Applications for Community Oncology

ASH Data Review

February 23, 2023

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2022 ASH Key Studies

Lymphomas

- TRIANGLE
- BRUIN
- CAPTIVATE
- L-MIND/First-MIND
- Glofitamab/NP30179

Multiple Myeloma

- GEM-CESAR
- ASCENT
- IFM2017-03
- MajesTEC-1

Leukemias

- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
- Momentum
- Study 2102-HEM-101

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CLINICAL QUESTION

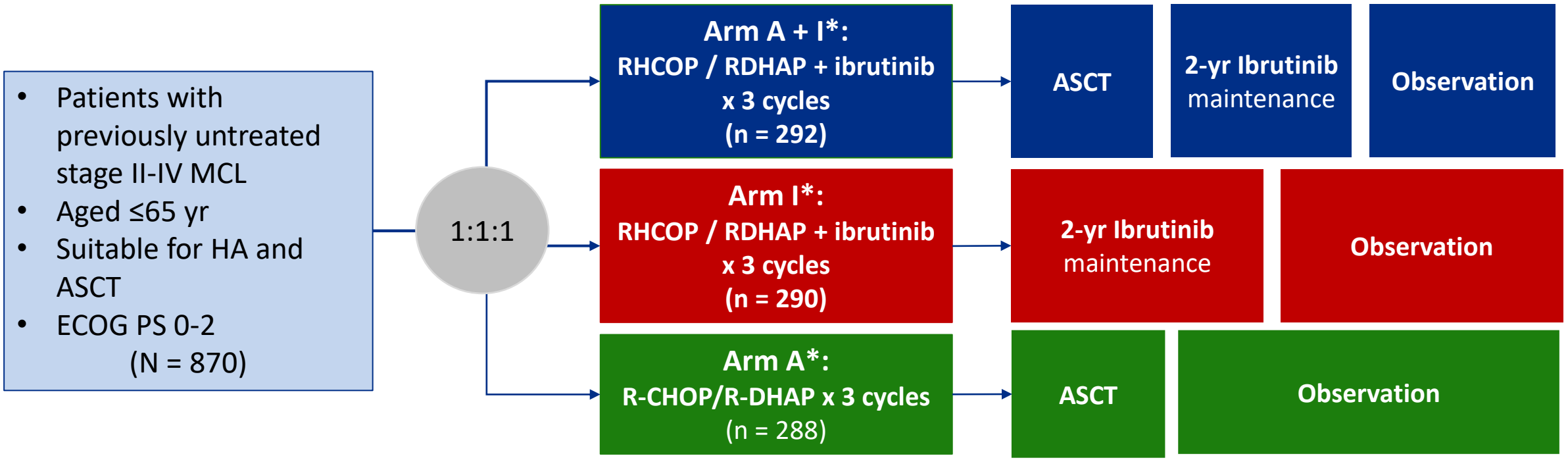
TRIANGLE Clinical Study

Does the addition of ibrutinib to induction immunochemotherapy followed by ASCT with ibrutinib maintenance provide benefit for patients with previously untreated mantle cell lymphoma?

KEY DATA

TRIANGLE Clinical Study

Study Design: randomized, open-label phase 3 trial



*R maintenance was added following national guidelines in all 3 arms (arm A + I: 57%; arm I: 54%; arm A: 58%).

Primary endpoint: Failure-free survival (FFS)

Secondary endpoints: Response rates, PFS, RD, OS, Safety

R-CHOP: (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone)
R-DHAP: (rituximab, dexamethasone, cytarabine, and cisplatin)

Dreyling. ASH 2022. Abstr 1.

TRIANGLE Clinical Study

Baseline Characteristics

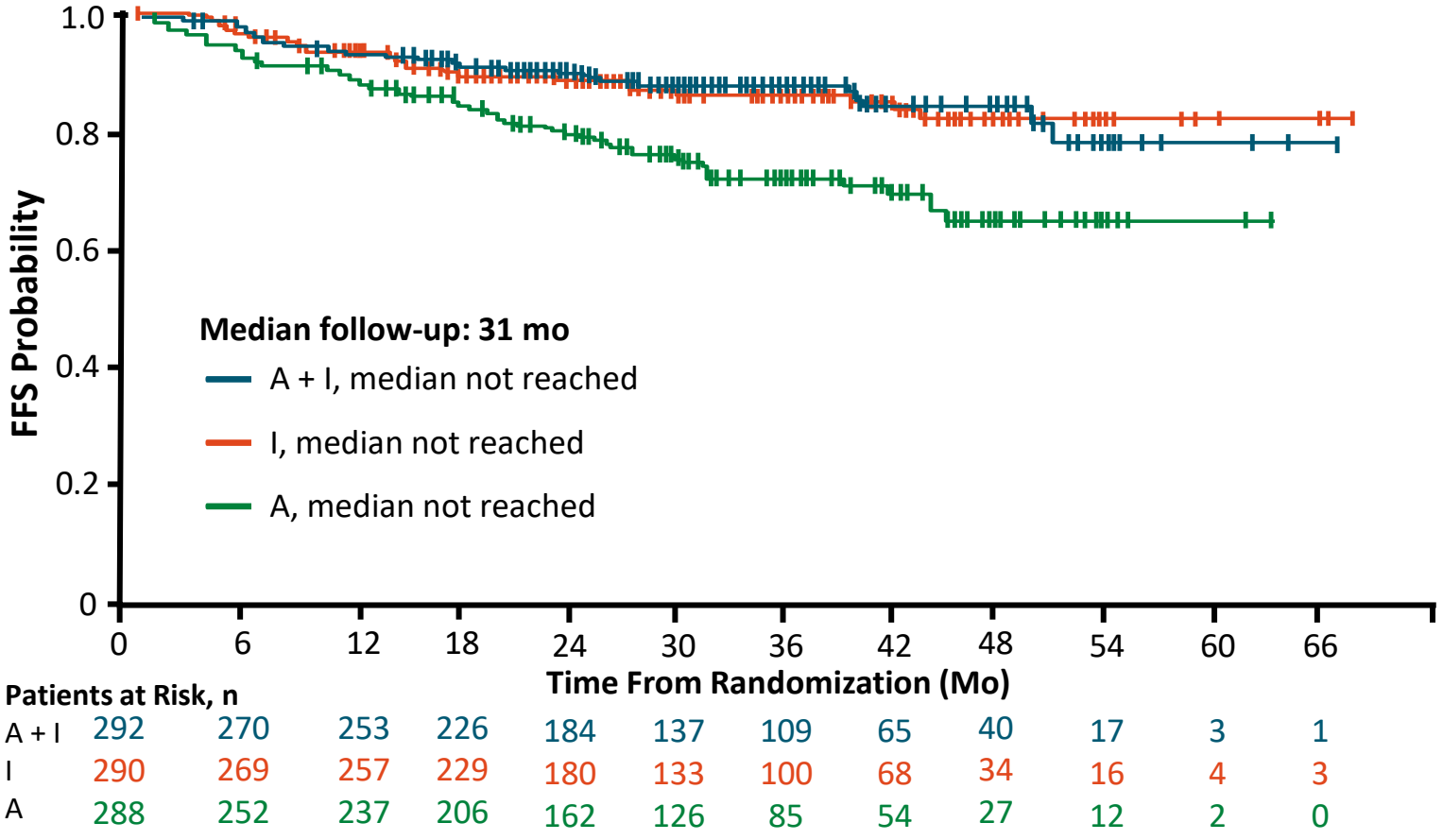
Characteristic, %	A + I* (n = 292)	I* (n = 290)	A* (n = 288)
Median age, yr (range)	**57** (36-68)	**58** (27-65)	**57** (31-65)
Male, %	**74**	**79**	**76**
Ann Arbor stage (n = 864), %			
• I	0	0	0
• II	4	6	4
• III	7	10	8
• IV	**89**	**84**	**88**
ECOG PS >1, %	1	2	2
MIPI, %			
• Low	58	58	58
• Intermediate	27	27	27
• High	15	16	14
No MCL, n	**4** (1 NHL NOS, 1 HD, 2 MZL)	**2** (1 HCL, 1 DLBCL)	**2** (1 CLL, 1 FL)

*A + I arm: IR-CHOP/R-DHAP + ASCT + I; I arm: IR-CHOP/R-DHAP + I. I: ibrutinib; A arm: R-CHOP/R-DHAP + ASCT.

KEY DATA

TRIANGLE Clinical Study

Primary Endpoint: FFS



Patients at Risk, n												
A + I	292	270	253	226	184	137	109	65	40	17	3	1
I	290	269	257	229	180	133	100	68	34	16	4	3
A	288	252	237	206	162	126	85	54	27	12	2	0

A + I vs A 3-Yr FFS Rate

- A + I: 88%;
- A: 72%
- HR (A + I vs A): 0.52, *P* = 0.0008 (superiority confirmed)

I vs A 3-Yr FFS Rate

- I: 86%
- A: 72%
- HR (A vs I): 1.77, *P* = 0.9979 (superiority rejected)

***A + I vs I**, ongoing*

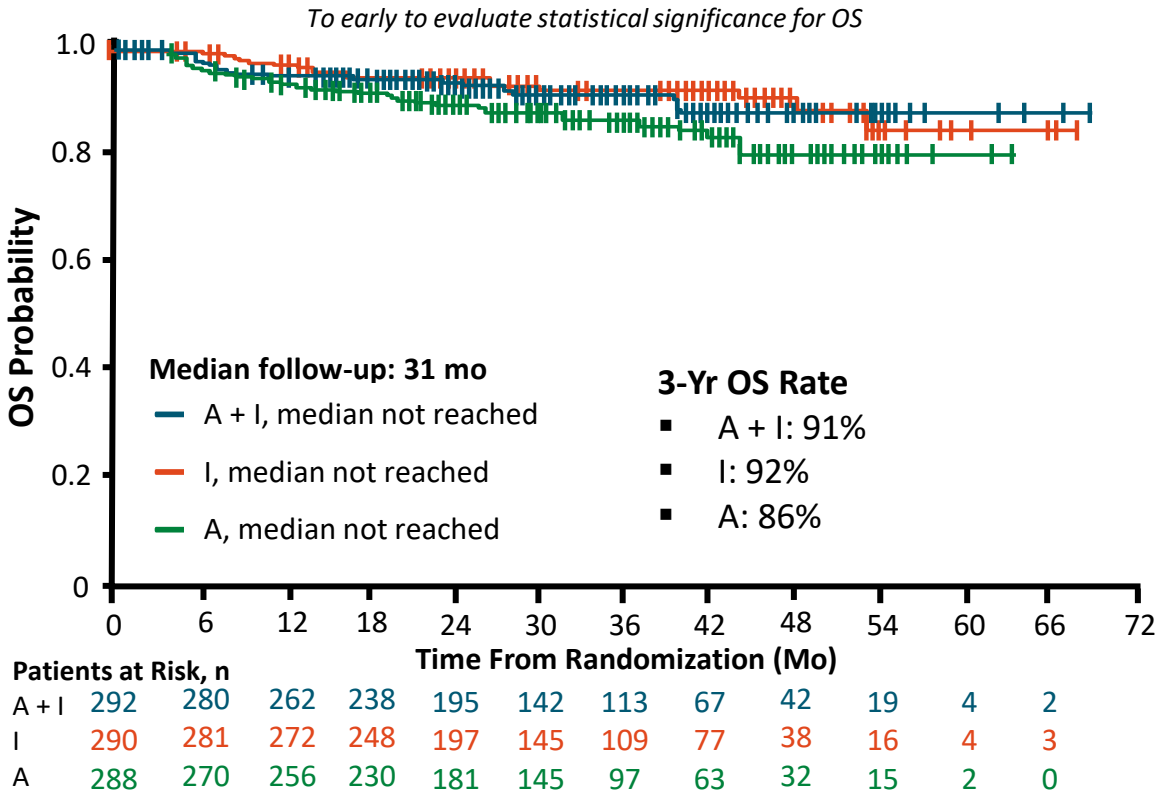
A + I arm: IR-CHOP/R-DHAP + ASCT + I; I arm: IR-CHOP/R-DHAP + I. I: ibrutinib.

Dreyling. ASH 2022. Abstr 1.

KEY DATA

TRIANGLE Clinical Study

Secondary Endpoint: OS



A arm: R-CHOP/R-DHAP + ASCT

A + I arm: IR-CHOP/R-DHAP + ASCT + I

I arm: IR-CHOP/R-DHAP + I. I: ibrutinib

Secondary Endpoint: Response Rates

Response	A + I*	I*	A*	A + I/I
ED, n (%)	1 (0.4)	0	1 (0.4)	1 (0.2)
PD, n (%)	3 (1)	3 (1)	11 (4)	6 (1)
SD, n (%)	1 (0.4)	2 (0.7)	4 (1)	3 (0.5)
PR, n (%)	152 (54)	148 (53)	158 (58)	300 (54)
CR, n (%)	124 (**44**)	125 (**45**)	98 (**36**)	249 (**45**)
CR + PR, n (%)	276 (**98**)	273 (**98**)	256 (**94**)	549 (**98**)
Total, n	281	278	272	559
NE, n	8	10	11	18
ND, n	3	2	5	5

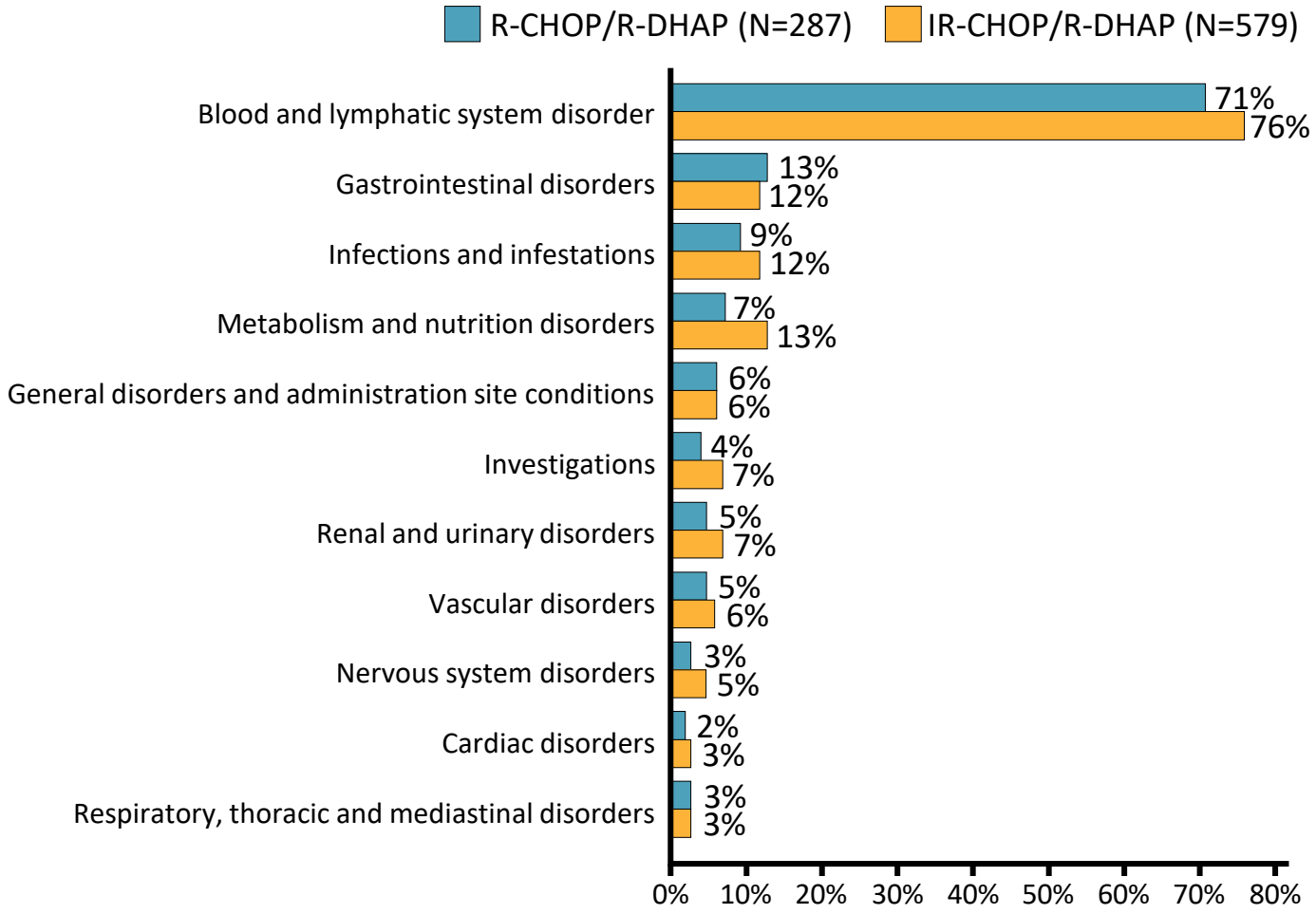
- Combined arms (A + I/I) yielded significantly higher CR (*P* = 0.0203) and ORR (*P* = 0.0025) rates vs control (A)
- In MCL younger R-CHOP/R-DHAP group, CR rates were 38%, and ORR was 94%

Dreyling. ASH 2022. Abstr 1.

KEY DATA

TRIANGLE Clinical Study

Safety: Grade 3-5 AEs (Induction) in >2% of patients



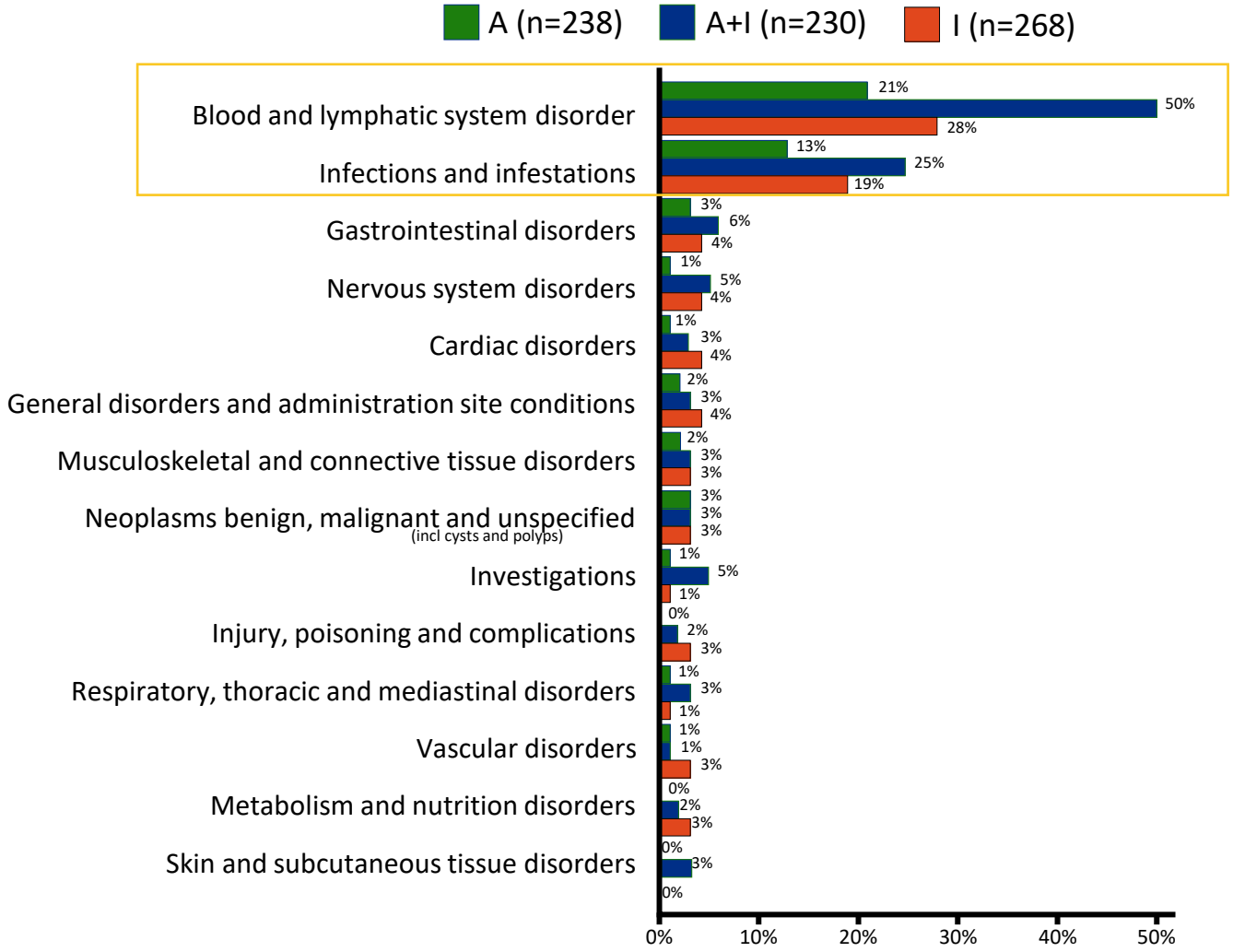
Grade 3-5 AEs by Preferred Term, n (%)	R-CHOP/R-DHAP (n = 287)	IR-CHOP/R-DHAP (n = 579)
Thrombocytopenia	169 (59)	351 (61)
Neutropenia	134 (47)	283 (49)
Anemia	62 (22)	140 (24)
Febrile neutropenia	44 (15)	88 (15)
Leukopenia	25 (9)	70 (12)
Lymphopenia	15 (5)	38 (7)

Grade 5 AEs by System Organ Class, n (%)	R-CHOP/R-DHAP (n = 287)	IR-CHOP/ R-DHAP (n = 579)
GI disorders	2 (1)	0
Infections and infestations	1 (0)	1 (0)
Psychiatric disorders	0	1 (0)

Dreyling. ASH 2022. Abstr 1.

TRIANGLE Clinical Study

Safety: Grade 3-5 AEs (Maintenance/Follow-up) in >2% of patients



Grade 3-5 AEs by Preferred Term, n (%)	A + I* (n = 230)	I* (n = 268)	A* (n = 238)
Neutropenia	**101 (44)**	**62 (23)**	**40 (17)**
Febrile neutropenia	14 (6)	7 (3)	6 (3)
Thrombocytopenia	13 (6)	8 (3)	5 (2)
Leukopenia	10 (4)	6 (2)	4 (2)
Anemia	6 (3)	4 (1)	4 (2)
Lymphopenia	1 (0)	5 (2)	3 (1)

Grade 5 AEs by System Organ Class, n (%)	A + I* (n = 230)	I* (n = 268)	A* (n = 238)
Infections and infestations	2 (1)	2 (1)	3 (1)
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	1 (0)	0	1 (0)
Cardiac disorders	0	1 (0)	0
Respiratory, thoracic, and mediastinal disorders	1 (0)	0	0
Vascular disorders	0 (0)	0	1 (0)

There were no substantial differences in the occurrence of grade 3-5 AEs during induction with R-CHOP/R-DHAP vs ibrutinib-R-CHOP/R-DHAP (neutropenia: 47%/49% of patients, leukopenia: 15%/15%, febrile neutropenia: 9%/12%, infections and infestations: 9%/12%, cardiac disorders: 2%/3%).

The two ASCT-containing arms did not substantially differ in grade 3-5 AEs (A/A+I: neutropenia: 36%/33%, febrile neutropenia: 20%/22%, leukopenia: 17%/17%, infections and infestations: 17%/20%).

Dreyling. ASH 2022. Abstr 1.

TRIANGLE Clinical Study

Safety: Causes of Death

Cause of Death, n (%)	A + I* (n = 292)	I* (n = 290)	A* (n = 288)
All cause	25 (8.6)	23 (7.9)	39 (13.5)
Lymphoma	4 (1.4)	11 (3.8)	16 (5.6)
Concomitant disease	7 (2.4)	5 (1.7)	11 (3.8)
Lymphoma and concomitant disease	1 (0.3)	1 (0.3)	0
Secondary malignancy	2 (0.7)	0	1 (0.3)
Therapy	3 (1.0)	0	4 (1.4)
Therapy and concomitant disease	0	0	1 (0.3)
Unknown	8 (2.7)	6 (2.1)	6 (2.1)

A arm: R-CHOP/R-DHAP + ASCT; A + I arm: IR-CHOP/R-DHAP + ASCT + I; I arm: IR-CHOP/R-DHAP + I. I: ibrutinib

Dreyling. ASH 2022. Abstr 1.

SUMMARY

TRIANGLE Clinical Study

- The addition of ibrutinib to standard CIT ± ASCT yielded strong efficacy with acceptable safety in younger patients with previously untreated MCL

- Based on primary endpoint of FFS, ASCT + ibrutinib is superior to ASCT standard of care arm
  - ASCT standard of care arm is not superior to ibrutinib without ASCT
  - No conclusion yet as to whether ASCT adds to ibrutinib, but safety profile favors ibrutinib-only arm

- Numerical OS benefit observed in ibrutinib-containing arms vs control arm, but data are immature

Dreyling. ASH 2022. Abstr 1.

TRIANGLE Clinical Study

Adding ibrutinib to induction immunochemotherapy and using ibrutinib as maintenance after autologous stem cell transplant (ASCT) improves failure-free survival (FFS) in patients with mantle cell lymphoma (MCL)

2022 ASH Key Studies

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BRUIN Clinical Study

Does pirtobrutinib provide benefit for patients previously treated with a covalent BTK inhibitor for relapsed/refractory mantle cell lymphoma?

