Updates in Leukemia

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Acute lymphoblastic leukemia

PhALLCON: Phase III study comparing Ponatinib vs Imatinib in Philadelphia chromosome positive ALL

- Newly diagnosed Ph+ ALL
- Ponatinib 30 mg daily or Imatinib 600 mg daily with reduced intensity chemotherapy
- End of induction (cycles 1-3) consolidation (cycle 4-9) post consolidation (cycles 10-20)
- After cycle 20, single agent ponatinib or imatinib until disease progression or unacceptable toxicity
- Composite primary endpoint :
  - MRD-neg (BCR::ABL1 ≤0.01%) complete remission (CR) for 4 weeks at end of induction
- Secondary endpoints:
  - EFS (any cause death, failure to achieve CR for 4 weeks by end of induction, relapse from CR)

Jabbour et al. Journal of Clinical Oncology 2023 41:36_suppl, 398868-398868

PhALLCON: Phase III study comparing Ponatinib vs Imatinib in Philadelphia chromosome positive ALL

	Ponatinib	Imatinib
Responses at end of induction, n (%)	**(N=154)**	**(N=78)**
MRD-neg (BCR::ABL1 ≤0.01%) CR	53 (34)	13 (17)
p value	0.0021	
MR 4 (≤0.01%)	64 (42)	16 (21)
MR 4.5 (≤0.0032%)	39 (25)	10 (13)
Adverse effects, n (%)	**(N=163)**	**(N=81)**
Grade 5 TEAEs/treatment-related AEs	8 (5) / 0	4 (5) / 1 (1)
Grade 3–4 TEAEs	139 (85)	71 (88)
TE aortic occlusion events (any Grade)	4 (2)	1 (1)

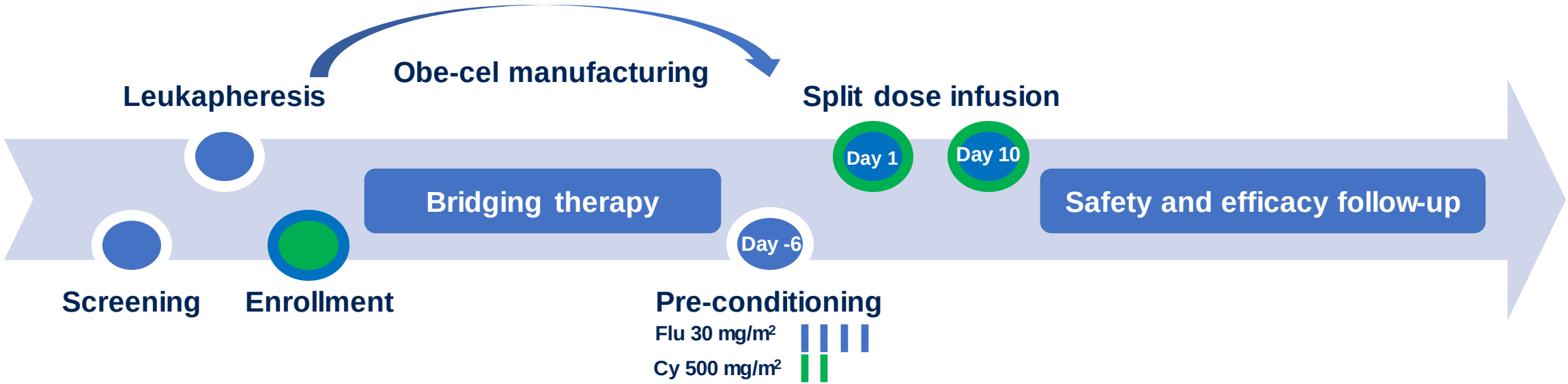
Jabbour et al. Journal of Clinical Oncology 2023 41:36_suppl, 398868-398868

PhALLCON: Phase III study comparing Ponatinib vs Imatinib in Philadelphia chromosome positive ALL

	Ponatinib	Imatinib
Hematopoietic cell transplantation (%)	31	37
Lack of efficacy (%)	7	26
Median Follow-up (months)	20 months	18 months
Median EFS	HR 0.652 (95% CI 0.385-1.104)	

Jabbour et al. Journal of Clinical Oncology 2023 41:36_suppl, 398868-398868

FELIX study on Obecabtagene- Autoleucel in R/R B-ALL



Pre-conditioning

Tumor burden-adjusted split dosing to maximize the therapeutic index

Pre-conditioning				
BM blasts ≤20%	→	100 x 10^6 CAR T cells	CRS Grade <2 No ICANS →	310 x 10^6 CAR T cells
BM blasts >20%	→	10 x 10^6 CAR T cells	→	400 x 10^6 CAR T cells

94% of infused patients received both obe-cel infusions

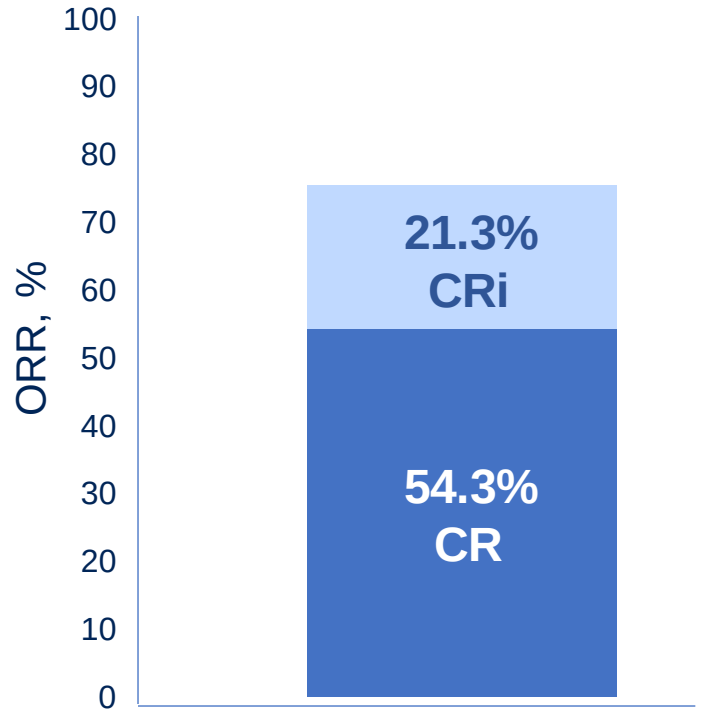
CRS, cytokine release syndrome; cy, cyclophosphamide; flu, fludarabine; ICANS, immune effector cell associated neurotoxicity syndrome

PRESENTED BY: Dr Claire Roddie, University College London, UK; Abstract 7000

Slides courtesy: Dr. Claire Roddie

FELIX study: Disease Response per IRRC Assessment

76% of infused patients achieved CR/CRi



ORR: 76%
95% CI (66, 84)
p<0.0001*

97% of responders with evaluable samples were MRD negative at 10^{-4} level by flow cytometry

*One-sided p-value from the exact test on H0: ORR ≤40% vs H1: ORR >40%
CR, complete remission, CRi, CR with incomplete blood count recovery; IRRC, independent response review committee; MRD, minimal residual disease; ORR, overall remission rate

