Disclosures

- Novartis, Gilead, Celgene speaker fees

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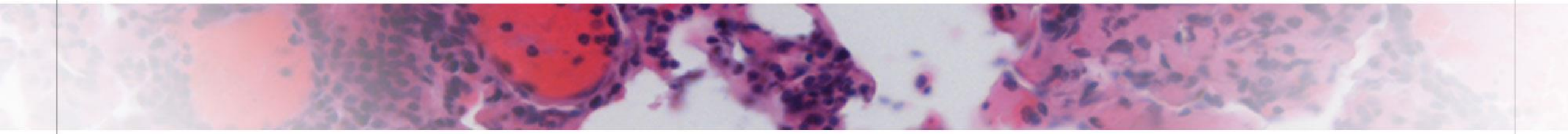


ALLCAR19: UPDATED DATA USING AUTO1, A NOVEL FAST-OFF RATE CD19 CAR IN ADULT RELAPSED/REFRACTORY B-ACUTE LYMPHOBLASTIC LEUKAEMIA

Claire Roddie, Maeve A O'Reilly, Maria A V Marzolini, Leigh Wood, Juliana Dias Alves Pinto, Mahnaz Abbasian, Ketki Vispute, Mark W Lowdell, Graham Wheeler, Joanna Olejnik, Bilyana Popova, Kim Champion, Alexia Gali, Yashma Pathak, Victoria Spanswick, Helen Lowe, John A Hartley, Farzin Farzaneh, David Linch, Martin Pule and Karl Peggs

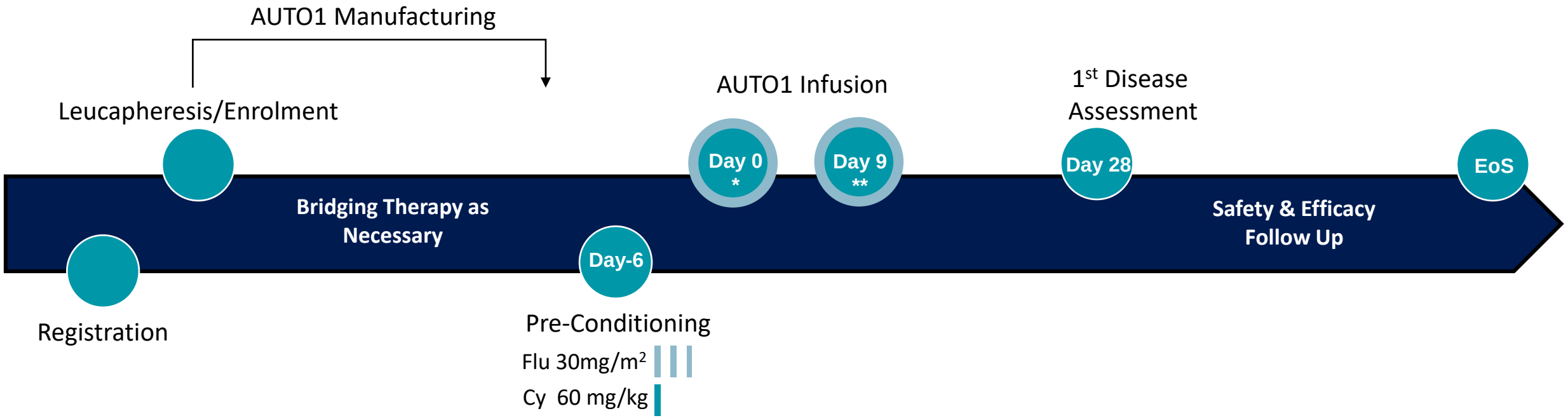
Adult B-Acute Lymphoblastic Leukemia:
Current standard of care

- Adult B-ALL prognosis is poor; long-term remission rates limited to 30-40%
  - 50% of all adult patients will relapse, with 5-year OS 7% (Fielding et al., 2007)
- Currently the only curative option for r/r ALL is allo-SCT in CR2, but <50% achieve CR2
- Blinatumomab and inotuzumab ozogamicin act as a bridge to allo-SCT (Topp et al. 2015; Kantarjian et al., 2019)
- CD19 CAR T can deliver excellent response rates but with considerable toxicity, particularly in elderly patients

- **Currently available CARs:** *high affinity CD19 binders*
- **AUTO1:** *Lower affinity CD19 binder with fast off-rate**
  - Physiological T-cell activation
  - Reduced toxicity
  - Improved engraftment
  - Potential long-term persistence, to deliver sustained responses

*Ghorashian S, Pule MA, Amrolia P et al. *Nature Medicine* 2019.