Additional patients and extended follow-up

*On **January 27, 2023**, the Food and Drug Administration (FDA) granted accelerated approval to pirtobrutinib (JAYPIRCA™, Eli Lilly and Company) for relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor*

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KEY DATA

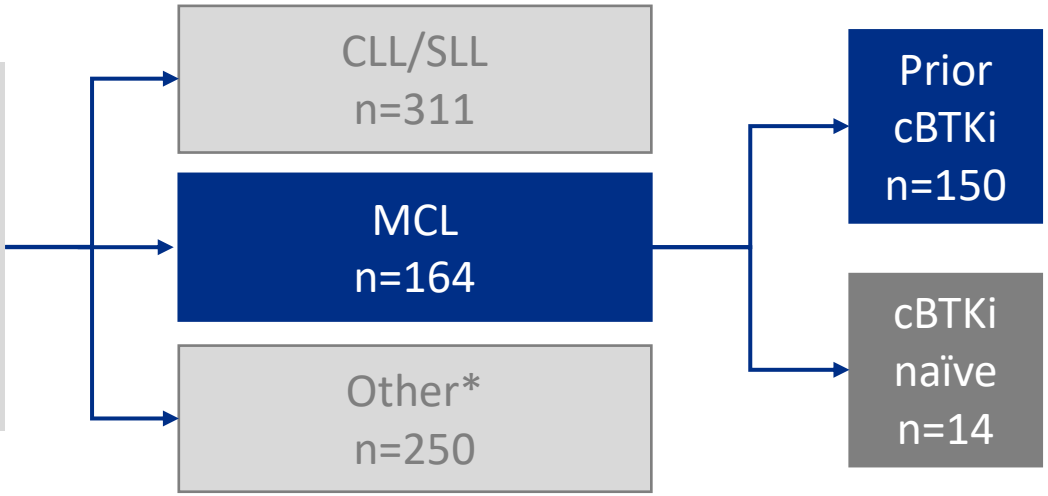
BRUIN Clinical Study

Study Design: open-label, multi-center Phase 1/2 trial

Pts with previously treated B-cell malignancies, including MCL, were eligible for treatment with pirtobrutinib monotherapy in either the dose escalation or expansion portion of the multicenter BRUIN study

- Age ≥18
- ECOG 0-2
- Active disease and in need of treatment
- Previously treated

N=725



The Primary Analysis Set comprises the first **90** patients who met the following criteria:

- Enrolled to either phase 1 or 2
- Had measurable disease
- Had received a prior cBTKi containing regimen
- Had no known central nervous system involvement

Overall, 86% (n=77) received the recommended phase 2 dose of 200 mg pirtobrutinib once daily as starting dose.

Key Endpoints: overall response rate (ORR) based on Lugano 2014 criteria, duration of response (DOR), and safety

*Other includes DLBCL, WM, FL, MZL, Richter's transformation, B-PLL, Hairy Cell Leukemia, PCNSL, and other transformation

A data cut of 31 January 2022 was chosen to ensure the majority of the cohort had a minimum of 9 months of follow-up from the initial response

KEY DATA

BRUIN Clinical Study

Baseline Characteristics

Characteristics	Prior cBTKi (n=90)	cBTKi Naïve (n=14)
Median age, years (range)	70 (46-87)	67 (60-86)
Male, n (%)	72 (80)	10 (71)
Histology, n (%)		
Classic	70 (78)	11 (79)
Pleomorphic/Blastoid	20 (22)	3 (21)
ECOG PS, n (%)		
0	61 (68)	5 (36)
1	28 (31)	8 (57)
2	1 (1)	1 (7)
sMIPI Score, n (%)		
Low risk (0-3)	20 (22)	3 (21)
Intermediate risk (4-5)	50 (56)	5 (36)
High risk (6-11)	20 (22)	6 (43)
Tumor Bulk (cm), n (%)		
<5 / ≥5	66 (73) / 24 (27)	9 (64) / 5 (36)
<10 / ≥10	87 (97) / 3 (3)	12 (86) / 2 (14)
Bone Marrow Involvement, n (%)		
Yes	46 (51)	4 (29)
No	44 (49)	10 (71)

Characteristics	Prior cBTKi (n=90)	cBTKi Naïve (n=14)
Reason discontinued any prior cBTKi[a], n (%)		
Progressive disease	74 (82)	-
Toxicity/Other	16 (18)	-
Median number prior lines of systemic therapy (range)	3 (1-8)	2 (1-3)
Prior therapy, n (%)		
BTK inhibitor	90 (100)	0 (0)
Anti-CD20 antibody	86 (96)	14 (100)
Chemotherapy	79 (88)	14 (100)
Immunomodulator	19 (21)	1 (7)
Stem cell transplant	19 (21)	7 (50)
Autologous	17 (19)	7 (50)
Allogeneic	4 (4)	0 (0)
BCL2 inhibitor	14 (16)	0 (0)
CAR-T	4 (4)	0 (0)
PI3K inhibitor	3 (3)	1 (7)

[a]Calculated as percent of patients who received prior cBTKi.

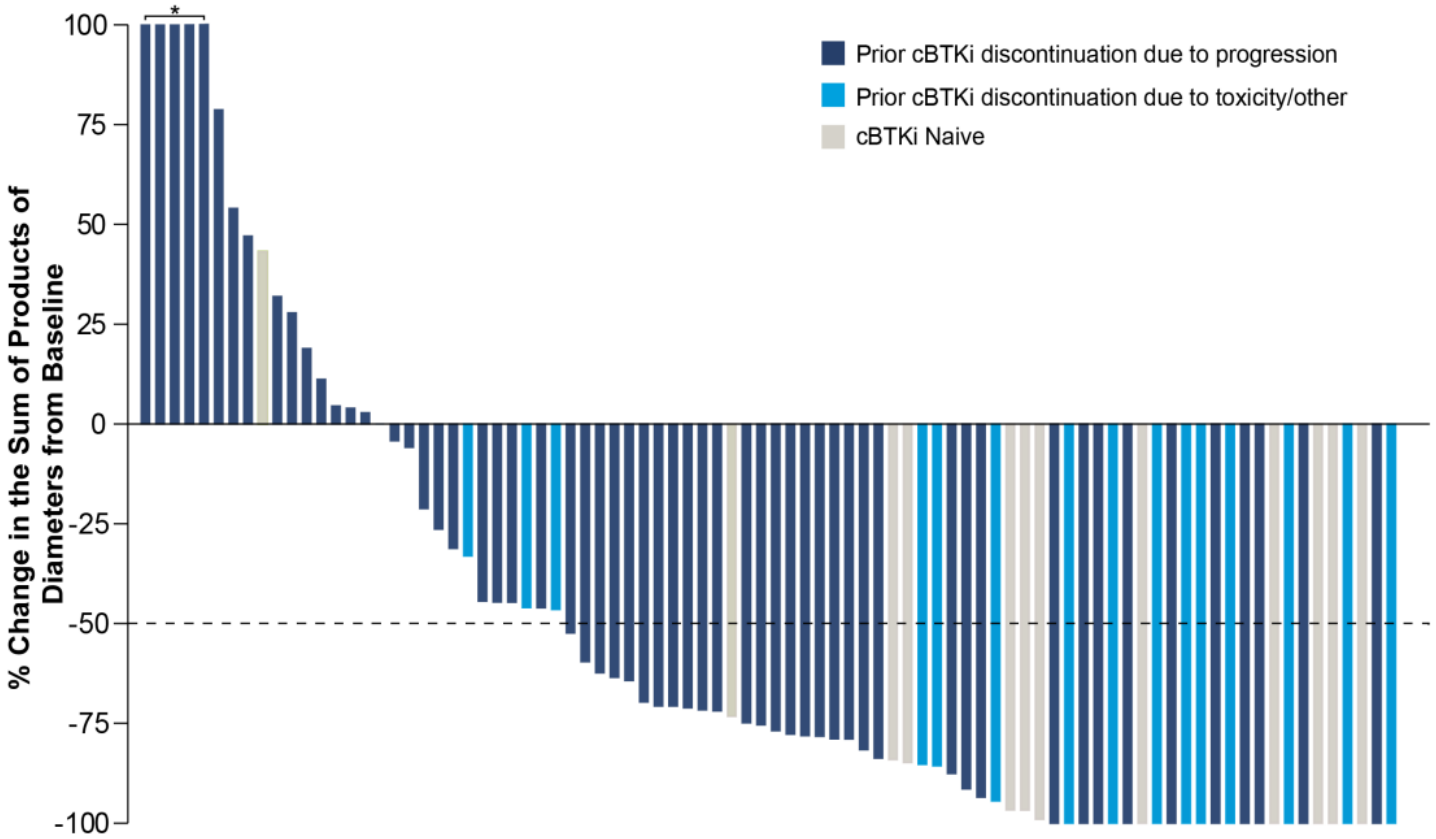
Wang. ASH 2022. Abstr 4218.

Data cutoff date of 31 January 2022.

KEY DATA

BRUIN Clinical Study

Response Rates



Prior cBTKi MCL Patients	n=90
Overall Response Rate[a], % (95% CI)	**57.8% (46.9-68.1)**
Best Response[b]	
CR, n (%)	18 (20.0)
PR, n (%)	34 (37.8)
SD, n (%)	14 (15.6)
PD, n (%)	15 (16.7)

cBTKi Naïve MCL Patients	n=14
Overall Response Rate[a], % (95% CI)	**85.7% (57.2-98.2)**
Best Response[c]	
CR, n (%)	5 (35.7)
PR, n (%)	7 (50.0)
SD, n (%)	0 (0.0)
PD, n (%)	1 (7.1)

Data cutoff date of 31 January 2022. Data for 18 patients are not shown in the waterfall plot due to no measurable target lesions identified by CT at baseline, discontinuation prior to first response assessment, or lack of adequate imaging in follow-up. *Indicates patients with >100% increase in SPD. [a]ORR includes patients with a best response of CR and PR. [b] 9 cBTKi pre-treated MCL patients were not evaluable. [C] 1 cBTKi naïve patient was not evaluable. Response status per Lugano 2014 criteria based on IRC assessment.
Responses were observed in 6/8 pts (75%) with blastoid MCL and in 6/12 pts (50%) with pleomorphic MCL.

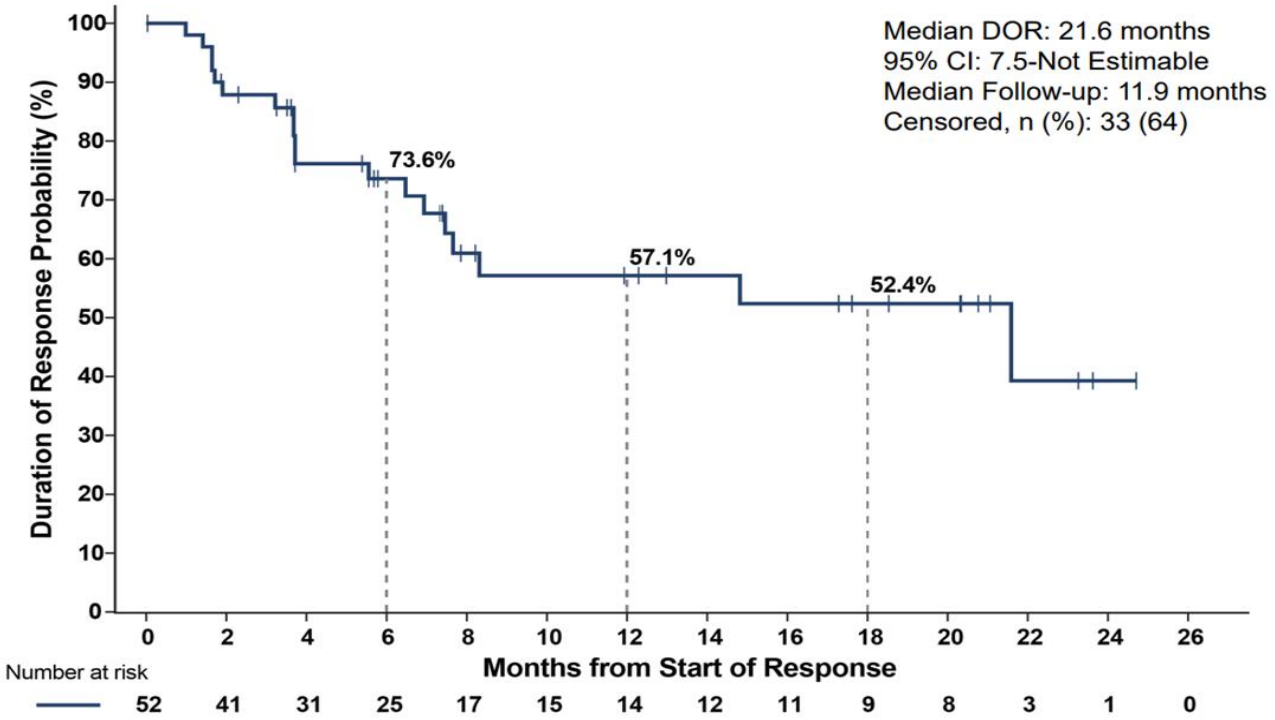
Wang. ASH 2022. Abstr 4218.

KEY DATA

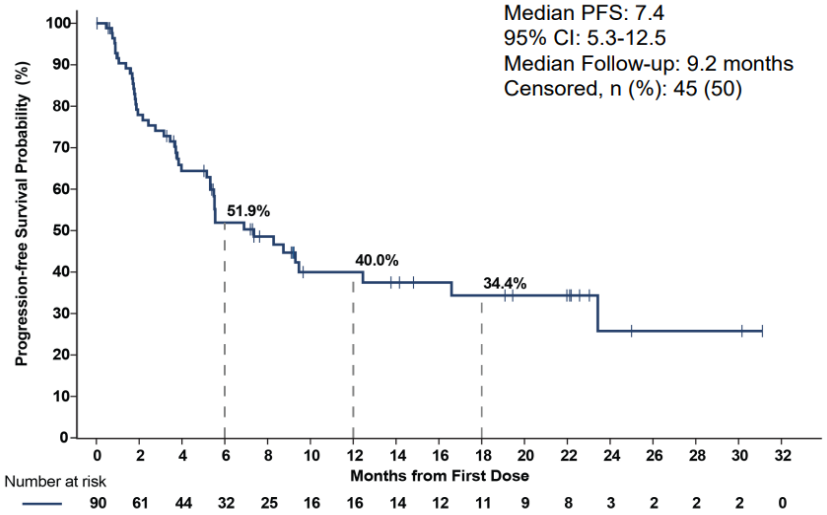
BRUIN Clinical Study

Efficacy: Duration of Response, PFS, and OS

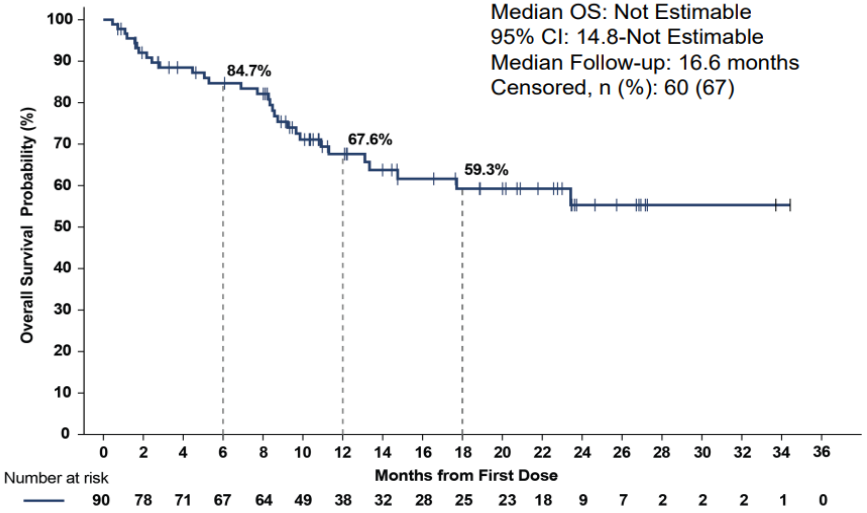
Duration of Response



Progression-Free Survival



Overall Survival



Patients who discontinued their prior BTKi due to disease progression (n=74) had an ORR of 50% (95% CI, 38-62) and a median DOR of 14.8 months (95% CI, 5.6-NE).

Data cutoff date of 31 January 2022. Response status per Lugano 2014 criteria based on IRC assessment.

Wang. ASH 2022. Abstr 4218.

KEY DATA

BRUIN Clinical Study

Safety

	All Doses and Patients (N=725)			
	Treatment-Emergent AEs, (≥15%), %		Treatment-Related AEs, %	
Adverse Event (AEs)	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Fatigue	26.3%	1.7%	9.1%	0.8%
Diarrhea	22.1%	0.8%	8.6%	0.3%
Neutropenia[a]	21.7%	18.6%	13.0%	10.5%
Contusion	19.0%	0.0%	12.6%	0.0%
AEs of Special Interest[b]	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Bruising[c]	23.2%	0.0%	14.9%	0.0%
Rash[d]	12.3%	0.4%	5.5%	0.3%
Arthralgia	13.0%	0.4%	3.2%	0.0%
Hemorrhage/Hematoma[e]	10.2%	1.7%	3.4%	0.4%
Hypertension	9.5%	2.8%	3.2%	0.6%
Atrial fibrillation/flutter[f, g]	2.6%	1.0%	0.7%	0.1%

- Median time on treatment for the overall population was 8 months
- Discontinuations due to TRAEs occurred in 2% (n=15) of overall patients
- Dose reductions due to TRAEs occurred in 5% (n=38) of overall patients
- Overall and MCL safety profiles were consistent

aAggregate of neutropenia and neutrophil count decreased.
bAEs of special interest are those that were previously associated with cBTKi.
cAggregate of contusion, petechiae, ecchymosis, and increased tendency to bruise.
dAggregate of all preferred terms including rash.
eAggregate of all preferred terms including hematoma or hemorrhage.
fAggregate of atrial fibrillation and atrial flutter.
gOf 19 total afib/aflutter TEAEs, 6 occurred in patients with a prior medical history of atrial fibrillation.

The safety cohort consisted of all pts with B-cell malignancies who received at least one dose of pirtobrutinib monotherapy (n=725)
Data cutoff date of 31 January 2022.

Wang. ASH 2022. Abstr 4218.

SUMMARY

BRUIN Clinical Study

- With over a year of additional data, pirtobrutinib continues to demonstrate promising efficacy in R/R MCL patients who have received a prior BTKi
  - Overall response rate consistent regardless of the number of prior systemic therapies, with a greater ORR for BTKi naïve patients
- Pirtobrutinib is well tolerated with low rates of AEs as well as low rates of discontinuation
- Pirtobrutinib is the first-and-only approved reversible BTK inhibitor
  - A randomized, global, Phase 3 trial comparing pirtobrutinib with investigator's choice of cBTKi in pretreated BTKi naïve MCL is ongoing (BRUIN MCL-321; NCT04662255)

Wang. ASH 2022. Abstr 4218.

BRUIN Clinical Study

Pirtobrutinib provides benefit for patients with relapsed/refractory mantle cell lymphoma (MCL) and should be standard of care in the 3L setting

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Leukemias

- VIALE-A
- ECOG-ACRIN E1910
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- Study 2102-HEM-101

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CAPTIVATE Clinical Study

Does continued ibrutinib after front-line treatment with ibrutinib plus venetoclax provide benefit for patients with CLL/SLL with undetectable MRD?

Additional year of follow-up

August 4, 2022: The European Commission approved IMBRUVICA® (ibrutinib) in a fixed-duration combination regimen with Venclexta (venetoclax) for adult patients with previously untreated chronic lymphocytic leukaemia (CLL)

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KEY DATA

CAPTIVATE Clinical Study

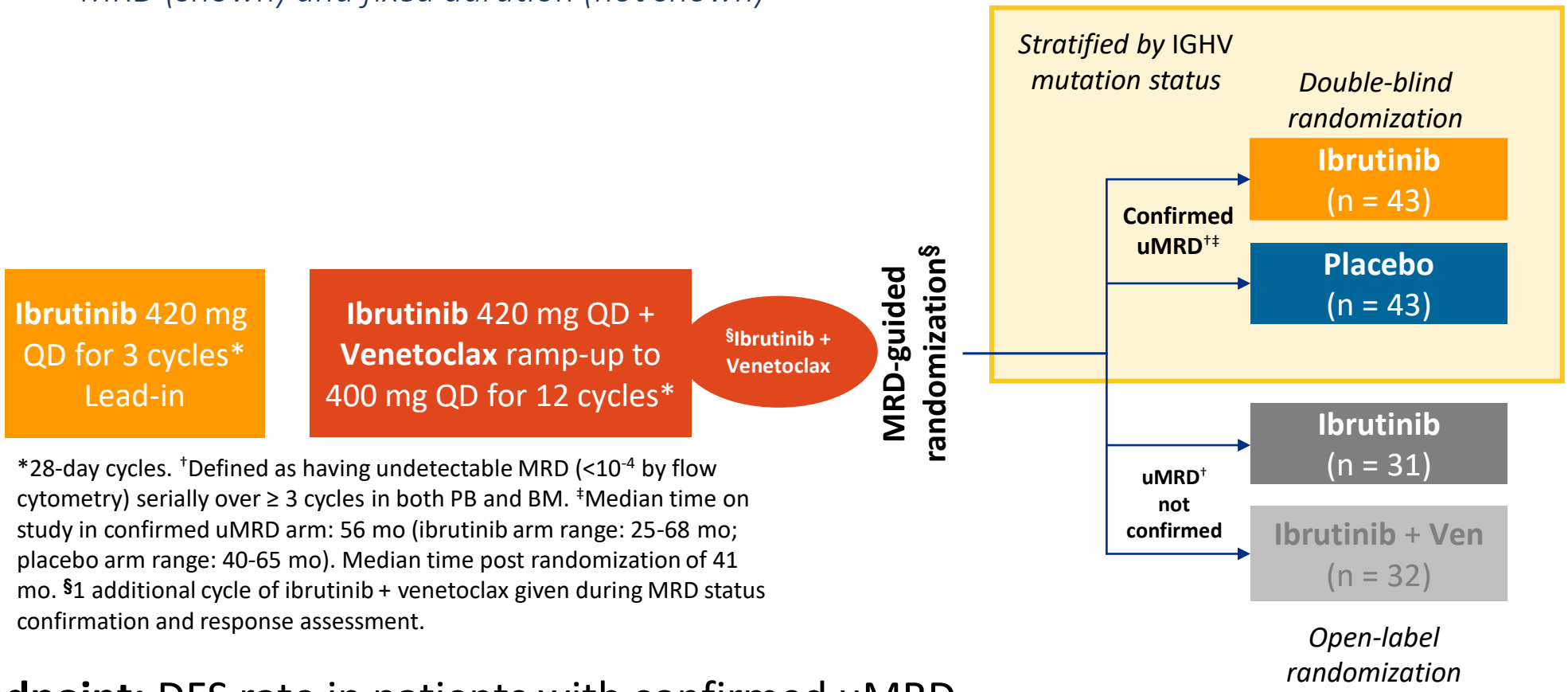
Study Design: Multicenter, randomized phase II study with 2 cohorts:

MRD (shown) and fixed duration (not shown)

MRD cohort

- Patients <70 yr with previously untreated, active CLL/SLL requiring therapy
- ECOG PS 0/1

(N = 164)



*28-day cycles. †Defined as having undetectable MRD ($<10^{-4}$ by flow cytometry) serially over ≥ 3 cycles in both PB and BM. ‡Median time on study in confirmed uMRD arm: 56 mo (ibrutinib arm range: 25-68 mo; placebo arm range: 40-65 mo). Median time post randomization of 41 mo. §1 additional cycle of ibrutinib + venetoclax given during MRD status confirmation and response assessment.

- **Primary endpoint:** DFS rate in patients with confirmed uMRD
- **Secondary endpoints:** undetectable MRD, response rates, safety

Allan. ASH 2022. Abstr 92.