Slides courtesy: Dr. Claire Roddie

FELIX study: Safety – CRS and ICANS

Low rates of Grade ≥3 CRS and/or ICANS were observed

	BM blasts ≤20% at pre-conditioning (N = 37)	BM blasts >20% at pre-conditioning (N = 57)	All infused patients (N = 94)
CRS			
Any grade, n (%)	24 (64.9)	47 (82.5)	71 (75.5)
Grade ≥3, n (%)	1 (2.7)	2 (3.5)	3 (3.2)
ICANS			
Any grade, n (%)	5 (13.5)	19 (33.3)	24 (25.5)
Grade ≥3, n (%)	1 (2.7)	6 (10.5)	7 (7.4)

- Tocilizumab and steroid was used to treat CRS in 53/94 (56%) and 16/94 (17%) patients, respectively
- 3/94 (3%) patients required vasopressor for treatment of CRS
- 6/7 (86%) Grade ≥3 ICANS were observed among patients with >75% BM blasts at pre-conditioning

CRS, cytokine release syndrome; ICANS, immune effector cell associated neurotoxicity syndrome

PRESENTED BY: Dr Claire Roddie, University College London, UK; Abstract 7000

Slides courtesy: Dr. Claire Roddie

Outcomes following Brexucabtagene Autoleucel for Adults with Relapse/Refractory B-ALL

- Brexucabtagene Autoleucel- anti CD-19 CAR T-cell therapy, approved for R/R B-ALL
- **Real-world post approval study**
- 76 adult patients from 13 centers in US
- Median age 44 (18-81); Female 46%; Non-Hispanic White 57%; Hispanic 25%

Ph-neg/ Ph +	71/29
Median number of lines of therapy (range)	4 (1-9)
Prior BLIN (%)	53
Prior INO (%)	37
Prior transplant (%)	46

Active disease at apheresis (%)	69
CR with MRD + (%)	19
CR with MRD- (%)	12
CNS-3 disease (%)	11
Median follow-up for survivors (months)	8.3

Roloff et al. Journal of Clinical Oncology 2023 41:16_suppl, 7001-7001.

Outcomes following Brexucabtagene Autoleucel for Adults with Relapse/Refractory B-ALL

Response rates at D+28 (n=70)	
CR/CRi	64 (91%)
MRD-	54
MRD +	10
No response	6 (9%)
Active CNS+	10
CR	8
No response	2

Roloff et al. Journal of Clinical Oncology 2023 41:16_suppl, 7001-7001.

Outcomes following Brexucabtagene Autoleucel for Adults with Relapse/Refractory B-ALL

Toxicity: CRS and ICANS	
CRS (any grade)	62 (83%)
CRS Grade 1-2	57
CRS Grade 3-4	5
No CRS	13 (17%)
ICANS (any grade)	46 (61%)
ICANS Grade 1-2	17
ICANS Grade 3-4	29
No ICANS	30

Roloff et al. Journal of Clinical Oncology 2023 41:16_suppl, 7001-7001.

Outcomes following Brexucabtagene Autoleucel for Adults with Relapse/Refractory B-ALL

Six-month outcomes	Duration of remission (%)	Progression Free Survival (%)	Overall Survival (%)
Post-CAR MRD negative CR	83	78	94
Post-CAR MRD positive CR	35	35	100
No response to Brexu-cel	-	0	50

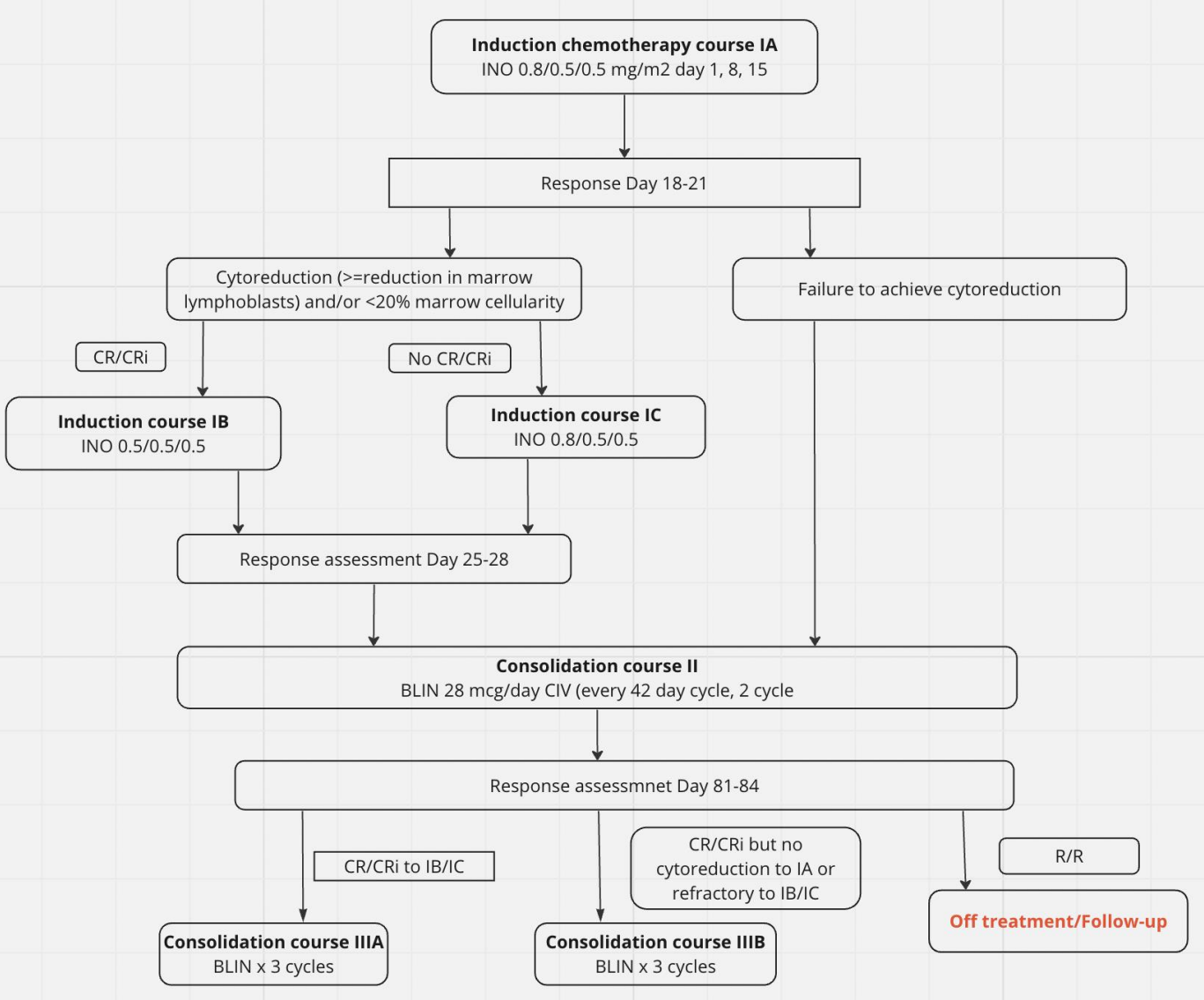
Roloff et al. Journal of Clinical Oncology 2023 41:16_suppl, 7001-7001.