ALLCAR19 Study Design:
B-ALL arm



BM blasts ≤20% → **Day 0** Infuse 100 x 10^6 CD19 CAR T-cells → **Day 9** Infuse 310 x 10^6 CD19 CAR T-cells

BM blasts >20% → **Day 0** Infuse 10 x 10^6 CD19 CAR T-cells → **Day 9** Infuse 400 x 10^6 CD19 CAR T-cells

No G3-5 CRS/ICANS

ALLCAR19 (NCT02935257)

ALLCAR19 Study:
Endpoints and Eligibility

Primary Endpoints

- Grade 3-5 toxicity causally related to the ATIMP
- Feasibility of adequate leucapheresis & generation of AUTO1 CAR T-cells

Secondary Endpoints

- Depth of response at 1 and 3 months post ATIMP
- Persistence of CD19CAR T-cells in peripheral blood
- Incidence and duration of hypogammaglobulinaemia & B-cell aplasia
- Relapse rate, disease-free, overall survival, 1 & 2 years

Inclusion

- Age 16 to 65 years
- High risk or relapsed histologically confirmed CD19+ B-ALL following standard therapy requiring salvage in whom alternative therapies are deemed inappropriate by their treating physician

Exclusion

- CD19 negative disease
- Overt CNS involvement/isolated extramedullary disease
- Active hepatitis B, C or HIV infection
- Stem Cell Transplant patients only: no active GVHD
- Significant neurotoxicity following blinatumomab

No exclusion for prior blinatumomab or inotuzumab ozogamicin

ALLCAR19 Manufacturing:
Product Characteristics & Feasibility

Registered
n = 26

1 progressed pre-harvest

Enrolled/Leucapheresed
n = 25

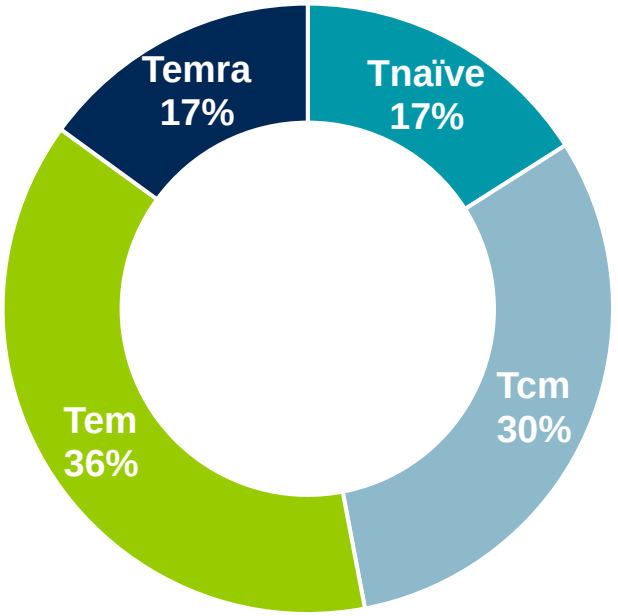
1 failed harvest

Manufactured
n = 24

4 died of PD or infection in bridging

Treated
n = 20

- 100% of successful harvests result in a QP released product
- Semi-automated closed manufacturing process was used in 18/24 products
- Advantages of closed process includes:
  - rapid, standardised manufacture
  - trend towards lower exhaustion markers
  - enrichment for Tcm and Tnaive CAR+ cells (47%)
- Mean transduction efficiency 66.5%
  - range 50 – 83%



