 ; 0,31)	0,0205	0,0169	0,9352
	Male	132	92 (69,7%)	186	99 (53,1%)	1,32 (1,11 ; 1,58)	2,07 (1,29 ; 3,30)	0,17 (0,06 ; 0,28)	0,0026	0,0024	

Subgroup		Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC					
		N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction
MLL Rearrangement	No or NA	231	157 (68,0%)	270	139 (51,3%)	1,33 (1,15 ; 1,54)	2,04 (1,42 ; 2,94)	0,17 (0,09 ; 0,25)	0,0001	0,0001	0,9112
	Yes	5	4 (80,0%)	9	6 (69,2%)	1,16 (0,63 ; 2,14)	1,78 (0,13 ; 23,98)	0,11 (-0,35 ; 0,57)	1,0000	0,9208	
Morphologic blast count in bone marrow	high	160	97 (60,6%)	78	52 (66,4%)	0,91 (0,75 ; 1,12)	0,78 (0,44 ; 1,38)	-0,06 (-0,19 ; 0,07)	0,3945	0,4456	0,0122
	low	73	61 (83,6%)	72	48 (66,9%)	1,25 (1,03 ; 1,51)	2,51 (1,14 ; 5,53)	0,17 (0,03 ; 0,30)	0,0217	0,0233	
	NA	3	3 (100,0%)	130	45 (35,0%)	NA (NA ; NA)	NA (NA ; NA)	NA (NA ; NA)	NA	NA	NA
Number of previous relapses	>=3			68	22 (31,9%)						
	0			20	11 (52,9%)						
	1			57	28 (50,4%)						
	2			135	84 (62,5%)						
	NA	236	161 (68,2%)			NA (NA ; NA)	NA (NA ; NA)	NA (NA ; NA)	NA	NA	NA
Previous HSCT	No	105	67 (63,8%)	128	91 (70,8%)	0,91 (0,76 ; 1,09)	0,74 (0,43 ; 1,28)	-0,07 (-0,19 ; 0,06)	0,3261	0,3613	0,0000
	Yes	131	94 (71,8%)	151	54 (35,9%)	2,01 (1,58 ; 2,55)	4,58 (2,77 ; 7,59)	0,36 (0,25 ; 0,47)	0,0000	0,0000	
Region	European Union (EU)	77	60 (77,9%)	278	145 (52,1%)	1,51 (1,28 ; 1,78)	3,30 (1,83 ; 5,93)	0,26 (0,15 ; 0,37)	0,0000	0,0002	0,3767
	Rest-of-the-World (ROW)	12	7 (58,3%)			NA (NA ; NA)	NA (NA ; NA)	NA (NA ; NA)	NA	NA	

Subgroup	Tisagenlecleucel		SOC		Tisagenlecleucel vs. SOC						
	N valid	Patients with event n (%)	N valid	Patients with event n (%)	RR (95%-KI)	OR (95%-KI)	RD (95%-KI)	p-value (Fisher)	p-value (Barnard)	p-value interaction	
United States (US)	147	94 (63,9%)	1	0 (0,0%)	2,20 (0,21 ; 22,76)	4,31 (0,16 ; 117,85)	0,35 (-0,33 ; 1,03)	0,3691	0,2861		
Status of disease	refractory to previous line of therapy	48	27 (56,2%)	60	32 (54,2%)	1,05 (0,75 ; 1,48)	1,12 (0,52 ; 2,39)	0,03 (-0,16 ; 0,22)	0,8465	0,7713	0,0426
	relapsed after previous line of therapy	188	134 (71,3%)	219	113 (51,3%)	1,40 (1,19 ; 1,64)	2,38 (1,58 ; 3,59)	0,20 (0,11 ; 0,29)	0,0000	0,0000	

RR: Risk Ratio; OR: Hazard Ratio; RD: Hazard Ratio; CI: Confidence interval; N: Number of patients; NA: not available/not reached/not estimable; p-value: Fisher, Barnard; p-value interaction: LRT