



CAR T cell Therapy for

Patients with CNS Involvement

and

Patients with Down Syndrome

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**CAR T CELL THERAPY FOR
RELAPSED AND/OR REFRACTORY
CNS/BONE MARROW OR
ISOLATED CNS B ALL
IN CHILDREN AND YOUNG ADULTS**

Phase 1/2a trial of CTL019 in pediatric acute lymphoblastic leukemia (ALL)

Patient Characteristics

N=60

Median Age (range)

11 years (1.7-24)

Post Allogeneic Transplant

39 (65%)

Baseline ALL burden

>5% Blasts

32 (53%)

0.01-5% Blasts

12 (20%)

<0.01% Blasts

16 (27%)

CNS status at infusion

CNS1

53 (88%)

CNS2

4 (7%)

CNS3 at infusion; within 12 months

3 (5%); 17 (28%)

Patients with CNS disease prior to CTL019

- 17 patients (pts) CNS3 within 12 months of infusion
 - 10 pts had isolated CNS relapses; 7 pts had combined marrow and CNS relapses
 - Ranged from 1st to 7th relapse prior to receiving CTL019
 - 16 pts had prior CNS XRT; 13 pts had prior BMT
 - 6 pts with ocular involvement
 - 3 pts with parenchymal changes on brain and spine MRI

Neurotoxicity for patients with CNS disease prior to CTL019

Neurotoxicity Manifestation	Prior to CTL019	
	CNS involvement	No CNS involvement
Encephalopathy (Grade 2-3)	3/17 (18%)	12/43 (28%)
Seizures (Grade 2-4)	1/17 (6%)	3/43 (7%)

Neurotoxicity is not increased in patients with CNS involvement.

Outcomes for patients with CNS disease prior to CTL019

CNS cohort

- 3 pts CNS3 on Day -1 evaluation
 - 1 in complete remission (CR) at day 28
 - 1 with pseudoprogression and CR by month 3
 - 1 not evaluable (NE)
- 17 pts CNS3 within 1 year of infusion
 - 16/17 were CNS1 by CSF at day 28
 - 12/17 in continuous CR 2-31 months post-infusion (median 11 months)
 - 5 BM relapses
 - 1 without a marrow response and CNS NE

Outcomes for patients with CNS disease prior to CTL019

Entire cohort

- 98% of all pts treated have CTL019 detectable in CSF
- Lumbar punctures demonstrate CTL019 in CSF 1 year after CTL019 infusion

CAR T CELL THERAPY IN PEDIATRIC PATIENTS WITH DOWN SYNDROME AND B ALL

Characteristics of patients with Down Syndrome (DS) who received CTL019/119

Patient Characteristics

N=10

Median age at CAR T cell infusion (range)	11.5 years (3-26)
Median age at ALL diagnosis (range)	6 years (0.8-14)
Sex	2 female, 8 male
Extramedullary disease	
CNS	2 (CNS2a, CNS2b)
Non-CNS	1
Comorbidities	
Congenital cardiac defects	5
Hypothyroidism	2
Pulmonary hypertension	1