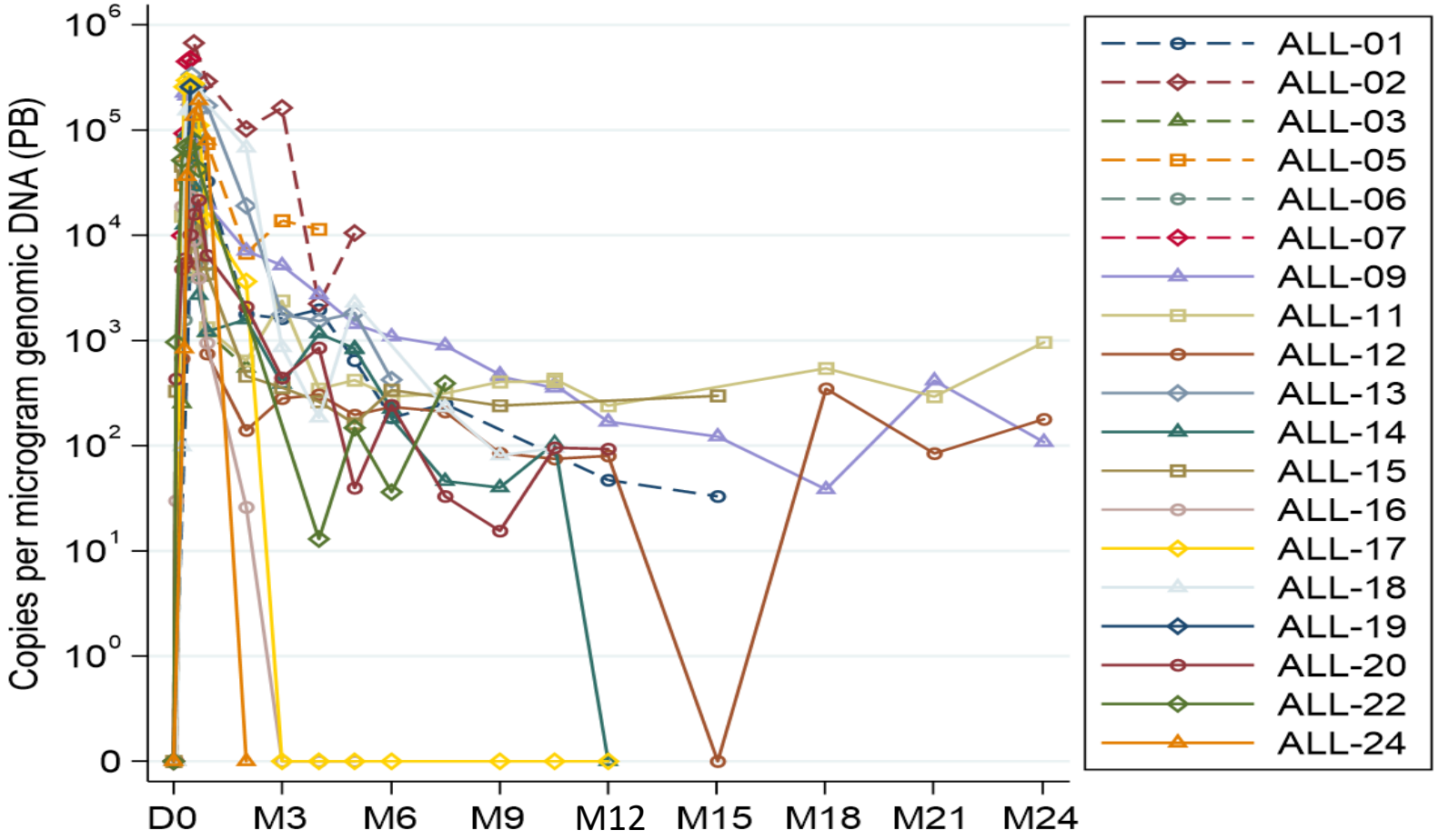
Patient Characteristics:
Treated (n=20)