Chemotherapy-free treatment with INO+BLIN for older adults with newly diagnosed Ph- CD22+ B-ALL

- **INDUCTION THERAPY:** Course IA (INO 0.8/0.5/0.5 mg/m2) day 1, 8, 15→ Response D18-21
  - CRi/CRi→ Induction course IB INO 0.5/0.5/0.5 → response D 25-28
  - No CR/CRi but cytoreduction→ Induction course IC INO 0.8/0.5/0.5 → response D 25-28
  - No cytoreduction
- **CONSOLIDATION II:** BLIN x 2 cycles (after IB, IC, no cytoreduction)→ response D 81-84
- **CONSOLIDATION III**
  - If CR/CRi to IB/IC→ consolidation course IIIA→ BLIN x 2 cycles
  - If CR/CRi but failure of ALL cytoreduction to IA or refractory to IB/IC→ consolidation course IIIB→ BLIN x 3 cycles

Wieduwilt et al. Journal of Clinical Oncology 2023 41:16_suppl, 7006-7006

Chemotherapy-free treatment with INO+BLIN for older adults with newly diagnosed Ph- CD22+ B-ALL



Wieduwilt et al. Journal of Clinical Oncology 2023 41:16_suppl, 7006-7006

Chemotherapy-free treatment with INO+BLIN for older adults with newly diagnosed Ph- CD22+ B-ALL

Best response	
Best cumulative response	
CR/CRh/CRi	20/11/1 (32, 96%)
Refractory/Progressive	1 (3)
Best response course (IA/B/C)	
CR/CRh/CRi	30 (85%)
Refractory	3 (9)
Undetermined	2 (6)
Best response end course II	
CR	19
CRh/CRi	13

Wieduwilt et al. Journal of Clinical Oncology 2023 41:16_suppl, 7006-7006

Chemotherapy-free treatment with INO+BLIN for older adults with newly diagnosed Ph- CD22+ B-ALL

1-year EFS	75% (90% CI, 63-89)
1-year OS	**84% (95% CI, 72-98%)**
Relapse	**9**
Systemic + CNS relapse	2
CD19 negative	3
CD22 negative	1
Death with refractory ALL	**1**
Death in remission	**2**
On study therapy	1
After allogeneic HCT	1

Wieduwilt et al. Journal of Clinical Oncology 2023 41:16_suppl, 7006-7006

Chemotherapy-free treatment with INO+BLIN for older adults with newly diagnosed Ph- CD22+ B-ALL

Grade ≥3 adverse events ≥10% evaluable patients	
Decreased ANC	29 (87.9%)
Decreased PLT	24 (72.7%)
Anemia	14 (42.2%)
Decreased WBC	13 (39.4%)
Decreased lymphocytes	9 (27.3%)
Febrile neutropenia	7 (21.2%)
Encephalopathy	4 (12.1%)

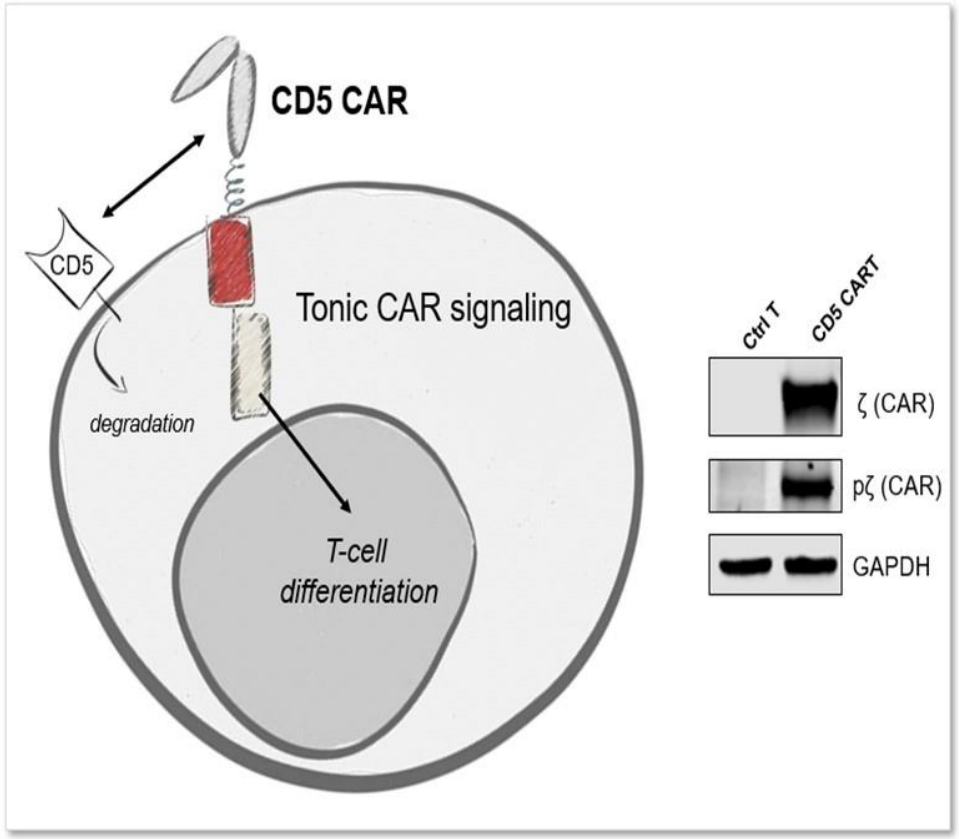
Wieduwilt et al. Journal of Clinical Oncology 2023 41:16_suppl, 7006-7006

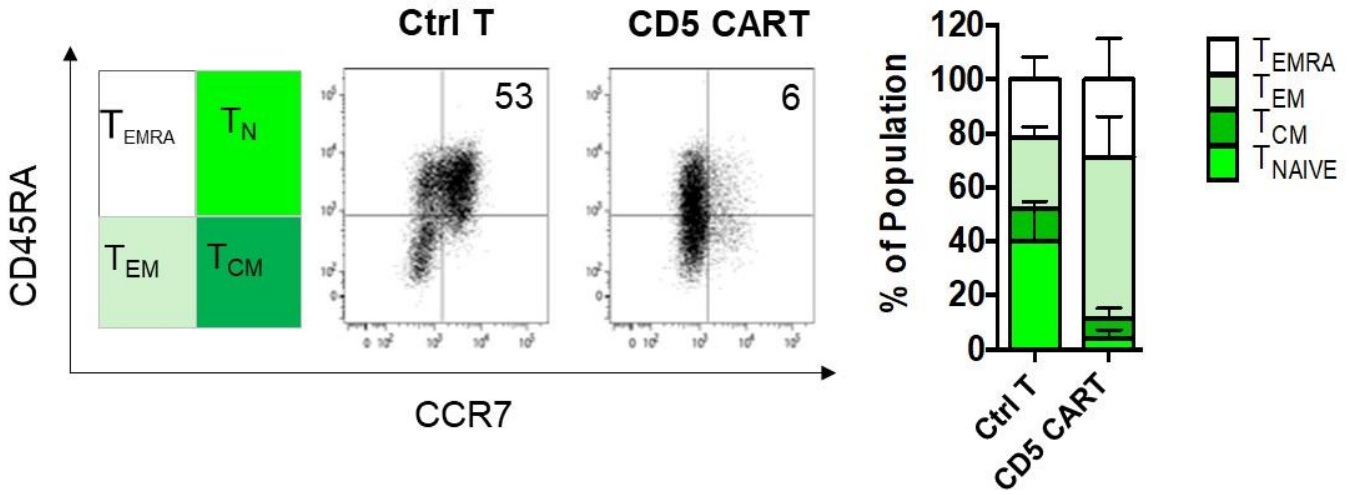
Chemotherapy-free treatment with INO+BLIN for older adults with newly diagnosed Ph- CD22+ B-ALL