Characteristics of patients with DS who received CTL019/119

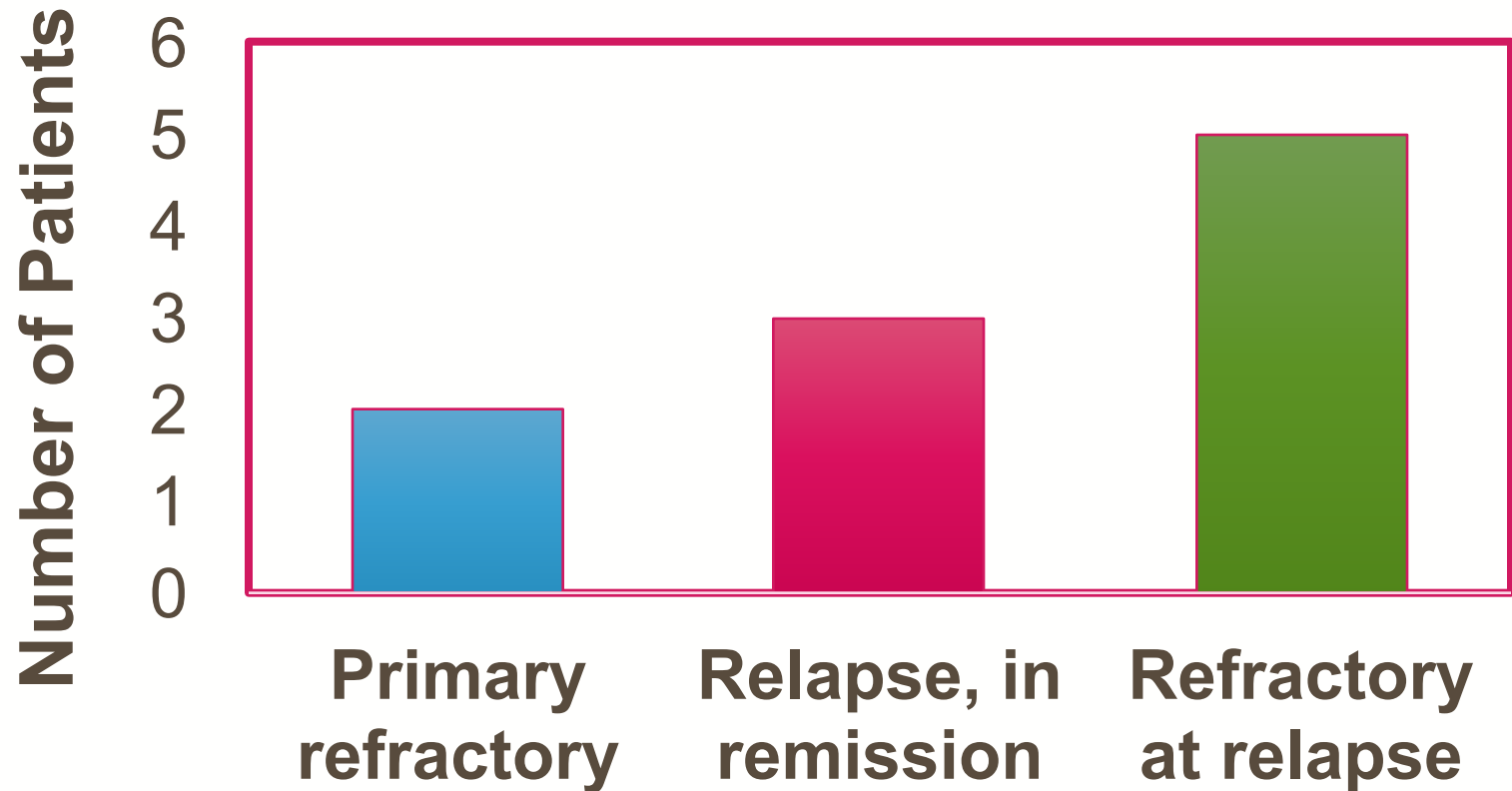
Pre-CAR treatment toxicity

Severe mucositis	3
Steroid induced diabetes	4
MTX-associated CNS toxicity	2
Kidney injury	3
Sepsis	4 (5 episodes)