CAPTIVATE Clinical Study

Baseline Characteristics

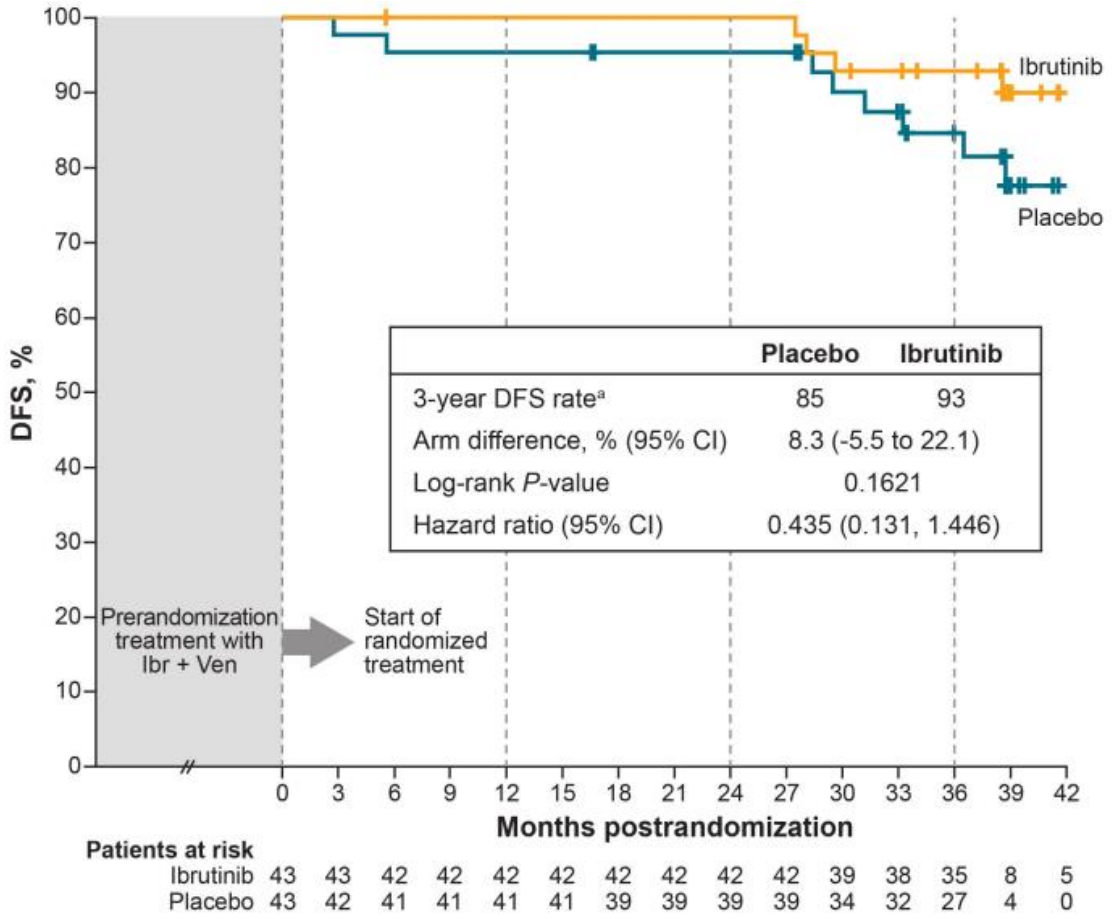
Characteristic	All Patients (N = 164)	Patients With Confirmed uMRD (n = 86)	
		Ibrutinib (n = 43)	Placebo (n = 43)
Median age, yr (range)	58 (28-69)	56 (34-69)	61 (43-69)
Rai stage III/IV, n (%)	53 (32)	8 (19)	15 (35)
High-risk genomic features, n (%)			
• del(17p)/TP53 mutation	32 (20)	13 (30)	2 (5)
• del(11q)	28 (17)	10 (23)	8 (19)
• Complex karyotype	31 (19)	13 (30)	4 (9)
• Unmutated IGHV	99 (60)	30 (70)	30 (70)
Any cytopenia, n (%)	59 (36)	6 (14)	19 (44)
• ANC ≤1.5 x 10^9/L	14 (9)	0	5 (12)
• Hemoglobin ≤11 g/dL	35 (21)	2 (5)	14 (33)
• Platelets ≤100 x 10^9/L	30 (18)	4 (9)	4 (9)
Lymph node diameter, n (%)			
• ≥5 cm	53 (32)	10 (23)	18 (42)
• ≥10 cm	5 (3)	1 (2)	1 (2)

Allan. ASH 2022. Abstr 92.

KEY DATA

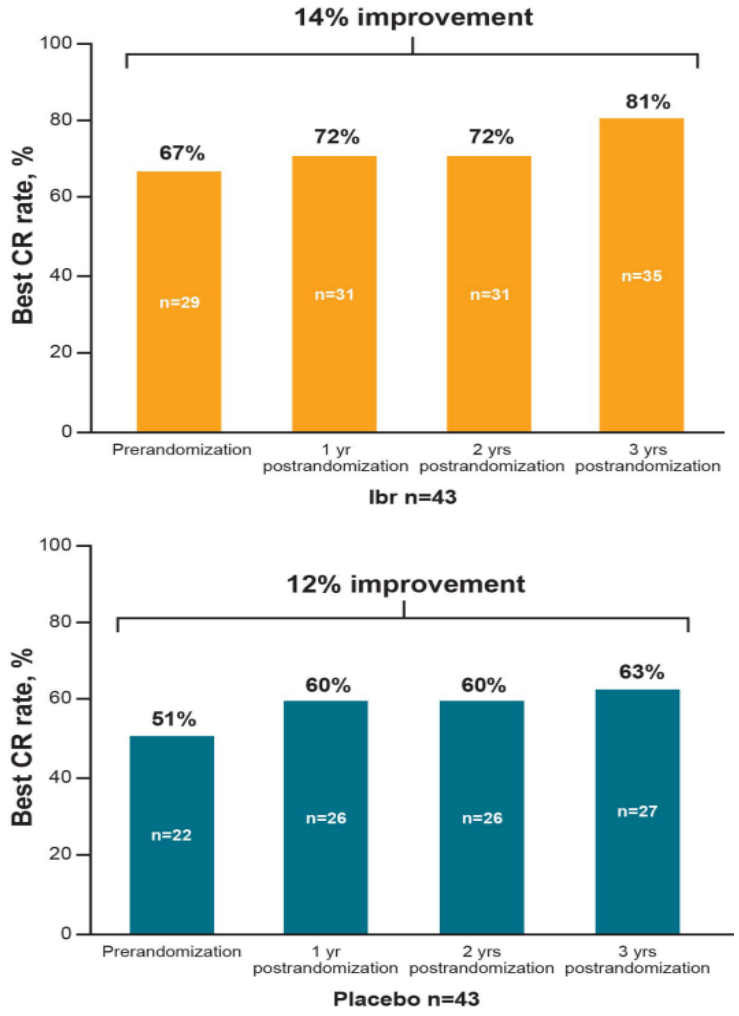
CAPTIVATE Clinical Study

Primary Endpoint: 3-year Disease-Free Survival



Complete Response Rates

CRs were durable, with no significant difference in duration of CR between treatment arms at 42 months of follow-up

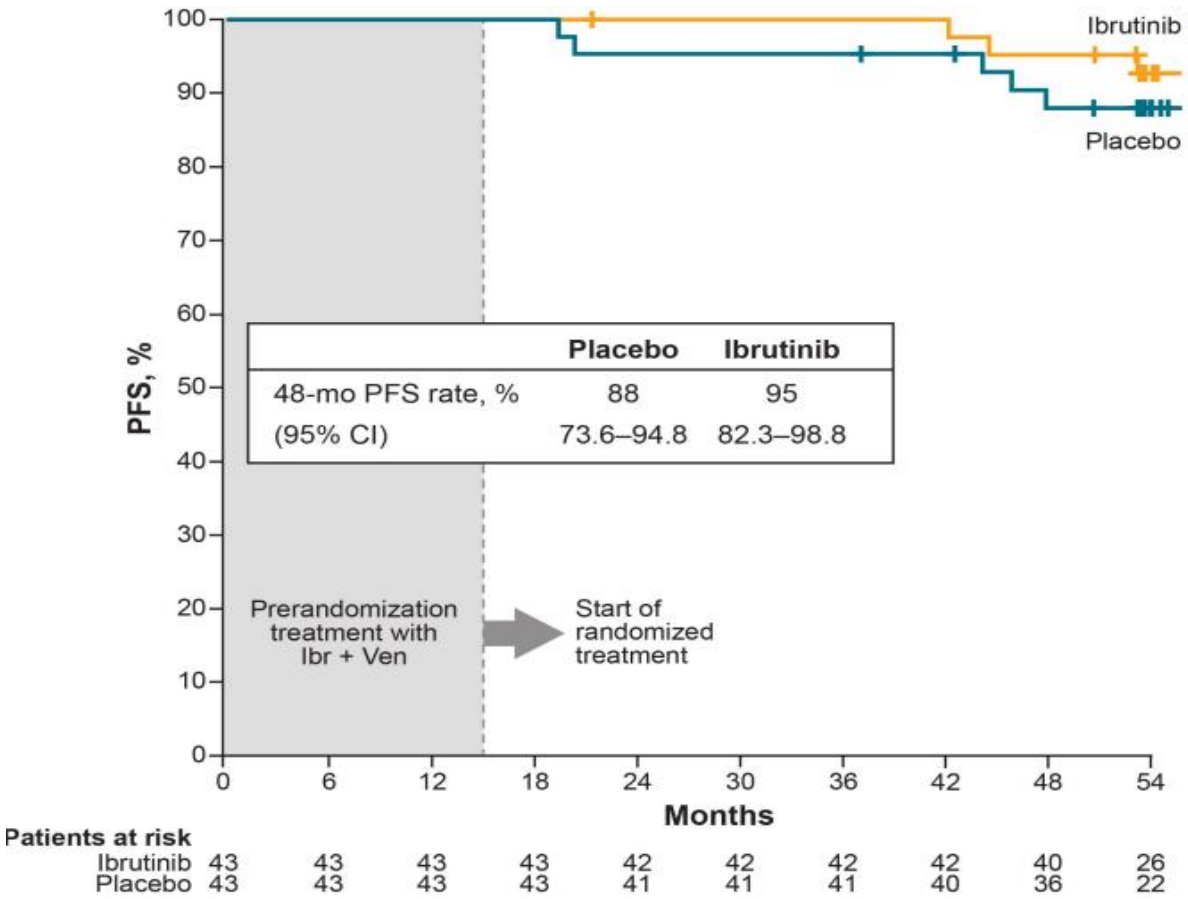


Allan. ASH 2022. Abstr 92.

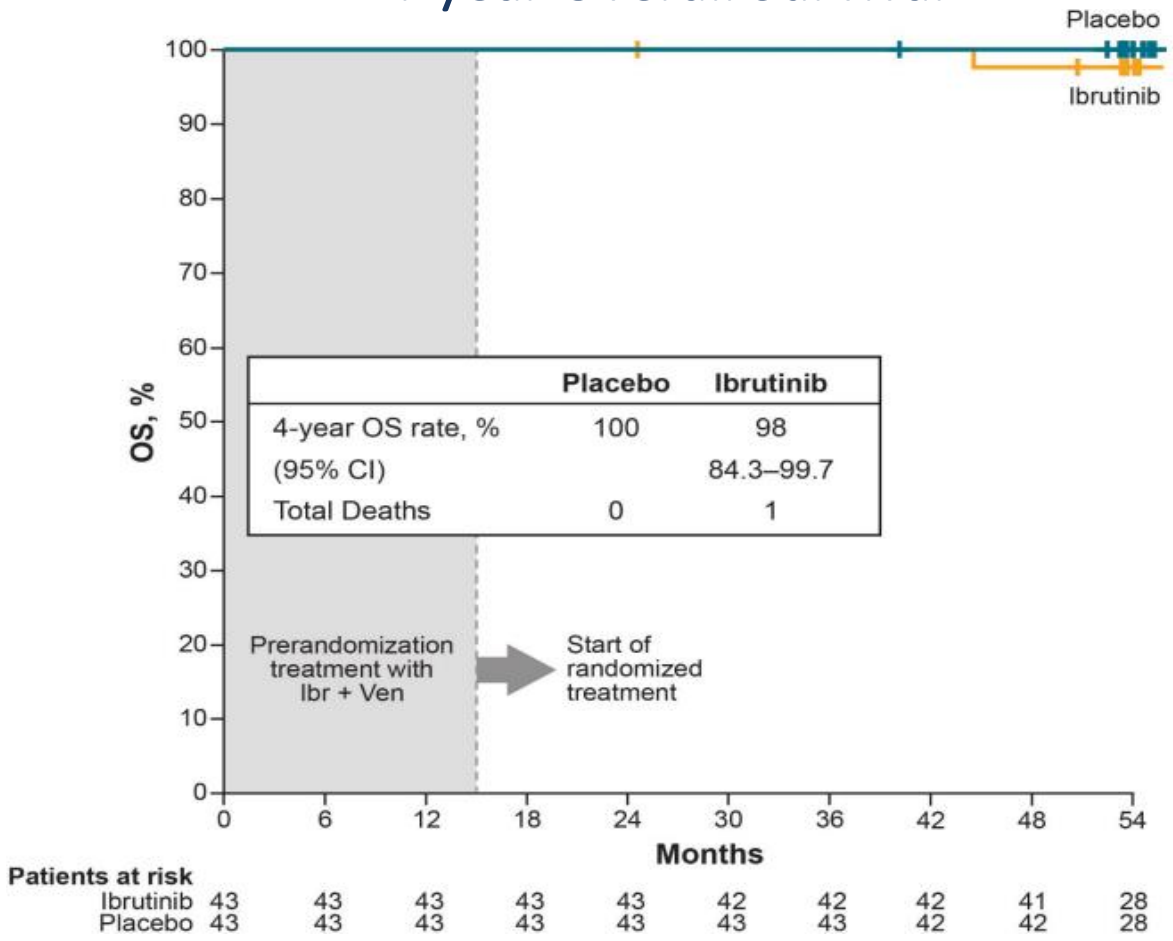
KEY DATA

CAPTIVATE Clinical Study

4-year Progression-Free Survival (PFS)



4-year Overall Survival



- 3 of 7 patients with PD in the placebo arm have initiated retreatment with ibrutinib; all 3 patients had PR
- 2 patients in the ibrutinib arm had PD; none have initiated retreatment

Allan. ASH 2022. Abstr 92.

SUMMARY

CAPTIVATE Clinical Study

- 3 years after being placed on placebo there is not a statistically significant difference in PFS when compared to patients that have been continued on ibrutinib; progression-free survival rates continue to be high and durable across the two study arms
  - At 48 months, PFS rates among patients with unmutated IGHV were similar to those of the total population
  - Efficacy Outcomes in Patients With del(17p), TP53 mutation or Complex Karyotype (CK) were consistent with the total population

Allan. ASH 2022. Abstr 92.

CAPTIVATE Clinical Study

Fixed duration of Ibrutuinib + Venetoclax leads to high PFS and OS, and the addition of continuing ibrutinib adds minimal benefit in patients that obtain MRD negativity

2022 ASH Key Studies

Lymphomas

- TRIANGLE
- BRUIN
- CAPTIVATE
- L-MIND/First-MIND
- Glofitamab/NP30179

Multiple Myeloma

- GEM-CESAR
- ASCENT
- IFM2017-03
- MajesTEC-1

Leukemias

- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
- Momentum
- Study 2102-HEM-101

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L-MIND Clinical Study

Does tafasitamab with lenalidomide provide benefit for patients with relapsed/refractory Diffuse Large B-cell Lymphoma?

5 year follow-up analysis

July 31, 2020: The FDA granted accelerated approval to tafasitamab-cxix (MONJUVI, MorphoSys US Inc.), a CD19-directed cytolytic antibody, indicated in combination with lenalidomide for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low grade lymphoma, and who are not eligible for autologous stem cell transplant.

cornerstone specialty network™

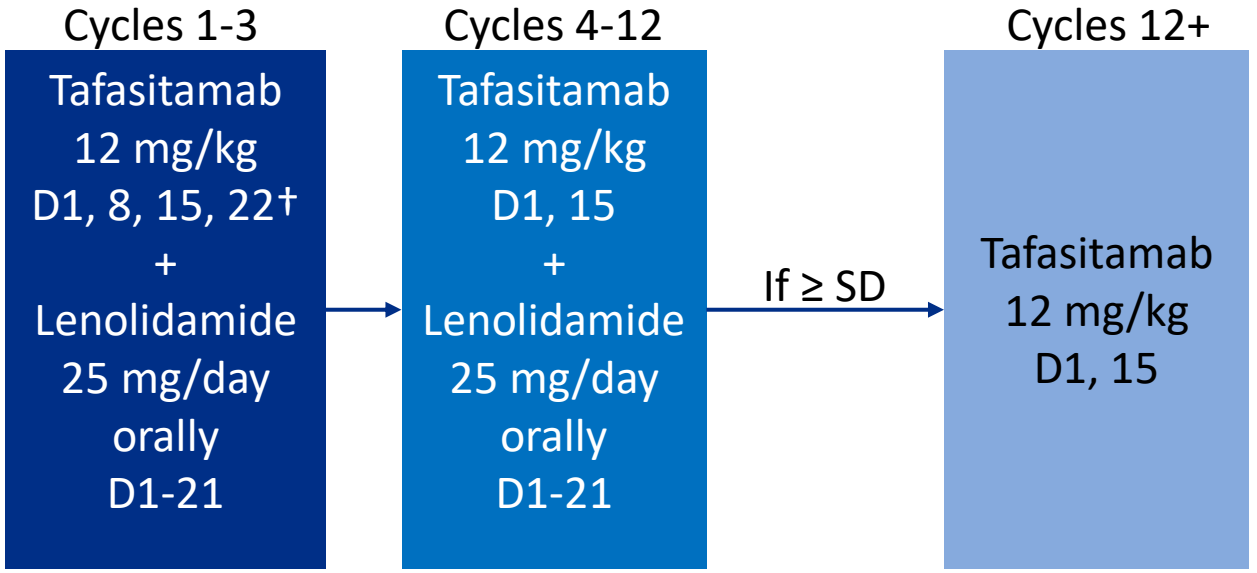
KEY DATA

L-MIND Clinical Study

Study Design: ongoing, open-label, multicenter, single-arm Phase II Study

- Patients aged ≥18 years with R/R DLBCL
- 1–3 prior systemic therapies, including ≥1 CD20-targeting regimen
- Ineligible for HDC plus ASCT
- Primary refractory patients were not eligible*
- ECOG status 0-2

N=81



Until PD

Primary endpoint: ORR (central read)
Secondary endpoints: ORR (by investigator), PFS, DoR, OS, Safety

Note: 80 patients received ≥1 dose of tafasitamab + LEN and were included in the full analysis set (FAS) for efficacy; all 81 patients were included in the safety analysis

- At data cut-off (February 15, 2022) 30 patients completed 12 cycles of tafasitamab + LEN and four patients discontinued LEN before 12 cycles
- 27 patients (34%) received treatment for ≥2 years (median: 4.3 years)
- Of these 27 patients, 23 are confirmed alive, one died from an unknown cause, two died following AEs unrelated to study treatment, and one was lost to follow-up; Thirteen patients remain on treatment; 14 patients discontinued the treatment

*Primary refractory is defined as no response to, or progression/relapse during or within 6 months of, front-line therapy; 15 refractory patients were included under an early version of the protocol. † A loading dose of tafasitamab was administered on Day 4 of Cycle 1. ASCT, autologous stem cell transplant; D, days; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HDC, high-dose chemotherapy; LEN, lenalidomide; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed or refractory; SD, stable disease.

Nowakowski. ASH 2022. Abstr 1619.

KEY DATA

L-MIND Clinical Study

Baseline Characteristics

Characteristic, n (%)	Treatment ≥ 2 years n=27	Safety analysis set n=81
Gender, male	12 (44)	44 (54)
Age, years	71 (41–81)	72 (41–86)
IPI Score		
• 0-2	19 (70)	40 (49)
• 3-5	8 (30)	41 (51)
Elevated LDH, n (%)*	12 (44)	45 (56)
Prior lines, n (%)*		
• 1	16 (59)	40 (49)
• 2	10 (37)	35 (43)
• 3	1 (4)	5 (6)
• 4	–	1 (1)

Characteristic, n (%)	Treatment ≥ 2 years n=27	Safety analysis set n=81
Primary refractory, n (%)*	4 (15)‡	15 (19)
Refractory to previous therapy line, n (%)*,†	12 (44)	36 (44)
Prior SCT, n (%)	4 (15)	9 (11)
Cell of origin (locally assessed)		
• GCB	11 (41)	37 (46)
• Non-GCB	9 (33)	20 (25)
• Missing or not evaluable	7 (26)	24 (29)
Ann Arbor disease stage		
• I-II	8 (30)	20 (25)
• III-IV	19 (70)	61 (75)

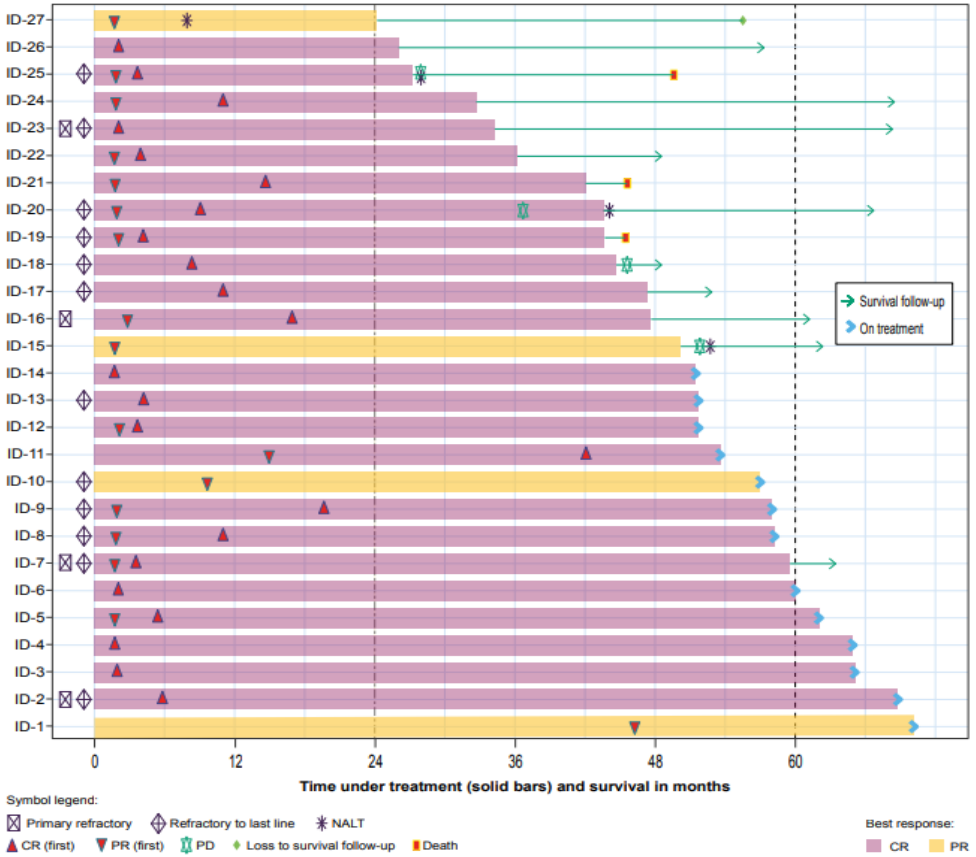
*At study entry. † Refractory to previous line is defined as having less than a partial response to the most recent systemic therapy. ‡ Primary refractory defined as no response to or progression/relapse during or within 6 months of front-line therapy; primary refractory patients had a DoR to 1L of 3–6 months. 1L, first line; DoR, duration of response; GCB, germinal center B-cell; IHC, immunohistochemistry; IPI, International Prognostic Index; LDH, lactate dehydrogenase; SCT, stem cell transplant.

Klinik ASH 2022. Abstr 2937.

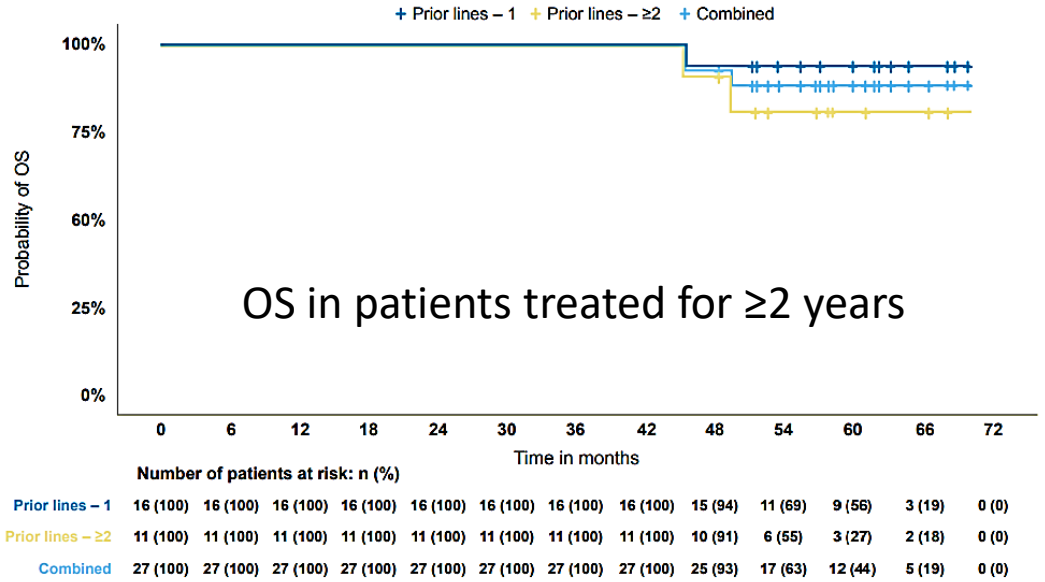
KEY DATA

L-MIND Clinical Study

Efficacy



- A complete response (CR) as a best response was achieved by 23 of 27 patients, including the patients who were primary refractory
- Four patients achieved a partial response (PR), of which two were still on treatment



- The 48-month OS rate was 92.6%; however, the median OS, PFS, and DoR were not reached
- Of 12 patients refractory to a previous therapy line, 11 (91.7%) were in follow-up at 48 months
- Twelve patients have been in OS follow-up for ≥5 years; of these, six are still on treatment, while six have discontinued treatment
  - Of the six patients who received treatment for ≥5 years, five achieved CR (one of whom had triple-hit R/R DLBCL [patient ID-7]) and one had a PR
  - All of the primary refractory patients (n=4) are in follow-up at 60 months

Klinik ASH 2022. Abstr 2937.

SUMMARY

L-MIND Clinical Study

- With long term follow-up, tafasitamab plus LEN can result in prolonged remission and overall survival of 5 years or greater for patients with R/R DLBCL ineligible for ASCT
- No new safety signals

Klinik ASH 2022. Abstr 2937.