Total deaths	9 (of N=33)
Relapsed ALL	**6 (18%)**
AE/refractory ALL	**1 (3%)**
Respiratory failure, liver failure, reported VOD	
AE/in remission	**2**
On study therapy (encephalopathy, pancytopenia, liver failure)	1
Complication of allogeneic HCT (respiratory failure)	1

Wieduwilt et al. Journal of Clinical Oncology 2023 41:16_suppl, 7006-7006

CD5 CAR-T cells are more terminally differentiated in T-ALL





Mamonkin M, et al. Cancer Immunol Res 2018
Srinivasan et al., unpublished data

Slides courtesy: Dr. LaQuisa Hill

Initial clinical responses in T-ALL

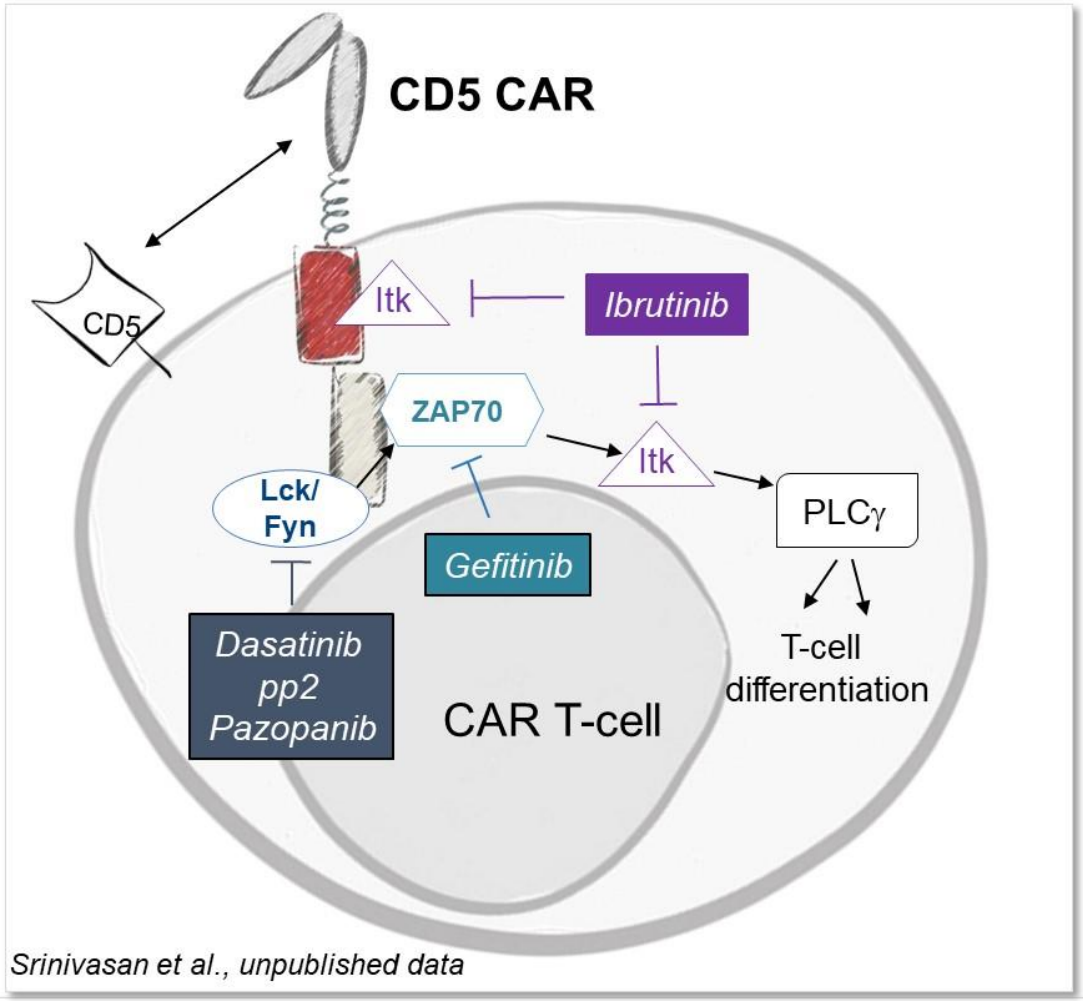
Baylor College of Medicine

Age/Sex	Disease Type	Disease status	Dose Level	Best Clinical Response
		ORR 12.5%		
39M	T-ALL	Primary Refractory	DL**1**	SD
51F	T-ALL	Relapsed post-SCT	DL**2**	SD
15F	T-ALL	Primary Refractory	DL**2**	**MRD+ CR**
40M	T-ALL	Relapsed	DL**2**	PD
19M	T-LBL	Primary Refractory	DL**2**	PD
11M	T-ALL	Relapsed	DL**3**	PD
36F	T-ALL	Primary Refractory	DL**3**	PD
12F	T-ALL	Relapsed post-SCT	DL**3**	PD