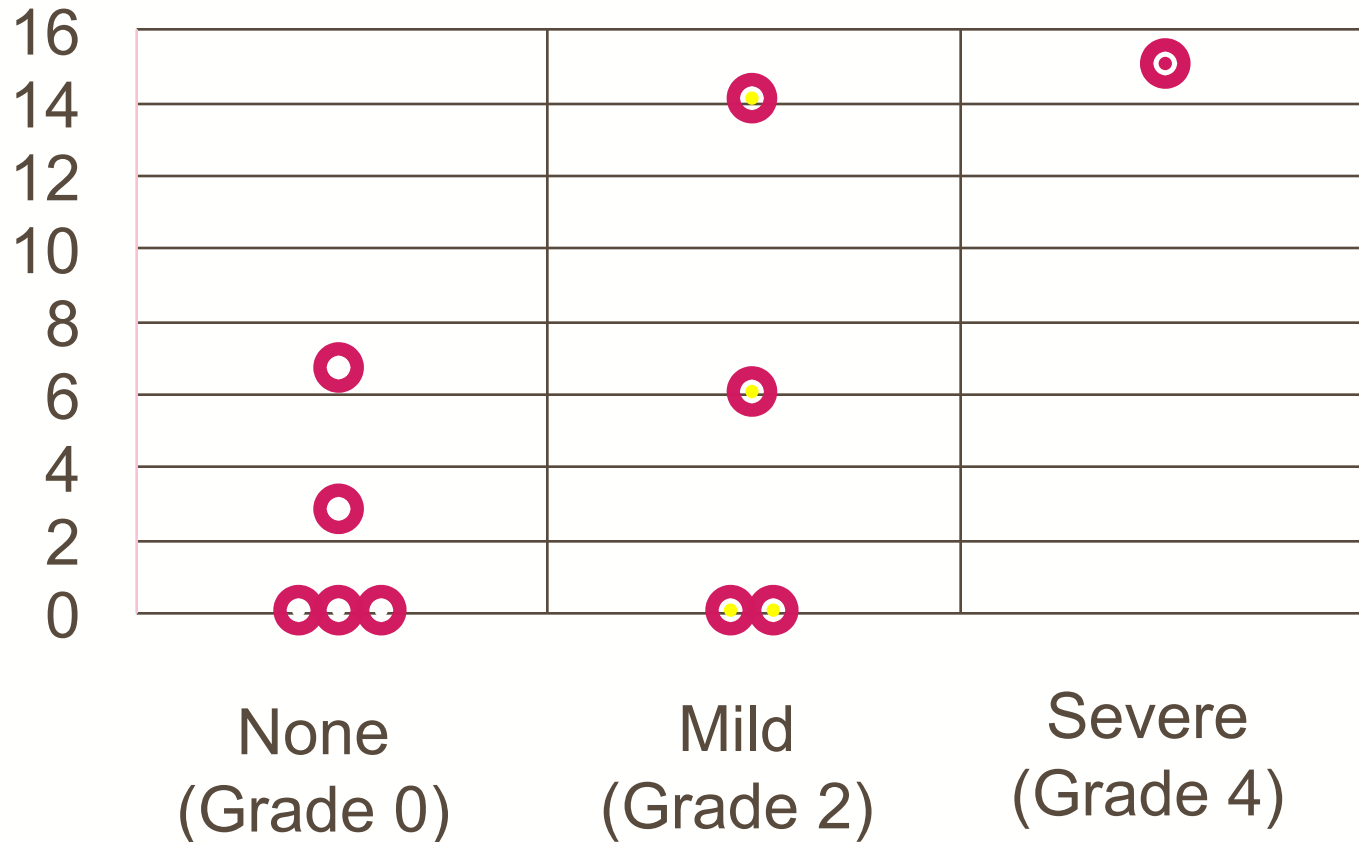
Prior cellular/immunotherapy

HSCT	2
CD19-directed CAR T cell therapy	1
CD22-directed CAR T cell therapy	1
Inotuzumab	1

Indications for treatment with CTL019/119 for patients with DS



Disease burden and cytokine release syndrome (CRS) in pts with DS



Severity of CRS

Adverse Events in pts with DS

CRS

- Fever 5
- ICU admission 1
- Vasopressor use 1
- Tocilizumab⁺ use 1
- Corticosteroid use 1
- Intubation 1