Baseline Characteristics	N=20 (%)
Median age, years (range)	43 (18-62)
Gender	13M/7F
Chromosomal/Molecular status	
• Ph+ (bcr-abl)	6 (30%)
• MLL	1 (5%)
• Other	8 (40%)
• Normal	4 (20%)
• Failed	1 (5%)
Prior lines of treatment	
• Median (range)	3 (2-6)
• **Prior Inotuzumab**	**10 (50%)**
• **Prior Blinatumomab**	**5 (25%)**
• **Prior allo-HSCT**	**13 (65%)**
- sibling/haplo/VUD	4p/1p/8p

Leukemia Burden Prior to Lymphodepletion	N=20 (%)
Morphological disease	
• ≤ 5% blasts	7 (35%)
• 5 - 49% blasts	4 (20%)
• **≥ 50% blasts**	**9 (45%)**
CNS status at registration	
• CNS 1	0 (0%)
• CNS II – III	0 (0%)
Other extranodal sites	3 (16%)

20 patients have been infused (data cut off 12-Nov-2020)

AUTO1 Pharmacokinetics:
Expansion and Persistence by qPCR



ALLCAR19 qPCR PK *all patients (n=19)*		***Mueller 2017** *(responders)*
AUC D0-28 *(Geometric Mean) (Copies/µg x days)*	**750 320**	**342 732**
Half life *(Median Days)*	17 *(Range 11-29)*	14.2
Max CAR T level *(Geometric Mean) (Copies/µg)*	117 670	47 988
T (Cmax) *(Median Days)*	14 *(Range 7-21)*	