CLINICAL QUESTION

First-MIND Clinical Study

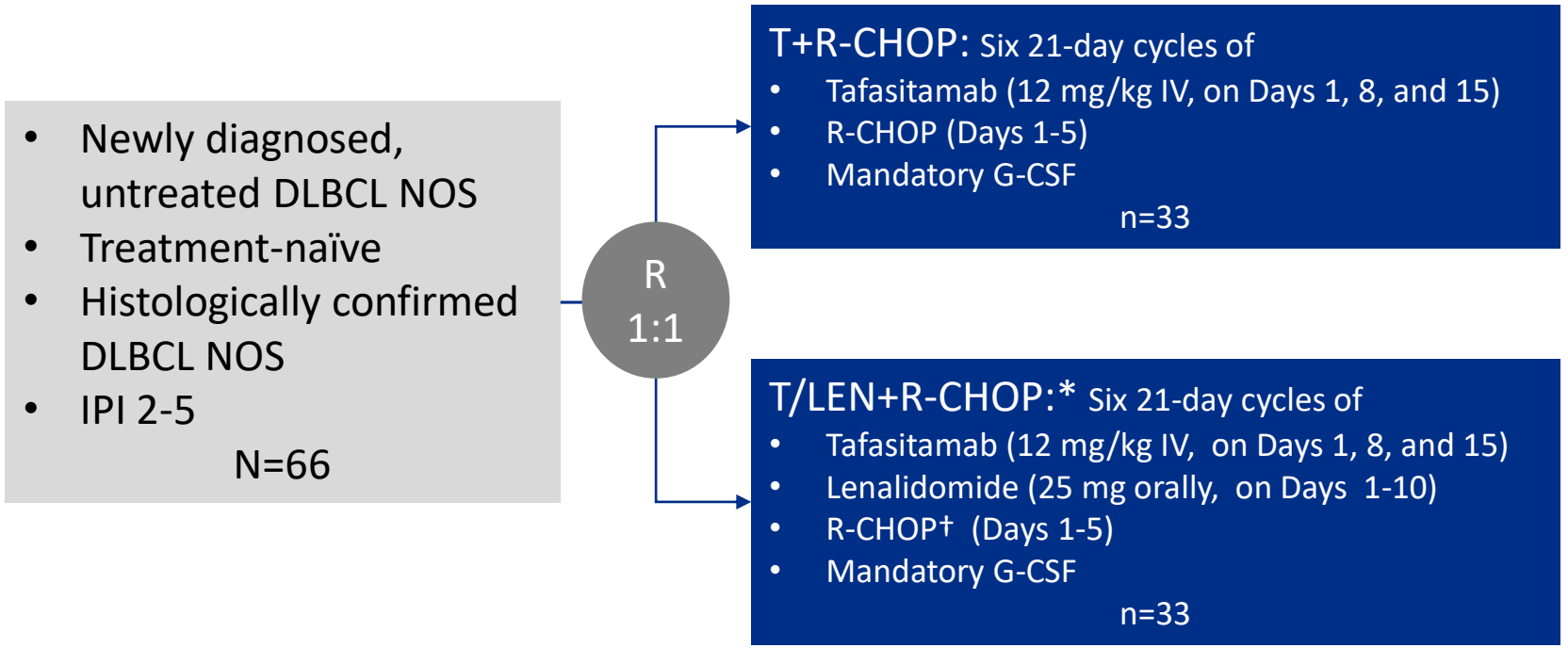
Does tafasitamab plus R-CHOP with or without lenalidomide provide benefit for patients with newly diagnosed Diffuse Large B-cell Lymphoma?

18 month follow-up analysis

KEY DATA

First-MIND Clinical Study

Study Design: Open-label, randomized Phase 1b study



The final analysis was conducted on August 10, 2022, and included ≥18 months' follow-up after the end of treatment (EoT) visit for all patients

Primary endpoint: Incidence and severity of TEAEs

Key secondary endpoints: ORR at EoT Metabolic, PET-negative CR rate at EoT Pharmacokinetics and immunogenicity

Exploratory endpoints: Pharmacodynamics/biomarker analysis

Data cut-off: May 5, 2022

*In the lenalidomide arm, venous thromboembolism prophylaxis with either low-molecular weight heparins or aspirin is mandatory (according to institutional guidelines).

† Rituximab (375 mg/m2) and CHOP chemotherapy included cyclophosphamide (750 mg/m2 IV), doxorubicin (50 mg/m2 IV), and vincristine (1.4 mg/m2 [maximum dose = 2 mg] IV) on Day 1 of every 21-day cycle and prednisone/prednisolone (100 mg/day PO) on Days 1 to 5. The Day 1 steroid dose being part of CHOP (100 mg prednisone/prednisolone, or equivalent, PO or IV) could be used as a further component of premedication prior to the tafasitamab infusion

Nowakowski. ASH 2022. Abstr 1619.

KEY DATA

First-MIND Clinical Study

Baseline Characteristics

Characteristic, n (%)	T + R-CHOP n=33	T/L + R-CHOP n=33	T/L +R-CHOP IPI 3-5 n=22
Gender, male	15 (45.5)	13 (39.4)	10 (45.5)
Age, >60 years	21 (63.6)	22 (66.7)	15 (68.2)
Race, White	31 (93.9)	33 (100)	22 (100)
IPI Score			
• 2	13 (39.4)	11 (33.3)	-
• 3	13 (39.4)	16 (48.5)	16 (72.7)
• 4	7 (21.2)	4 (12.1)	4 (18.2)
• 5	0	2 (6.1)	2 (9.1)
• 3-5	**20 (60.6)**	**22 (66.7)**	22 (100)
ECOG Score			
• 0	**19 (57.6)**	**12 (36.4)**	7 (31.8)
• 1	**12 (36.4)**	**17 (51.5)**	12 (54.5)
• 2	2 (6.1)	4 (12.1)	3 (13.6)

Characteristic, n (%)	T + R-CHOP n=33	T/L + R-CHOP n=33	T/L +R-CHOP IPI 3-5 n=22
Cell of origin (locally assessed)			
• GCB	9 (27.3)	10 (30.3)	12 (54.5)
• Non-GCB	15 (45.5)	14 (42.2)	9 (40.9)
• Missing or not evaluable	9 (27.3)	9 (27.3)	1 (4.5)
Ann Arbor disease stage			
• I	2 (6.1)	1 (3.0)	-
• II	0	1 (3.0)	-
• III	8 (24.2)	7 (21.2)	3 (13.6)
• IV	23 (69.7)	24 (72.7)	19 (86.4)
• I & II	2 (6.1)	2 (6.1)	-
• III & IV	**31 (93.9)**	**31 (93.9)**	22 (100)

ECOG PS, Eastern Cooperative Oncology Group performance status; GCB, germinal center B-cell; IPI, International Prognostic Index; L, lenalidomide; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; T, tafasitamab.

Nowakowski. ASH 2022. Abstr 1619.

KEY DATA

First-MIND Clinical Study

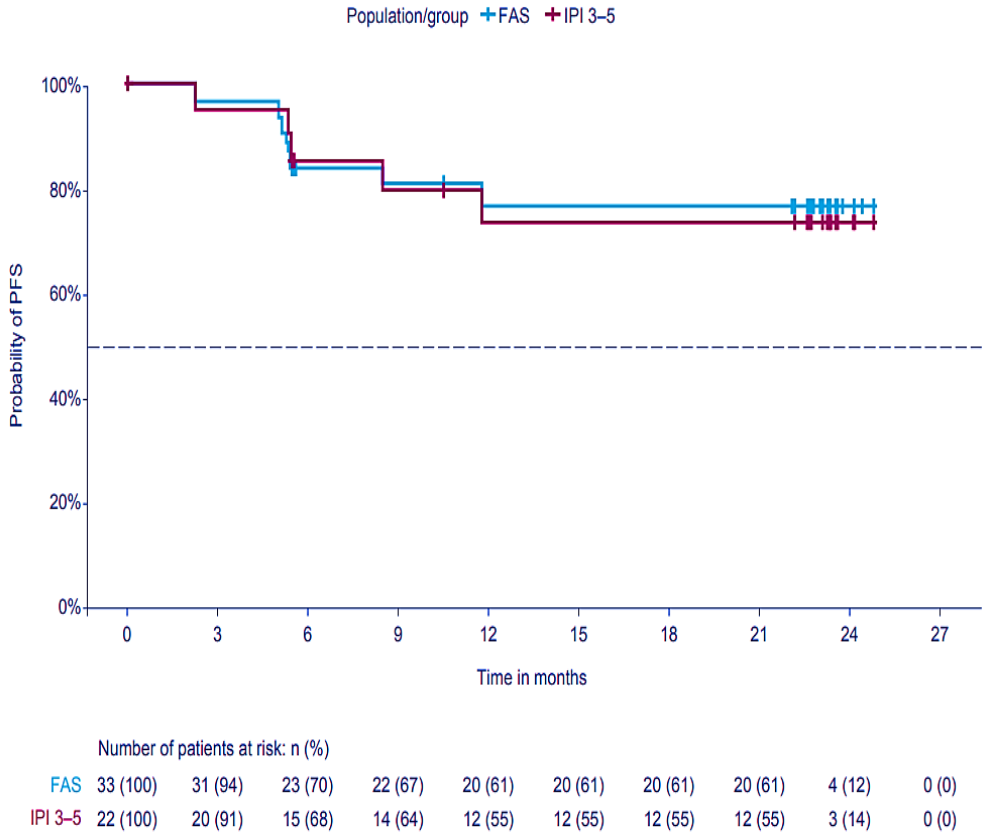
Efficacy

	T + R-CHOP n=33	T/L + R-CHOP n=33	T/L +R-CHOP IPI 3-5 n=22
ORR, n (%) [95% CI]			
• CR or PR (at EoT)	25 (75.8) [57.7, 88.9]	27 (81.8) [64.5, 93.0]	18 (81.8) [59.7, 94.8]
• CR or PR (best response across all visits)	30 (90.9) [75.7, 98.1]	31 (93.9) [79.8, 99.3]	20 (90.9) [70.8, 98.9]
18-month DoR rate, % [95% CI]	72.7 [52.7, 85.3]	78.7 [58.5, 89.9]	76.6 [48.8, 90.5]
18-month DoCR rate, % [95% CI]	74.5 [53.8, 87.0]	86.5 [63.8, 95.5]	80.0 [50.0, 93.1]
24-month PFS rate, % [95% CI]	72.7 [52.7, 85.3]	76.8 [57.1, 88.3]	73.6 [47.3, 88.2]
24-month OS rate, % [95% CI]	90.3 [72.9, 96.8]	93.8 [77.3, 98.4]	95.2 [70.7, 99.3]

DoCR, duration of complete response; DoR, duration of response

Note: The 18-month PFS rate by MRD status at EoT in the T/L+R-CHOP arm was 92.3% in MRD-negative patients (n=12) and 66.6% in MRD-positive patients (n=3)

PFS in the overall T/L+R-CHOP cohort and patients treated with T/L+R-CHOP with an IPI score of 3–5



FAS, full analysis set; IPI, International Prognostic Index; L, lenalidomide; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; T, tafasitamab.

Nowakowski. ASH 2022. Abstr 1619.

SUMMARY

First-MIND Clinical Study

- The addition of tafasitamab to lenolidamide and R-CHOP has no unexpected safety signals and there is a potential signal for efficacy

- No new safety signals
  - Tafasitamab + LEN can be added to R-CHOP without impairing dosing and scheduling, with minimal increased toxicities as expected from the additional therapies added R-CHOP
  - Toxicities similar to those experienced with R-CHOP alone (Grade ≥ 3 for R-CHOP: 65.8%
    (GOYA Phase III study: Sehn et al. Journal of Hematology & Oncology (2020) 13:71)

The combination of R-CHOP and tafasitamab + LEN as first-line therapy is being investigated further in the global, randomized, Phase III frontMIND study (NCT04824092) in untreated patients with DLBCL and an IPI score of 3–5.

Nowakowski. ASH 2022. Abstr 1619.

L-MIND / First-MIND Clinical Study

Tafasitamab with lenalidomide provides benefit for patients with relapsed/refractory Diffuse Large B-cell Lymphoma

Potential to benefit patients with treatment naïve R/R DLBCL

More to come…

2022 ASH Key Studies

Lymphomas

- TRIANGLE
- BRUIN
- CAPTIVATE
- L-MIND/First-MIND
- Glofitamab/NP30179

Multiple Myeloma

- GEM-CESAR
- ASCENT
- IFM2017-03
- MajesTEC-1

Leukemias

- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
- Momentum
- Study 2102-HEM-101

Glofitamab/NP30179 Clinical Study

Does glofitamab provide benefit for patients with Large B-cell Lymphoma?

January 5, 2023: *The U.S. Food and Drug Administration (FDA) accepted the company's Biologics License Application (BLA) and granted Priority Review for glofitamab, an investigational CD20xCD3 T-cell engaging bispecific antibody, for the treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma (LBCL) after two or more lines of systemic therapy.*

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KEY DATA

Glofitamab/NP30179 Clinical Study

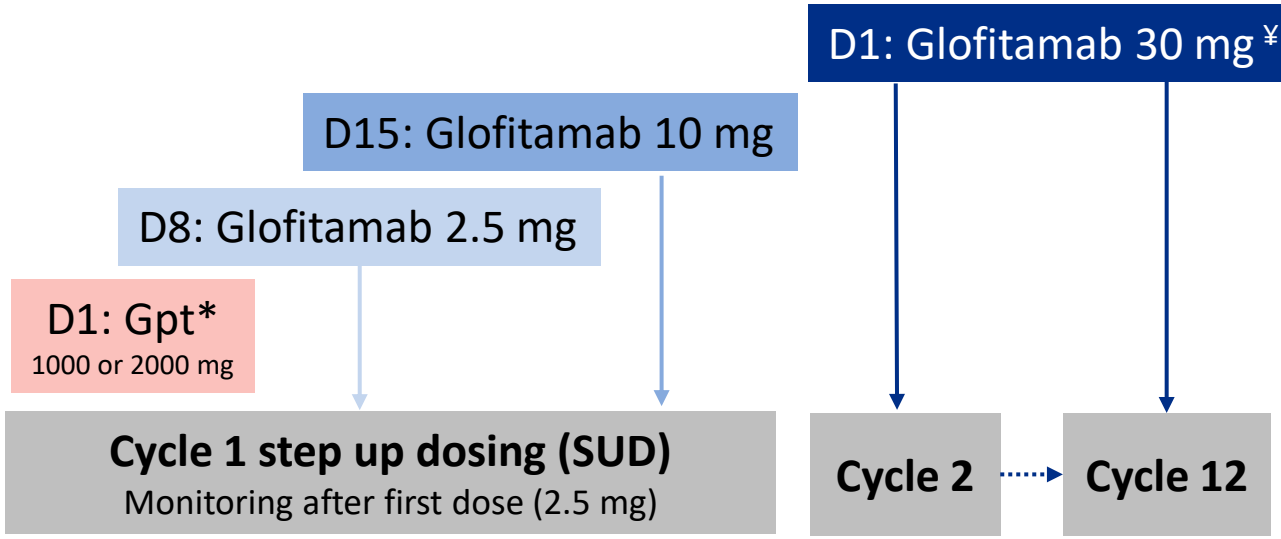
Study Design: Phase I/II Study

- DLBCL NOS, HGBCL, transformed FL or PMBCL
- ECOG PS0-1
- ≥2 prior therapies, including anti-CD20 antibody and anthracycline

n=37

BCL, B-cell lymphoma; FL, follicular lymphoma; HGBCL, high grade BCL; NOS, not otherwise specified; PMBCL, primary mediastinal large BCL

Fixed-duration treatment: every 3 weeks, maximum of 12 cycles



*Obinutuzumab pretreatment (Gpt , 1 x **1000 mg [n=16]** or **2000 mg [n=21]**) is given 7 days prior to the first dose of glofitamab to mitigate the risk of cytokine release syndrome (CRS)

¥ In the glofitamab SUD + 1000 mg Gpt cohort, two patients had 16 mg glofitamab as their target dose.

Patients were hospitalized for receipt of the first dose of glofitamab; hospitalization requirements evolved during the study, such that subsequent doses were administered in the outpatient setting unless cytokine release syndrome of grade 2 or higher was reported after the first dose. N Engl J Med 2022;387:2220-31

Primary Endpoints: CR (best response) rate by IRC

Secondary Endpoints: ORR, DoR (by IRC and investigator), DoCR, PFS (by IRC and investigator), and OS

Response rates were assessed by Lugano criteria

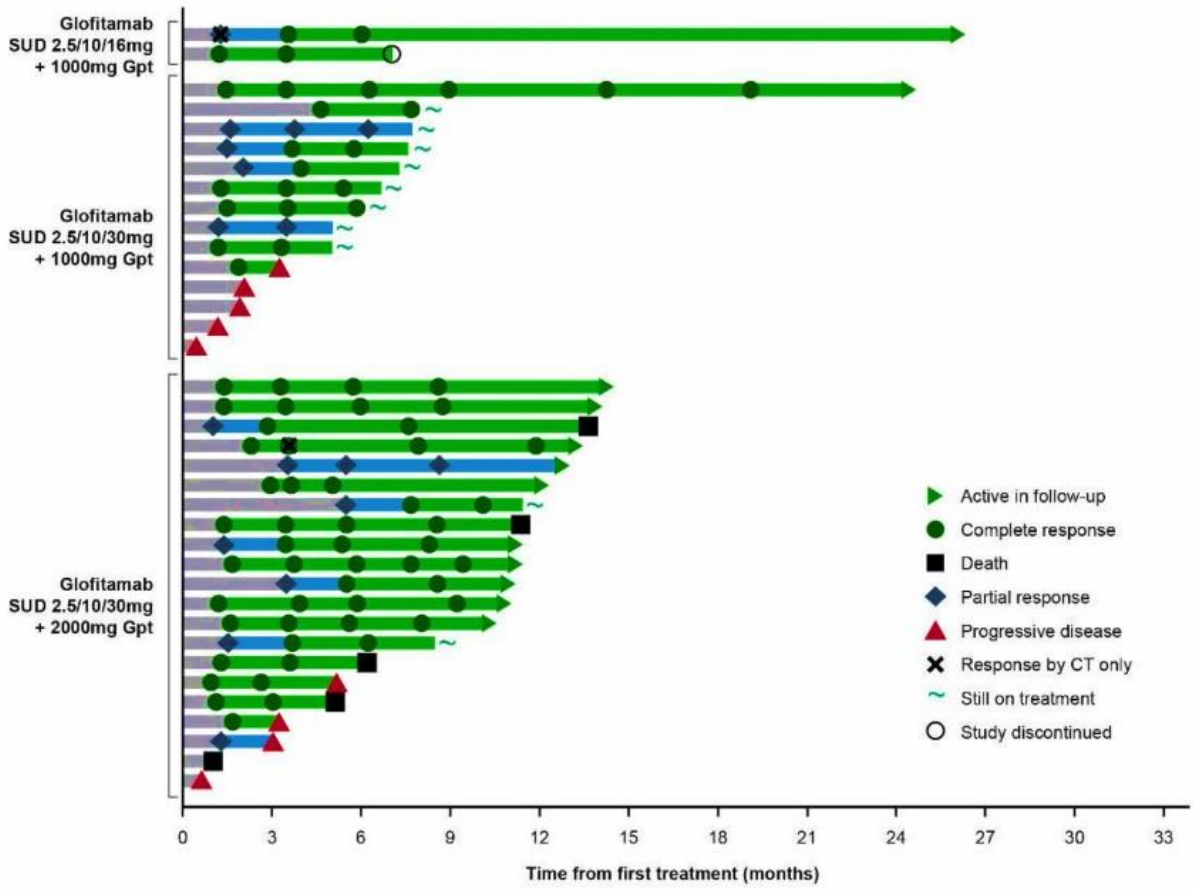
Cutoff date: March 14, 2022

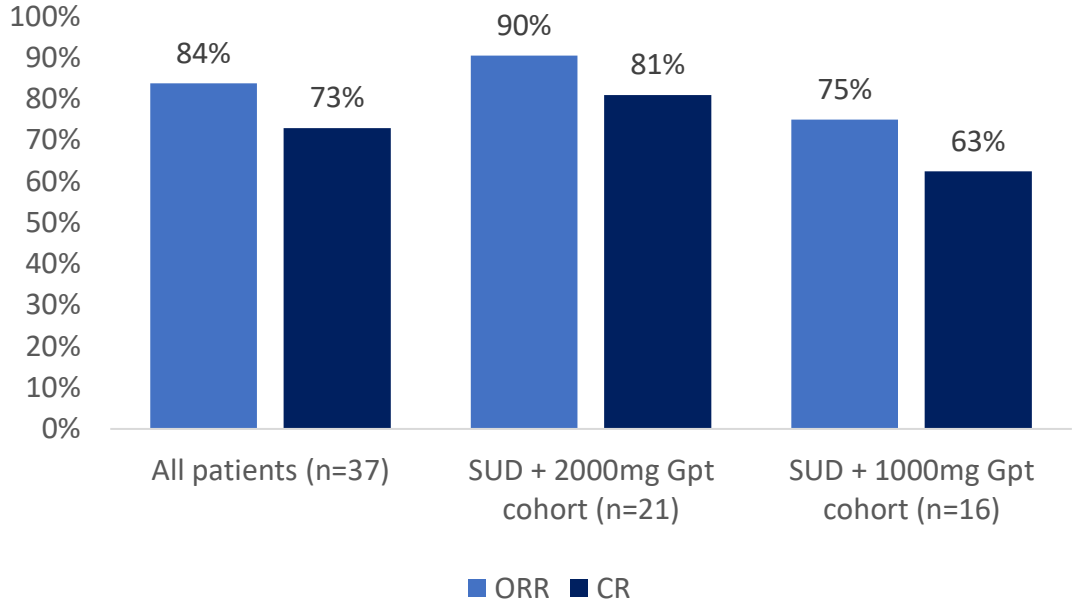
Philips. ASH 2022. Abstr 74.
Dickinson. ASCO 2022 Abstr 7500
N Engl J Med 2022; 387:2220-2231

KEY DATA

Glofitamab/NP30179 Clinical Study

Efficacy: Time on Treatment and Response Rates





- Median time to CR was 51 days
- Majority of CRs (20/27; 74.1%) were ongoing at the data cut-off and an estimated 71.6% of patients with a CR remained in response at 9 months.
- Median duration of response was 12.6 months (95% CI: 10.0–NE) and median duration of CR was 10.0 months (95% CI: 4.9–NE)

Philips. ASH 2022. Abstr 74.
Dickinson. ASCO 2022 Abstr 7500
N Engl J Med 2022; 387:2220-2231

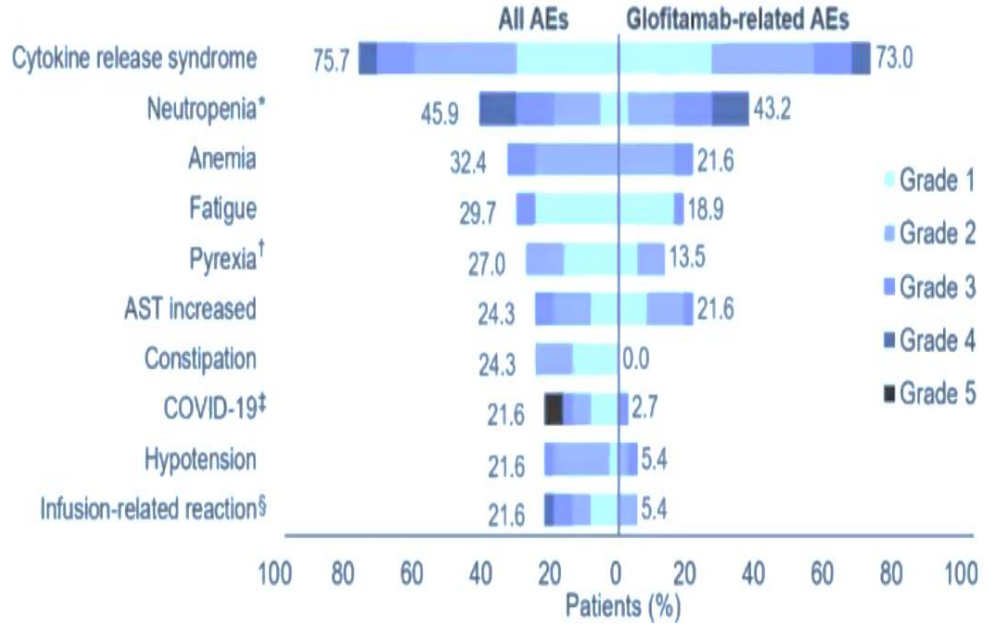
KEY DATA

Glofitamab/NP30179 Clinical Study

Safety

Adverse event, n (%)	Glofitamab SUD + 1000 mg Gpt n=16	Glofitamab SUD + 2000 mg Gpt n=21	Glofitamab SUD + Gpt, All patients n=37
Any Grade AE	16 (100)	21 (100)	37 (100)
• Glofitamab related	16 (100)	19 (90.5)	35 (94.6)
Serious AE	13 (81.3)	16 (76.2)	29 (78.4)
• Glofitamab related	12 (75.0)	11 (52.4)	23 (62.2)
Grade 3/4 AE	14 (87.5)	11 (52.4)	25 (67.6)
• Glofitamab related	12 (75.0)	11 (52.4)	23 (62.2)
Grade 5 AE	0	4 (19.0)	4 (10.8)
• Glofitamab related	0	0	0
AE leading to discontinuation	0	0	0
Deaths	2 (12.5)	9 (38.1)	10 (27.0)

AEs with an incidence of ≥20% in all patients (N=37)



- CRS rates were lower in the 2000 mg Gpt (14/21; 66.7%, Grades 1-3) vs the 1000 mg Gpt (14/16; 87.5%, Grades 1-4) cohort.
- No Grade 5 AEs related to glofitamab or AEs leading to treatment discontinuation reported

*Includes neutrophil count decrease. †Events occurred separately from CRS. ‡There were 3 serious COVID-19 AEs: Grade 3 (n=1), Grade 5 (n=2).§ IRR AEs related to glofitamab are reported as such if cytokine levels were normal. Most IRRs were related to Obitnutuzumab.

