Comprehensive Cancer Center
Tübingen-Stuttgart

Post ASH 2023 San Diego

Zelluläre Therapie und Stammzelltransplantation

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Themen

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Plenary #1:Wolff: Safety and efficacy of Axatilimab for chronic GVHD

Plenary Session

American Society *of* Hematology
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Safety and Efficacy of Axatilimab at 3 Different Doses in Patients with Chronic Graft-Versus-Host Disease (AGAVE-201)

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*†Authors contributed equally to this work.

ASH Plenary Session, December 10, 2023

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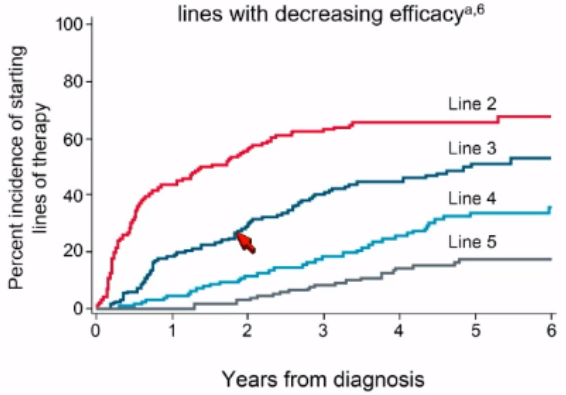
Chronic Graft-Versus-Host Disease Is a Heterogeneous Immune-Mediated Complication of allo-HSCT

- Major cause of late morbidity in 30% to 50% of patients[1-3]
- Inflammatory and fibrotic multiorgan disease[2,4]
- Significant impairment in QOL[5]

There is an unmet need for novel treatments that are well tolerated and provide rapid, durable responses as well as improved QOL

More than 50% of patients receive ≥3 therapy lines with decreasing efficacy[a,6]



allo-HSCT, allogeneic hematopoietic stem cell transplant; QOL, quality of life.
[a]A line of therapy was defined as 1 or more treatments prescribed at the same time.

1. Arai et al. *Biol Blood Marrow Transplant.* 2015;21:266-274. **2.** Arora et al. *Biol Blood Marrow Transplant.* 2016;22:449-455. **3.** Velickovic et al. *Ther Adv Hematol.* 2020;11:1-18. **4.** Wood et al. *Bone Marrow Transplant.* 2013;48:1429-1436. **5.** Yu et al. *Cancer Med.* 2023;12:3823-3833. **6.** Lee et al. *Biol Blood Marrow Transplant.* 2018;24:555-562.

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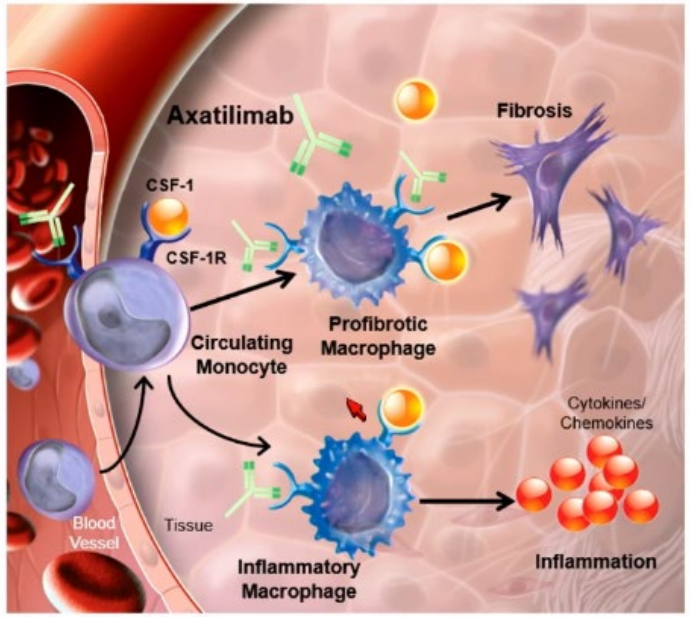
Plenary #1:Wolff: Safety and efficacy of Axatilimab for chronic GVHD

Axatilimab Targets Key Mediators of cGVHD Pathology

- CSF-1R–dependent monocytes and macrophages mediate inflammation and fibrosis[1,2]
- Axatilimab is an investigational monoclonal antibody that targets CSF-1R on monocytes and macrophages[2]
- Axatilimab has shown favorable safety and promising efficacy in recurrent/refractory cGVHD, with an ORR of 67% in the first 6 cycles[2]

cGVHD, chronic graft-versus-host disease; CSF-1R, colony-stimulating factor 1 receptor; ORR, overall response rate.

Axatilimab Mechanism of Action[1-3]



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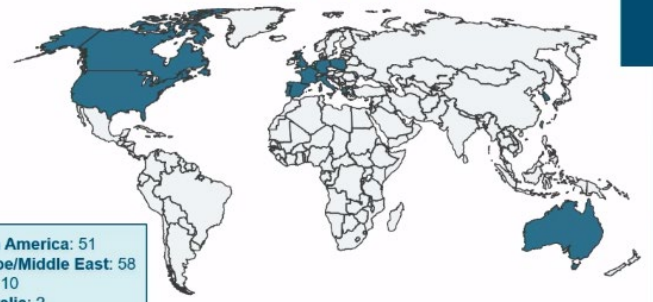
1. MacDonald et al. *Blood*. 2017;129:13-21. 2. Kitko et al. *J Clin Oncol*. 2022;41:1864-1875. 3. Jardine et al. *J Clin Invest*. 2020;130:4574-4586.

3

AGAVE-201: Study Design and Methods

Phase 2 study evaluated safety and efficacy of axatilimab in patients with cGVHD[1]

121 Global Study Sites



North America: 51
Europe/Middle East: 58
Asia: 10
Australia: 2

Randomization
3 axatilimab doses[a]
N=241

- **0.3 mg/kg Q2W** n=80
- **1.0 mg/kg Q2W** n=81
- **3.0 mg/kg Q4W** n=80

Q2W, every 2 weeks; Q4W, every 4 weeks.
[a]Patients were randomized 1:1:1 and stratified by severity of cGVHD and prior use of ibrutinib, ruxolitinib, or belumosudil.

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1. ClinicalTrials.gov. https://www.clinicaltrials.gov/study/NCT04710576. Accessed October 13, 2023.

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Plenary #1:Wolff: Safety and efficacy of Axatilimab for chronic GVHD

AGAVE-201: Study Design and Methods

Key eligibility criteria

- Age ≥2 years with ≥2 prior lines of systemic therapy
- Active cGVHD defined per 2014 NIH Consensus Criteria[1]
- Concomitant use of corticosteroids (65%), calcineurin inhibitors (28%), or mTOR inhibitors (12%) was allowed but not required
- No additional systemic cGVHD therapy was allowed

Primary endpoint

- ORR in the first 6 cycles as defined by NIH 2014 Consensus Criteria[1]
- Endpoint was met if lower bound of 95% CI >30%

Secondary and exploratory endpoints

- Clinically meaningful improvement in mLSS (≥7 points)
- Organ-specific response rates, DOR, FFS, OS
- Safety

DOR, duration of response; FFS, failure-free survival; mLSS, modified Lee Symptom Scale; mTOR, mammalian target of rapamycin; NIH, National Institutes of Health; OS, overall survival.

1. Jagasia et al. *Biol Blood Marrow Transplant.* 2015;21:389-401.

Baseline Characteristics (ITT Population)

Patient characteristic	Total cohort (N=241)
Age, median (min, max), y	53 (7, 81)
Sex, male, n (%)	151 (63)
Race, White, n (%)	200 (83)
Time from cGVHD diagnosis to randomization, median (max), y	4 (18)
Patients with severe disease, n (%)	192 (80)
Number of organs involved at baseline, median (max)	4 (8)
≥ 4 organs involved, n (%)	130 (54)
Number of prior systemic cGVHD therapies, median (max)	4 (15)
Refractory to last prior cGVHD treatment,[a] n (%)	132 (55)
Prior ruxolitinib, ibrutinib, and/or belumosudil, n (%)	204 (85)
Prior ruxolitinib, n (%)	179 (74)
Prior ibrutinib, n (%)	75 (31)
Prior belumosudil, n (%)	56 (23)

Patient characteristics were well balanced among cohorts

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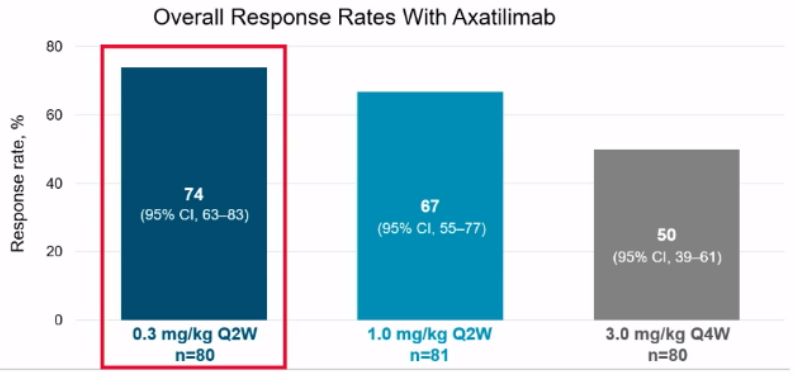
ITT, intention to treat. [a]Defined as patients with a best response to last prior treatment of no change or progressive disease reported at baseline.

Plenary #1:Wolff: Safety and efficacy of Axatilimab for chronic GVHD

Primary Efficacy Endpoint[a] Met in All Cohorts

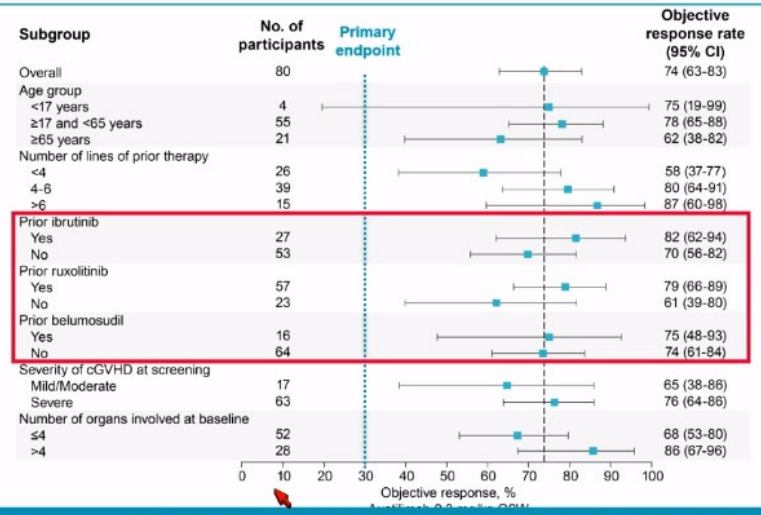


	0.3 mg/kg Q2W n=80	1.0 mg/kg Q2W n=81	3.0 mg/kg Q4W n=80
Time to response, median months (range)	1.7 (0.9–8.1)	1.9 (0.9–8.6)	1.4 (0.9–5.6)
Response maintained for ≥12 months, % (95% CI)	60 (43–74)	60 (43–74)	53 (30–71)

Q2W, every 2 weeks; Q4W, every 4 weeks.
[a]Primary endpoint was overall response rate in the first 6 cycles as defined by NIH 2014 Consensus Criteria.[1]

1. Lee et al. *Biol Blood Marrow Transplant.* 2015;21:984-999.

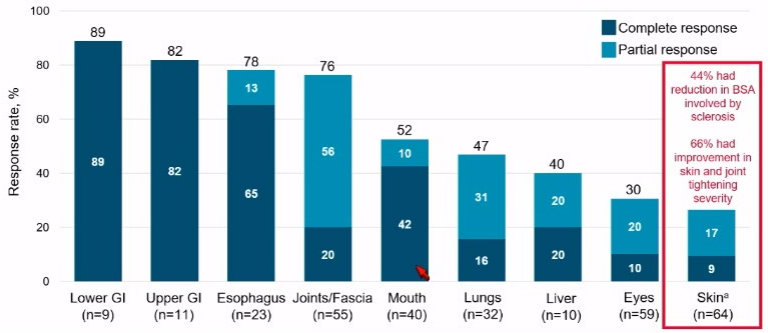
Efficacy Across Subgroups in 0.3 mg/kg Q2W



High response rates (≥75%) were seen in patients who received prior FDA-approved therapies

Q2W, every 2 weeks.