Acute Neurologic Toxicity

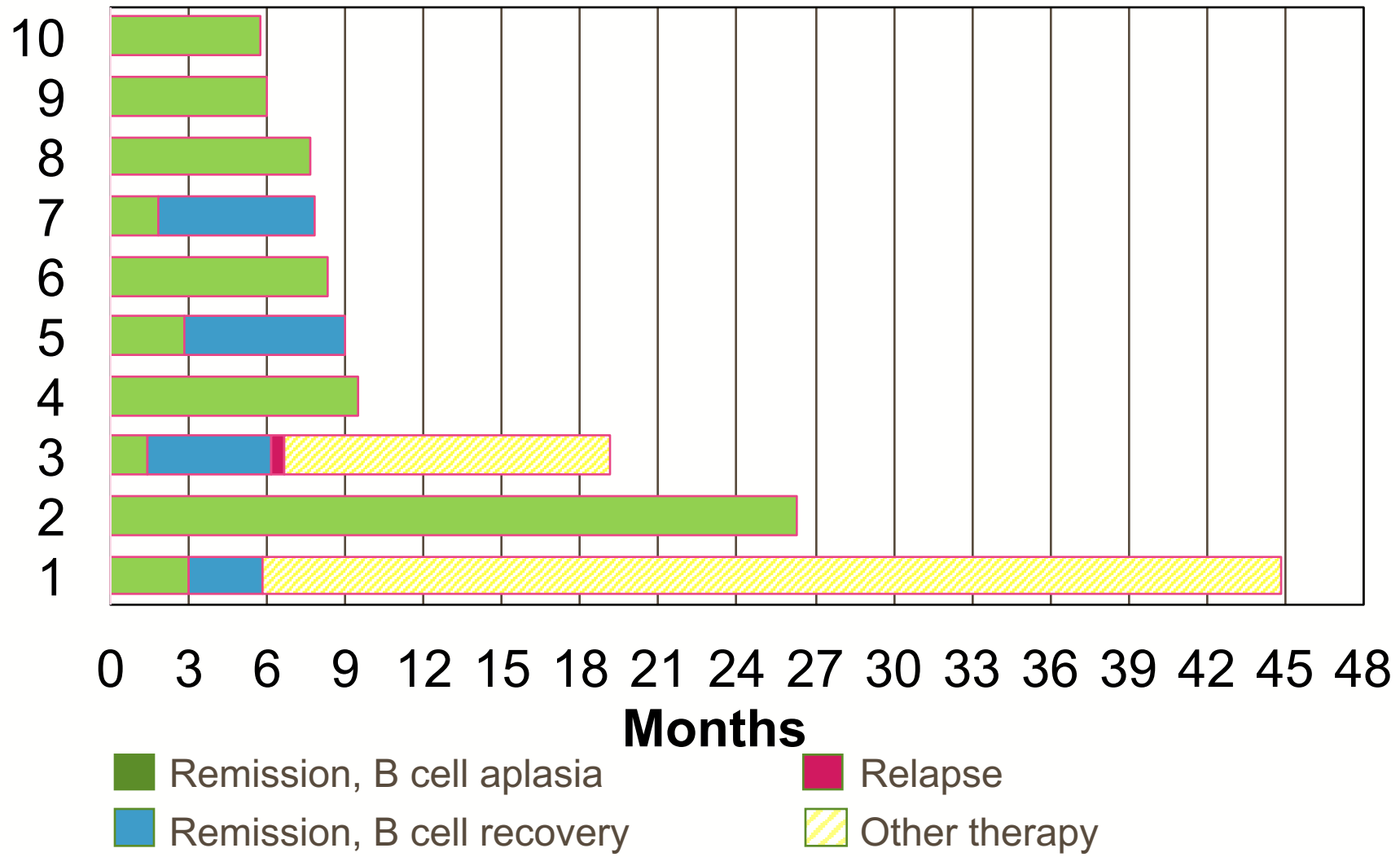
- Seizure/Syncopal episode 1

Infection

- ≤ 30 days post-infusion 0
- > 30 days post-infusion 2*

*1) Parainfluenza respiratory infection, outpatient
2) Human Metapneumovirus infection during lymphodepletion for re-infusion

Outcomes for patients with DS after receiving CAR T cell therapy



Conclusions

- CAR T cells can induce durable CNS remissions in pts with relapsed and/or refractory B ALL with CNS involvement.
- Neurotoxicity is not increased in CNS relapsed pts treated with CAR T cell therapy
- The risk of severe CRS and infectious complications in the acute period after CAR T cell infusions appears to be similar between DS and non-DS patients.
- CAR T cell therapy induced MRD and CNS negative remission in 10/10 DS pts.

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