Philips. ASH 2022. Abstr 74.
Dickinson. ASCO 2022 Abstr 7500
N Engl J Med 2022; 387:2220-2231

SUMMARY

Glofitamab/NP30179 Clinical Study

- Fixed duration glofitamab can achieve early, high, and durable CR rates in heavily pretreated patients with prior BTKi therapy
- All CRS events were manageable (17 patients received tocilizumab to manage CRS) and most resolved by data cut-off
- Off-treatment progression is rarely observed
  - Results not shown (Hutchings ASH 2022 Abstr 441)

Philips. ASH 2022. Abstr 74.
Dickinson. ASCO 2022 Abstr 7500
N Engl J Med 2022; 387:2220-2231

Glofitamab/NP30179 Clinical Study

Glofitamab has the potential to provide benefit for patients with Large B-cell Lymphoma

More to come…

The FDA is expected to make a decision on approval of this novel cancer immunotherapy by July 1, 2023

If approved, glofitamab would be the first fixed-duration, off-the-shelf CD20xCD3 T-cell engaging bispecific antibody available to treat people with an aggressive lymphoma who have previously received multiple courses of treatment.

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2022 ASH Key Studies

Lymphomas

- TRIANGLE
- BRUIN
- CAPTIVATE
- L-MIND/First-MIND
- Glofitamab/NP30179

Multiple Myeloma

- GEM-CESAR
- ASCENT
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Leukemias

- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
- Momentum
- Study 2102-HEM-101

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GEM-CESAR

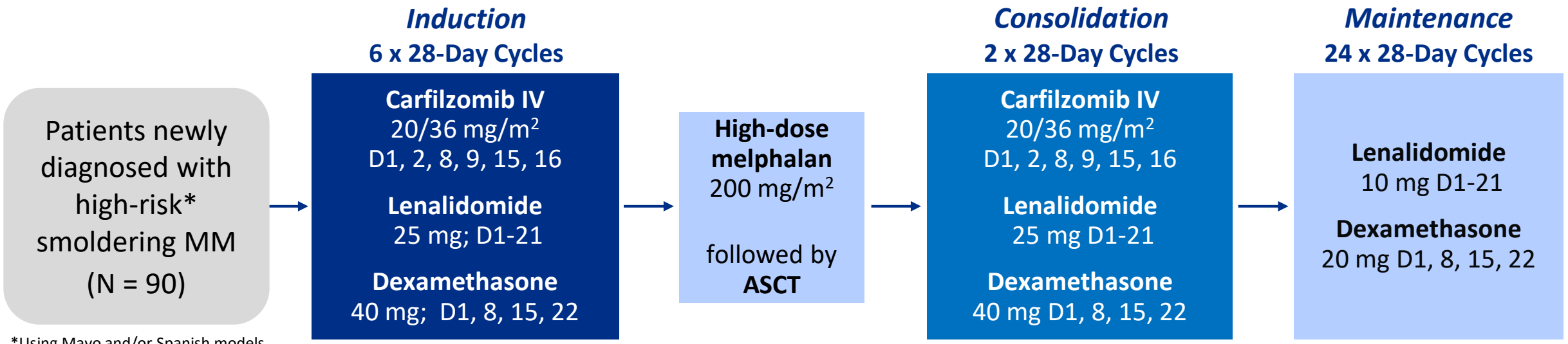
Is KRd followed by ASCT, KRd consolidation, and lenalidomide maintenance therapy potentially curative for patients with high-risk smoldering multiple myeloma ?

Post Hoc Analyses

KEY DATA

GEM-CESAR

Study Design: multicenter, open-label phase II trial



*Using Mayo and/or Spanish models (pre-2014 diagnostic criteria): ≥3 g/dL serum M-protein and ≥10% PCs in BM or either ≥3 g/dL serum M-protein or ≥10% PCs in BM and >95% of aberrant PCs within PCs in BM by immunophenotyping and immunoparesis.

- Patients included with ≥1 biomarker predictive for imminent risk of progression
- Patients with bone disease on CT or PET/CT at screening excluded

Primary endpoint: MRD negativity (by flow cytometry) after HDT-ASCT and at 3 yr and 5 yr after HDT-ASCT
(MRD assessment at 3 yr amended to 4 yr due to COVID-19 pandemic)

Secondary endpoints: response rates (sCR/CR/VGPR/PR), TTP, PFS, OS, safety, biochemical progression

Mateos. ASH 2022. Abstr 118.

GEM-CESAR

Baseline Characteristics

Characteristic	Patients (N = 90)
Median age, yr (range)	59 (33-70)
Median serum / urine M-protein, g/dL (range) / g/24 hr (range)	2.77 (0-8.6) / 0.43 (0-7.2)
Plasma cells bone marrow infiltration, % (range)	22 (10-80)
High-risk definition, n (%)	
• Mayo Clinic model only	19 (21)
• Spanish model only	47 (52)
• Both	24 (27)
Ultra high risk (≥1 biomarker), n (%)	30 (33)
• Serum FLC ratio >100	18 (20)
• >1 focal lesion on MRI	11 (12)
• ≥60% PCs in bone marrow	7 (8)
PET positive without lytic lesions, n (%)	5 (6)
Cytogenetic abnormalities, n (%)	
• Standard risk	54 (60)
• High risk: t(4;14), t(14;16), del17, del1p	31 (34)
• Unknown risk	5 (6)

Mateos. ASH 2022. Abstr 118.

KEY DATA

GEM-CESAR

Primary Endpoint: Undetectable MRD rate after HDT-ASCT and sustained at 4/5 years post HDT-ASCT

Undetectable MRD, n (%)	3 Months After HDT-ASCT (n = 82)	4 Years After ASCT (n = 58)
MRD negative at 10^{-5}	56 (68)	25 (43)
MRD negative at 10^{-6}	39 (48)	28 (48)

Evaluable patients include: patients at risk with the bone marrow and MRD assessment performed as well as those who discontinued earlier than the specific time point due to progressive or biochemical progressive disease.

Mateos. ASH 2022. Abstr 118.

GEM-CESAR

Efficacy: ITT population

Response Category, n (%)	Induction (N = 90)	HDT-ASCT (N = 90)	Consolidation (N = 90)	Maintenance (N = 90)
ORR, n (%)	**85 (94)**	**82 (91)**	**85 (94)**	**80 (95)**
• ≥ CR	**37 (41)**	**54 (60)**	**64 (70)**	**58 (64)**
• VGPR	35 (39)	17 (19)	14 (16)	9 (10)
• PR	13 (14)	11 (12)	7 (8)	3 (3)
Stable disease	1 (1)	1 (1)	--	--
Progressive disease	2 (3)*	--	--	7 (7)†
Not evaluable	2 (3)	7 (8)	5 (5)	13 (14)
MRD negative at 10^{-5}	36 (40)	56 (63)	51 (63)	47 (52)

*Both biochemical progression.
†All biochemical progression, with 1 patient progressing to active disease during maintenance.

- Median follow-up: 70.1 mo (range: 6.2-88.8)
- 70 patients completed all treatment, including 2 years of maintenance therapy

Mateos. ASH 2022. Abstr 118.

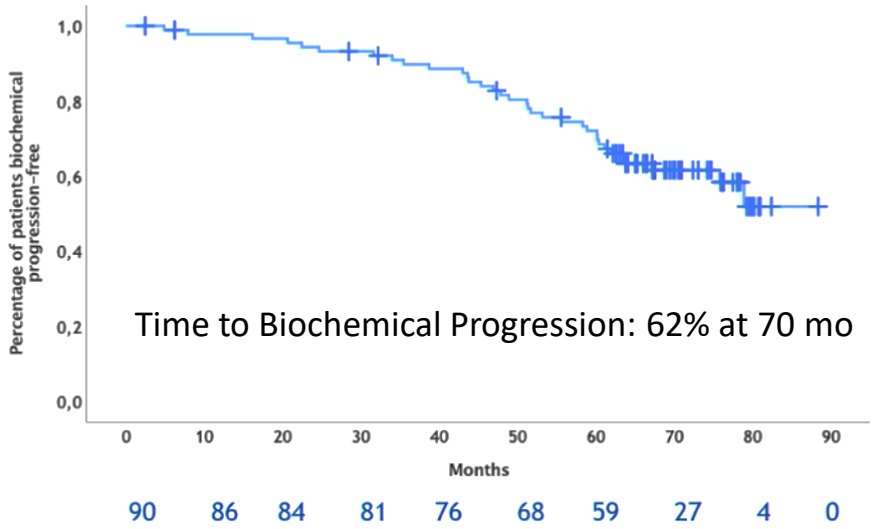
GEM-CESAR

Time to Biochemical Progression to MM

34 patients progressed biochemically:

- 9 patients during treatment phase
- 8 patients during the first 4 years after treatment
- 17 (50%) between the 4th and 5th year post transplant

Type of Biochemical Progression	n (%)
Progressive disease	8 (24%)
Relapse from CR	19 (56%)
Ultrasensitive MRD relapse: • Conversion from MRD-ve to +ve confirmed twice with sensitivity ≥10^{-5} or increase in >1log between 1st and 2nd determination (if sensitivity 10^{-6})	7 (21%)



Time to Biochemical Progression: 62% at 70 mo

- 21 of 34 (62%) patients with biochemical progression received continuous DaraPd rescue therapy
- After a median of 14 cycles 72% achieved response:
  - 29% ≥ CR
  - 19% VGPR
  - 24% PR

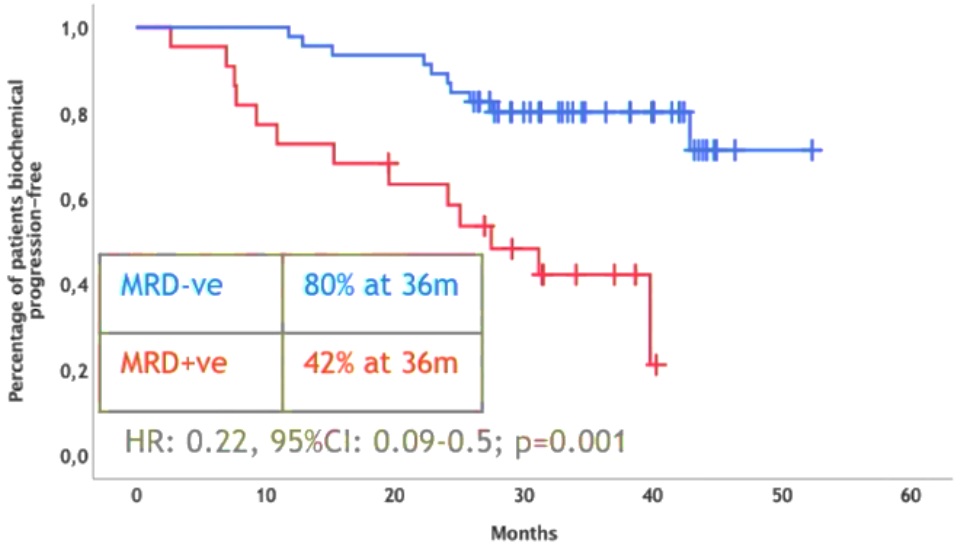
Progressed to MM: 2 (6%); 1 death due to MM progression

Mateos. ASH 2022. Abstr 118.

GEM-CESAR

Factors Predicting Biochemical Progression to MM

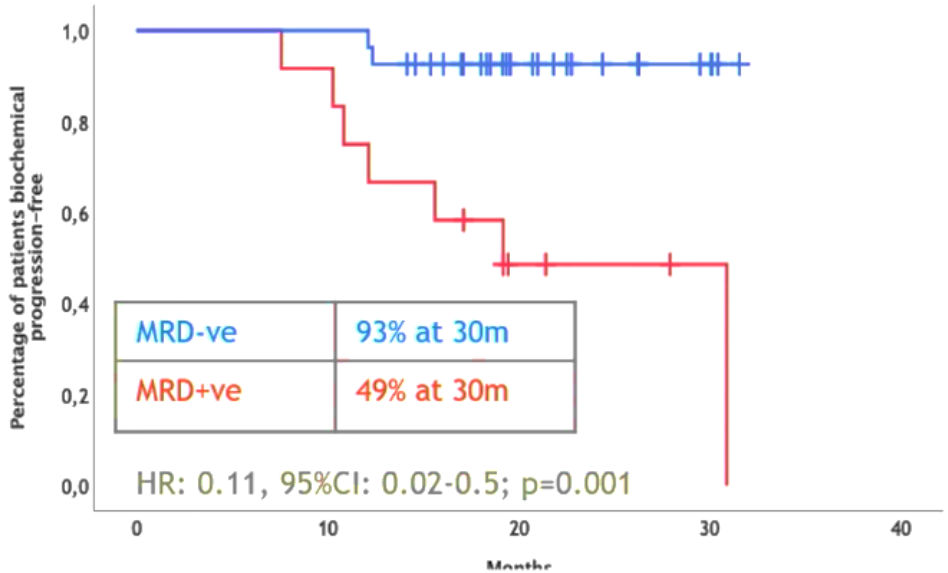
Landmark Time to Biochemical Progression
by MRD at End of Maintenance



Number of patients at risk

MRD-ve	46	45	42	28	14	1	0
MRD+ve	22	16	12	7	0		

Landmark Time to Biochemical Progression
by MRD 4 Yr After Treatment



Number of patients at risk

MRD-ve	27	27	27	18	0
MRD+ve	12	12	11	6	1

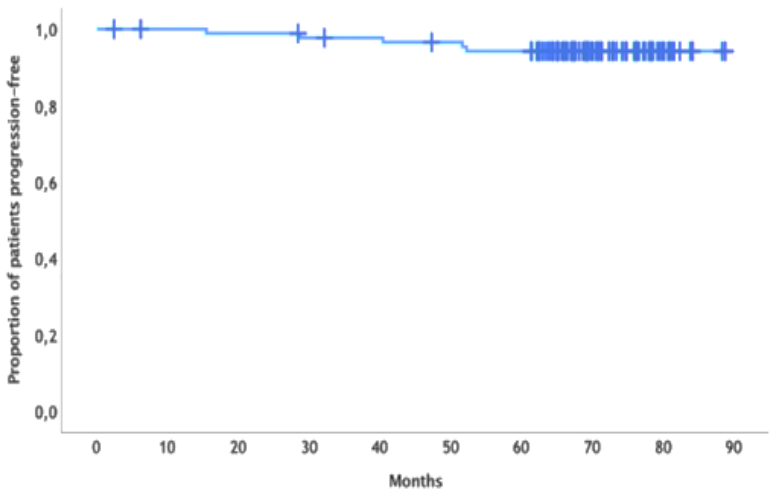
Mateos. ASH 2022. Abstr 118.

KEY DATA

GEM-CESAR

Time to Progression to MM

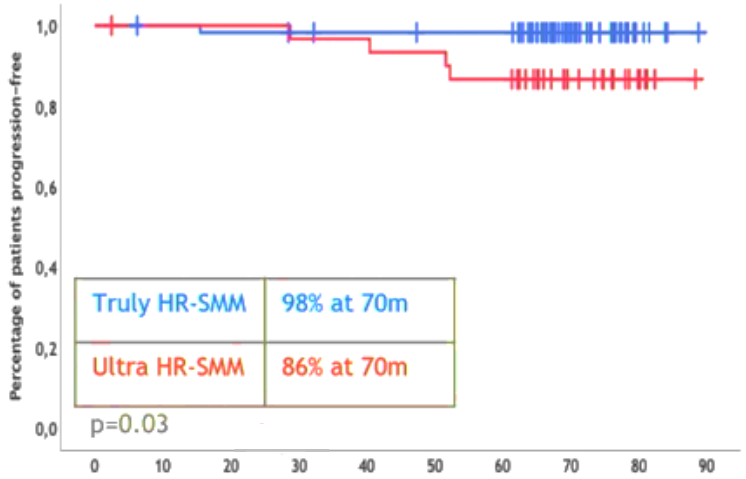
Time to active MM at 70 mo: 94%



Number of patients at risk

90	88	86	85	83	82	80	41	10	0

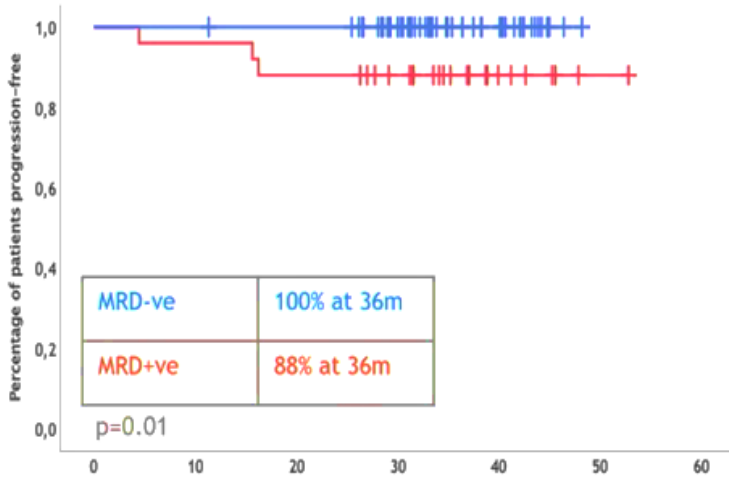
Time to Progression to Active MM by Risk



Number of patients at risk

HR-SMM	59	58	57	57	55	54	53	27	4
Ultra HR	31	30	30	29	28	27	26	13	4

Landmark Time to Progression to Active MM by MRD After Maintenance



Number of patients at risk

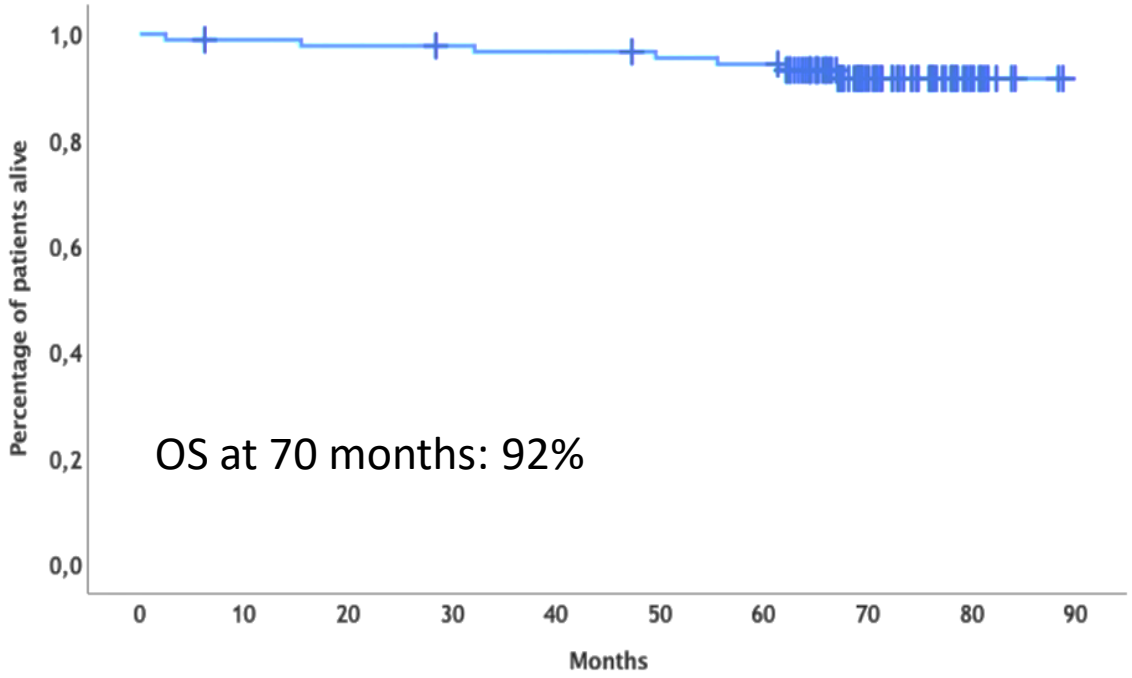
MRD-ve	46	45	42	28	14	0
MRD+ve	22	16	12	7	0	0

- 5 patients progressed to active, symptomatic MM
- Progression was initially asymptomatic in 4 patients

Mateos. ASH 2022. Abstr 118.

GEM-CESAR

Overall Survival



- 7 patients have died
  - 3 related to PD (1 after rescue therapy with DaraPd)
  - 1 cardiac arrest, not related to treatment
  - 1 massive ischemic stroke during induction
  - 1 related to lung cancer
  - 1 related to MDS

Mateos. ASH 2022. Abstr 118.

SUMMARY

GEM-CESAR

- 68% of evaluable patients were MRD negative at 3 mo after ASCT, and 43% remained negative at 4 yr post ASCT
- 94% of patients had not progressed to active MM at 70 mo
  - Presence of SLiM criteria and presence of MRD at end of maintenance predicted for progression to MM
- 48% of patients had progressed biochemically at 70 mo
  - Rescue therapy with DaraPd led to response in 79% of evaluable patients, allowing majority to continue with no myeloma-defining events
- MRD negativity after maintenance and sustained MRD negativity at 4 yr after ASCT was predictive for lack of biochemical progression

Mateos. ASH 2022. Abstr 118.

GEM-CESAR

Curative therapy with KRd followed by ASCT, KRd consolidation, and lenalidomide maintenance in high-risk smoldering MM appears achievable

2022 ASH Key Studies

Lymphomas

- TRIANGLE
- BRUIN
- CAPTIVATE
- L-MIND/First-MIND
- Glofitamab/NP30179

Multiple Myeloma

- GEM-CESAR
- ASCENT
- IFM2017-03
- MajesTEC-1

Leukemias

- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
- Momentum
- Study 2102-HEM-101

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CLINICAL QUESTION

ASCENT

Does fixed duration therapy with daratumumab, carfilzomib, lenalidomide, and dexamethasone provide benefit for high-risk smoldering multiple myeloma?

ASCENT

Study Design: multicenter, open-label phase II trial

Patients with untreated, high-risk smoldering MM*; adequate marrow and organ function; no evidence of amyloidosis or significant comorbidities (N = 87)

→

Induction
6 x 4-week Cycles

Carfilzomib 36 mg/m^2 twice weekly or 56 mg/m^2 weekly

Lenalidomide 25 mg daily x 3 wk per cycle

Daratumumab weekly for 8 wk; every other wk for 16 wk

Dexamethasone 40 mg weekly

→

Consolidation
6 x 4-week Cycles

Carfilzomib 36 mg/m^2 twice weekly or 56 mg/m^2 weekly

Lenalidomide 25 mg daily x 3 wk per cycle

Daratumumab every 4 wk

Dexamethasone 20 mg weekly

→

Maintenance
12 x 4-week Cycles

Lenalidomide 10 mg daily x 3 wk per cycle

Daratumumab every 8 wk

*Defined with IMWG updated risk stratification with any 2 of the following: serum M spike >2 g/dL or involved to uninvolved FLC ratio >20 or bone marrow PC % >20%, or score of ≥9 using risk scoring system of FLC ratio, serum M spike, marrow plasma cell %, and presence of high-risk FISH.

Primary endpoint: rate of confirmed sCR
Secondary endpoints: rate of MRD negativity (10^{-5} by flow cytometry), OS, PFS, safety, and toxicities

Kumar. ASH 2022. Abstr 757.

ASCENT

Baseline Characteristics

Characteristic	Patients (N = 87)
Median age, yr (range)	64 (41-76)
Male, n (%)	44 (51)
Race, n (%)	
• White	73 (84)
• Black	6 (7)
High-risk by FISH, n (%)	17 (20)
IMWG 20/2/20 high-risk criteria, n (%)	59 (68)
• M spike >2 g/dL	63 (72)
• FLC ratio >20	27 (31)
• BMPCs >20%	64 (74)
IMWG score ≥9, n (%)	28 (32)
Serum B_2M, mg/dL (range)	2.4 (1.5-5.0)
Serum creatinine, mg/dL (range)	0.9 (0.5-1.9)
Serum LDH, IU/dL (range)	169 (109-529)

- Median follow up: 26.2 mo (95% CI: 23.8-33.2)
  - 27 (31%) patients remained on treatment
  - 48 (55%) patients completed 24 cycles
- Median number of cycles: 23 (range: 1-24)
- 12 (14%) discontinued prior to completion of 24 cycles due to:
  - Withdrawal by subject (n = 3)
  - Adverse events (n = 3)
  - Physician decision (n = 3)
  - Progression (n = 2)
  - Death (n = 1)

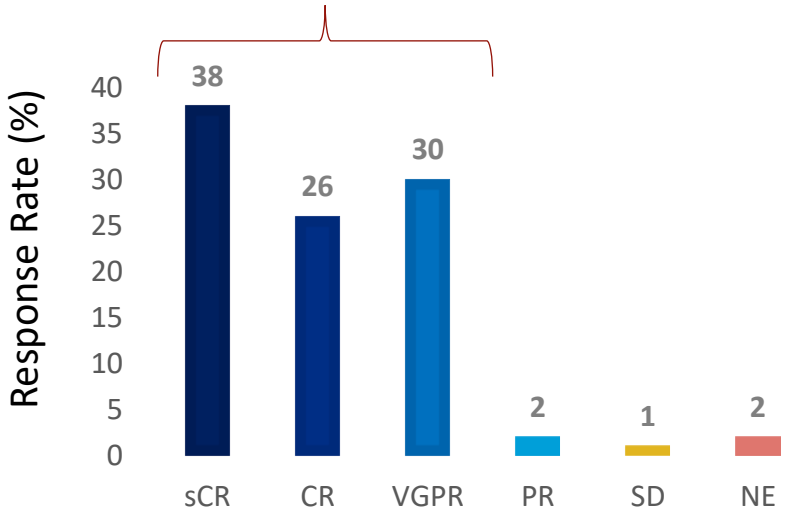
Kumar. ASH 2022. Abstr 757.