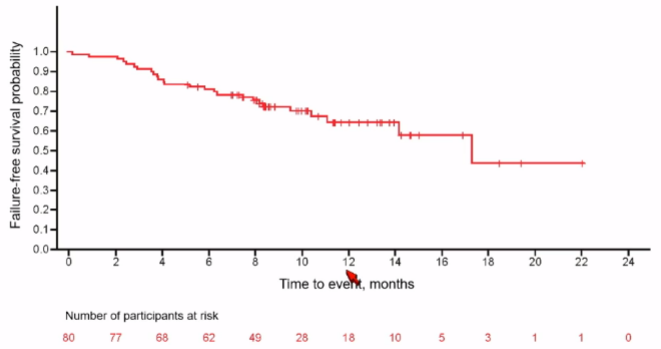
Organ Responses in 0.3 mg/kg Q2W



Responses were notable in fibrosis-dominated organs, including esophagus (78%), joints and fascia (76%), lung (47%), and skin (27%)

BSA; body surface area; GI, gastrointestinal; Q2W, every 2 weeks. [a]Due to rounding, complete response and partial response numbers may not add up to total response rate.

Failure-free Survival[a] in 0.3 mg/kg Q2W



Median FFS was 17.3 (95% CI, 14.2–NE) months

NE, not estimable; Q2W, every 2 weeks.
[a]Defined as time from randomization to death or new systemic cGVHD therapy, where axatilimab dose increase is not considered new therapy.

Plenary #1:Wolff: Safety and efficacy of Axatilimab for chronic GVHD

Axatilimab Safety Profile

	Axatilimab 0.3 mg/kg Q2W n=79	Axatilimab 1.0 mg/kg Q2W n=81	Axatilimab 3.0 mg/kg Q4W n=79
Axatilimab dose changes owing to AE, n (%)			
Discontinuation	5 (6.3)	18 (22.2)	14 (17.7)
Dose decrease	5 (6.3)	6 (7.4)	13 (16.5)
Any grade AE in ≥20% of total patients			
Fatigue	18 (22.8)	16 (19.8)	21 (26.6)
Headache	15 (19.0)	14 (17.3)	16 (20.3)
Periorbital edema	2 (2.5)	19 (23.5)	23 (29.1)
COVID-19	13 (16.5)	18 (22.2)	11 (13.9)
Laboratory-based abnormalities			
AST increase	11 (13.9)	31 (38.3)	43 (54.4)
CPK increase	9 (11.4)	26 (32.1)	49 (62.0)
Lipase increased	9 (11.4)	21 (25.9)	39 (49.4)
Lactate dehydrogenase increased	11 (13.9)	22 (27.2)	32 (40.5)
ALT increase	10 (12.7)	18 (22.2)	31(39.2)
Amylase increase	3 (3.8)	10 (12.3)	34 (43.0)
At least 1 related Grade ≥3 AE, n (%)	14 (17.7)	28 (34.6)	37 (46.8)
Fatal AE	1 (1.3)[a]	7 (8.6)[b]	6 (7.6)[c]

Conclusions

- Axatilimab at 0.3 mg/kg Q2W is highly effective and has a manageable safety profile in recurrent/refractory cGVHD
- Rapid and durable responses were documented in all organs and patient subgroups
- Significant reduction of symptom burden was reported by most patients, including those with fibrotic cGVHD manifestations
- Adverse events were mostly low grade, reversible, and increased with higher doses
- Unique mechanism of action may represent a new therapeutic strategy in cGVHD

Q2W, every 2 weeks.

#425 Othman: Benefit of allogeneic HCT in CR1 in NPM-1 mutated AML restricted to MRD positivity after Induction

The benefit of allogeneic transplant in 1st complete remission in *NPM1* mutated AML with or without *FLT3* ITD is restricted to those testing MRD positive after induction – an analysis of the UK NCRI AML17 and AML19 studies

J Othman*, N Potter*, A Ivey, J Jovanovic, SD Freeman, A Gilkes, I Thomas, S Johnson, J Canham, J Cavenagh, P Kottaridis, C Arnold, UM Overgaard, M Dennis, C Wilhelm-Benartzi, R Dillon*, NH Russell*

On behalf of the UK NCRI AML working group

*equal contribution

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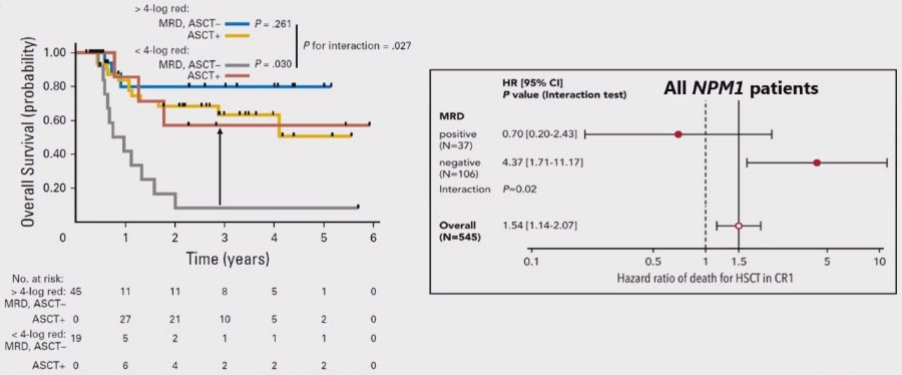
Background

- In ELN 2022, *NPM1* mutated (*NPM1*^{mut}) AML is:
  - Generally favorable risk
  - Intermediate risk if co-mutated *FLT3* ITD
  - Adverse risk if adverse karyotype
- The role of allogeneic transplant in first remission (CR1-allo) in *NPM1*^{mut} AML remains controversial, with significant variation in practice worldwide

#425 Othman: Benefit of allogeneic HCT in CR1 in NPM-1 mutated AML restricted to MRD positivity after Induction

Post induction MRD may identify patients who benefit from CR1-allo



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Balsat *et al. JCO.* 2017;35(2)
Fenwarth L et al. Blood. 2021;137(4)

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Methods

Aim – describe the impact of CR1-allo in *NPM1*^{mut} AML according to MRD status and baseline clinical and molecular features

- Data from NCRI AML17 (2009-2014) and AML19 (2015-2020)
  - Sequential prospective RCTs of intensive chemotherapy for younger adults with newly diagnosed AML
  - Both prior to the availability of midostaurin and *FLT3* ITD MRD assays
- *NPM1* MRD performed by RT-qPCR at the same reference laboratory in both trials

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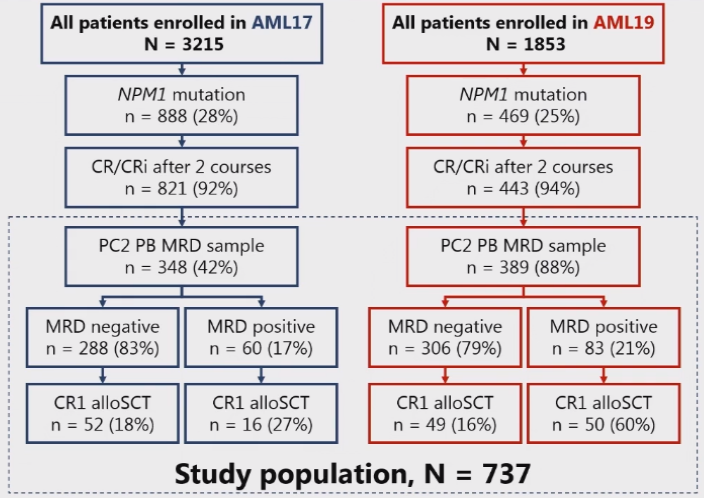

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Characteristic	All N = 737	AML17 N = 348	AML19 N = 389
Median age (range)	52 (6 - 71)	52 (6 - 70)	52 (18 - 71)
Female	406 (55%)	187 (54%)	219 (56%)
Prior myeloid malignancy	30 (4.1%)	19 (5.5%)	11 (2.8%)
Previous chemo/radiotherapy	11 (1.5%)	5 (1.4%)	6 (1.5%)
Adverse cytogenetic risk	9 (1.2%)	4 (1.1%)	5 (1.3%)
***FLT3* ITD**	286 (39%)	139 (40%)	147 (38%)
Low allelic ratio	174 (61%)	75 (54%)	99 (68%)
High allelic ratio	111 (39%)	64 (46%)	47 (32%)
***FLT3* TKD**	121 (17%)	53 (15%)	68 (17%)
Induction regimen			
DA, ADE or CPX-351	549 (74%)	348 (100%)	201 (52%)
FLAG-Ida	188 (26%)	0 (0%)	188 (48%)
Gemtuzumab with induction	378 (52%)	116 (34%)	262 (67%)
Allogeneic transplant	297 (40%)	140 (40%)	158 (41%)
Transplant in CR1	167 (23%)	68 (20%)	99 (25%)
Transplant at other stage	131 (18%)	72 (21%)	59 (15%)
No transplant	439 (60%)	208 (60%)	231 (59%)