* Mueller, KT et. al. Blood 130(21) 2017

★ *ALL-16 developed a HAMA reaction to reject CAR*

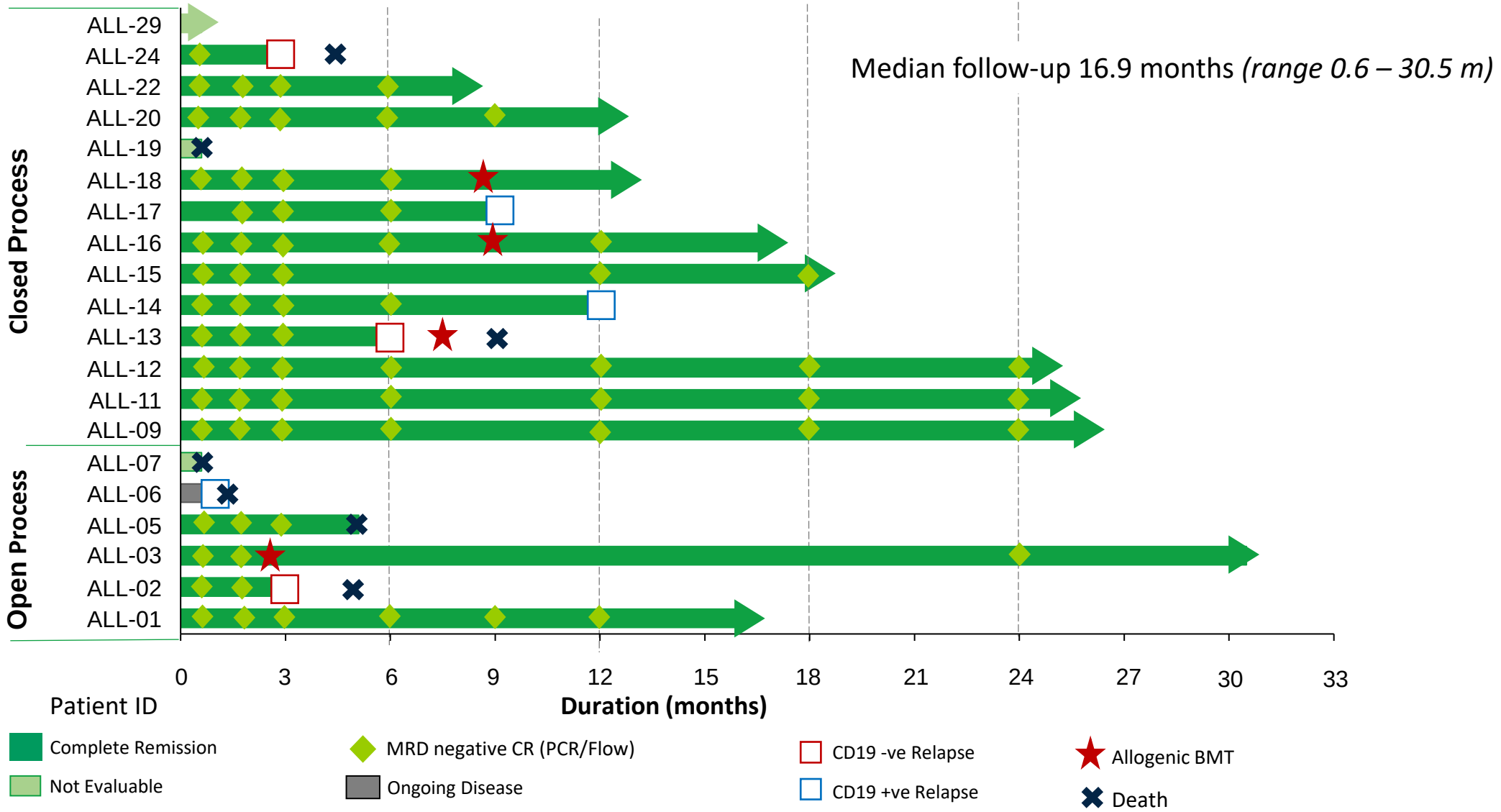
Safety Profile

CRS (Lee Criteria)	Neurotoxicity (ICANS#)	≥ Grade 3 Cytopenia	Day -6	At Day 28
• CRS (any) in 10/20 • Grade 2 in 7/20 • ≥ Grade 3 CRS in 0/20	• ICANS (any) in 4/20 • Grade 2 in 1/20 • Grade 3 in 3/20	• ≥ Grade 3 Neutropenia	7/20	8/17

- **CRS**
  - All patients who developed Grade 2 CRS had high burden B-ALL
  - Tocilizumab was used in 7/20 patients (35%)
- **Neurotoxicity (ICANS)**
  - ≥ Grade 2 ICANS was reported in 4/20 patients: all had ≥ 50% blasts; all cases were preceded by CRS
  - 3/4 cases resolved to G1 in <24h with steroids, 1/4 cases resolved to G1 in 72h with steroids
- **≥ Grade 3 neutropenia:**
  - Pre-dated treatment in 7/20 patients
  - At Day 28, 8/17 evaluable patients had ≥ Grade 3 neutropenia with most resolving by Month 2/3
- **7/20 patients died on study:**
  - 2/20 died from progressive B-ALL
  - 1/20 died post-progression from allo-transplant-related complications (VOD/sepsis)
  - 4/20 from infection: 2/4 before D28 (sepsis; invasive fungal); 1/4 at M6 in CR (MDR-pseudomonas in blood); 1/4 at M3 of COVID-19