KEY DATA

ASCENT

Response

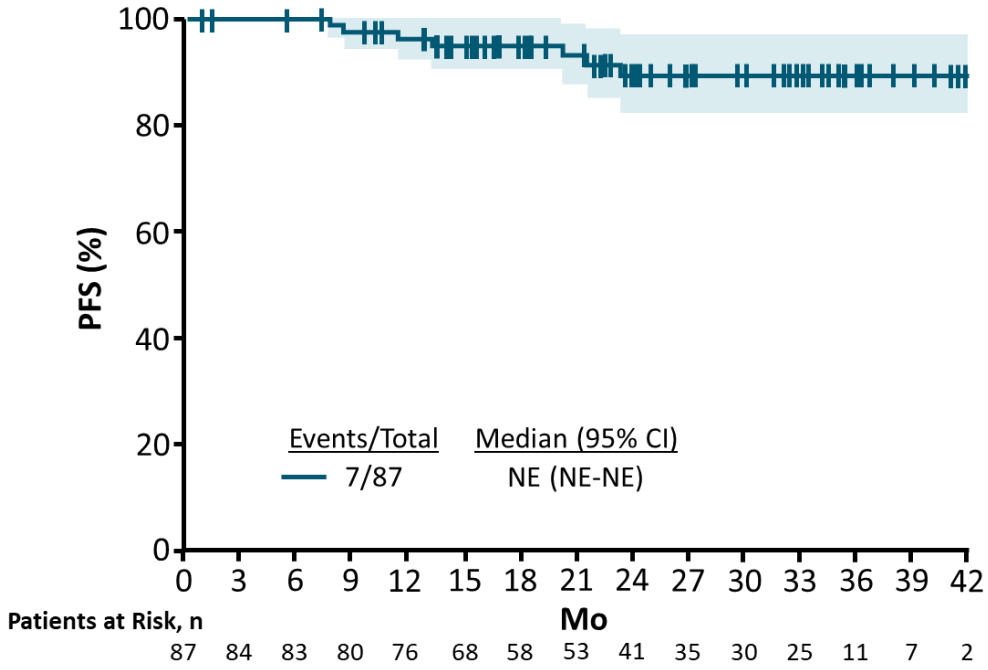
- **ORR: 97%**
  - 92% ≥ VGPR
- Marrow MRD_{neg}: 84% (n = 73)
  - 61% (n = 53) of patients also in complete response and MRD_{neg}
- Median time to MRD negativity: 6.6 mo
  - End of induction: n = 53
  - End of consolidation: n = 16
  - End of maintenance: n = 4



Progression-Free Survival

3-yr PFS rate: 89.9% (95% CI: 82.3%-98.3%)

- 4 patients progressed:
  - 3 with biochemical progression and 1 who developed plasma cell leukemia 6 mo after completing treatment



Note: Median PFS for cohort not yet reached

Kumar. ASH 2022. Abstr 757.

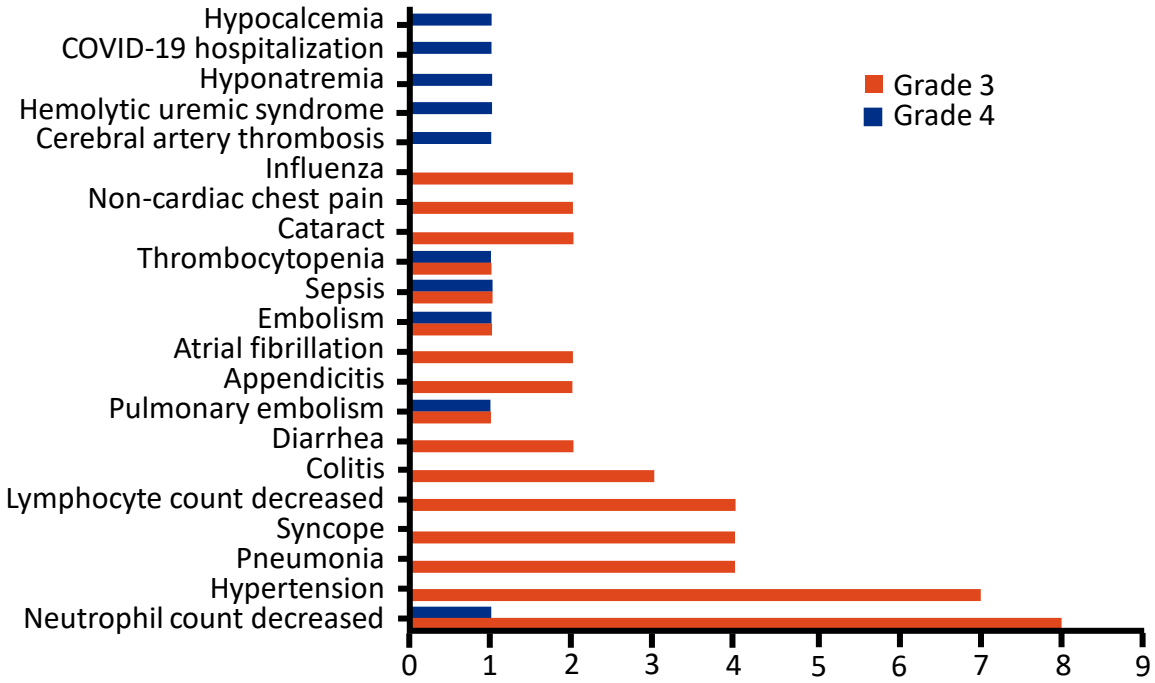
KEY DATA

ASCENT

Safety

Event	Patients (N = 87)
Any-grade AE possibly related to Tx, n (%)	81 (92)
Hematologic EA grade ≥3, n (%)	16 (18)
Nonhematologic AE grade ≥3, n (%)	44 (51)
Dose reductions, n	
▪ Carfilzomib	12
▪ Lenalidomide	12
▪ Dexamethasone	14
Median dose per cycle, mg	
▪ Daratumumab	1600
▪ Carfilzomib	312
▪ Lenalidomide	210
▪ Dexamethasone	80

Grade 3 AEs Observed in ≥2 Patients or Grade 4 AEs in ≥1 Patient



Deaths on trial: COVID-19 (n = 2), RSV (n = 1), PD (n = 1)

Kumar. ASH 2022. Abstr 757.

SUMMARY

ASCENT

- The combination of daratumumab, carfilzomib, lenalidomide, and dexamethasone given for fixed duration of 2 year in patients with high-risk SMM was associated with a high response rate including high rates of MRD negativity

- No new toxicity signals observed
  - Toxicities similar to those observed with this regimen in active MM

Kumar. ASH 2022. Abstr 757.

ASCENT Clinical Trial

The quadruplet regimen of daratumumab, carfilzomib, lenalidomide, and dexamethasone provides benefit for patients with high-risk smoldering MM

2022 ASH Key Studies

Lymphomas

- TRIANGLE
- BRUIN
- CAPTIVATE
- L-MIND/First-MIND
- Glofitamab/NP30179

Multiple Myeloma

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- ASCENT
- IFM2017-03
- MajesTEC-1

Leukemias

- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
- Momentum
- Study 2102-HEM-101

CLINICAL QUESTION

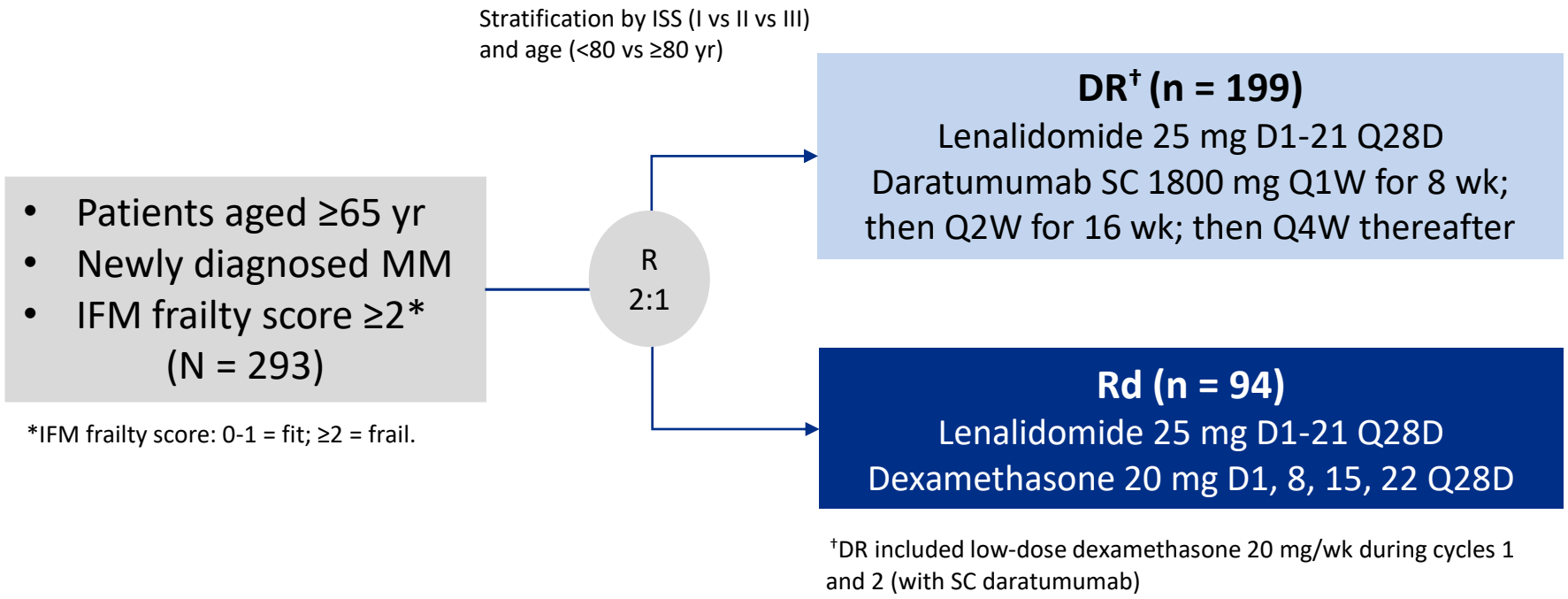
IFM2017-03

Does a dexamethasone dose sparing-regimen of daratumumab plus lenalidomide benefit frail patients with newly diagnosed multiple myeloma?

KEY DATA

IFM2017-03

Study Design: randomized, multicenter, open-label phase III trial



*IFM frailty score: 0-1 = fit; ≥2 = frail.

†DR included low-dose dexamethasone 20 mg/wk during cycles 1 and 2 (with SC daratumumab)

- **Primary endpoint:** PFS
- **Interim analysis at 12 mo of therapy:** ORR, VGPR or better rate, MRD rate, grade ≥3 AEs

Broome. ASH 2022. Abstr 3.

IFM2017-03

Baseline Characteristics

Characteristic	DR (n = 199)	Rd (n = 94)
Median age, yr (range)	81 (68-92)	81 (68-90)
Age category, n (%)		
• 65 to <70 yr	2 (1)	2 (2)
• 70 to <75 yr	30 (15)	13 (14)
• 75 to <80 yr	49 (25)	19 (20)
• ≥80 yr	118 (59)	61 (65)
Female, n (%)	101 (51)	48 (51)
ECOG PS 0/1/2, %	10/46/44	10/50/40
Charlson ≤1, n (%)	113 (58)	57 (61)
IFM frailty score, n (%)		
• ≤1	0	0
• 2	57 (29)	35 (37)
• 3	81 (41)	26 (28)
• 4	44 (22)	24 (26)
• 5	17 (9)	9 (10)

Characteristic	DR (n = 199)	Rd (n = 94)
ISS disease stage I/II/III, %	17/51/32	19/53/28
Measurable disease type, n (%)		
• IgG	113 (57)	49 (52)
• IgA	38 (19)	20 (21)
• PBJ only	21 (11)	10 (11)
• SFLC only	27 (14)	15 (16)
Cytogenetics profile,* n (%)		
• Standard risk	148 (83)	60 (78)
• High risk	31 (17)	17 (22)
• del17p	16 (9)	11 (14)
• t(4;14)	9 (5)	5 (6)
• t(14;16)	6 (3)	3 (3)
Creatinine clearance, n (%)		
• <30 mL/min	1 (1)	3 (3)
• 30 to <60 mL/min	119 (60)	50 (53)
• ≥60 mL/min	79 (40)	41 (44)

*Cytogenetic profile NA for DR (n=20); Rd (n=17)

IFM2017-03

Response Rates

Response	DR (n = 199)	Rd (n = 94)	P Value
ORR, %	**96%**	**85%**	**0.001**
• CR	17	10	
• VGPR	47	33	
• PR	32	42	
≥ VGPR, %	**64%**	**43%**	
MRD at 10^{-5} by NGS,* %	10	3	0.012

*In ITT analysis. MRD was assessed in patients with ≥ VGPR at 12 mo and was not assessable or missing for 20.6% of patients in DR arm and 14.1% of patients in Rd arm. Patients with missing data were considered MRD positive.

Rate of Response Over Time	Proportion of Patients With ≥ VGPR, %	
	DR (n = 199)	Rd (n = 94)
Mo 4	41	26
Mo 8	68	48
Mo 12	71	55

Similar improvement in rate of ≥ VGPR with DR across all subgroups analyzed, including IFM frailty score (*P* = 0.87) and cytogenetic risk (*P* = 0.29)

Fewer discontinuations in DR arm vs Rd arm (32% vs 45%)

IFM2017-03

Safety

Most Common Grade ≥3 AEs	DR (n = 199)	Rd (n = 94)	P Value
Any grade ≥3 AE, n (%)	164 (82)	64 (68)	0.010
SAE, n (%)	109 (55)	59 (63)	0.21
Grade ≥3 hematologic AEs, n (%)	109 (55)	24 (26)	<0.0001
• Anemia	21 (11)	2 (2)	0.010
• Neutropenia	91 (46)	17 (18)	<0.0001
• Thrombocytopenia	18 (9)	3 (3)	0.089
Grade ≥3 infection, n (%)	26 (13)	17 (18)	0.29
• Non–COVID-19 infections	17 (9)	13 (14)	0.21
• Pneumonia	5 (3)	7 (7)	0.060
• COVID-19	9 (5)	4 (4)	1.0
Treatment discontinuation for AE, n (%)	27 (14)	15 (16)	0.65

Broome. ASH 2022. Abstr 3.

SUMMARY

IFM2017-03

- The combination of daratumumab and lenalidomide *without* dexamethasone demonstrated significantly superior ORR, rates of VGPR or better, and rates of MRD negativity
- The safety profile was similar
- PFS analysis is ongoing

Broome. ASH 2022. Abstr 3.

IFM2017-03

Daratumumab plus lenalidomide provides benefit and should be considered for newly diagnosed frail patients with Multiple Myeloma

Dexamethasone can be safely omitted from treatment in this population

2022 ASH Key Studies

Lymphomas

- TRIANGLE
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- CAPTIVATE
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- Glofitamab/NP30179

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- MajesTEC-2

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- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
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- Study 2102-HEM-101

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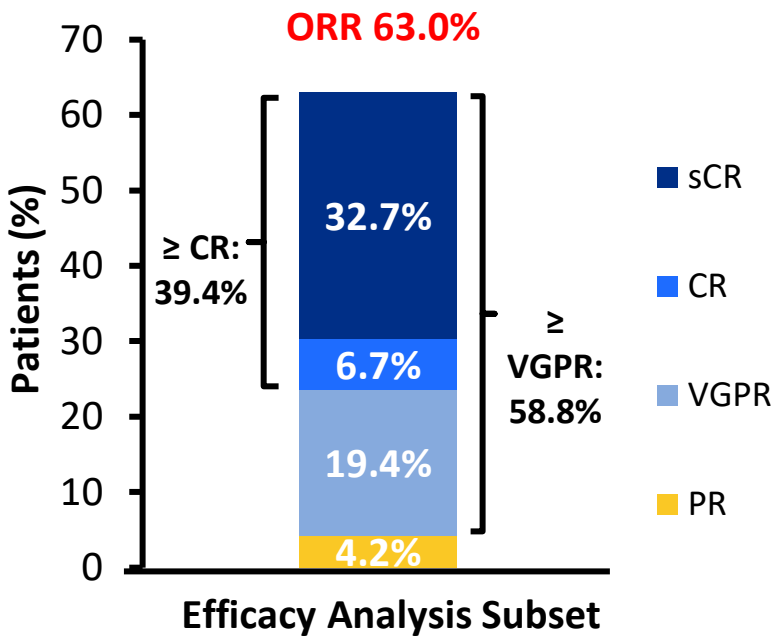
FDA Approval

MajesTEC-1

On October 25, 2022, the FDA granted accelerated approval to teclistamab-cqyv (brand name Tecvayli), the first bispecific B-cell maturation antigen-directed CD3 T-cell engager, for adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

Previously reported at ASCO 2022: a single-arm, multi-cohort, open-label, multi-center study



- Median follow-up: 14.1 mo (range: 0.3-24.4)
- Median treatment duration: 8.5 mo (range: 0.2-24.4)
- Median relative dose intensity: 93.7%

Responses were durable and deepened over time

MRD Event	All Patients (N = 165)
MRD negative (10^{-5}), n/N (%)	
• All treated	44/165 (26.7)
• MRD evaluable	44/54 (81.5)
MRD negativity with ≥CR, %	46.2

Event	All Patients (N = 165)
Median time to first response, mo (range)*	1.2 (0.2-5.5)
Median time to best response, mo (range)*	3.8 (1.1-16.8)
Median DoR, mo (95% CI)	18.4 (14.9-NE)

*n = 104.

- Median PFS: 11.3 mo (95% CI: 8.8-17.1)
- Median OS: 18.3 mo (95% CI, 15.5-NE)
  - (Not yet mature; data from 97 patients (58.8%) censored.)

Nooka. ASCO 2022. Abstr 8007. Moreau. NEJM. 2022;[Epub].

CLINICAL QUESTION

MajesTEC-2

Does the bispecific antibody teclistamab in combination with daratumumab and lenalidomide provide benefit for patients with multiple myeloma?

KEY DATA

MajesTEC-2

Study Design: ongoing, phase Ib, multicohort trial

- Patients with measurable MM
- 1-3 prior lines of therapy, including an IMiD and a PI

→ **Teclistamab**
step-up dosing
0.72 mg/kg or 1.5 mg/kg SC QW,
with transition to 3 mg/kg SC Q2W
starting at cycle 3

\+ **Daratumumab**
1800 mg SC
(per approved schedule)
Cycles 1–2: QW
Cycles 3–6: Q2W
Cycles 7+: Q4W

\+ **Lenalidomide**
25 mg PO daily for 21 days of a 28-day cycle, starting at cycle 2
Cycles 2–4: dexamethasone 40 mg PO given QW

IMiD: immunomodulatory drug
PI: proteasome inhibitor

Primary endpoint: Safety, dose-limiting toxicities

Key secondary endpoints: ORR, rate of ≥VGPR and ≥CR, duration of response, time to response

Hospitalization and premedication with dexamethasone (16 mg), acetaminophen, and diphenhydramine required for step-up doses and first full dose of teclistamab.

Searle. ASH 2022. Abstr 160.

MajesTEC-2

Baseline Characteristics

Characteristic	Dara 1800 mg SC Len 25 mg PO	
	Tec 0.72 g/kg SC n=13	Tec 1.5 mg/kg SC n=13
Median age, yr (range)	65 (38-71)	60 (46-75)
Male, n (%)	11 (84.6)	17 (89.5)
Race, n (%)		
• White	9 (69.2)	17 (89.5)
• Black	0	1 (5.3)
• Asian	1 (7.7)	0
• Unknown/not reported	3 (23.1)	1 (5.3)
Extramedullary plasmacytomas ≥1, n (%)†	1 (7.7)	1 (5.3)
High-risk cytogenetics, n (%)‡	3/12 (25)	7/15 (46.7)
ISS stage, n (%)§		
• I	8/11 (72.7)	9/16 (56.3)
• II	2/11 (18.2)	4/16 (25.0)
• III	1/11 (9.1)	3/16 (18.8)

Characteristic	Dara 1800 mg SC Len 25 mg PO	
	Tec 0.72 g/kg SC n=13	Tec 1.5 mg/kg SC n=13
Median time since dx, yr (range)	3.9 (0.4-7.8)	3.4 (1.1-6.3)
Median prior lines of therapy, n (range)	2 (1-3)	2 (1-3)
Prior stem cell transplant, n (%)	8 (61.5)	18 (94.7)
Prior proteasome inhibitor, n (%)	13 (100)	19 (100)
Prior immunomodulatory drug, n (%)	13 (100)	19 (100)
Prior anti-CD38 mAb, n (%)	5 (38.5)	5 (26.3)
Refractory status, n (%)		
• To lenalidomide	6 (46.2)	3 (15.8)
• To an anti-CD38 mAB	3 (23.1)	3 (15.8)

Data cut-off Oct 17, 2022.
aCytogenetic risk is based on FISH or karyotype testing and is defined as ≥1 of the following: del(17p), t(4;14), or t(14;16).
bAll daratumumab; no patients were refractory to isatuximab.

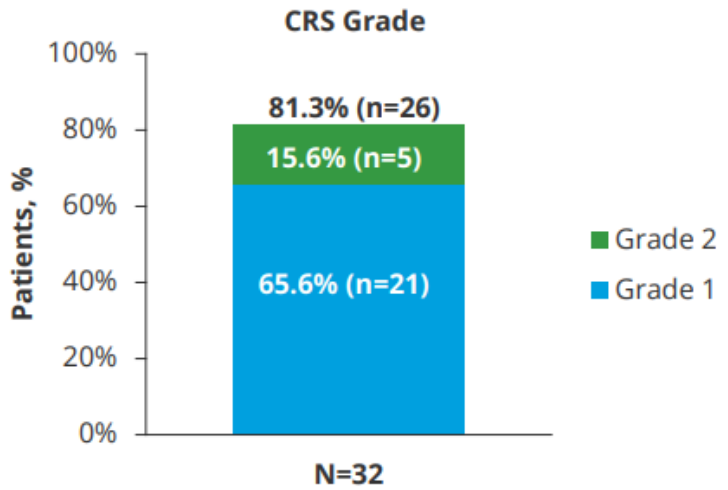
MajesTEC-2

Safety

AE (any Grade: ≥25% and/or Grade 3/4: ≥10%), n (%)	N=32	
	Any Grade	Grade 3/4
CRS	26 (81.3)	0
Fatigue	15 (46.9)	2 (6.3)
Diarrhea	15 (46.9)	0
Cough	13 (40.6)	1 (3.1)
COVID-19	12 (37.5)	4 (12.5)
Insomnia	12 (37.5)	1 (3.1)
Hypophosphatemia	10 (31.3)	2 (6.3)
Pyrexia	10 (31.3)	1 (3.1)
Upper respiratory tract infection	10 (31.3)	0
Nausea	10 (31.3)	0
ALT increase	9 (28.1)	3 (9.4)
Pneumonia	8 (25.0)	5 (15.6)

Per protocol, tocilizumab was given for all grade 2 CRS events and at investigator discretion for grade 1 events.
Prophylactic tocilizumab was not required per protocol

Hematologic AE (any Grade: ≥25% and/or Grade 3/4: ≥10%), n (%)	N=32	
	Any Grade	Grade 3/4
Neutropenia	27 (84.4)	25 (78.1)
Thrombocytopenia	8 (25.0)	5 (15.6)
Anemia	7 (21.9)	4 (12.5)
Febrile neutropenia	4 (12.5)	4 (12.5)
Lymphopenia	4 (12.5)	4 (12.5)



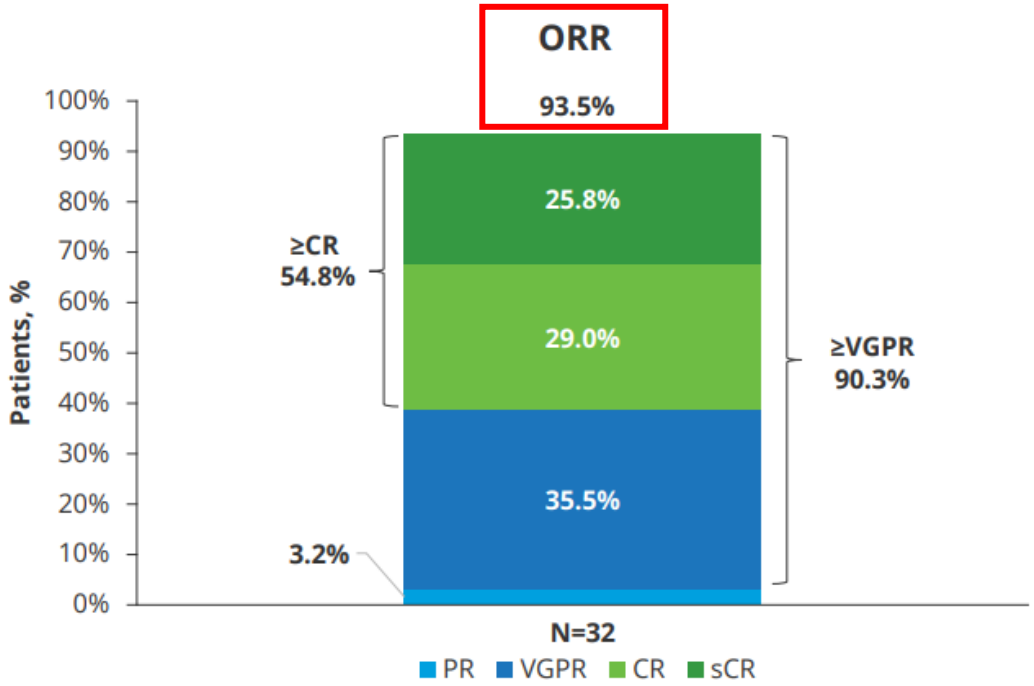
- 97% of CRS events occurred during cycle 1

Searle. ASH 2022. Abstr 160.