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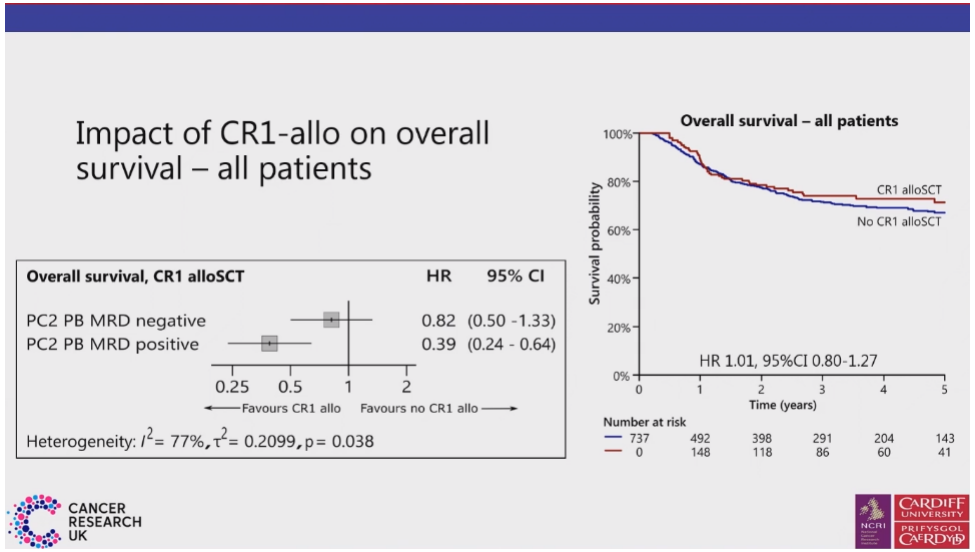
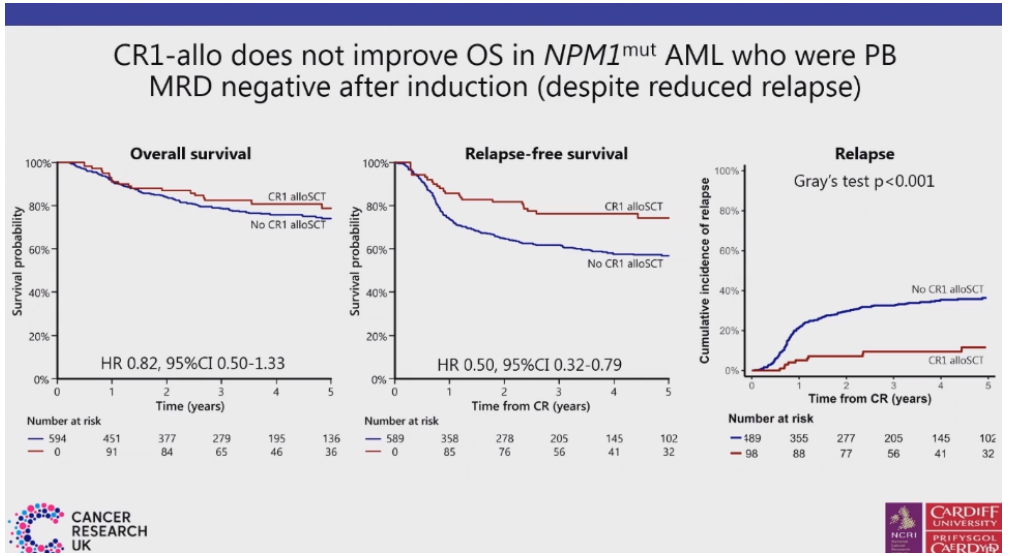
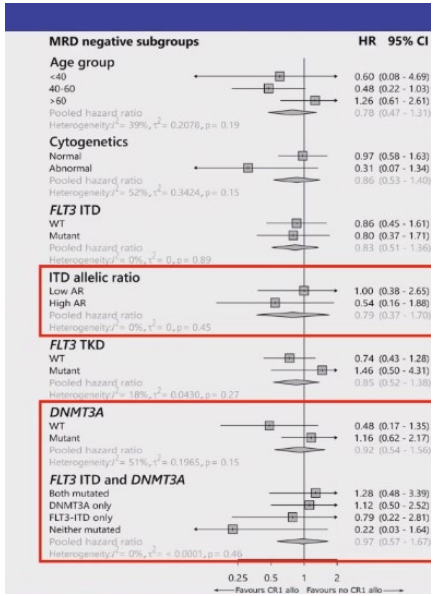
#425 Othman: Benefit of allogeneic HCT in CR1 in NPM-1 mutated AML restricted to MRD positivity after Induction

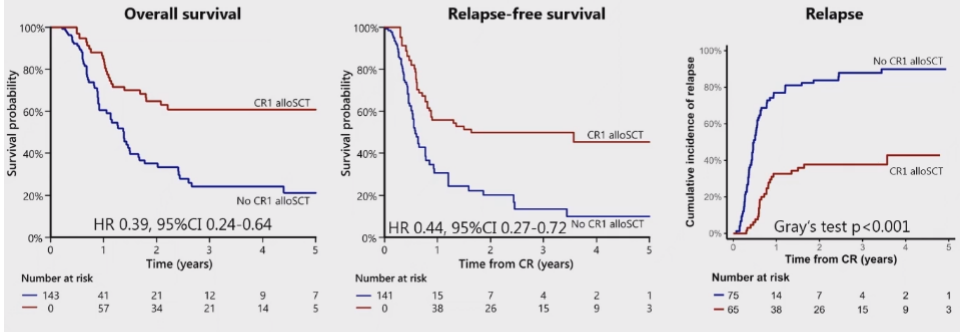




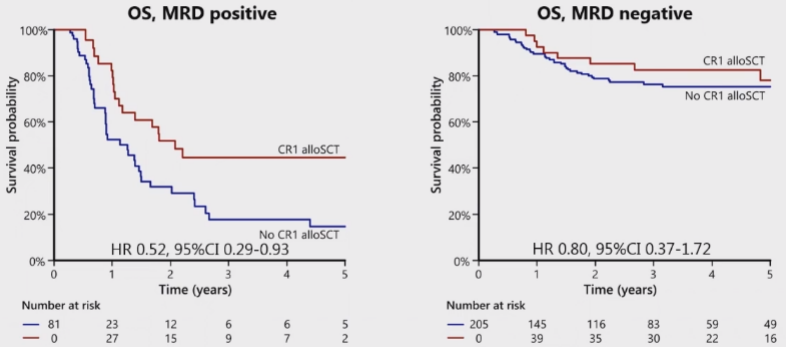


#425 Othman: Benefit of allogeneic HCT in CR1 in NPM-1 mutated AML restricted to MRD positivity after Induction

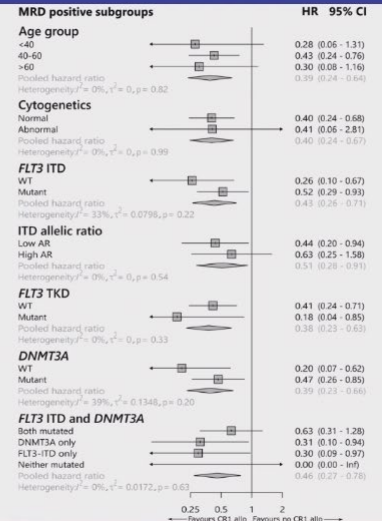
CR1-allo improves OS in *NPM1*^{mut} AML who were PB MRD positive after induction



Results in *NPM1*^{mut} + *FLT3* ITD patients were similar to the overall population



No subgroup heterogeneity in CR1-allo benefit for MRD positive patients

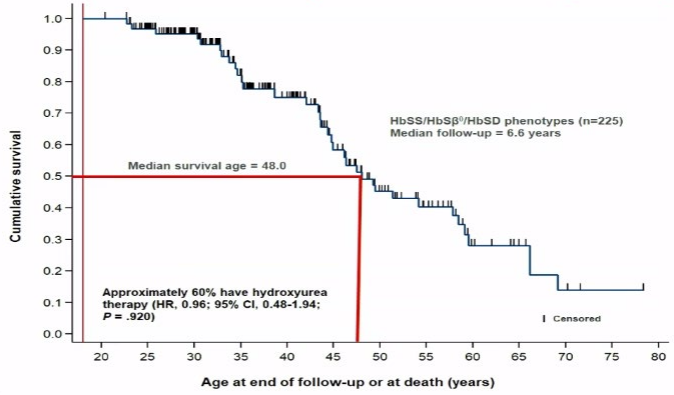


Conclusions

- Molecular MRD after induction chemotherapy identifies patients with *NPM1*^{mut} AML who benefit from allogeneic transplant in first remission
- Patients achieving MRD negativity in blood after second induction show no survival benefit from CR1 transplant, even if *FLT3* ITD co-mutated

#LBA#4: RIC Haploidentical Marrow Transplantation in Adults with Severe Sickle Cell Disease CTN 1507

Adults with sickle cell disease have a shortened life-span median survival for HbSS: 48.0 years with no change in 25 years



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DeBaun M et al. Blood, 2019. 133(6): 615-617.

For children with SCD, excellent outcomes with matched sibling donor (MSD) allogeneic hematopoietic stem cell transplantation (allo-HSCT) for over 3 decades

- Non-myeloablative HLA-MSD transplant is preferred for adults with severe SCD
- How do we address the unmet needs, namely
  - Children with strokes with no MSD
  - Adults with severe disease have organ dysfunction, typically excluded
  - Only ~8-14% of eligible patients have an HLA-MSD

Need less toxicity and alternative donors!

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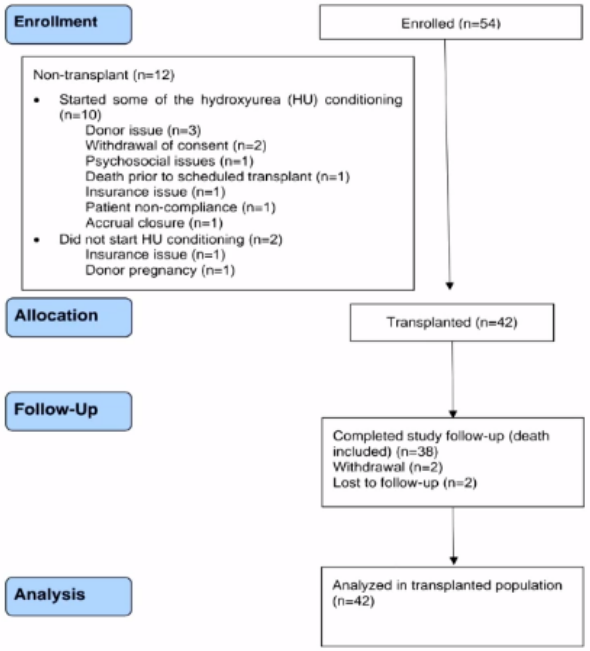
Blood, 16 March 2017. Volume 129, Number 11

#LBA#4: RIC Haploidentical Marrow Transplantation in Adults with Severe Sickle Cell Disease CTN 1507

Participant disposition and follow-up

- Participant demographics
  - 59.3% are male
  - 92.6% are Black
  - 3.7% are Hispanic
- Participant visit delays and cancellations due to COVID-19



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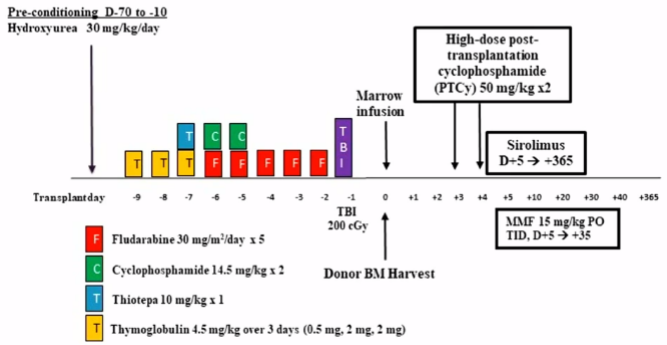
Common Conditioning Platform for Haplo-BMT



Study design

- This is a Phase II, single-arm, multi-center trial designed to estimate the efficacy and toxicity of haploidentical bone marrow transplantation (BMT) in patients with sickle cell disease (SCD).
- Eligibility criteria
  ≥ 2 episodes of ACS in the preceding 2 years
  ≥ 3 episodes of VOC in the preceding 2 years
  ≥ 8 transfusions per year for ≥ 1 year to prevent SCD-related complications
  Tricuspid valve regurgitant jet (TRJ) ≥ 2.7 m/sec

Demographic and clinical characteristics of participants

Variable	≥15 yrs(n=42)	Percentage (%)
Age at transplant, median (IQR)	22.8 (15.5-43.2)	n/a
Follow-up time (months), median (IQR) (n=42)	24.4 (7.0-45.8)	n/a
SCD genotype (SS and Sβ⁰-thalassemia), n (%)	47 (54)	87%
Indications for transplant (n%): Recurrent vaso-occlusive pain episodes Acute chest syndrome Overt stroke Chronic RBC transfusion Elevated TRJ velocity ≥2.7 m/sec	 25 (59.5%) 7(16.7%) 6 (14.3%) 16 (38.1%) 1 (2.4%)	 59.5 16.7 14.3 38.1
Participants achieved the intended 30 mg/kg of HU preconditioning	13	31
HLA Match Score	4/8 5/8 6/8	75.9% 14.8% 9.3%

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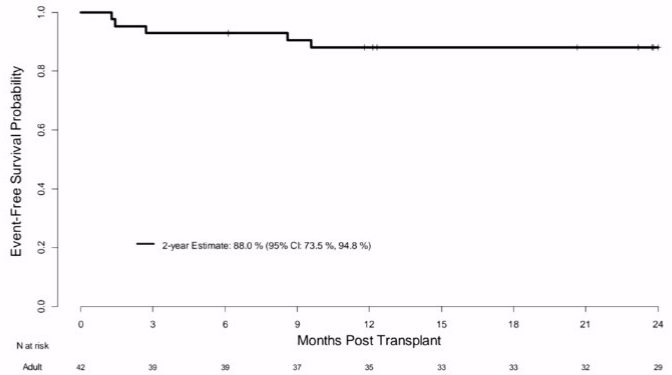
#LBA#4: RIC Haploidentical Marrow Transplantation in Adults with Severe Sickle Cell Disease CTN 1507