CD5 expression remained detectable in all patients

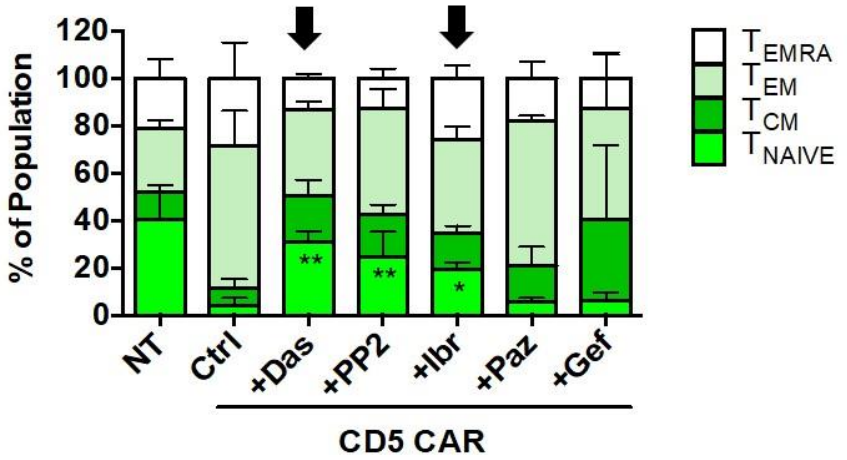
Slides courtesy: Dr. LaQuisa Hill

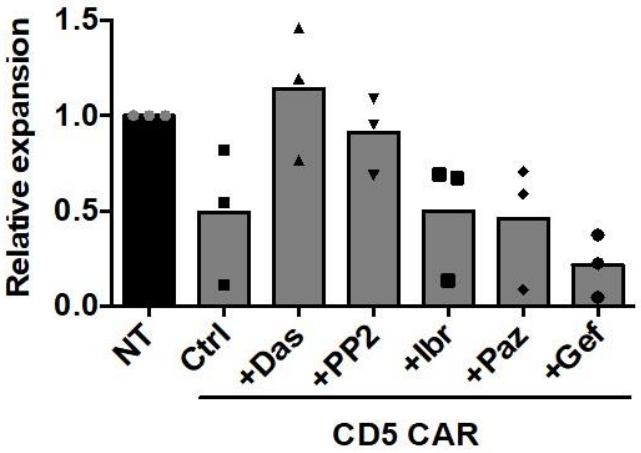
Inhibition of tonic CD5 CAR signaling prevents excessive T-cell differentiation



Srinivasan et al., unpublished data

Phenotype of CD5 CAR T-cells expanded with TKIs





Madhu Srinivasan

PRESENTED BY: LaQuisa Hill MD

Slides courtesy: Dr. LaQuisa Hill

Improved responses with TKI inhibition

Age/Sex	Disease Type	Disease status	Dose Level	Best Clinical Response
ORR 57%				
Autologous (+TKI)				
14M	T-ALL	Primary refractory	DL**2**	PD
65F	T-LBL	Relapsed	DL**3**	SD
17M	T-ALL	Primary refractory	DL**3**	**MRD- CR**
70F	T-ALL	Relapsed	DL**3**	**MRD- CR**
Donor-derived (+TKI)				
13F*	T-ALL	Relapsed post-alloSCT	DL**1**	**MRD- CR**
43M	T-ALL	Relapsed post-alloSCT	DL**1**	**MRD- CR**
45F	T-ALL	Relapsed post-alloSCT	DL**1**	SD

* Treated on DL3 in non-TKI arm with no response

No increase in severity of CRS/ICANS with TKI inhibition

	Cohort 1 (N=8)	Cohort 2 (N=7)
Responses		
CR, n (%)	1 (12.5)	4 (57)
MRD neg, n (%)	0 (0)	4 (57)
Toxicities		
CRS, n (%)	2 (25)	5 (71)
Grade 1-2	2 (25)	5 (71)
Grade ≥3	0 (0)	0 (0)
NT/ICANS, n (%)	1 (12.5)	0 (0)
Grade 1-2	1 (12.5)	0 (0)
Grade ≥3	0 (0)	0 (0)
aGVHD, n (%)	0 (0)	0 (0)

Acute myeloid leukemia

CPX-351 vs 7+3: survival outcomes based on bone marrow blasts percentage in AML

- Phase III, newly diagnosed or secondary AML patients 60-75 years
- 5-year follow-up (median follow-up 60.9 months)

Baseline BM blasts	< 20%[a]		20%–40%		> 40%–60%		> 60%	
Treatment	CPX-351	7+3	CPX-351	7+3	CPX-351	7+3	CPX-351	7+3
N	**21**	**22**	**62**	**65**	**34**	**34**	**32**	**29**
Median OS, mo	**12.6**	**7.3**	**11.6**	**6.0**	**8.1**	**4.9**	**4.7**	**2.9**
HR (95% CI)	0.38 (0.19, 0.75)		0.62 (0.42, 0.91)		0.72 (0.43, 1.21)		0.67 (0.40, 1.14)	
Median EFS, mo	3.0	1.1	2.5	2.2	5.0	1.0	2.0	1.2
HR (95% CI)	0.60 (0.32, 1.14)		0.81 (0.55, 1.18)		0.45 (0.27, 0.77)		0.54 (0.31, 0.95)	
CR, n (%)	7 (33)	5 (23)	25 (40)	21 (32)	16 (47)	8 (24)	9 (28)	4 (14)
OR (95% CI)	3.78 (0.68, 21.05)		1.22 (0.56, 2.66)		2.89 (0.99, 8.44)		1.72 (0.41, 7.21)	
Median 5-years OS% (95% CI)	26.0 (9.6, 46.1)	0	22.4 (12.9, 33.4)	9.2 (3.8, 17.7)	19.4 (8.1, 34.4)	8.8 (2.3, 21.1)	6.3 (1.1, 18.1)	3.4 (0.30, 14.9)

Ritchie et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 7027-7027.

Myelodysplastic syndrome

The COMMANDS study

The COMMANDS study (NCT03682536) is a global, phase 3, open-label, randomized trial comparing the efficacy and safety of luspatercept versus epoetin alfa for the treatment of anemia due to IPSS-R LR-MDS in ESA-naive patients who require RBC transfusions

Key eligibility criteria

- ≥ 18 years of age
- IPSS-R Very low-, Low-, or Intermediate-risk MDS (with or without RS) by WHO 2016, with < 5% blasts in bone marrow[a]
- Required RBC transfusions (2–6 pRBC units/8 weeks for a minimum of 8 weeks immediately prior to randomization)
- Endogenous sEPO < 500 U/L
- ESA-naive

Patients stratified by:

- Baseline sEPO level
- Baseline RBC transfusion burden
- RS status

Randomized 1:1

Luspatercept (N = 178)
1.0 mg/kg s.c. Q3W
titration up to 1.75 mg/kg

Epoetin alfa (N = 178)[b]
450 IU/kg s.c. QW
titration up to 1050 IU/kg

Response assessment at day 169 and every 24 weeks thereafter

End treatment
Due to lack of clinical benefit[c] or disease progression per IWG criteria

Post-treatment safety follow-up

- Monitoring for other malignancies, HR-MDS or AML progression, subsequent therapies, survival
- For 5 years from first dose or 3 years from last dose, whichever is later