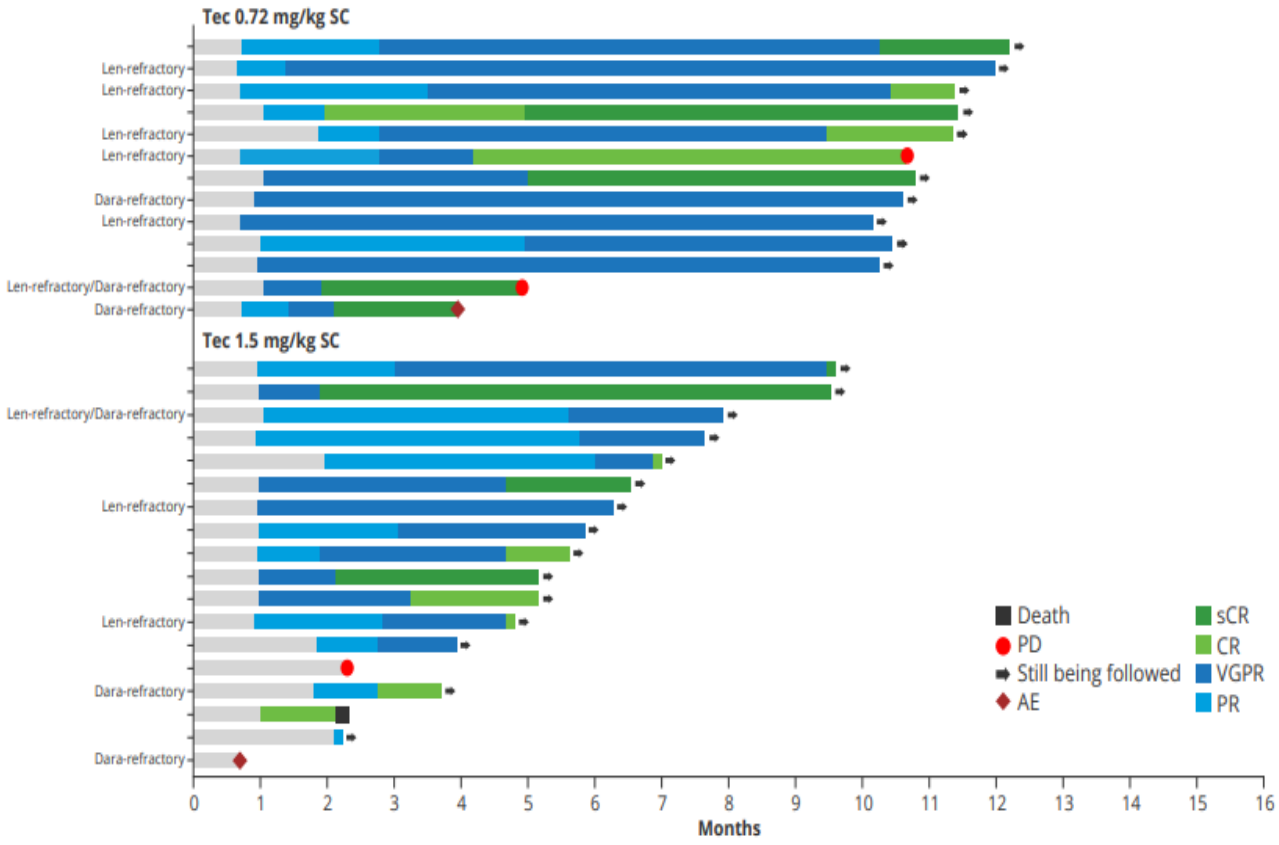
KEY DATA

MajesTEC-2

Response



	Median (range)
Follow-up months	8.4 (1.1–12.9)
Time to first response, months	1.0 (0.7–3.3)
Time to ≥CR, months	3.0 (1.0–10.4)



- Responses were observed in patients who were refractory to daratumumab and/or lenalidomide

Searle. ASH 2022. Abstr 160.

SUMMARY

MajesTEC-2

- The combination of teclistamab with daratumumab and lenalidomide has potential with 80.6% (25/31) of response-evaluable patients remaining progression-free and on treatment at data cut-off

- The safety profile was consistent with the individual components of the regimen
  - No grade 3 or 4 CRS events or ICANS

MajesTEC-7 (NCT05552222) is a randomized, open-label phase 3 study that will compare tec-dara-len vs D-Rd in patients with NDMM who are transplant-ineligible or for whom ASCT is not intended

Searle. ASH 2022. Abstr 160.

MajesTEC-2

The combination of teclistamab with daratumumab and lenalidomide has potential to benefit patients with relapsed/refractory Multiple Myeloma

More to come…

2022 ASH Key Studies

Lymphomas

- TRIANGLE
- BRUIN
- CAPTIVATE
- L-MIND/First-MIND
- Glofitamab/NP30179

Multiple Myeloma

- GEM-CESAR
- ASCENT
- IFM2017-03
- MajesTEC-1

Leukemias

- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
- Momentum
- Study 2102-HEM-101

VIALE-A Clinical Study

Does azacitidine with or without venetoclax provide benefit for patients with treatment naïve AML ineligible for standard induction chemotherapy?

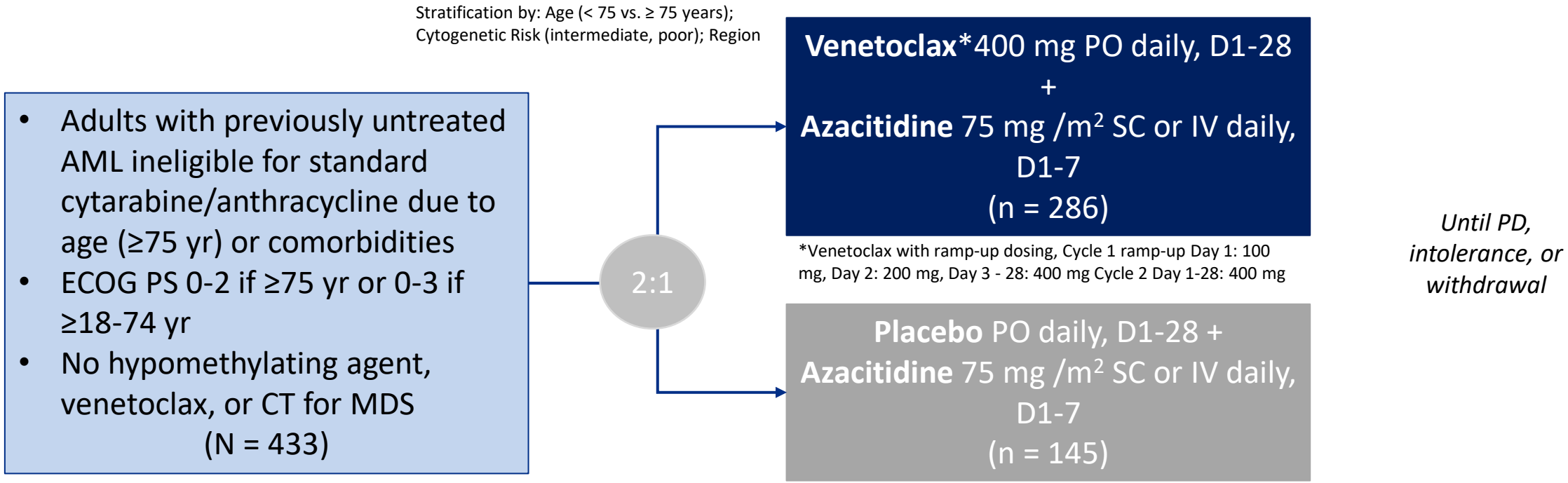
Extended 2 year follow-up

100% OS analysis

KEY DATA

VIALE-A Clinical Study

Study Design: multicenter, double-blind, placebo-controlled, randomized phase 3 trial



Primary endpoint: OS, (CR + CRi coprimary endpoint in EU/EU reference countries)

Key secondary endpoints: CR + CRi rate, CR rate, EFS, OS by molecular subtype, MRD negativity remission rate

100% OS analysis with 360/431 survival events with the data cut-off of Dec 1, 2021

Pratz. ASH 2022. Abstr 219.

KEY DATA

VIALE-A Clinical Study

Baseline Characteristics

Characteristic	Ven-Aza (n = 286)	Pbo-Aza (n = 145)
Median age, yr (range)	76 (49-91)	76 (60-90)
Age, yr, n (%)		
▪ 18 to <65	10 (3.5)	5 (3.4)
▪ 65 to <75	102 (35.7)	53 (36.6)
▪ ≥75	174 (60.8)	87 (60.0)
De novo AML, n (%)	214 (74.8)	110 (75.9)
▪ Secondary	72 (25.2)	35 (24.1)
Secondary AML, n (%)		
▪ Post MDS or CMML	46 (63.9)	26 (74.3)
▪ Tx-related AML	26 (36.1)	9 (25.7)
AML w/myelodysplasia-related changes, n (%)	92 (32.2)	49 (33.8)

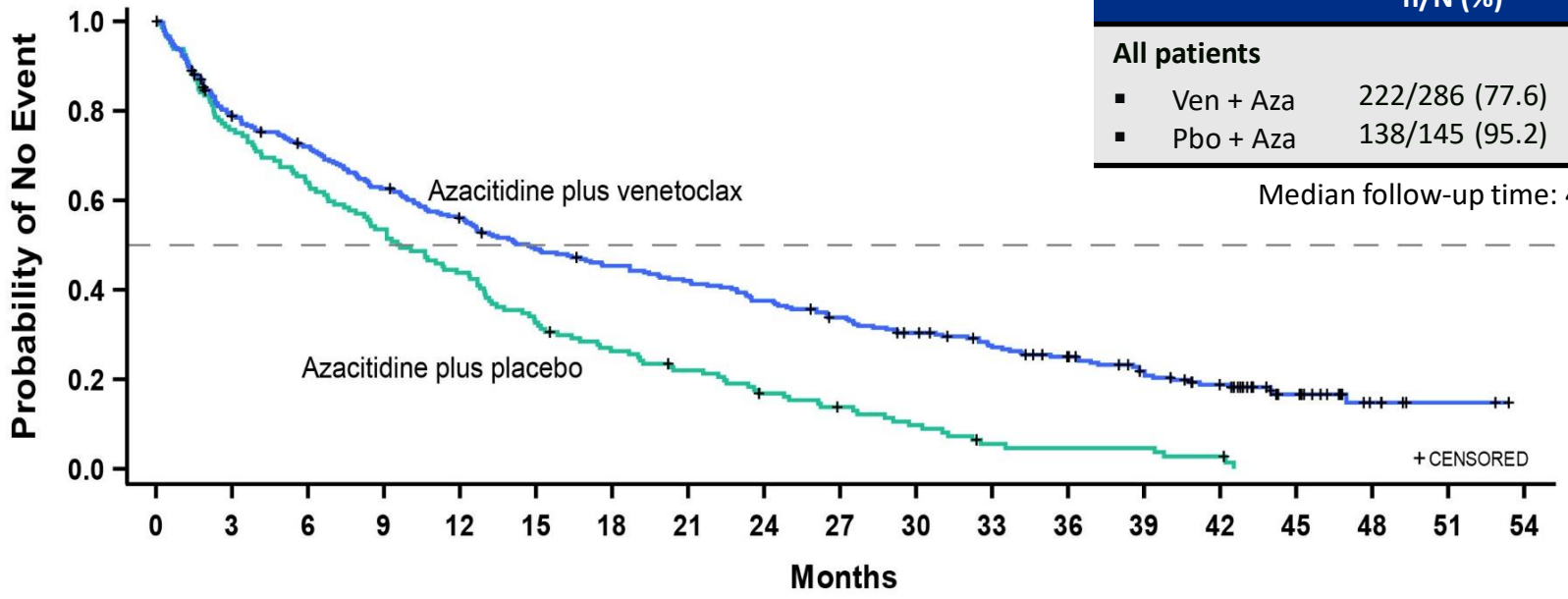
Characteristic	Ven-Aza (n = 286)	Pbo-Aza (n = 145)
Blast count, n (%)		
▪ <30%	85 (29.6)	41 (28.1)
▪ ≥30% to <50%	61 (21.3)	33 (22.6)
▪ ≥50%	140 (49.1)	71 (49.3)
ECOG PS, n (%)		
▪ 0-1	157 (54.9)	81 (55.9)
▪ 2-3	129 (45.1)	64 (44.1)
Cytogenetic risk, n (%)		
▪ Intermediate	182 (63.6)	89 (61.4)
▪ Poor	104 (36.4)	56 (38.6)
Somatic mutations, n/N (%)		
▪ IDH1 or IDH2	61/245 (24.9)	28/127 (22.0)
▪ FLT3	29/206 (14.1)	22/108 (20.4)
▪ NPM1	27/163 (16.6)	17/86 (19.8)
▪ TP53	38/163 (23.3)	14/86 (16.3)

AML, acute myeloid leukemia; Aza, azacitidine; CMML, chronic myelomonocytic leukemia; ECOG, Eastern Cooperative Oncology Group; Pbo, placebo; PS, performance status; Ven, venetoclax.

Pratz. ASH 2022. Abstr 219.

VIALE-A Clinical Study

Overall Survival



Population	Events/Patients, n/N (%)	Median OS, Mo (95% CI)	HR (95% CI)	P Value
All patients				
▪ Ven + Aza	222/286 (77.6)	14.7 (12.1-18.7)	**0.58**	<.001
▪ Pbo + Aza	138/145 (95.2)	9.6 (7.4-12.7)	(0.465-0.723)	

Median follow-up time: 43.2 months (range: < 0.1 - 53.4)

Patients at Risk

Azacitidine plus placebo	145	109	92	77	63	47	37	30	22	17	12	6	5	5	3	0			
Azacitidine plus venetoclax	286	220	199	173	153	133	122	113	101	89	78	67	57	45	34	18	6	2	0

Aza, azacitidine; MRD, minimal residual disease; mut, mutations; NR, not reported; OS, overall survival; Pbo, placebo; Ven, venetoclax.

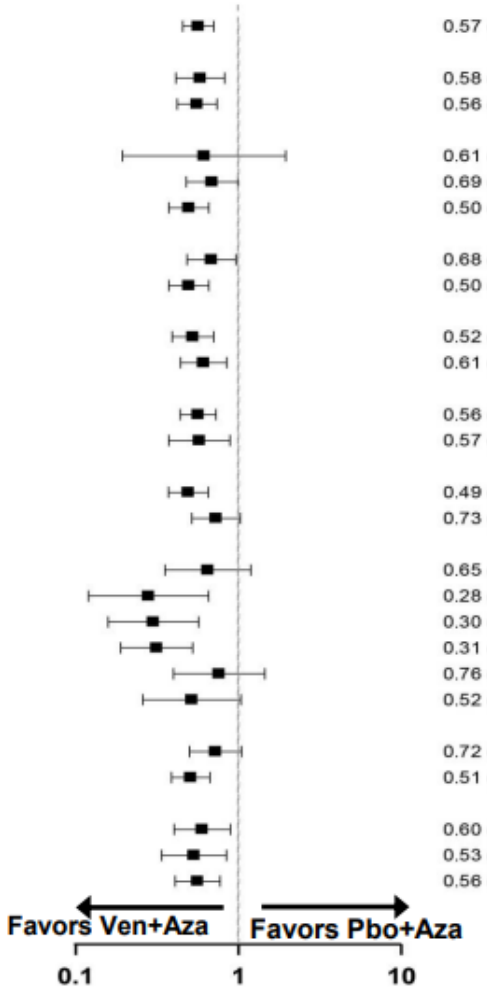
Pratz. ASH 2022. Abstr 219.

KEY DATA

VIALE-A Clinical Study

Overall Survival by subgroups

	Ven+Aza n/N (%)	Pbo+Aza n/N (%)	HR (95% CI)
All Patients	222/286 (77.6)	138/145 (95.2)	0.57 (0.45, 0.70)
Gender			
Female	88/114 (77.2)	55/ 58 (94.8)	0.58 (0.41, 0.82)
Male	134/172 (77.9)	83/ 87 (95.4)	0.56 (0.42, 0.74)
Age (Years)			
18 - < 65	8/ 10 (80.0)	5/ 5 (100.0)	0.61 (0.19, 1.95)
65 - < 75	79/102 (77.5)	49/ 53 (92.5)	0.69 (0.48, 0.99)
≥ 75	135/174 (77.6)	84/ 87 (96.6)	0.50 (0.37, 0.66)
Age (Years)			
< 75	87/112 (77.7)	54/ 58 (93.1)	0.68 (0.48, 0.96)
≥ 75	135/174 (77.6)	84/ 87 (96.6)	0.50 (0.37, 0.66)
Baseline ECOG			
Grade < 2	127/157 (80.9)	78/ 81 (96.3)	0.52 (0.39, 0.70)
Grade ≥ 2	95/129 (73.6)	60/ 64 (93.8)	0.61 (0.44, 0.85)
Type of AML			
De Novo	162/214 (75.7)	104/110 (94.5)	0.56 (0.44, 0.73)
Secondary	60/ 72 (83.3)	34/ 35 (97.1)	0.57 (0.37, 0.89)
Cytogenetic risk			
Intermediate	130/182 (71.4)	84/ 89 (94.4)	0.49 (0.37, 0.65)
Poor	92/104 (88.5)	54/ 56 (96.4)	0.73 (0.52, 1.02)
Molecular Marker			
FLT3	23/ 29 (79.3)	20/ 22 (90.9)	0.65 (0.35, 1.19)
IDH1	21/ 23 (91.3)	11/ 11 (100.0)	0.28 (0.12, 0.65)
IDH2	30/ 40 (75.0)	18/ 18 (100.0)	0.30 (0.16, 0.57)
IDH1/2	49/ 61 (80.3)	28/ 28 (100.0)	0.31 (0.19, 0.52)
TP53	36/ 38 (94.7)	13/ 14 (92.9)	0.76 (0.40, 1.45)
NPM1	17/ 27 (63.0)	17/ 17 (100.0)	0.52 (0.26, 1.03)
AML-MRC			
Yes	81/ 92 (88.0)	46/ 49 (93.9)	0.72 (0.50, 1.04)
No	141/194 (72.7)	92/ 96 (95.8)	0.51 (0.39, 0.67)
Bone marrow blast count			
< 30%	72/ 85 (84.7)	40/ 41 (97.6)	0.60 (0.40, 0.89)
30 -< 50%	47/ 61 (77.0)	32/ 33 (97.0)	0.53 (0.34, 0.84)
≥ 50%	103/140 (73.6)	66/ 71 (93.0)	0.56 (0.41, 0.77)



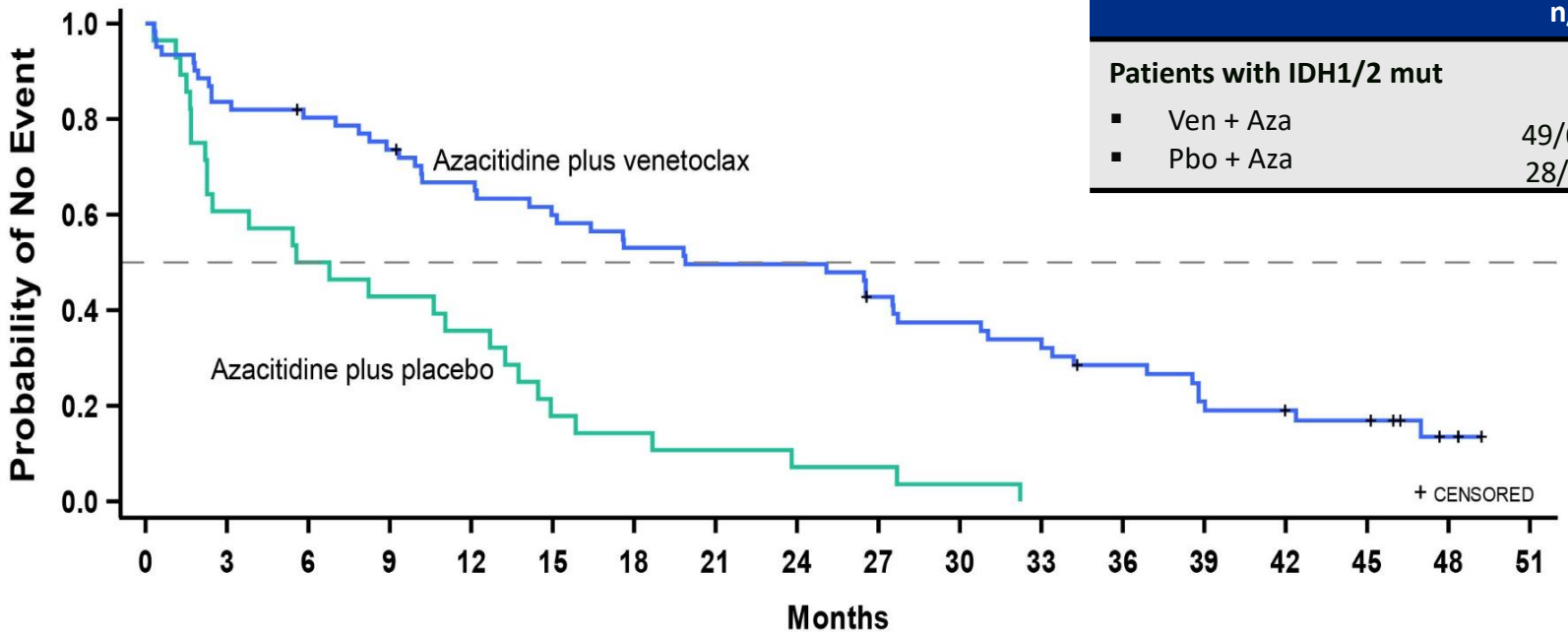
Pratz. ASH 2022. Abstr 219.

KEY DATA

VIALE-A Clinical Study

Median OS for pts with IDH1/2 mutations

Population	Events/Patients, n/N (%)	Median OS, Mo (95% CI)	HR (95% CI)	P Value
Patients with IDH1/2 mut				
▪ Ven + Aza	49/61 (80.3)	19.9 (12.2-27.7)	**0.314** (0.189-0.522)	<.001
▪ Pbo + Aza	28/28 (100)	6.2 (2.3-12.7)		



Patients at Risk

Azacitidine plus placebo	28	17	14	12	10	5	4	3	2	2	1	0						
Azacitidine plus venetoclax	61	51	48	44	39	35	31	29	29	24	21	19	15	11	9	8	3	0

Aza, azacitidine; MRD, minimal residual disease; mut, mutations; NR, not reported; OS, overall survival; Pbo, placebo; Ven, venetoclax.

Pratz. ASH 2022. Abstr 219.

KEY DATA

VIALE-A Clinical Study

Overall Survival

Population	Events/Patients, n/N (%)	Median OS, Mo (95% CI)	HR (95% CI)	P Value
All patients				
▪ Ven + Aza	222/286 (77.6)	14.7 (12.1-18.7)	0.58 (0.465-0.723)	<.001
▪ Pbo + Aza	138/145 (95.2)	9.6 (7.4-12.7)		
Patients with IDH1/2 mut				
▪ Ven + Aza	49/61 (80.3)	19.9 (12.2-27.7)	0.314 (0.189-0.522)	<.001
▪ Pbo + Aza	28/28 (100)	6.2 (2.3-12.7)		
Patients with CR/CRi and MRD <10^{-3}				
▪ Ven + Aza	43/69 (62)	34.2 (27.7-44.0)	NR	NR
▪ Pbo + Aza	9/11 (82)	25.0 (7.0-39.8)		
Patients with CR/CRi and MRD ≥10^{-3}				
▪ Ven + Aza	76/96 (79)	18.7 (12.9-23.5)	NR	NR
▪ Pbo + Aza	23/24 (96)	15.1 (7.4-26.4)		

Aza, azacitidine; MRD, minimal residual disease; mut, mutations; NR, not reported; OS, overall survival; Pbo, placebo; Ven, venetoclax.