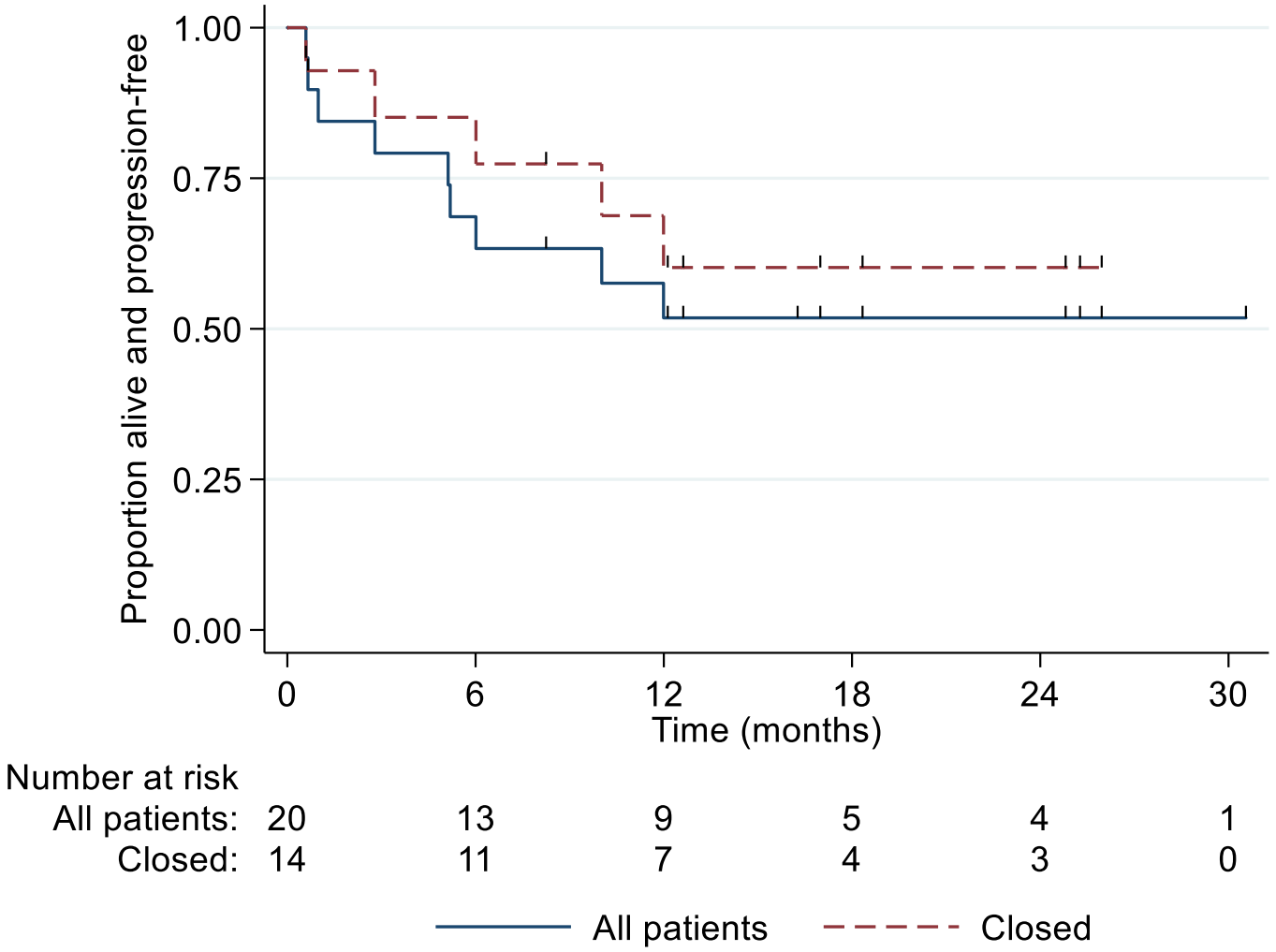
 # Immune Effector Cell Associated Neurotoxicity Syndrome
CRS & NT will be graded using the ASTCT/ASBMT Consensus Grading (Lee et al. 2019)

Efficacy & Duration



MRD < 10^{-4} by PCR or < 5 x 10^{-4} based on limits of detection of assay
Data cutoff 12-Nov-2020, Evaluable = All patients with at least M1 follow-up or death prior to Month 1.

AUTO1: Efficacy Overview



		All patients Est [95% CI]	Closed process Est [95% CI]
	N *	19	13
	ORR	84%	92%
	MRD Neg CR	84%	92%
DOR			
	Median	Not reached	Not reached
	6 months	81% [52%, 94%]	83% [48%, 96%]
	12 months	68% [39%, 85%]	65% [31%, 85%]
EFS			
	Median	Not reached	Not reached
	6 months	69% [43%, 85%]	85% [52%, 96%]
	12 months	52% [28%, 71%]	60% [29%, 81%]
OS			
	Median	Not reached	Not reached
	6 months	68% [43%, 84%]	85% [51%, 96%]
	12 months	63% [37%, 80%]	76% [43%, 92%]