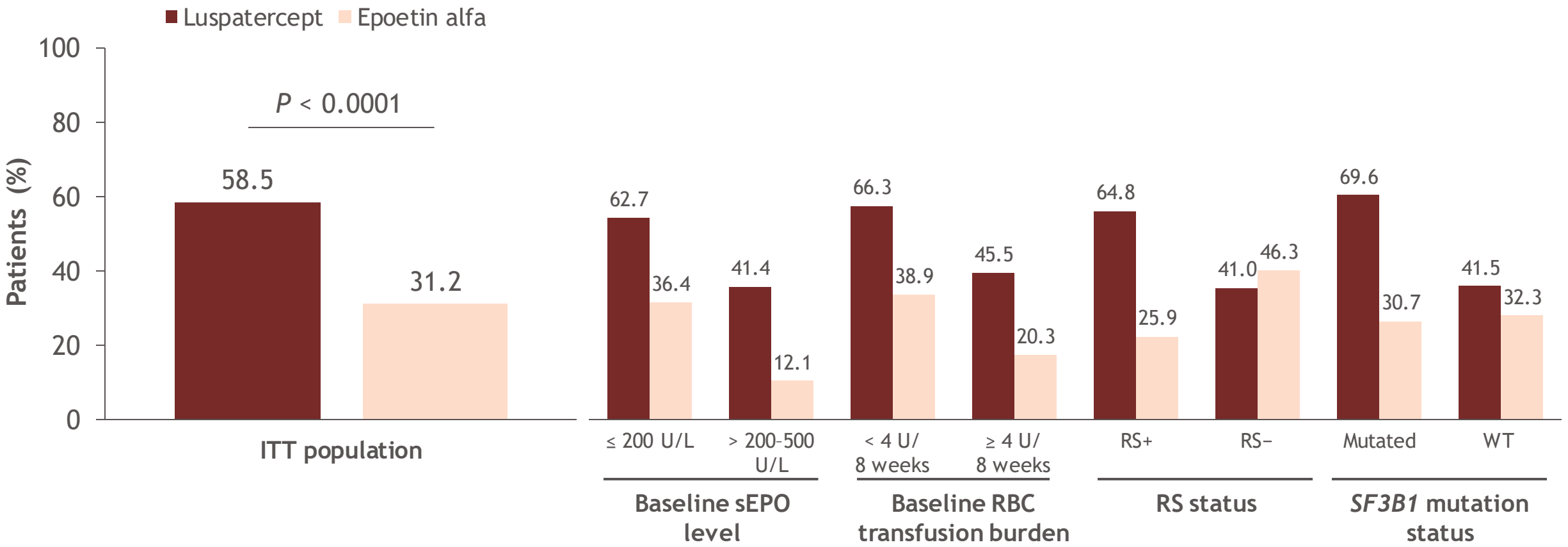
[a]MDS with del(5q) were excluded; [b]2 patients randomized to the epoetin alfa arm withdrew consent prior to receiving their first dose; [c]Clinical benefit defined as transfusion reduction of ≥ 2 pRBC units/8 weeks versus baseline. AML, acute myeloid leukemia; HR, high risk; IPSS-R, Revised International Prognostic Scoring System; IWG, International Working Group; pRBC, packed RBC; QW, once weekly; Q3W, every 3 weeks; RBC, red blood cell; s.c., subcutaneously; sEPO, serum erythropoietin; WHO, World Health Organization.

Garcia-Manero G, et al. ASCO 2023 [Abstract #7003]

Slides courtesy: Dr. Guillermo Garcia-Manero

COMMANDS: achievement of primary endpoint in different patient subgroups

- Primary endpoint: RBC-TI ≥ 12 weeks with concurrent mean Hb increase ≥ 1.5 g/dL (weeks 1–24)



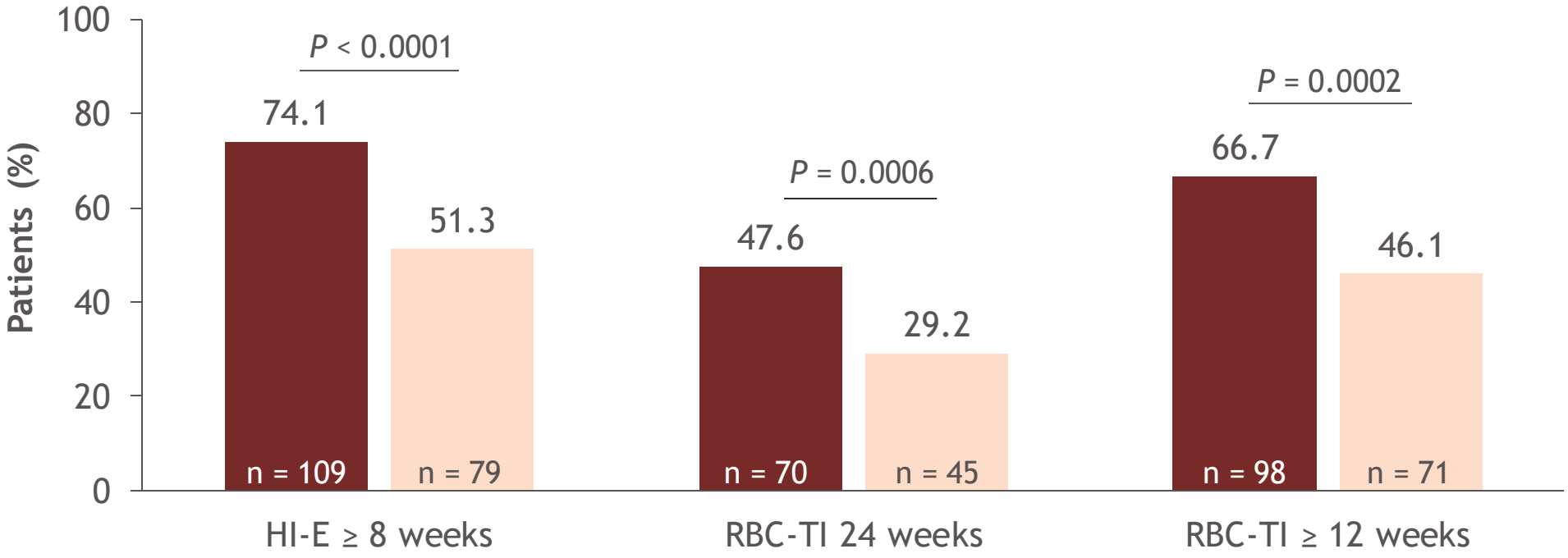
RS status, baseline sEPO level, and baseline RBC transfusion burden were prespecified factors for randomization. *SF3B1* mutation status was a post hoc subgroup analysis. WT, wild type.

Garcia-Manero G, et al. ASCO 2023 [Abstract #7003]

Slides courtesy: Dr. Guillermo Garcia-Manero

COMMANDS secondary endpoints: luspatercept superior to epoetin alfa

	Luspatercept (N = 147)	Epoetin alfa (N = 154)
Time to first RBC transfusion (week 1-EOT), median (range), weeks	n = 93 168.0 (64.0–323.0)	n = 116 42.0 (22.0–55.0)



Garcia-Manero G, et al. ASCO 2023 [Abstract #7003]

