Real-World Evidence of Tisagenlecleucel for pediatric acute lymphoblastic leukemia and Non-Hodgkin Lymphoma

Supplemental Materials:

Figure S1: Summary of release specifications (Manufacturing Infused Set). Boxplots illustrating the distribution of (A) dose and (B) cell viability for both indications in the registry vs. pivotal trials. (C) Summary of out-of-specification batches captured in the registry.

Table S1: Detailed demographic / baseline information and subgroups for ALL (A) and NHL (B) comparing to ELIANA and JULIET clinical trials.

Table S2: Safety and efficacy analyses for unique subgroups within recipients with ALL (A) and NHL (B)

Table S3: Overview of safety endpoints other than CRS and ICANS

Table S1: Detailed demographic / baseline information and subgroups for ALL (A) and NHL (B) comparing to ELIANA and JULIET clinical trials. (Infused Set)

A	**CIBMTR; ALL (N=255), n (%)**	**ELIANA (N=79), n (%)**
Median age at infusion, years (range)	13.2 (0.41-26.17)	11.0 (3-24)
Age <3 years	15 (5.9)	0
Gender, male / female	150 (58.8) / 105 (41.2)	45 (57.0) / 34 (43.0)
Down Syndrome	12 (4.7)	6 (7.6)
Prior CNS involvement	24 (9.4)	11 (13.9)
Disease status at time of cellular therapy infusion (or at enrollment in clinical trial):		
Primary refractory/Relapsed	159 (62.3)	79 (100)
CR	95 (37.2)	0
Unknown	1 (0.5)	0
MRD negative prior to infusion	44 (17.3)	NA
Median number of prior therapies (range)	3 (0-15)	3 (1-8)
Prior blinatumomab	38 (14.9)	0
Prior inotuzumab	27 (10.6)	3 (3.8)
Prior HCT:		
Allogeneic	71 (27.8)	48 (60.8)
Autologous	1 (0.4)	0
Both	1 (0.4)	0
Karnofsky/Lansky performance status prior to cellular therapy:		
90-100	174 (68.2)	53 (67.1)
80	37 (14.5)	13 (16.5)
<80	31 (12.2)	13 (16.5)
Not reported	13 (5.1)	-
Median time from leukapheresis acceptance (or enrollment in clinical trial) to infusion, days	33 (21-91)	46
Median time of follow-up since infusion, months	13.4 (3.5-27.9)	38.8 (19.1-49.7)

B

	CIBMTR; NHL (N=155), n (%)	**JULIET (N=115), n (%)**
Median age at infusion, years (range)	65.4 (18.45-88.99)	56.0 (22.0-76.0)
Age ≥ 65 years	83 (53.3)	26 (22.6)
Gender, male / female	91 (53.5) / 64 (41.3)	71 (61.7) / 44 (38.3)
Double/triple hit	17 (11)	20 (17.4)
Disease status at time of cellular therapy infusion (or at enrollment in clinical trial):		
Primary refractory/Relapsed	147 (94.8)	115 (100)
CR	7 (4.5)	0
Unknown	1 (0.7)	0
Median number of prior therapies (range)	4 (0-11)	3 (1-6)
Prior HCT:		
Allogeneic	5 (3.2)	0
Autologous	40 (25.8)	56 (48.7)
Both	1 (0.6)	0
ECOG performance status prior to cellular therapy:		
0-1	129 (83.2)	115 (100)
2-4	8 (5.2)	0
Not reported	18 (11.6)	0
Median time from leukapheresis acceptance (or enrollment in clinical trial) to infusion, days	31.5 (22-130)	54
Median time of follow-up since infusion, months	11.9 (3.8-19.0)	32.6 (16.3-44.9)

Table S2: Safety and efficacy analyses for unique subgroups within recipients with ALL (A) and NHL (B)