N = All patients with at least M1 follow-up or RIP prior to Month 1.
Event = death or morphological relapse.
DOR, EFS and OS data are preliminary considering the small n

ALLCAR19 Study:
Extending Eligibility to Indolent NHL, HG-NHL and CLL

Cohort 1: Indolent B-NHL

(Dose = 200 million CD19 CAR T-cells)

- relapsed/refractory (r/r) Follicular Lymphoma
- r/r Mantle Cell Lymphoma
- r/r Marginal Zone Lymphoma
- ≥2 prior lines of therapy including Rituximab and anthracycline

Cohort 2: High grade B-NHL

(Dose = 200 million CD19 CAR T-cells + Pembrolizumab)

- r/r DLBCL, PMBCL, transformed FL
- not Richter's transformation
- ≥2 prior lines of therapy including Rituximab and anthracycline

Cohort 3: CLL/SLL

(Dose = 230 million CD19 CAR T-cells/ split dose)

- r/r CLL/SLL
- ≥2 prior lines of therapy including Ibrutinib/BTKi

ALLCAR19 Study:
Cohort 1:Indolent NHL- products and demographics

Registered
n = 8

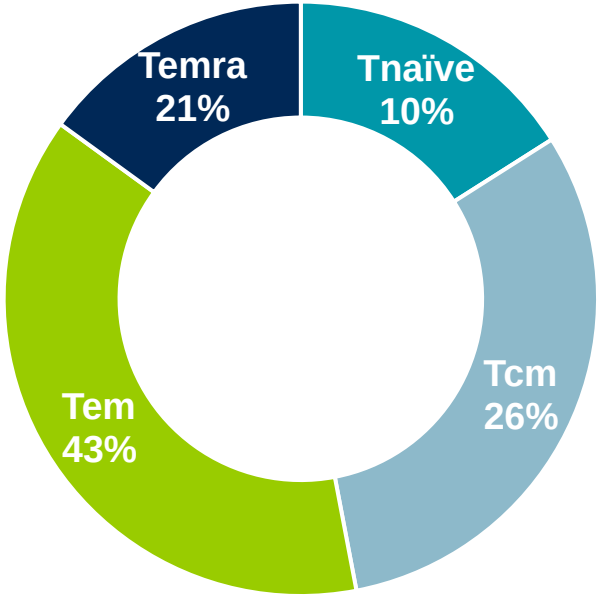
Enrolled/Leucapheresed
n =8

2 currently in manufacture

Manufactured
n = 6

2 pending infusion

Treated
n = 4



- N=6 products QP released
- Semi-automated, closed manufacturing
- Tcm/Tnaive CAR+ (36%)
- Transduction efficiency (mean 76%)

Baseline Characteristics	N=8 (%)
Median age, years (range)	57 (39 - 68)
Gender	6M/2F
Histological diagnoses	
• MCL	2 (25%)
• FL	6 (75%)
Disease Stage	
• Stage I/II	0 (0)
• Stage III/IV	8 (100%)
Prior lines of treatment	
• Median (range)	3 (2-4)
• Prior ASCT	4 (50%)
• Prior allo-HSCT	1 (12.5%)
- sibling/haplo/VUD	0p/0p/1p

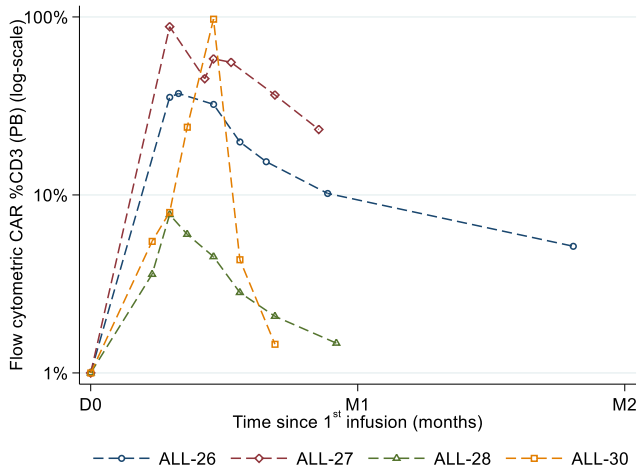
4 patients have been infused (data cut off 12-Nov-2020)