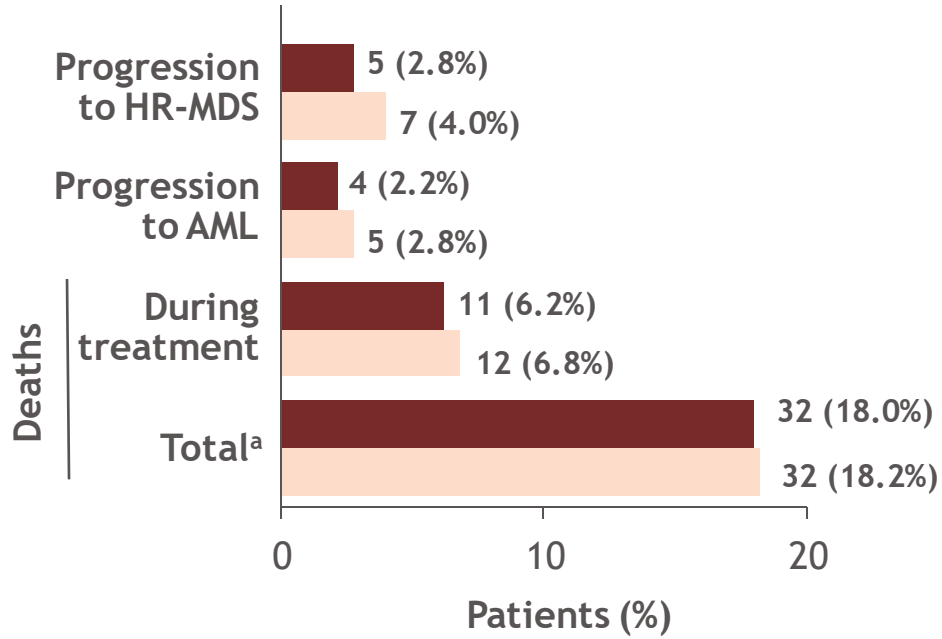
Slides courtesy: Dr. Guillermo Garcia-Manero

COMMANDS: safety

Patients, n (%)	Luspatercept (N = 178)		Epoetin alfa (N = 176)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Heme-related TEAEs				
Anemia	17 (9.6)	13 (7.3)	17 (9.7)	12 (6.8)
Thrombocytopenia	11 (6.2)	7 (3.9)	3 (1.7)	1 (0.6)
Neutropenia	9 (5.1)	7 (3.9)	13 (7.4)	10 (5.7)
Leukocytopenia	2 (1.1)	0	3 (1.7)	0
TEAEs of interest				
Fatigue	26 (14.6)	1 (0.6)	12 (6.8)	1 (0.6)
Diarrhea	26 (14.6)	2 (1.1)	20 (11.4)	1 (0.6)
Peripheral edema	23 (12.9)	0	12 (6.8)	0
Asthenia	22 (12.4)	0	25 (14.2)	1 (0.6)
Nausea	21 (11.8)	0	13 (7.4)	0
Dyspnea	21 (11.8)	7 (3.9)	13 (7.4)	2 (1.1)
TEE	8 (4.5)	5 (2.8)	5 (2.8)	1 (0.6)

TEAEs of any grade
164 (92.1%) luspatercept
150 (85.2%) epoetin alfa

Treatment duration, median (range)
41.6 (0–165) weeks luspatercept
27.0 (0–171) weeks epoetin alfa



Safety data are not exposure-adjusted. [a]Deaths during treatment period and post-treatment period. TEE, thromboembolic event.

Garcia-Manero G, et al. ASCO 2023 [Abstract #7003]

Slides courtesy: Dr. Guillermo Garcia-Manero

IMerge Phase 3 Trial Design (MDS3001; NCT02598661)

Phase 3
Double-blind, randomized
118 Clinical sites in 17 countries

Patient Population (ITT N = 178):
- IPSS low- or intermediate 1- risk MDS
- Relapsed/refractory[a] to ESA or EPO >500 mU/mL (ESA ineligible)
- **Transfusion dependent: ≥4 units RBCs/8 weeks over 16-week pre-study**
- Non-deletion 5q
- No prior treatment with lenalidomide or HMAs

RANDOMIZE

2:1

Imetelstat
7.5 mg/kg IV/4 weeks
(N = 118)

Placebo
(N = 60)

Stratification:
- Transfusion burden (4-6 vs >6 units)
- IPSS risk category (low vs intermediate-1)

Supportive care, including RBC and platelet transfusions, myeloid growth factors (e.g., G-CSF), and iron chelation therapy administered as needed on study per investigator discretion

Safety population (treated) N = 177
Imetelstat N = 118
Placebo N = 59

Primary End Point:
- 8-week RBC-TI[b]

Key Secondary End Points:
- 24-week RBC-TI[b]
- Duration of TI
- Hematologic Improvement-Erythroid
- Safety

Key Exploratory End Point:
- VAF changes
- PRO (fatigue measured by FACIT-Fatigue)

[a]Received ≥8 weeks of ESA treatment (epoetin alfa ≥40,000 U, epoetin beta ≥30,000 U or darbepoetin alfa 150 µg or equivalent per week) without Hgb rise ≥1.5 g/dL or decreased RBC transfusion requirement ≥4 U/8 weeks *or* transfusion dependence or reduction in Hgb by ≥1.5 g/dL after hematologic improvement from ≥8 weeks of ESA treatment.

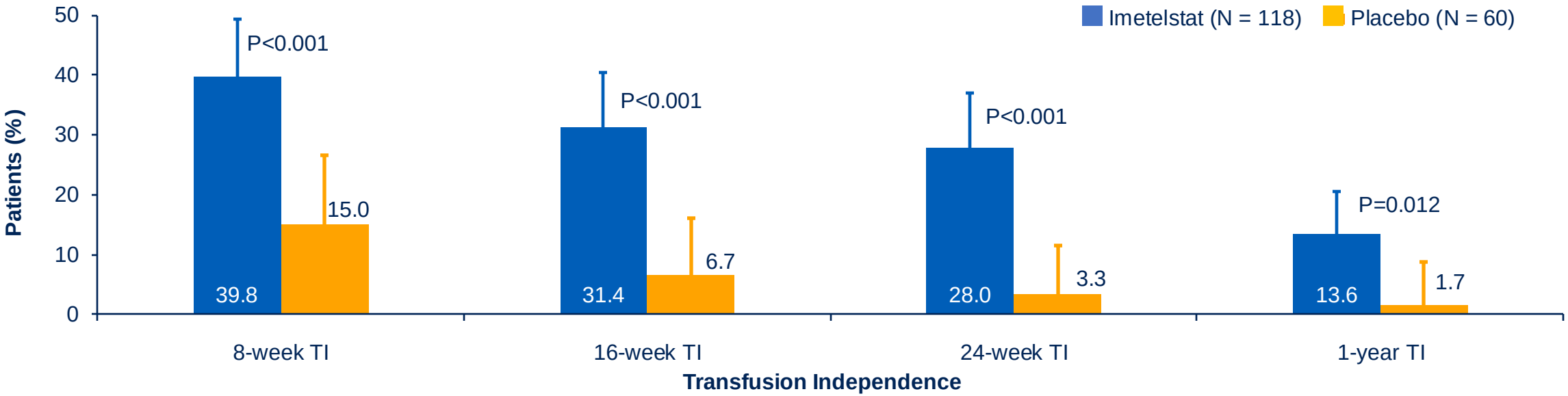
[b]Proportion of patients without any RBC transfusion for ≥8 consecutive weeks since entry to the trial (8-week TI); proportion of patients without any RBC transfusion for ≥24 consecutive weeks since entry to the trial (24-week TI)

EPO, erythropoietin; ESA, erythropoiesis stimulating agent; G-CSF, granulocyte colony-stimulating factor; Hgb, hemoglobin; HMA, hypomethylating agent; IPSS, International Prognostic Scoring System; ITT, intent-to-treat; IV, intravenous; MDS, myelodysplastic syndromes; PRO, patient-reported outcome; RBC, red blood cell; TI, transfusion independence, VAF, variant allele frequency.