A

Group	N=410	BOR of CR % (95% CI)	6-mo DOR % (95% CI)	6-mo OS % (95% CI)	CRS Gr. ≥3 % (95% CI)	ICANS Gr. ≥3 % (95% CI)
Overall	***N=249/255***	***85.5%*** (80.6, 89.7)	***78.1%*** (70.5, 84.0)	***88.5%*** (83.6, 92.0)	***16.1%*** (11.8, 21.2)	***9.0%*** (5.8, 13.2)
<3 years	N=15/15	86.7% (59.5, 98.3)	*	*	6.7% (0.2, 31.9)	13.3% (1.7, 40.5)
Down's	N=12/12	100.0% (73.5, 100.0)	*	100.0% (NE, NE)	16.7% (2.1, 48.4)	16.7% (2.1, 48.4)
Prior CNS involvement	N=23/24	82.6% (61.2, 95.0)	*	79.7% (54.1, 92.0)	25.0% (9.8, 46.7)	8.3% (1.0, 27.0)
Prior blinatumomab[1]	N=37/38	78.4% (61.8, 90.2)	67.2% (42.5, 83.1)	88.5% (72.1, 95.5)	13.2% (4.4, 28.1)	7.9% (1.7, 21.4)
Prior inotuzumab[1]	N=26/27	65.4% (44.3, 82.8)	*	64.2% (42.5, 79.5)	7.4% (0.9, 24.3)	11.1% (2.4, 29.2)
Primary refractory	N=37/38	86.5% (71.2, 95.5)	*	87.8% (70.5, 95.3)	10.5% (2.9, 24.8)	7.9% (1.7, 21.4)
MRD negative	N=42/44	97.6% (87.4, 99.9)	85.9% (69.2, 93.9)	97.1% (81.4, 99.6)	0.0% (0.0, 8.0)	2.3% (0.1, 12.0)

*Number of patients at risk is <10 patients [1]Among 37 patients who received blinatumomab prior to tisagenlecleucel, 17 (45.9%) patients experienced treatment failure, relapse, and/or death due to primary disease (median follow up 10.9 months). Among 26 patients who received inotuzomab, 16 (61.5%) experienced treatment failure, relapse, and/or death due to primary disease (median follow up 10.9 months).

B

Group	N=410	ORR / BOR of CR % (95% CI)	3-mo DOR % (95% CI)	6-mo OS (95% CI)	CRS Gr. ≥3 % (95% CI)	ICANS Gr. ≥3 % (95% CI)
Overall	***N=152/155***	61.8% (53.6, 69.6) / 39.5% (31.6, 47.7)	70.4% (58.8, 79.3)	70.7% (62.2, 77.6)	4.5% (1.8, 9.1)	5.2% (2.3, 9.9)
Double/triple hit	N=17/17	70.6% (44.0,89.7) / 47.1% (23.0, 72.2)	*	*	0.0% (0.0, 19.5)	5.9% (0.1, 28.7)
<65 years	N=71/72	62.0% (49.7,73.2) / 39.4% (28.0, 51.7)	64.4% (46.6, 76.6)	76.9% (65.0, 85.2)	4.2% (0.9, 11.7)	5.6% (1.5, 13.6)
≥65 years	N=81/83	61.7% (50.3, 72.3) / 39.5% (28.8, 51.0)	76.1% (60.0, 86.4)	64.3% (51.4, 74.6)	4.8% (1.3, 11.9)	4.8% (1.3, 11.9)