ALLCAR19 Study:
Cohort 1:Indolent NHL- toxicity, responses, engraftment

Toxicity

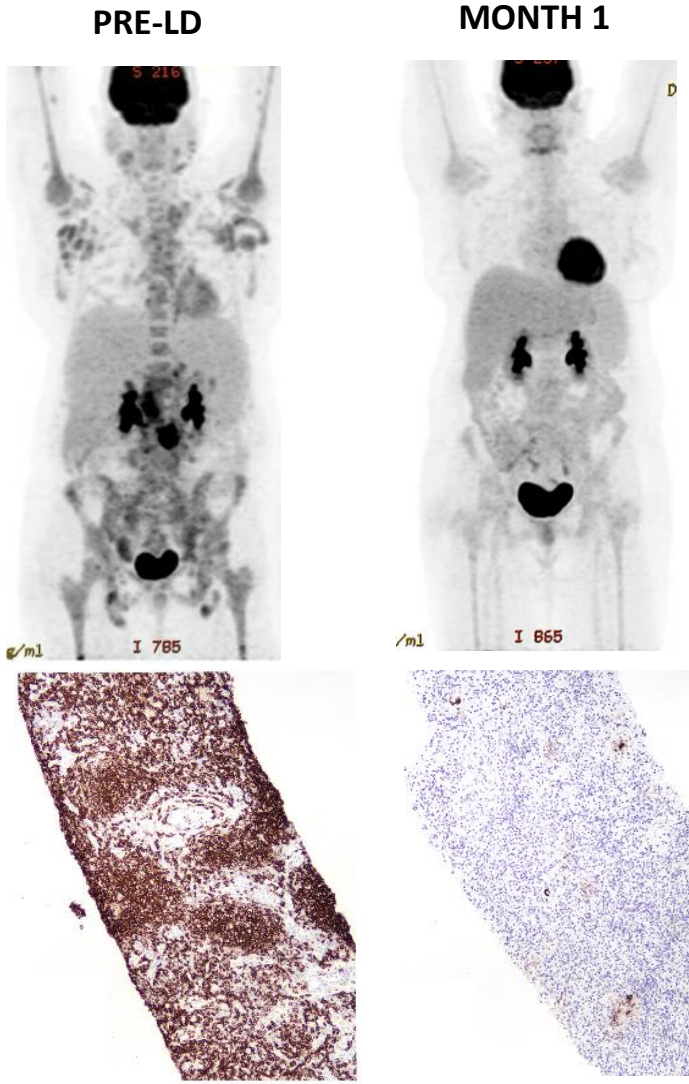
	n = 4
CRS	
any grade	3/4
≥ Grade 2	0/4
Neurotoxicity (ICANS)	
any grade	0/4
≥ Grade 3 Neutropenia	
Day -6	0/4
Day 28	0/4

Engraftment



Responses based on Lugano Criteria and IHC (CD20)

	n = 4
CMR	4/4
PR	0/4
SD	0/4
PD	0/4



Serial LN Biopsies, CD20 by IHC, Dr Teresa Marafioti, UCL

AUTO1:
Conclusions

- **Tolerable Safety Profile was observed:**
  - Despite high disease burden and despite heavily pre-treated patient population on study
    - No Grade 3 CRS was observed
    - Only 3/20 patients developed Grade 3 ICANS (rapid resolution with steroids)
- **Robust expansion and prolonged CAR persistence was observed**
- **Efficacy in adult r/r ALL:**
  - MRD negative CR was achieved in 16/19 (84%) patients at 1 month
  - EFS at 6 and 12 months is 69% and 52% respectively, in all treated patients
  - Responses are durable and ongoing CRs observed beyond 24 months, supporting the development of AUTO1 as a stand-alone therapy
- ***Promising early activity and safety has been observed in indolent NHL***

Global Phase Ib/II AUTO1 study in r/r ALL has started

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