Event-free survival was 88% at 2 years post-transplant



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Engraftment

- Cumulative incidence of neutrophil recovery at 42 days
  - 92.9% (95% CI: 77.4%, 97.9%)
- Cumulative incidence of platelet recovery to 50k was
  - at 60 days 88.1% (95% CI: 72.6%, 95.1%)
  - at 100 days 92.9% (95% CI: 77.4%, 97.9%)
- **On Day 28, 88.1% achieved full donor chimerism (donor >95%), and 4.8% had low chimerism (donor <5%)**

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Maximum acute and chronic GVHD severity post-transplant

	Adult	
	N	%
Maximum Acute GVHD Grade by Algorithm		
Grade 0, no aGVHD	23	54.8
Grade 1	8	19.0
Grade II	9	19.0
Grade III	2	4.8
Grade IV	0	0.0
Total transplanted	**42**	**100.0**

	Adult	
	N	%
Maximum Severity of Chronic GVHD		
None, no chronic GVHD	33	78.6
Mild	3	7.1
Moderate	3	7.1
Severe	3	7.1
Total transplanted	**42**	**100.0**

- The Day 100 Grades II-IV acute GVHD rate was 26.2% (95% CI: 14.0%, 40.2%).
- The Day 100 Grades III-IV acute GVHD rate was 4.8% (95% CI: 0.9%, 14.4%).
- Cumulative incidence plot for 2-year chronic GVHD rate estimate of 22.4% (95% CI: 10.9, 36.4%) at two-years post-transplant

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Deaths on study

Study ID	Age at Transplant (years)	Days post-transplant	Cause of Death
#1	28	Day – 63 (23 days after the start of hydroxyurea therapy, prior to transplant)	Intracranial hemorrhage from a left posterior inferior cerebellar artery with evidence of subarachnoid hemorrhage. Progression of ischemic changes involving the left temporoparietal lobes with multifocal bilateral cerebral infarctions and vasospasm
#2	29	261	Organ failure after a febrile episode
#3	18	291	Acute respiratory distress syndrome from COVID-19
#4	26	969 – (> 2 years post-transplant will not count toward the primary endpoint of two-year EFS)	Hemorrhagic shock from SVC rupture. Secondary to ARDS from COVID pneumonia

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#LBA#4: RIC Haploidentical Marrow Transplantation in Adults with Severe Sickle Cell Disease CTN 1507

Participants who received Nonmyeloablative Haplo-BMT had more overlapping co-morbidities compared to those who received gene therapy (LentiGlobin) and gene editing (Exagamglogene Autotemcel)

Variable	BMT CTN 1507	Vanderbilt (VGC²)	LentiGlobin	CRISPR/Cas9
Study	Phase-2 study	Phase-2 study	Phase 1-2	Phase-3 study
Donor availability	>90%	>90%	43/51	Unknown
Conditioning	Non-myeloablative	Non-myeloablative	Myeloablative	Myeloablative
Sites	Multicenter	Multicenter	Multicenter	Multicenter
Age at transplant, median (IQR)	22.8 (15.5-43.2)	24.9 (20.4 – 31.3)	24 (12–38)	21.2 (12-34)
Lag-time from enrollment to transplant	1-2 months	1-2 months	6-12 months?	6-12 months?
Evaluable for study end-points (n)	42	38	35	20
Follow-up time (months), median (IQR) (n=42)	24.4 (7.0-45.8)	37.2 (20.4-56.4)	17.3 (3.7-37.6).	21.8 (12.3-41.4)
Study End-points	Graft failure, death	Graft failure, death	VOC	VOC and hospitalization

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N Engl J Med. 2022 Feb 17;386(7):617-628
Blood (2023) 142 (Supplement 1): 1052

Haplo-BMT is as effective as gene therapy and gene editing in improving donor engraftment and hemoglobin level at 1/5th the cost

Variable	BMT CTN1507	Vanderbilt (VGC²)	LentiGlobin	CRISPR/Cas9
SCD genotype (SS and Sβ⁰-thal), n (%)	92.5%	36 (94.7)	35 (100%)	20 (100%)?
Median time to neutrophil engraftment (days)	25.5	21.0	20	27
Median time to platelet engraftment (days)	34.5	32.5	36	34.5
Mean Hemoglobin gm/dL (%) post-transplant	13.5	>13.0	11	≥11.0 g/dL
EFS OS	88% 95%	94.7% 94.7%	85% (HbA^{T87Q}) 96%	90% 100%?
Cost in US Dollars	$200-400,000	$200-400,000	$3.1 million	$2.2 million

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N Engl J Med. 2022 Feb 17;386(7):617-628
Blood (2023) 142 (Supplement 1): 1052

Conclusion

- Reduced intensity haploidentical-BMT in adults with SCD shows durable donor engraftment at 2 years with low mortality.
- The 2-year EFS 88% and OS 95% are comparable to that reported after MSD myeloablative BMT.
- These results support haploidentical BMT with PTCy as a suitable and tolerable curative therapy for adults with SCD and severe end-organ toxicity such as stroke and pulmonary hypertension, a population typically excluded from participating in myeloablative gene therapy and gene editing trials.

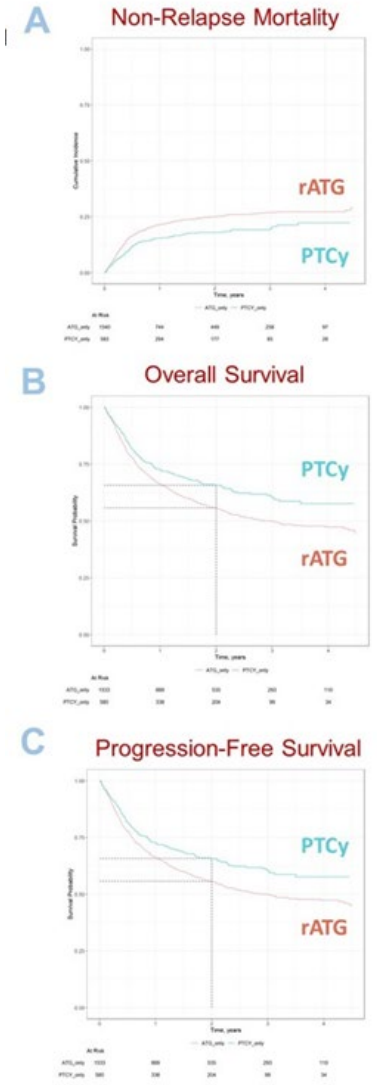
#2179 and #3558 Penack: Post Cy or ATG as GVHD Prophylaxis in mismatched and matched unrelated stem cell transplantation EBMT

Mismatched MUD

Table 1

	ATG_only (N=1540)	PTCy_only (N=583)	Total (N=2123)	p value
Patient Gender				0.48[1]
Male	893 (58.0%)	348 (59.7%)	1241 (58.5%)	
Female	647 (42.0%)	235 (40.3%)	882 (41.5%)	
Age at Transplant, yrs				< 0.01[2]
median [Q1, Q3]	56.1 (44.7, 63.8)	51.7 (40.0, 62.2)	55.3 (43.6, 63.3)	
[Min, Max]	18.1 - 80.4	18.2 - 79.2	18.1 - 80.4	
Age at Diagnosis, yrs				< 0.01[2]
median [Q1, Q3]	53.9 (42.6, 62.1)	49.0 (37.0, 60.3)	52.8 (40.6, 61.6)	
[Min, Max]	10.0 - 79.9	10.6 - 78.6	10.0 - 79.9	
Missing count	2	0	2	
Karnofsky =>90				0.30[1]
< 90	375 (25.5%)	132 (23.3%)	507 (24.9%)	
>= 90	1094 (74.5%)	434 (76.7%)	1528 (75.1%)	
Missing count	71	17	88	
HCT Comorbidity Index				0.35[1]
0	716 (51.2%)	265 (49.6%)	981 (50.8%)	
1-2	324 (23.2%)	115 (21.5%)	439 (22.7%)	
>=3	359 (25.7%)	154 (28.8%)	513 (26.5%)	
Missing count	141	49	190	
DRI				0.14[1]
Low	128 (8.3%)	56 (9.6%)	184 (8.7%)	
Int	975 (63.3%)	362 (62.1%)	1337 (63.0%)	
High	355 (23.1%)	146 (25.0%)	501 (23.6%)	
Very high	82 (5.3%)	19 (3.3%)	101 (4.8%)	
Hematological Malignancies				
AML	768 (49.9%)	257 (44.1%)	1025 (48.3%)	
MDS	215 (14.0%)	83 (14.2%)	298 (14.0%)	
ALL	187 (12.1%)	86 (14.8%)	273 (12.9%)	
MPN	142 (9.2%)	36 (6.2%)	178 (8.4%)	
MDS & MPN overlap	49 (3.2%)	16 (2.7%)	65 (3.1%)	
CML	31 (2.0%)	16 (2.7%)	47 (2.2%)	
NHL	103 (6.7%)	55 (9.4%)	158 (7.4%)	
Hodgkins	30 (1.9%)	26 (4.5%)	56 (2.6%)	
CLL	15 (1.0%)	8 (1.4%)	23 (1.1%)	
Transplant Year				< 0.01[1]
2018	487 (31.6%)	145 (24.9%)	632 (29.8%)	
2019	455 (29.5%)	160 (27.4%)	615 (29.0%)	
2020	359 (23.3%)	172 (29.5%)	531 (25.0%)	
2021	239 (15.5%)	106 (18.2%)	345 (16.3%)	
Myeloablative Conditioning				0.49[1]
No	678 (44.2%)	247 (42.5%)	925 (43.7%)	
Yes	857 (55.8%)	334 (57.5%)	1191 (56.3%)	
Missing count	5	2	7	
TBI				< 0.01[1]
No	1320 (85.7%)	464 (79.6%)	1784 (84.0%)	
Yes	220 (14.3%)	119 (20.4%)	339 (16.0%)	
GVHD Prevention Regimen				
CSA+MTX based	881 (57.2%)	3 (0.5%)	884 (41.6%)	
CSA+MMF based	446 (29.0%)	313 (53.7%)	759 (35.8%)	
MMF+TACRO/SIRO based	95 (6.2%)	174 (29.8%)	269 (12.7%)	
CSA based	47 (3.1%)	15 (2.6%)	62 (2.9%)	
TACRO/SIRO based	4 (0.3%)	54 (9.3%)	58 (2.7%)	
MTX+TACRO based	54 (3.5%)	0 (0.0%)	54 (2.5%)	
Other	13 (0.8%)	24 (4.1%)	37 (1.7%)	