*number of patients at risk is <10 patients

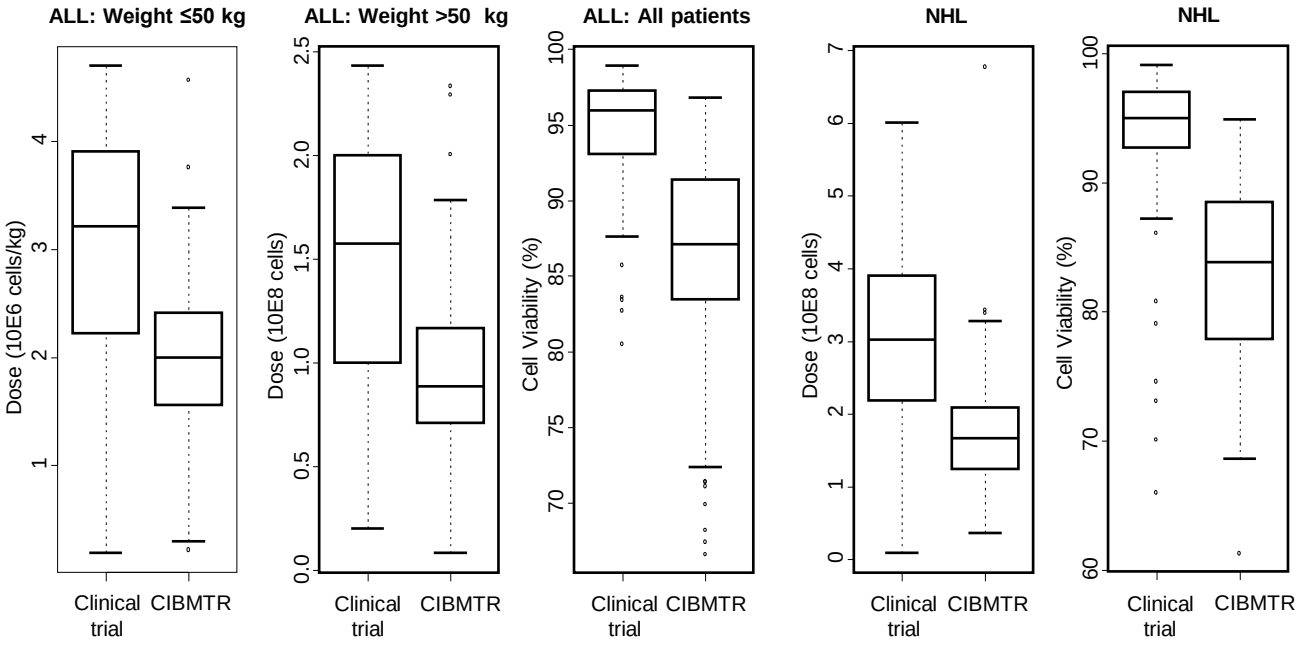
Table S3: Overview of safety endpoints other than CRS and ICANS (Safety Set)

	ALL (N=255), n (%)	**NHL (N=155), n(%)**
Hypogammaglobulinemia	134 (52.5)	56 (36.1)
Treated with IVIG	124 (48.6)	26 (16.8)
Prolonged cytopenia	71 (27.8)	23 (14.8)
Neutropenia	55 (21.6)	8 (5.2)
Thrombocytopenia	46 (18)	20 (12.9)
Clinically significant infections	118 (46.3)	39 (25.2)
Bacterial	59 (23.1)	18 (11.6)
Viral	57 (22.4)	22 (14.2)
Gr. 3/4 organ toxicities	21 (8.2)	3 (1.9)
Secondary malignancies	6 (2.4)	6 (3.9)
AML	4 (1.6)	0 (0.6)
MDS	2 (0.8	1(0.6)
Other	0	5 (3.2)
Deaths overall	47 (18.4)	51 (32.9)
Deaths within 30 days of infusion	8 (3.1)	6 (3.9)
Progressive disease	3 (1.2)	4 (2.6)
Other	5 (2.0)	2 (1.2)

Figure S1: Summary of release specifications (Manufacturing Infused Set): Boxplots illustrating the distribution of dose and cell viability for ALL (A) and NHL (B) in the registry vs. pivotal trials. (C) Summary of out-of-specification batches captured in the registry.

A

B



C

OOS specification	ALL (N=245), n (%)	NHL (N=138), n (%)	Total (N=383), n (%)
Any parameter	***39 (15.9)***	***47 (34.1)***	***86 (22.5)***
Viability (low)	33 (13.5)	43 (31.2)	76 (19.8)
IFN-gamma release (low or high)	4 (1.6)	2 (1.4)	6 (1.6)
CAR-positive viable T-cells dose (low or high)	0	3 (2.2)	3 (0.8)
CAR expression (low)	3 (1.2)	0	3 (0.8)