PRESENTED BY: Amer Zeidan, MBBS MHS, Associate Professor of Internal Medicine (Hematology)

Slides courtesy: Dr. Amer Zeidan

Higher Rates of Longer-Term Duration of RBC TI Observed With Imetelstat vs Placebo[a]



Patients With Response, n (% [95% CI])				
Imetelstat	47 (39.8 [30.9–49.3])	37 (31.4 [23.1–40.5])	33 (28.0 [20.1–37.0])	16 (13.6 [8.0–21.1])
Placebo	9 (15.0 [7.1–26.6])	4 (6.7 [1.9–16.2])	2 (3.3 [0.4–11.5])	1 (1.7 [0.0–8.9])

Data cutoff: October 13, 2022.

[a]Primary end point 8-week and the first secondary end point 24-week TI are statistically significant by study prespecified gatekeeping testing procedure. One-year TI represented a preliminary assessment. P-values determined by the Cochran-Mantel-Haenszel test, with stratification for prior RBC transfusion burden (≥4 to ≤6 vs >6 RBC units/8-weeks during a 16-week period prior to randomization) and baseline IPSS risk category (low vs intermediate-1) applied to randomization.

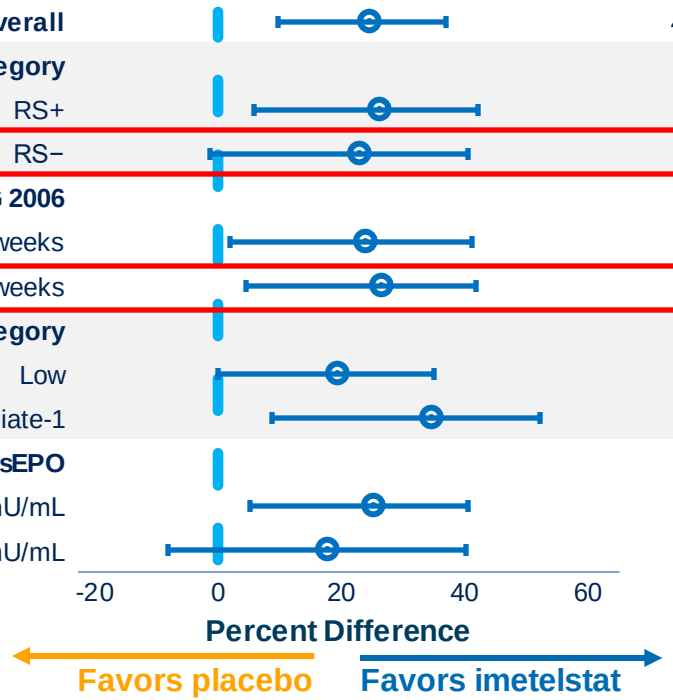
IPSS, International Prognostic Scoring System; RBC, red blood cell; TI, transfusion independence.

PRESENTED BY: Amer Zeidan, MBBS MHS, Associate Professor of Internal Medicine (Hematology)

Slides courtesy: Dr. Amer Zeidan

Primary End Point: 8-Week RBC-TI Rate Significantly Higher With Imetelstat vs Placebo Across Key LR-MDS Subgroups

	Imetelstat, n/N (%)	Placebo, n/N (%)	% Difference (95% CI)	P-Value
Overall	47/118 (39.8)	9/60 (15.0)	24.8 (9.9–36.9)	**<0.001**
WHO category				
RS+	33/73 (45.2)	7/37 (18.9)	26.3 (5.9–42.2)	**0.016**
RS−	14/44 (31.8)	2/23 (8.7)	23.1 (−1.3 to 40.6)	**0.038**
Prior RBC transfusion burden per IWG 2006				
4–6 units/8 weeks	28/62 (45.2)	7/33 (21.2)	23.9 (1.9–41.4)	**0.027**
>6 units/8 weeks	19/56 (33.9)	2/27 (7.4)	26.5 (4.7–41.8)	**0.023**
IPSS risk category				
Low	32/80 (40.0)	8/39 (20.5)	19.5 (−0.1 to 35.2)	**0.034**
Intermediate-1	15/38 (39.5)	1/21 (4.8)	34.7 (8.8–52.4)	**0.004**
Baseline sEPO				
≤500 mU/mL	39/87 (44.8)	7/36 (19.4)	25.4 (5.3–40.7)	**0.011**
>500 mU/mL	7/26 (26.9)	2/22 (9.1)	17.8 (−8.2 to 40.3)	**0.107**



Data cutoff: October 13, 2022.

P-values determined by the Cochran-Mantel-Haenszel test, with stratification for prior RBC transfusion burden (≥4 to ≤6 vs >6 RBC units/8-weeks during a 16-week period prior to randomization) and baseline IPSS risk category (low vs intermediate-1) applied to randomization.

IPSS, International Prognostic Scoring System; IWG, International Working Group; LR-MDS, lower-risk myelodysplastic syndromes; RBC, red blood cell; RS, ring sideroblast; sEPO, serum erythropoietin; TI, transfusion independence.

Consistent With Prior Clinical Experience, the Most Common AEs Were Hematologic

Grade 3–4 thrombocytopenia and neutropenia were the most frequently reported AEs, most often reported during Cycles 1–3

Nonhematologic AEs were generally low grade

Although ≈75% of patients treated with imetelstat had dose modifications due to AEs, <15% of patients discontinued treatment due to TEAEs

No cases of Hy's Law or drug-induced liver injury observed

The incidence of grade 3 liver function test laboratory abnormalities was similar in both treatment groups

AE (≥10% of patients), n (%)	Imetelstat (N = 118)		Placebo (N = 59)	
	Any Grade	Grade 3–4	Any Grade	Grade 3–4
Hematologic				
Thrombocytopenia	89 (75)	73 (62)	6 (10)	5 (8)
Neutropenia	87 (74)	80 (68)	4 (7)	2 (3)
Anemia	24 (20)	23 (19)	6 (10)	4 (7)
Leukopenia	12 (10)	9 (8)	1 (2)	0
Other				
Asthenia	22 (19)	0	8 (14)	0
COVID-19	22 (19)[a]	2 (2)[b]	8 (14)[a]	3 (5)[b]
Headache	15 (13)	1 (1)	3 (5)	0
Diarrhea	14 (12)	1 (1)	7 (12)	1 (2)
ALT increased	14 (12)	3 (3)	4 (7)	2 (3)
Edema peripheral	13 (11)	0	8 (14)	0
Hyperbilirubinemia	11 (9)	1 (1)	6 (10)	1 (2)
Pyrexia	9 (8)	2 (2)	7 (12)	0
Constipation	9 (8)	0	7 (12)	0

Data cutoff: October 13, 2022.

[a]Included COVID-19, asymptomatic COVID-19, and COVID-19 pneumonia. [b]Only COVID-19 pneumonia events were grade 3–4 COVID-19.

AE, adverse event; ALT, alanine aminotransferase.

Slides courtesy: Dr. Amer Zeidan

Thank you !!

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