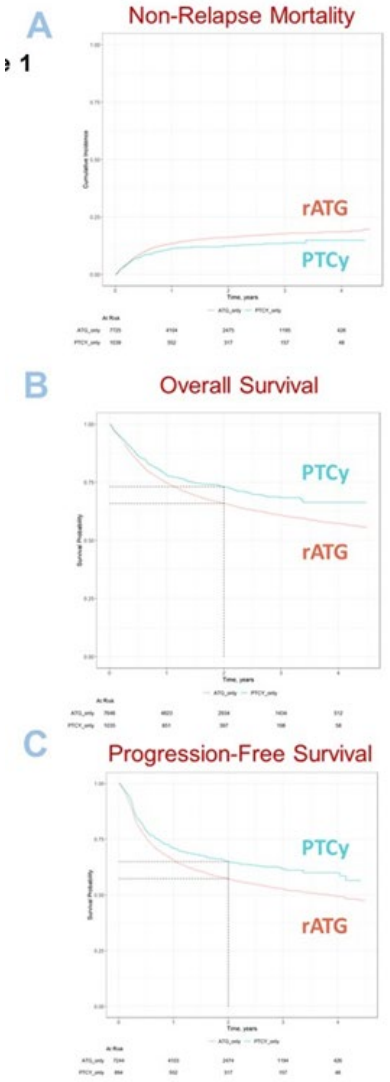
Figure 1



Matched MUD

Table 1

	ATG_only (N=7725)	PTCy_only (N=1039)	Total (N=8764)	p value
Patient Gender				0.33[1]
Male	4427 (57.3%)	612 (58.9%)	5039 (57.5%)	
Female	3298 (42.7%)	427 (41.1%)	3725 (42.5%)	
Age at Transplant, yrs				< 0.01[2]
median [Q1, Q3]	58.6 (48.1, 65.4)	53.0 (38.6, 62.3)	58.1 (46.9, 65.1)	
[Min, Max]	18.0 - 79.1	18.2 - 79.5	18.0 - 79.5	
Karnofsky =>90				0.83[1]
< 90	2271 (31.0%)	311 (31.4%)	2582 (31.1%)	
>= 90	5045 (69.0%)	680 (68.6%)	5725 (68.9%)	
Missing count	409	48	457	
SORROR Comorbidity Index				0.14[1]
0	3367 (48.6%)	494 (50.7%)	3861 (48.9%)	
1-2	1694 (24.5%)	210 (21.6%)	1904 (24.1%)	
>=3	1861 (26.9%)	270 (27.7%)	2131 (27.0%)	
Missing count	803	65	868	
DRI				< 0.01[1]
Low	585 (7.6%)	124 (11.9%)	709 (8.1%)	
Int	4959 (64.2%)	649 (62.5%)	5608 (64.0%)	
High	1839 (23.8%)	243 (23.4%)	2082 (23.8%)	
Very high	342 (4.4%)	23 (2.2%)	365 (4.2%)	
Hematological Malignancies				
AML	3728 (48.3%)	412 (39.7%)	4140 (47.2%)	
MDS	1185 (15.3%)	158 (15.2%)	1343 (15.3%)	
ALL	791 (10.2%)	157 (15.1%)	948 (10.8%)	
MPN	781 (10.1%)	67 (6.4%)	848 (9.7%)	
NHL	543 (7.0%)	123 (11.8%)	666 (7.6%)	
MDS & MPN	350 (4.5%)	34 (3.3%)	384 (4.4%)	
CML	189 (2.4%)	35 (3.4%)	224 (2.6%)	
Hodgkins	84 (1.1%)	36 (3.5%)	120 (1.4%)	
CLL	74 (1.0%)	17 (1.6%)	91 (1.0%)	
Transplant Year				0.03[1]
2018	2132 (27.6%)	242 (23.3%)	2374 (27.1%)	
2019	2311 (29.9%)	333 (32.1%)	2644 (30.2%)	
2020	2086 (27.0%)	302 (29.1%)	2388 (27.2%)	
2021	1196 (15.5%)	162 (15.6%)	1358 (15.5%)	
Myeloablative Conditioning				< 0.01[1]
No	3664 (48.0%)	391 (37.7%)	4055 (46.7%)	
Yes	3975 (52.0%)	646 (62.3%)	4621 (53.3%)	
Missing count	86	2	88	
TBI				< 0.01[1]
No	6607 (85.5%)	782 (75.3%)	7389 (84.3%)	
Yes	1118 (14.5%)	257 (24.7%)	1375 (15.7%)	
GVHD Prevention Regimen				
CSA+MTX	3849 (49.8%)	6 (0.6%)	3855 (44.0%)	
CSA+MMF	2690 (34.8%)	260 (25.0%)	2950 (33.7%)	
MMF+TACRO/SIRO	459 (5.9%)	461 (44.4%)	920 (10.5%)	
CSA	470 (6.1%)	101 (9.7%)	571 (6.5%)	
TACRO/SIRO	36 (0.5%)	159 (15.3%)	195 (2.2%)	
MTX+TACRO	143 (1.9%)	0 (0.0%)	143 (1.6%)	
Other	78 (1.0%)	52 (5.0%)	130 (1.5%)	



#2231: Schröder: AZA-Bridging vor Allo-SZT bei MDS

PATIENTS WITH HIGH-RISK MDS DO NOT BENEFIT FROM REMISSION INDUCTION WITH HMAs PRIOR TO HCT

J. C. SCHROEDER[1], J. F. Weller[1], P. Faustmann[1], L. Mix[1], C. Faul[1], C. Lengerke[1], W. A. Bethge[1]

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Universitätsklinikum Tübingen

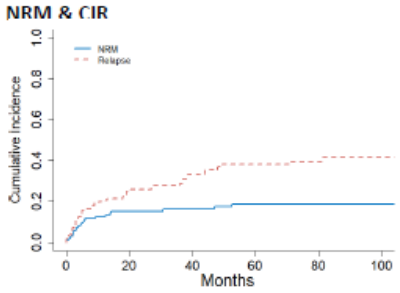
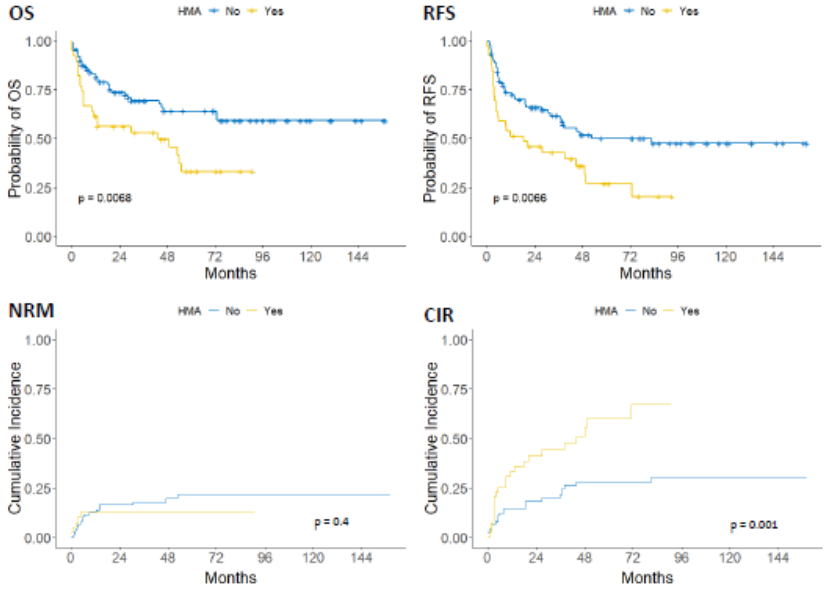


Figure 1: Long-term HCT outcomes of the entire cohort (n=128). Kaplan-Meier plots for long-term outcome variables of the entire cohort, median follow-up duration 60 months. Non-relapse mortality (NRM) and cumulative incidence of relapse (CIR) were analyzed as competing risks. OS, overall survival. RFS, relapse-free survival.



n=128		Relapse-free survival		
Parameter	Strata	5y RFS (95% CI)	Univariate HR (95% CI, p value)	Multivariate HR (95% CI, p value)
Age	< 60 y	46.6 (34.8 - 62.4)	1.01 (0.99-1.04, p=0.269)	-
	≥ 60 y	38.5 (25 - 59.4)	-	-
Sex	Male	43.4 (31.6 - 59.7)	-	-
	Female	44.2 (31.4 - 62.4)	0.88 (0.55-1.43, p=0.618)	-
HMA	No	51.3 (40 - 65.7)	-	-
	Yes	27.7 (15.3 - 50.1)	1.95 (1.19-3.18, p=0.008)	1.76 (1.03-3.00, p=0.038)
Cytogenetic risk	Good	64.1 (51.3 - 80.2)	-	-
	Intermediate	23.6 (9.9 - 56.3)	1.74 (0.93-3.27, p=0.085)	1.56 (0.83-2.95, p=0.17)
	Poor	28.1 (12 - 65.7)	2.58 (1.32-5.05, p=0.006)	2.71 (1.38-5.33, p=0.004)
	Very poor	23.5 (10 - 55.4)	3.14 (1.59-6.19, p=0.001)	3.13 (1.58-6.21, p=0.001)
BM blasts	< 5%	58.5 (42.4 - 80.7)	1.04 (1.01-1.06, p=0.006)	1.02 (0.99-1.06, p=0.11)
	5 - 9%	49.6 (27.4 - 89.7)	-	-
	10 - 19%	30.4 (18.9 - 49.2)	-	-
	≥ 20%	37 (14.4 - 95.5)	-	-

Due to the inherent limitations of retrospective studies **we currently prepare a prospective randomized clinical trial** to determine optimal pre-HCT treatment strategies and develop clinical tools to stratify MDS and hypoproliferative AML patients to **either upfront HCT or remission induction with HMAs or intensive chemotherapy**.

Themen

Stammzelltransplantation:

#1:Wolff: Safety and efficacy of Axatilimab for chronic GVHD

#425 Othman: Benefit of allogeneic HCT in CR1 in NPM-1 mutated AML restricted to MRD positivity after Induction

#2179 Penack: Post Cy or ATG as GVHD Prophylaxis in mismatched unrelated stem cell transplantation

#LBA#4: Kassim: RIC Haploidentical Marrow Transplantation in Adults with Severe Sickle Cell Disease CTN 1507

#2231: Schröder: AZA-Bridging vor Allo-SZT bei MDS

Zelluläre Therapie:

#108 Kittai: Anti-CD19 CAR T-cell therapy for Richter‘s Transformation

#220: Mueller: CD19-targeted CAR-T cells in refractory systemic autoimmune diseases

#228: Iacoboni: Efficacy of CAR-T cell therapy is not impaired by previous bispecific antibody treatment in LBCL

#108 Kittai: Anti-CD19 CAR T-cell therapy for Richter's Transformation

Anti-CD19 Chimeric Antigen Receptor T-Cell Therapy for Richter's Transformation: An International Multicenter Retrospective Study

Adam S Kittai, MD, David A. Bond, MD, Ying Huang, MS, MA, Seema A Bhat, MD, Emily Blyth, B.Med(Hons), FRACP, FRCPA, PhD, John C. Byrd, MD, Julio C Chavez, MD, Matthew S. Davids, MD, MMSc, Jamie P Dela Cruz, Mark R Dowling, MBBS, PhD, Caitlyn Duffy, Carrie I Ho, MD, Caron A Jacobson, MD, MMSc, Samantha M. Jaglowski, MD, MPH, Nitin Jain, MD, Kevin H Lin, MD, Christine McCarthy, BS, Erin M Parry, MD, PhD, Manoj Rai, MD, Kerry A Rogers, MD, Aditi Saha, MBBS, Levanto Schachter, DO, MS, Hamish Scott, MD, Jayastu Senapati, MD, MBBS, DM, Mazyar Shadman, MD, MPH, Tanya Siddiqi, MD, Deborah M. Stephens, DO, Vinay Vanguru, MBBS, FRACP, FRCPA, William G. Wierda, MD, PhD, Omer Zulfa, MD, Jennifer A. Woyach, MD and Philip A. Thompson, MBBS

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65th ASH® Annual Meeting and Exposition

Introduction

- Richter's transformation (RT) is defined as the transformation of CLL into an aggressive lymphoma, typically Large B-cell Lymphoma (LBCL).[1]
- No standard of care treatment options, as survival is measured in months.
- Outcomes of patients with RT that has developed on small molecule inhibitors with no prior chemotherapy remains poor.[2]
  - Median overall survival 8.2 months
- Therefore, RT represents a true area of unmet need.

[1]Tsimberidou et al JCO 2006, [2]Kittai et al ASH Oral 2023

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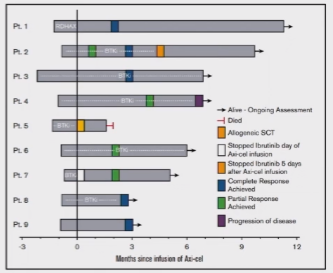
Methods

- International multicenter retrospective study of patients with RT who received FDA approved CD19 CART
  - Including axi-cel, tisa-cel, liso-cel, and brexu-cel
- 12 academic centers in the US and Australia
- RT defined as patients with LBCL with preceding or concurrently diagnosed CLL
- PFS and OS measured from date of CD19 CART
- Cox regression model used to associate prognostic factors with OS

Background – Anti-CD19 CART for RT

- Anti-CD19 CAR T-cell therapy (CD19 CART) has revolutionized the way we treat LBCL.
- RT was mostly excluded from clinical trials with CD19 CART.
- We published our experience treating patients with RT with axicabtagene ciloleucel showing impressive response rates.[1]



[1]Kittai et al Blood Advances 2020

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#108 Kittai: Anti-CD19 CAR T-cell therapy for Richter's Transformation

Baseline CLL Characteristics

CLL Treatment History	N=69
Prior Chemo for CLL, N (%)	39 (56.5)
Prior BTKi for CLL, N (%)	44 (63.8)
Prior Ven for CLL, N (%)	23 (33.3)
Prior Allo-SCT for CLL, N (%)	3 (4.4)
Prior CART for CLL, N (%)	1 (1.4)
Median # of CLL TRMT prior to RT	2 (0-10)
De novo RT (0 TRMT for CLL), N (%)	12 (17.4)

Median years from CLL dx to RT – 6 (0-28)

CLL Molecular Data	N=69
IGHV, N (%)	
Mutated	8 (13.3)
Unmutated	52 (86.7)
Unknown	9
del(17p), N (%)	23 (41.8)
Unknown	14
del(11q), N (%)	13 (23.6)
Unknown	14
Tri 12, N (%)	9 (16.4)
Unknown	14
Del(13q), N (%)	21 (38.2)
Unknown	14
TP53 mut, N (%)	20 (50.0)
Unknown	29
NOTCH1 mut, N (%)	6 (18.8)
Unknown	37
Complex KT (≥3 abn), N (%)	22 (51.2)
Unknown	26

RT Characteristics and TRMT	N=69
Age at RT Dx, median (range)	63 (26-80)
Clonal relationship to CLL, N (%)	
Related	23 (100)
Unknown	46
Complex KT (≥3 abn) at RT, N (%)	19 (65.5)
Unknown	40
del17p (RT), N (%)	12 (41.4)
Unknown	40
TP53 mut (RT), N (%)	14 (58.3)
Unknown	45
NOTCH1 mut (RT), N (%)	4 (21.1)
Unknown	50
MYC translocation, N (%)	8 (20.0)
Unknown	29
Median Ki-67 (%)	80 (40-100)
Unknown	9
Prior BTKi alone or in combo for RT	46 (66.7)
Prior Ven alone or in combo for RT	35 (50.7)
Prior BTKi or Ven for RT or CLL, N (%)	58 (84%)

RT Characteristics collected at CAR19

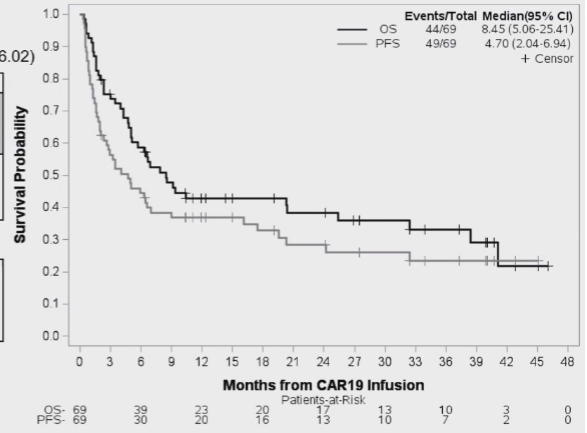
RT at CART Baseline Characteristics and TRMT	N=69
Median age at CART infusion	64 (27-80)
Median months from RT dx to CART	7.3 (0.4-65.6)
Median # TRMT for RT prior to CART	2 (0-7)
Median Total # of prior TRMT	4 (1-15)
Received bridging, N (%)	59 (85.5)
CAR-T product given, N (%)	
Axi-cel[1]	45 (65.2)
Liso-cel	7 (10.1)
Tisa-cel	17 (24.6)
Median days from Apheresis to CART infusion	34 (24-100)
Concurrent BTKi therapy, N (%)	31 (44.9)
Median LDH prior to CART	258 (96-2878)
Median largest LN (cm) prior to CART	3.5 (0.7-16)
Unknown	9
Median highest SUV on PET prior to CART	14.8 (3-50.6)
Unknown	7

Progression free and Overall survival

Median follow-up in months (range) – 24.13 (2.14-46.02)

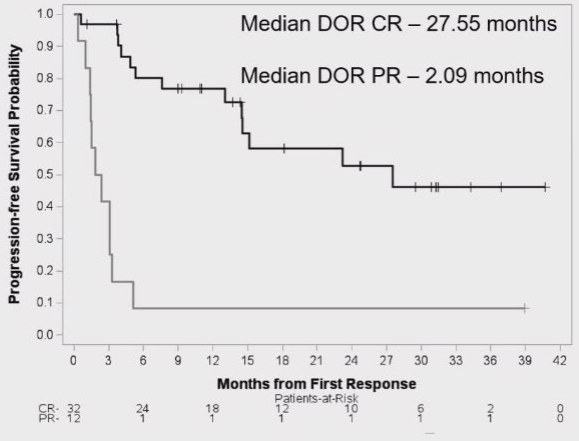
	N=69
PFS from CART Infusion	
Number of events	49
Median in months (95% CI)	4.70 (2.04-6.94)
OS from CART Infusion	
Number of events	44
Median in months (95% CI)	8.45 (5.06-25.41)

OS from RT Diagnosis	
Number of events	**44**
Median in months (95% CI)	**29.4 (15.7-33.5)**
Median follow-up (range)	**36.1 (8.2-82.9)**



Duration of response by CR or PR

Best response to CART, N (%)	
CR	32 (46.4)
PR	12 (17.4)
SD	1 (1.5)
PD	21 (30.4)
Died prior to assessment	3 (4.4)



#108 Kittai: Anti-CD19 CAR T-cell therapy for Richter's Transformation

Safety Outcomes

	N=69
Cause of Death (N=44), N (%)	
Disease	32 (72.7)
Non-disease	12 (27.3)
Non-relapse Mortality from CART Infusion, % (95% CI)	
Number of events	12
3-month estimate	7.3% (2.7-15.0)
6-month estimate	10.3% (4.5-18.9)
12-month estimate	13.4% (6.5-22.8)

CAR-T Outcomes	N=69
Grade 3-4 neutropenia, N (%)	60 (87.0)
Grade 3-4 thrombocytopenia, N (%)	49 (71.0)
Febrile neutropenia, N (%)	46 (66.7)
CRS max grade, N (%)	
0	8 (11.6)
1	24 (34.8)
2	26 (37.7)
3	9 (13.0)
4	2 (2.9)
ICANS max grade, N (%)	
0	23 (33.8)
1	12 (17.7)
2	8 (11.8)
3	17 (25.0)
4	8 (11.8)
Unknown	1
Grade 3-4 infection, N (%)	14 (20.3)

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MVA for OS – Independent prognostic factors

	Univariable Models		Multivariable Model	
	HR (95% CI)	p-value	HR (95% CI)	p-value
# prior lines of therapy for RT prior to CART	1.33 (1.05-1.70)	0.02	1.58 (1.23-2.03)	0.0004
Total prior lines of therapy	1.18 (1.04-1.35)	0.01		
Ki-67, 10% higher	1.29 (1.03-1.60)	0.03	1.49 (1.20-1.87)	0.0004
LDH, 2-fold increase	1.84 (1.36-2.49)	<.0001	1.91 (1.35-2.69)	0.0002

Conclusions

- This is the largest cohort of pts with RT to receive CD19 CART.
- Heavily pretreated group - 84% exposed to either BTKi or BCL2i, with 4 total prior lines of TRMT.
- Median OS from CAR19 was 8.5 months in this study.
- Median DOR from CAR19 for those patients that attained a CR was 27.55 months.
- Higher number of prior therapies is associated with worse OS.
  - Earlier use of CD19 CART in the RT disease course may be warranted.
- Prospective clinical trials ongoing.

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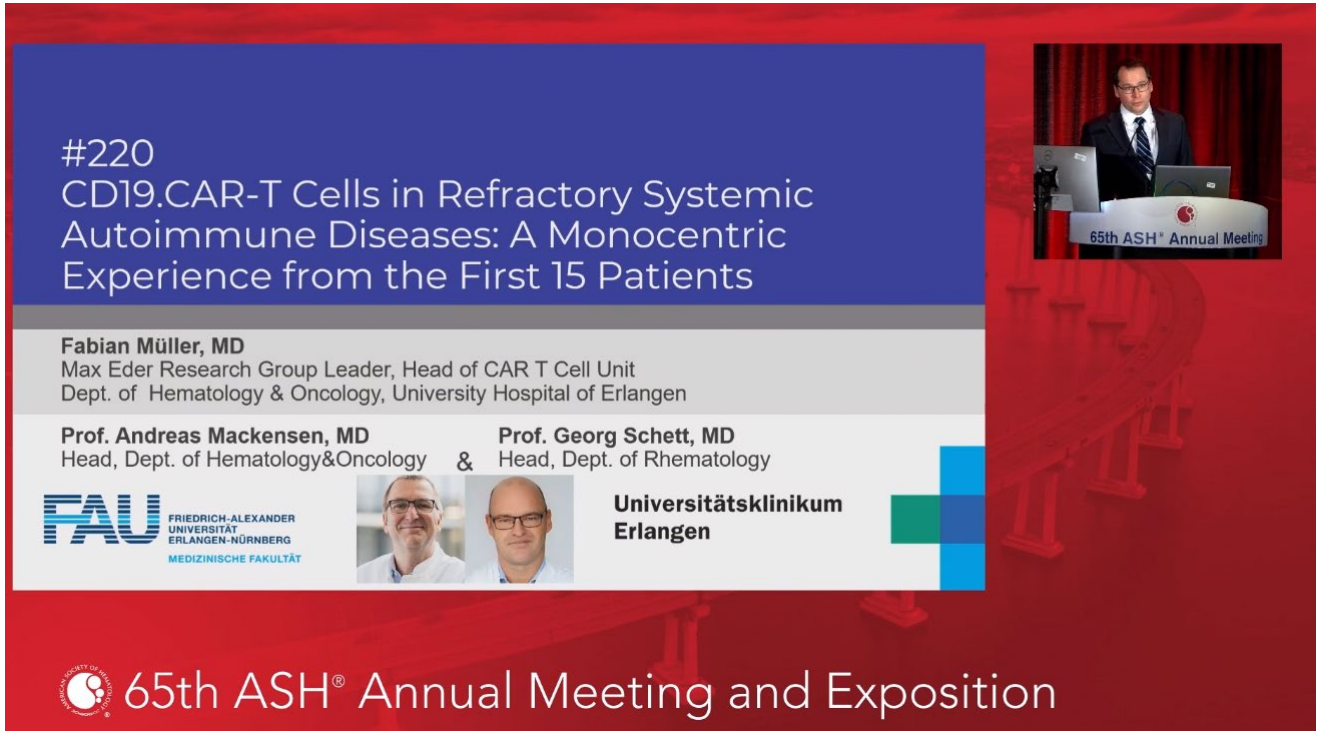
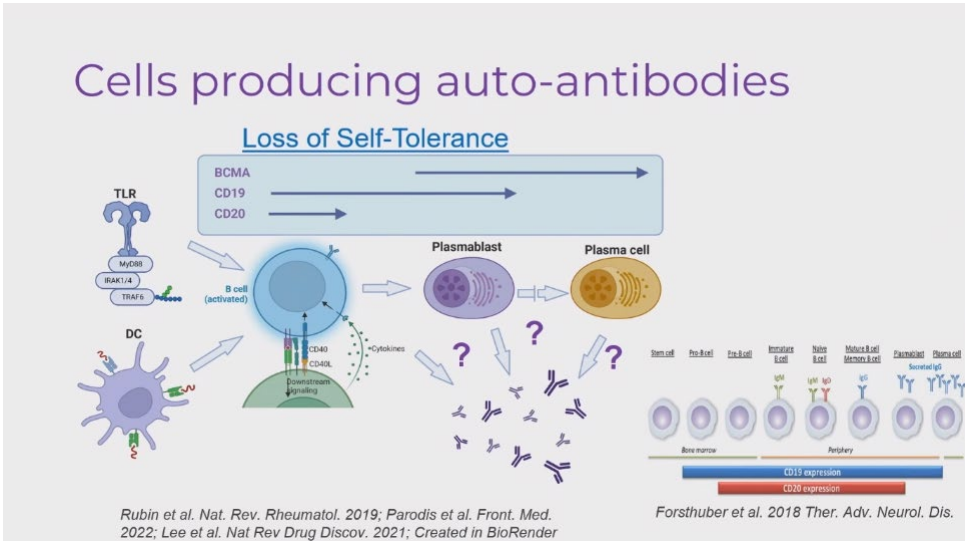
#220: Mueller: CD19-targeted CAR-T cells in refractory systemic autoimmune diseases





CAR-T in Auto-Immune Disease

– The Why & The How?

Advantages of CD19.CAR-Ts

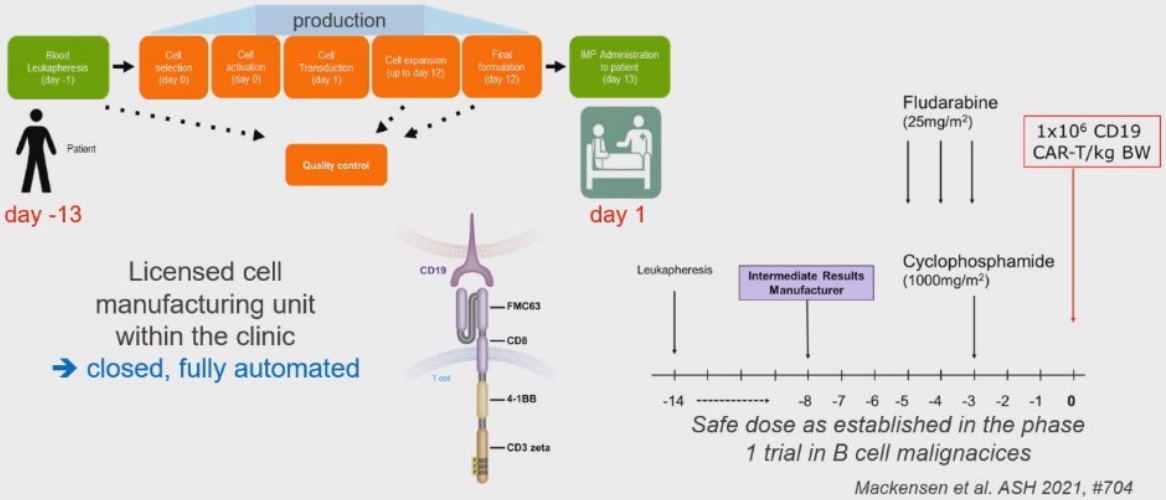
- ✓ Plasmablasts are targeted
- ✓ CAR-T cells invade tissue
- ✓ Depletion of B cells is deeper
- ✓ 2 SLE mouse models responded to CD19 CAR-Ts

Schett et al. Lancet 2023; Kansal et al.
Jin et al. Cell Mol Immunol. 2021.
Sci Transl Med. 2019;

#220: Mueller: CD19-targeted CAR-T cells in refractory systemic autoimmune diseases

CD19-Targeted CAR-T Cells in Refractory SLE

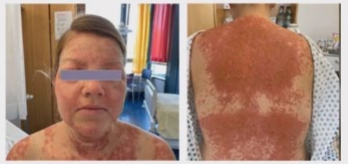
Production Pipeline & Time Line



Mackensen et al. ASH 2021, #704

The three diseases treated at our center

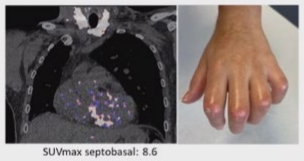
Systemic Lupus Erythematosus (SLE)



Kidney, Skin, Lung, Heart, Brain

Mougiakakos et al. NEJM, 2021
Mackensen et al. Nat Med. 2022

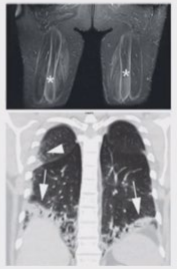
Systemic Sclerosis (SSc)



Skin, Lung, Heart, Kidney

Bergmann et al. Annals Rheum. Dis. 2023

Myositis (IIM)



Muscle, Lung, Heart

Müller et al. Lancet 2023

Patient Characteristics at Baseline

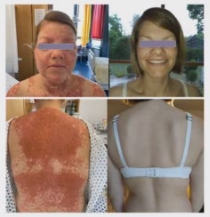
Total of **15 Patients**

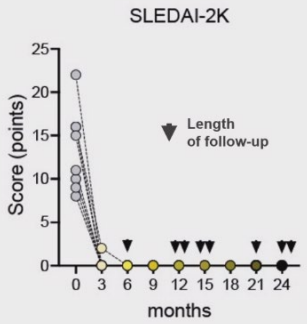
Disease Type:	8x SLE, 3x IIM, 4x SSc
Median Age (y):	36 (18-60)
Median Disease Duration:	4 years (1-20)
Median Follow-Up (mo):	15 months (4-29)
Auto-antibodies present:	15/15
For all at least 2 organs:	13 skin, 11 lung, 9 kidney, 9 joints, 4 heart, 3 muscle, others

➔ Heavily Pretreated, active & progressive disease at time of indication

#220: Mueller: CD19-targeted CAR-T cells in refractory systemic autoimmune diseases

Clinical responses - SLE

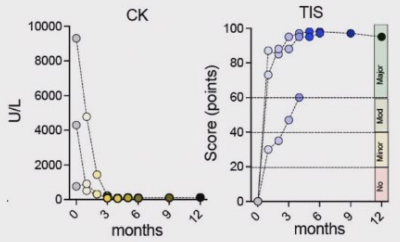




- Disease-activity rapidly abrogated
- Patients remain in complete remission
- No disease-specific therapy since CAR T

➔ CD19 CAR T achieves lasting remission in SLE

Clinical responses - IIM

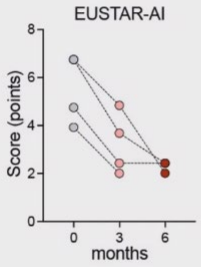


CK = creatinine kinase, TIS = Total improvement Score

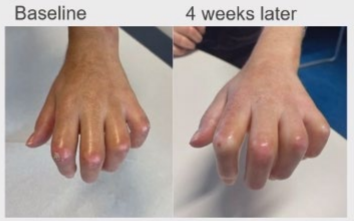
- Creatinine Kinase (CK) normalizes
- Muscle strength normalizes
- Patients remain in remission at data cut-off
- No disease-specific therapy since CAR T

➔ CD19 CAR T achieves lasting remission in IIM

Clinical responses - SSc



***EUSTAR** = European League Against Rheumatism Scleroderma Trials*
***AI** = activity index*

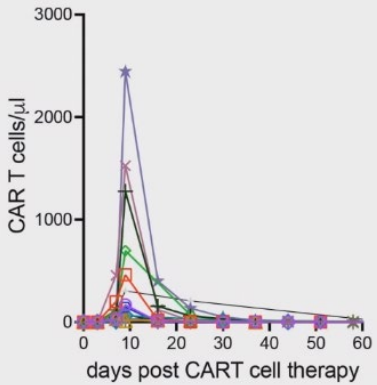


- Reduced skin stiffness
- Reversal of lung fibrosis
- Reduction of vasculitis (clinical symptoms)
- No flair or disease-specific therapy since CAR T

➔ Stop of disease activity / improved symptoms.

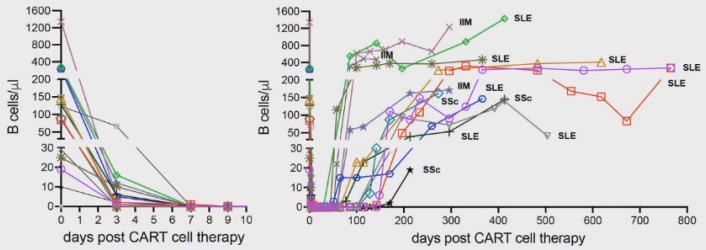
#220: Mueller: CD19-targeted CAR-T cells in refractory systemic autoimmune diseases

CAR Expansion



- CAR-T cells expand as expected reaching their peak at day 9
- Height of the peak is comparable to those in malignant disease

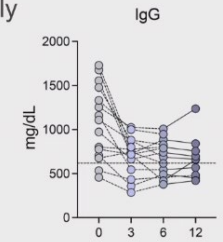
Initially abrogated B cells reappear after a median of 119 days



Patients remain treatment-free despite reoccurring B cells!

Patient Safety

- CRS grade 0/**1**/2 in n= 4/**10**/1 patients, respectively
- One possible ICANS grade 1 (vertigo)
  → only patient receiving glucocorticoids
- 6 of 15 patients needed Tocilizumab
- Few patients with hypogammaglobulinemia and need of substitution
- 14/15 patients with respiratory or urinary tract infections including pneumonia requiring hospitalization.
- 2 herpes zoster reactivation



➔ CD19 CAR T is well tolerated with some infections

Clinical Summary & Outlook

- CD19 CAR T cells were successfully produced from patients with auto-immune diseases
- Tapering immune suppression was well tolerated
- CAR T cells expand in a typical fashion and are detectable for months
- CD19 CAR T cell therapy is very well tolerated
- B cells and disease-defining auto-antibodies are quickly abrogated
- Naïve B cells remain the dominant phenotype up to 12 months after CART
- Disease-specific treatment was stopped and symptom control achieved in all patients treated up to date

#228: Iacoboni: Efficacy of CAR-T cell therapy is not impaired by previous bispecific antibody treatment in LBCL

Methods

1. Retrospective study of patients with R/R LBCL treated with CD19-targeted CAR T-cells at 15 centers in France and Spain between July 2018 and January 2023 who had been exposed to BsAbs prior to apheresis.
   - Patients exposed to BsAb targeting CD19/CD3 were excluded
2. Identified a control cohort from the DESCAR-T Registry and carried out a 1:1 propensity score matching (PSM) including 13 baseline covariates.
   - Response, survival and toxicity after CAR T-cell therapy, according to previous BsAb exposure.

Results – Prior bispecific antibody treatment

N=47

- Target CD20/CD3 (91%) or CD22/CD3 (9%)
- Monotherapy (87%) or combination (11%)
- Median number of prior lines before BsAb therapy was 2 (range 1-6)
- BsAb as the last line before CAR T-cell therapy in 26 (55%) patients

Toxicity	Patients
CRS any grade, n (%)	27 (57)
- Grade ≥2, n (%)	7 (15)
- Grade ≥3, n (%)	1 (2)
ICANS, %	0

Efficacy	Patients
Best ORR, n (%)	22 (47)
Best CR, n (%)	9 (19)
PFS, median mo (95% CI)	3.1 (2.7-4.4)
6-mo PFS, % (95% CI)	21 (11-34)
DoR, median days (range)	85 (24-526)

#228: Iacoboni: Efficacy of CAR-T cell therapy is not impaired by previous bispecific antibody treatment in LBCL

Results – Baseline characteristics at time of CAR T-cell therapy

Characteristics	N=47
Age, median years (range)	65 (31-82)
Male gender, n (%)	31 (66)
ECOG ≥2, n (%)	4 (9)
DLBCL, n (%)	38 (81)
Disease stage III-IV, n (%)	42 (89)
Prior therapies, median (range)	3 (2-9)
Previous ASCT, n (%)	9 (19)
Bulky disease (>5 cm), n (%)	17 (36)

Characteristics	N=47
Bridging therapy, n (%)	42 (89)
- Chemotherapy	29 (62)
Responder to bridging, n (%)	11 (28)
CAR T-cell therapy, n (%)	
- Axi-cel	22 (47)
- Tisa-cel	20 (42)
- Liso-cel	5 (11)
BsAb to apheresis, median days	51 (13-512)
Apheresis to CAR-T, median days	43 (34-103)

Results – CAR T-cell therapy toxicity

Toxicity	N=47
CRS any grade, n (%)	37 (79)
- Grade ≥3, n (%)	3 (6)
ICANS any grade, n (%)	11 (23)
- Grade ≥3, n (%)	1 (2)
Neutropenia grade ≥3, %	66
Thrombocytopenia grade ≥3, %	45

No grade 5 CRS or ICANS

During follow-up, 18 patients (38%) died due to:
- Disease progression (n=12)
- Infections (n=5)
- Unknown (n=1)

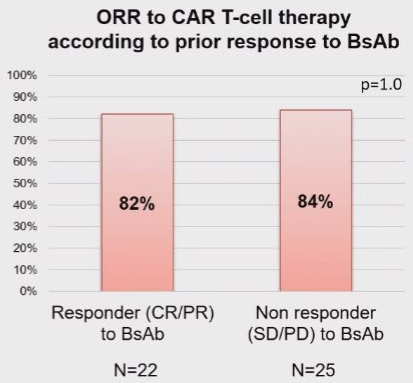
CRS, any grade		BsAb: No	BsAb: Yes	p
CAR-T	No	21% (4/19)	22% (6/27)	1.0
	Yes	79% (15/19)	78% (21/27)	

CRS after bispecific antibodies **did not predict** for an increased rate of CRS after CAR-T

Results – CAR T-cell therapy efficacy

Median follow-up of 10.5 months

Efficacy	N=47
Best ORR (CR), %	85 (43)
PFS, median mo (95% CI)	6.6 (2.6-NR)
OS, median mo (95% CI)	NR (9.0-NR)
DoR, median mo (95% CI)	8.8 (2.3-NR)



Results – CAR T-cell therapy efficacy

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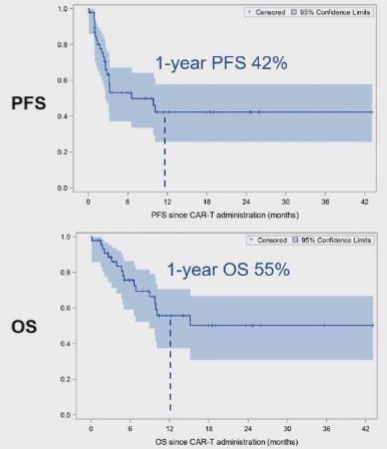
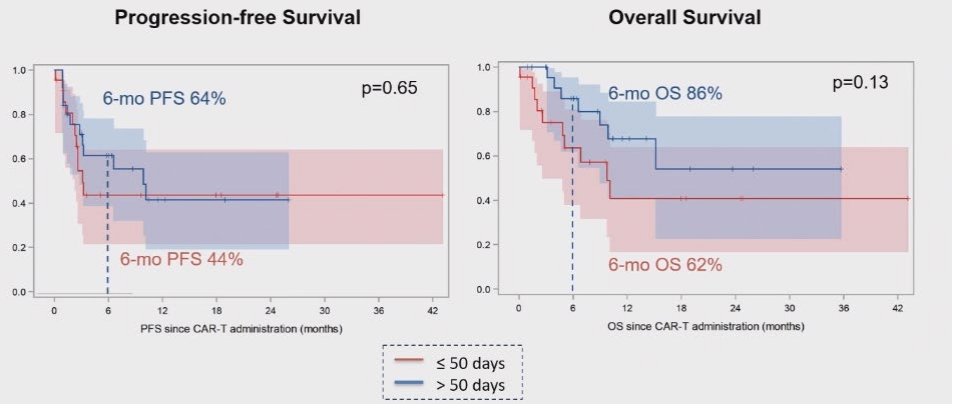


#228: Iacoboni: Efficacy of CAR-T cell therapy is not impaired by previous bispecific antibody treatment in LBCL

Results - Survival according to washout between BsAb and apheresis

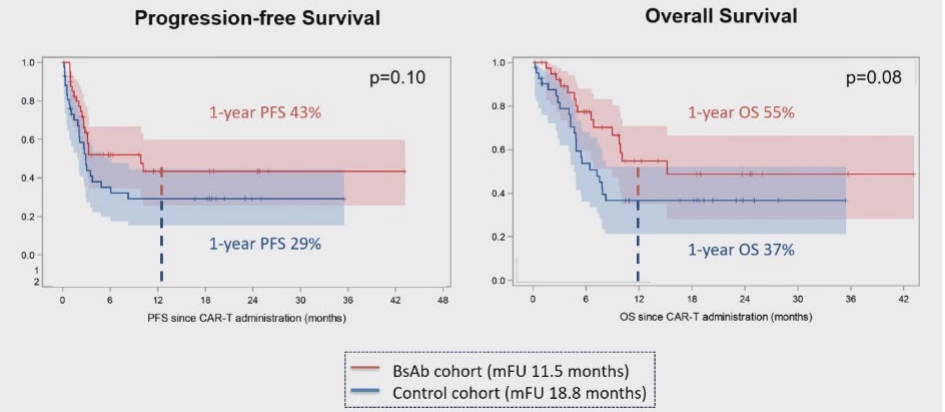


Results – Toxicity and efficacy according to prior BsAb exposure

Toxicity, n (%)	BsAb Cohort	Control Cohort	p
CRS, any	36 (86)	32 (76)	0.41
- Grade ≥2	16 (38)	17 (40)	
- Grade ≥3	3 (7)	8 (19)	
ICANS, any	11 (26)	11 (26)	1.00
- Grade ≥2	7 (17)	8 (19)	
- Grade 3	1 (2)	6 (14)	

Efficacy	BsAb Cohort	Control Cohort	p
ORR, n (%)	36 (86)	22 (55)	0.02
CR, n (%)	18 (43)	15 (38)	0.50

Results – Survival outcomes according to prior BsAb exposure



1. The safety profile of CAR T-cell therapy in patients with prior BsAb exposure was in line with published data and not modified by previous BsAb-related adverse events.
2. Response rates in our BsAb-exposed cohort were similar to control patients and independent of prior response to BsAb therapy.
3. Survival outcomes after CAR T-cell therapy in the BsAb-treated patients were comparable to the control group.

Innere Medizin II: Zugelassene CAR-T Zellen

- **Gilead: Axucabtagene Cliloleucel (Yescarta®), second generation, CD28, CD19**
  EMA: Zulassung bei Erwachsenen NHL August 2018
  Relapsed/refractory NHL (diffuse large B-cell lymphoma (**DLBCL**), primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma, **Follikuläres Lymphom** mit Rezidiv >3 Vortherapien (2022)
  zertifiziert, Erste Therapie Mai 2019

- **Novartis: Tisagenlecleucel (CTL019, Kymriah®), second generation, 4-1BB, CD19**
  EMA: Zulassung **ALL** bei Kindern und jungen Erwachsenen ≤25, Erwachsenen mit diffusem großzelligem B-Zell-Lymphom ((**DLBCL**) August 2018), **Follikuläres Lymphom** mit Rezidiv >2 Vortherapien (2022)
  zertifiziert, Erste Therapie September 2019

- **Gilead: Tecartus®, second generation, CD28 CD19**
  EMA: Zulassung zur Behandlung von erwachsenen Patienten mit rezidiviertem oder refraktärem Mantelzell-Lymphom (**MCL**) nach zwei oder mehr systemischen Therapien, die einen Bruton-Tyrosinkinase-(BTK-)Inhibitor einschließen (Dezember 2020), **R/R ALL**>= 26 Jahre
  zertifiziert

- **BMS/Celgene: Abecma®** (idecabtagene vicleucel, zugelassen 2021), Anti-BCMA CAR-T (bb121) für Behandlung von Erwachsenen Patienten mit Multiplen Myelom >3 Vortherapien (inkl. Immunmodulator, anti-CD38 und Proteasominh.), **Breyanzi®** (lisocabtagene maraleucel) Anti CD19 für **LBCL**, zugelassen 2022 LBCL >3 Vortherapien, **zertifiziert**

- **Janssen:** Ciltacabtagene Autoleucel (**Cilta-cel, Carvykti®**) Anti-BCMA, **Myelom, zertifiziert**

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CAR-T Zellen Studien

Entität	Beschreibung	Rahmenbedingungen
Lymphome/ Car-T-Zellen	**Phase-II-Studie zur Bewertung der Wirksamkeit und Sicherheit von MB-CART2019.1 im Vergleich zur Standardtherapie bei Teilnehmern mit rezidiviertem/refraktärem diffus-großzelligem B-Zell-Lymphom (R-R DLBCL) |** DALY 2-EU	**geöffnet** Infos: Prof. Dr. Bethge
Myelom/ Car-T-Zellen	**Linientherapie für nicht-transplant-fähige Patienten mit VRD gefolgt von Ciltacabtagene Autoleucel vs VRD gefolgt von Lenalidomid Erhaltung |** Cartitude-5	**geöffnet** Infos: Dr. Besemer
Lymphome/ALL CAR-T Zellen	**Behandlungsmöglichkeit mit eigenhergestellten anti-CD19 gerichteten CAR-T Zellen bei rezidivierten oder therapie-refraktären akuten lymphatischen Leukämien und B-Zell-Lymphomen** **A phase I/II safety, dose finding and feasibility trial of MB-CART19.1 in patients with relapsed or refractory CD19 positive B cell malignancies**	**geöffnet** Infos: Prof. Dr. Bethge
Lymphome/ALL CAR-T Zellen	**A phase I/II dose finding and efficacy study of MB-CART-CD19/CD22 in patients with relapsed/refractory B-cell malignancies**	**geplant** Infos: Prof. Dr. Bethge

Stammzelltransplantation Studien

Entität	Beschreibung	Rahmenbedingungen
Spender	A randomized controlled trial comparing outcome after hematopoietic cell transplantation from a partially matched unrelated versus haploidentical donor (Hamlet Studie)	geöffnet Infos: Prof. Dr. Bethge
Spender	Matched Unrelated vs. Haploidentical Donor for Allogeneic Stem Cell Transplantation in Patients with Acute Leukemia with Identical GVHD Prophylaxis – A Randomized Prospective European Trial (HaploMUD Studie)	geöffnet Infos: Prof. Dr. Bethge
Immunsuppression	Graft vs Host Disease Prophylaxis in unrelated donor transplantation: a randomized clinical trial comparing PTCY vs ATG (GRAPPA)	geöffnet Infos: Prof. Dr. Bethge
GVHD	A Randomised, Open-label, Multicentre, Phase 3 Trial of First-line Treatment with Mesenchymal Stromal Cells MC0518 Versus Best Available Therapy in Adult and Adolescent Subjects with Steroid-refractory Acute Graft-versus-host Disease After Allogeneic Haematopoietic Stem Cell Transplantation (IDUNN Trial)	geöffnet Infos: Prof. Dr. Bethge

und am Ende….

Vielen Dank für Ihre Aufmerksamkeit

Universitätsklinikum Tübingen