Pratz. ASH 2022. Abstr 219.

KEY DATA

VIALE-A Clinical Study

Patient Disposition and Follow-up

Follow-up	Ven-Aza (n = 286)	Pbo-Aza (n = 145)
Median duration of follow-up, mo (range)	43.2 (0.0-53.4)	42.1 (0.2-42.5)
Patients remaining on treatment at time of current analysis, n (%)	25 (9)	0 (0)
Discontinued treatment, n (%)	261 (91.3)	145 (100)

Duration of Response

	Treatment Arm	DoR at 75% OS Analysis,* Median Mo (95% CI)	DoR at 100% OS Analysis,† Median Mo (95% CI)
Duration of CR + CRi	Ven + Aza (n = 190,‡ 191§)	17.5 (13.6-NE)	18.2 (13.6-23.1)
	Pbo + Aza (n = 41,‡ 42§)	13.4 (5.8-15.5)	10.7 (5.0-15.1)

	Treatment Arm	DoR at 75% OS Analysis,* Median Mo (95% CI)	DoR at 100% OS Analysis,† Median Mo (95% CI)
Duration of CR	Ven + Aza (n = 105,‡ 111§)	17.5 (15.3-NE)	22.1 (16.7-27.0)
	Pbo + Aza (n = 26)	13.3 (8.5-17.6)	13.4 (10.3-15.1)

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VIALE-A Clinical Study

Safety

Adverse Events (Aes), n (%)	Aza-Ven (n = 283)	Aza-Pbo (n = 144)
Any adverse event	283 (100)	144 (100)
Grade ≥3 AEs	279 (98.6)	139 (96.5)
Serious AEs	242 (85.5)	111 (77.1)
AE leading to Ven/Pbo discontinuation	85 (30.0)	32 (22.2)
AE leading to Ven/Pbo interruption	207 (73.1)	86 (59.7)
AE leading to Ven/Pbo reduction	7 (2.5)	6 (4.2)
Fatal AEs	71 (25.1)	31 (21.5)
Deaths, n (%)	220 (77.7)	138 (95.8)
▪ ≤30 days after first study drug dose	21 (7.4)	9 (6.3)
▪ ≥30 days after last study drug dose	90 (31.8)	46 (31.9)

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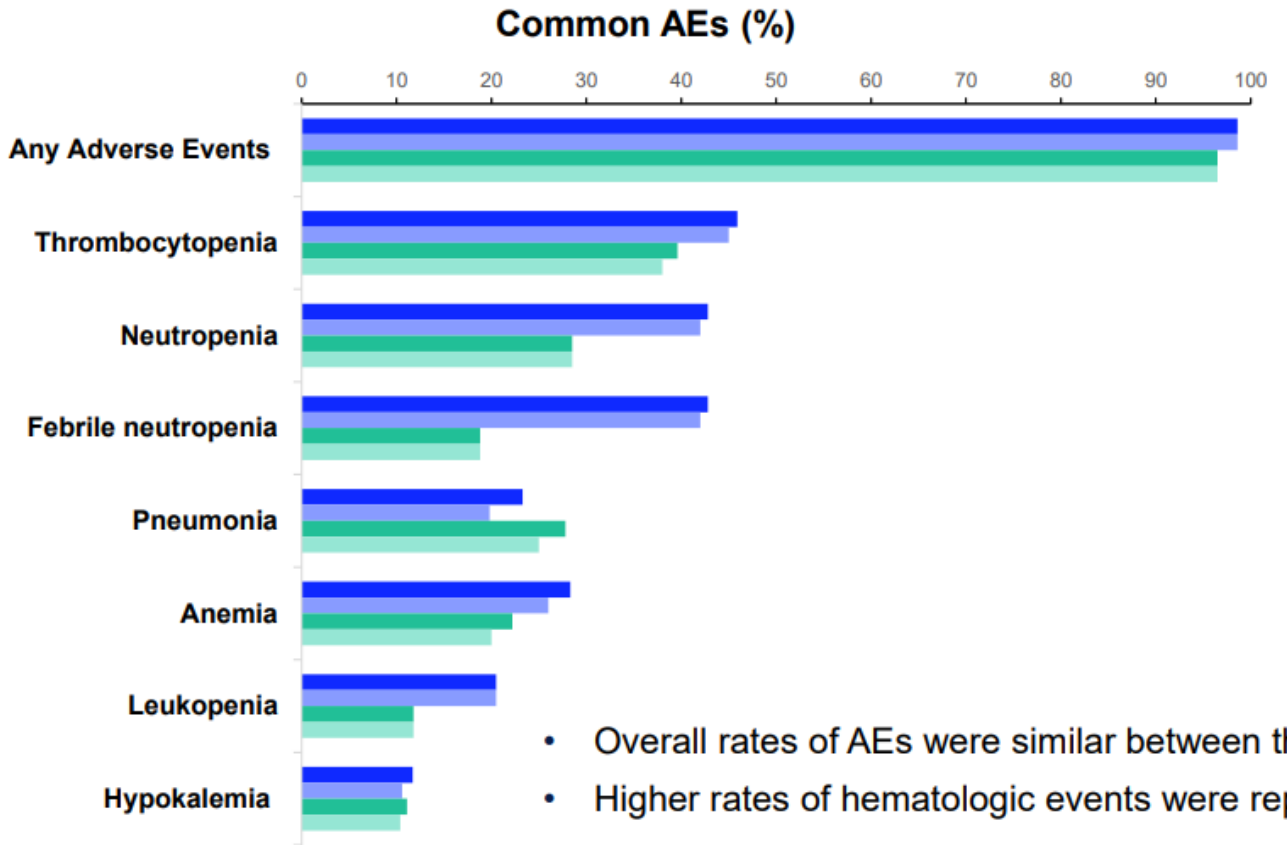
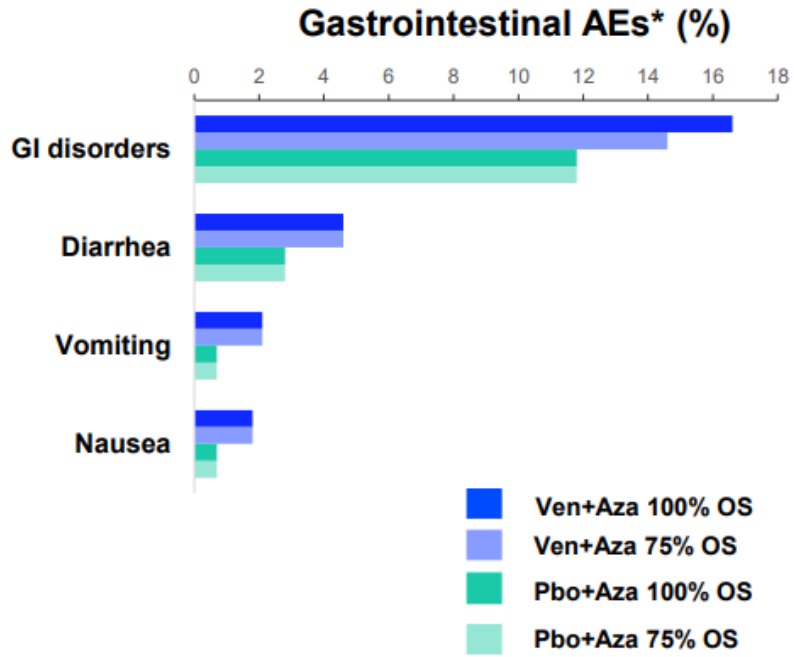
KEY DATA

VIALE-A Clinical Study

Safety





- Overall rates of AEs were similar between the two arms
- Higher rates of hematologic events were reported in the Ven+Aza arm

With longer follow up on treatment, grade ≥ 3 TEAEs reported in ≥ 10% are slightly higher than at 75% OS analysis

Pratz. ASH 2022. Abstr 219.

SUMMARY

VIALE-A Clinical Study

- With long term follow up, OS benefit with Ven +Aza continues to be observed compared to azacytidine monotherapy
  - HR 0.58 (95% CI 0.465 – 0.723, *P* value < 0.001)
- OS benefit was observed across all analyzed subgroups
  - Duration of CR and CR/CRi in those receiving venetoclax + azacitidine was longer than that of patients receiving azacitidine monotherapy and increased with long-term follow-up
- No new safety concerns

Pratz. ASH 2022. Abstr 219.

VIALE-A Clinical Study

Use of azacitidine in combination with venetoclax provides benefit and is the standard of care for patients with treatment naïve AML who are ≥ 75 years of age or ineligible for intensive chemotherapy

2022 ASH Key Studies

Lymphomas

- TRIANGLE
- BRUIN
- CAPTIVATE
- L-MIND/First-MIND
- Glofitamab/NP30179

Multiple Myeloma

- GEM-CESAR
- ASCENT
- IFM2017-03
- MajesTEC-1

Leukemias

- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
- Momentum
- Study 2102-HEM-101

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CLINICAL QUESTION

ECOG-ACRIN E1910 Clinical Trial

Does addition of Blinatumomab to consolidation chemotherapy provide benefit for patients with ALL who are MDR negative (<0.01%) after induction chemotherapy?

On July 11, 2017: The US FDA approved blinatumomab (BLINCYTO, Amgen Inc.) for the treatment of relapsed or refractory CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL)

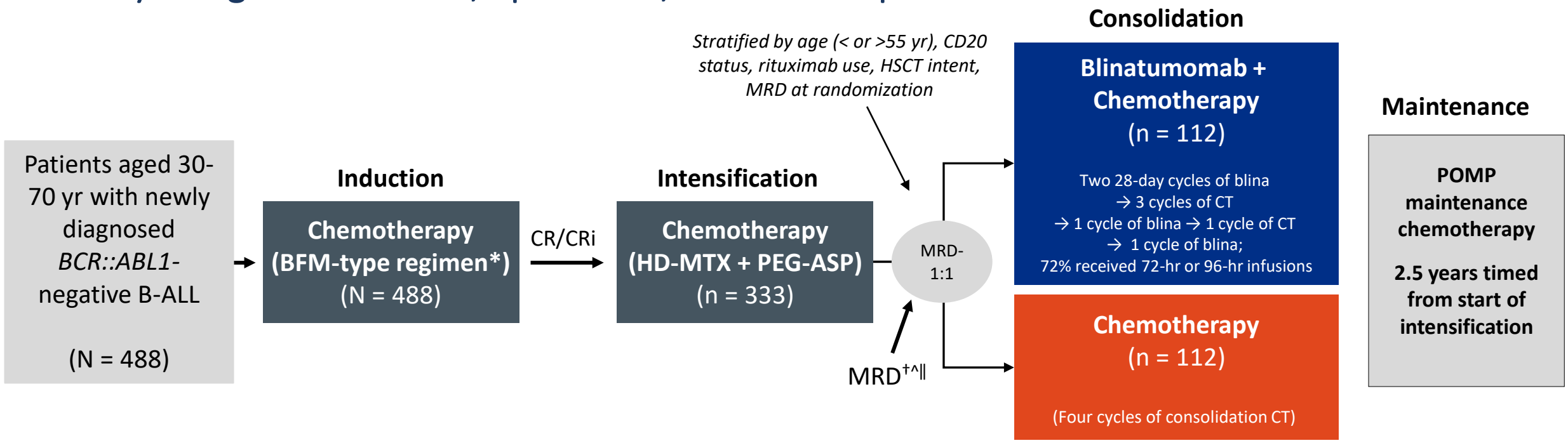
On March 29, 2018: The US FDA expanded approval of BLINCYTO® for the treatment of CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% in adults and children

cornerstone specialty network™

KEY DATA

ECOG-ACRIN E1910 Clinical Trial

Study Design: Multicenter, open-label, randomized phase 3 trial



*Regimen adapted from E2993/UKALLXII trial, including extended remission induction, addition of PEG-ASP for patients <55 yr of age, and addition of rituximab for CD20+ disease.

Patients could undergo alloHSCT at discretion of treating physician, ideally after first 2 cycles of blina in experimental arm or at any time following intensification in control arm.

Primary endpoint: OS in MRD^{neg} patients

Key secondary endpoints: MRD status, RFS

Litzow. ASH 2022. Abstr LBA1.

KEY DATA

ECOG-ACRIN E1910 Clinical Trial

Patient Characteristics

Characteristic	Blinatumomab + Chemotherapy (n = 152)	Chemotherapy (n = 134)
Median age, yr (range)	51 (30-70)	
MRD^{neg}, n	112	112
• Proceeded to HSCT, n	22	22
MRD^{pos}, n	40	22

- MRD assessed centrally by 6-color flow cytometry, with cutoff of ≤0.01% for MRD negativity.
- 286 patients underwent MRD assessment, with 224 being negative and 62 being positive.
- After blinatumomab regulatory approval in March 2018 for MRD^{pos} *BCR::*$ABL1^{neg}$ B-ALL, MRD^{pos} patients were assigned to blina arm and no longer randomized.

- Postinduction CR/CRi rate: 81% (395/488)
  - CR rate: 75% (364/488)
  - CRi rate: 6% (31/488)
- MRD status after intensification
  - MRD^{neg}: 78% (224/286)
  - MRD^{pos}: 22% (62/286)

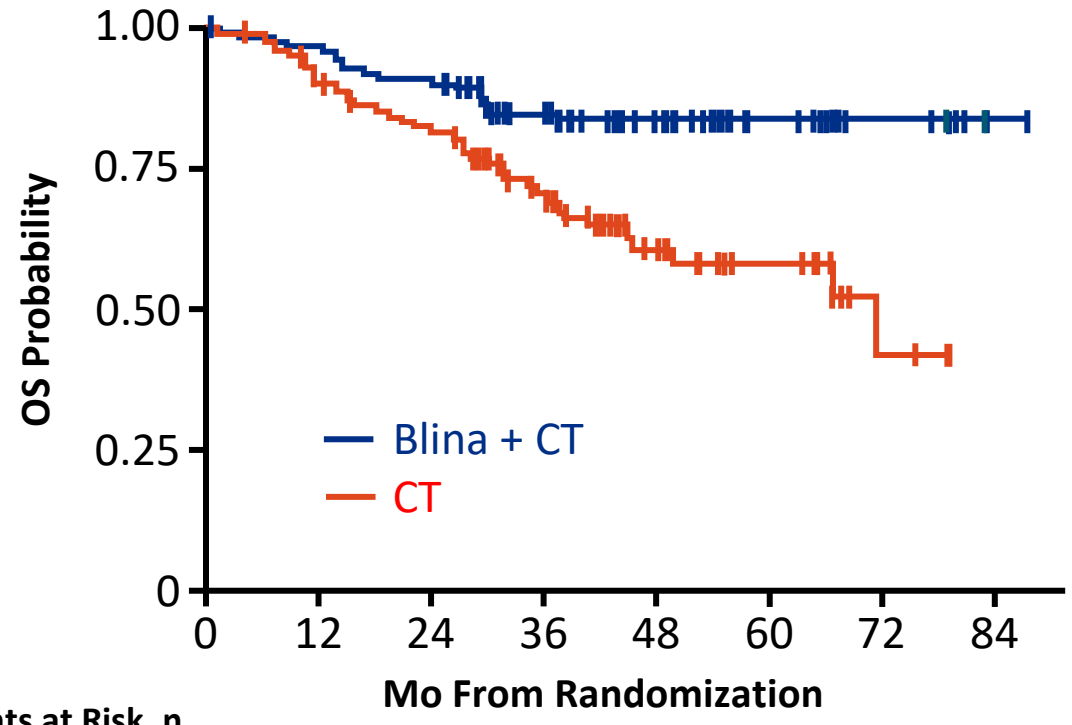
- At third interim analysis, 80% of patients assigned to experimental arm received ≥2 cycles of blinatumomab

Litzow. ASH 2022. Abstr LBA1.

KEY DATA

ECOG-ACRIN E1910 Clinical Trial

Primary Endpoint: Overall Survival in MRD^{neg} Disease



Patients at Risk, n								
Blina + CT	112	106	99	65	41	18	7	1
CT	112	96	85	53	28	14	4	0

	Blina + CT (n = 112)	CT (n = 112)	HR (95% CI)	P
mOS, mo	NR	71.4	**0.42** (0.24-0.75)	0.003
• 3.6-yr OS, %	83	65		
• Deaths, n	17[†]	39[‡]		
mRFS, mo	NR	22.4	**0.46** (0.27-0.78)	0.004

[†]n = 8 secondary to ALL, n = 9 NRM.
[‡]n = 20 secondary to ALL, n = 17 NRM, n = 2 unknown.

- *At third interim efficacy analysis, ECOG-ACRIN DSMB recommended releasing results due to benefit observed with blinatumomab in MRD^{neg} disease*

Litzow. ASH 2022. Abstr LBA1.

KEY DATA

ECOG-ACRIN E1910 Clinical Trial

Overall Survival in MRD^{pos} Disease

OS in MRD^{pos} Disease	Blina + Ct (n = 40)	CT (n = 22)	HR (95% CI)	P Value
mOS, mo	NR	22.4	**0.39** (0.14-1.10)	0.066
• Deaths, n	9	13	--	--

Litzow. ASH 2022. Abstr LBA1.

SUMMARY

ECOG-ACRIN E1910 Clinical Trial

- Significant OS benefit with the addition of blinatumomab to chemotherapy as consolidation therapy for patients with MRD^{neg} *BCR::ABL1*-negative B-ALL

- No new safety concerns

Litzow. ASH 2022. Abstr LBA1.

ECOG-ACRIN E1910 Clinical Trial

The addition of blinatumomab to consolidation chemotherapy provides benefit to patients with MRD^{neg} BCR::ABL1-negative B-ALL and may be considered as a new standard of care treatment option

2022 ASH Key Studies

Lymphomas

- TRIANGLE
- BRUIN
- CAPTIVATE
- L-MIND/First-MIND
- Glofitamab/NP30179

Multiple Myeloma

- GEM-CESAR
- ASCENT
- IFM2017-03
- MajesTEC-1

Leukemias

- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
- Momentum
- Study 2102-HEM-101

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CLINICAL QUESTION

Ruxolitinib for CMML

Does ruxolitinib provide benefit for patients with symptomatic chronic myelomonocytic leukemia?

KEY DATA

Ruxolitinib for CMML

Study Design: Open-label, multicenter phase 2 expansion study

- Diagnosis of CMML
- Symptomatic splenomegaly or MPN TSS ≥ 17
- Previously untreated or after therapy with hypomethylating agents
- ANC ≥250/ul
- Platelets ≥35,000 u/l

→ **Ruxolitinib, 20 mg po BID**
N=29

First dose of oral Ruxolitinib, 20 mg followed by Ruxolitinib at a dose of 40 mg daily divided into two equal doses approximately 12 hours apart.

Serial blood counts, chemistry and bone marrow assessment were conducted to assure safety and assess efficacy. Spleen volume was measured by CT imaging and the percentage of spleen volume reduction (SVR) was captured. Daily measurements of the MPN-SAF were performed for up to 17 weeks while on study.

→ Treated for a total of 16 weeks if no clear progression

Monthly follow-up

Primary Outcomes:

- Clinical benefit / Overall response rate per International Working Group (IWG) criteria for MDS/MPNs and symptom improvement was assessed using the MPN-SAF TSS

Secondary Outcomes:

- Time to acute myeloid leukemia transformation
- Overall survival (OS)
- Duration of response
- Other: change in symptom score, pathological response, mutational status

Padron ASH 2022 Abstract 457.

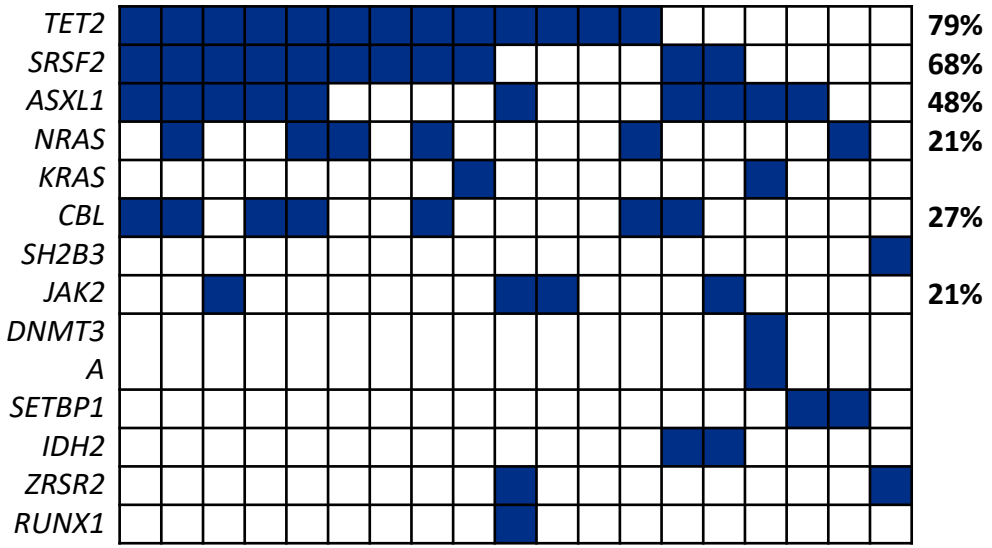
KEY DATA

Ruxolitinib for CMML

Baseline characteristics

Characteristics	N=29
Median age (range)	74 (63 -87)
Male	27 (93%)
WHO Classification	
• CMML-0	18 (62%)
• CMML-1	10 (35%)
• CMML-2	1 (3%)
FAB Classification	
• MDS-CMML	9 (31%)
• MPN-CMML	20 (69%)
Risk Stratification (MDASC)	
• Lower risk	21 (72%)
• Higher risk	8 (28%)
Risk stratification (MAYO)	
• Lower risk	12 (41%)
• Higher risk	17 (59%)
Prior treatment with hypomethylating agent	2 (7%)
Splenomegaly	20 (67%)
Baseline MPN-SAF TSS	31 (11-59)

Somatic Mutations at Baseline



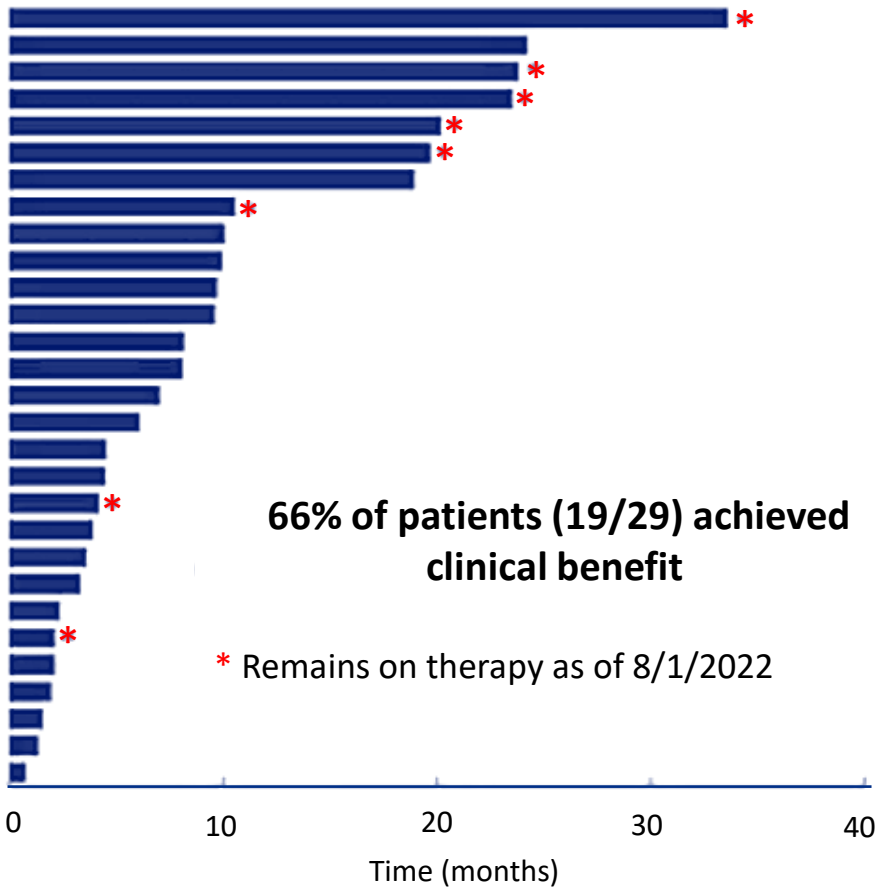
- The most common somatic mutations at baseline were *TET2 (79%)*, *SRSF2 (68%)* and *ASXL1(48%).*
- *NRAS (21%), CBL (37%), and JAK2 (21%)* were seen at higher proportions than previously reported likely due to study inclusion criteria.

Padron ASH 2022 Abstract 457.

KEY DATA

Ruxolitinib for CMML

Response Rates per MDS/MPN IWG



Note: The median duration of follow up was 16 months.
The median duration on treatment was 4 mo (0.5-23 mo).

Response	N = 29
Bone marrow response rate, n (%) • PR • Marrow response • SD • Not evaluable	5 (17) 3 (10) 2 (7) 20 (69) 4 (14)
Median DoR, mo (range)	9.6 (0.75-33)
Remaining on study for >12 mo, n	7
Patients who discontinued treatment, n • Due to PD • Due to AE (platelets) • Due to lack of efficacy	15 8 4 3
Patients who transitioned to BMT, n	1
Deaths on study, n (unrelated to treatment)	1

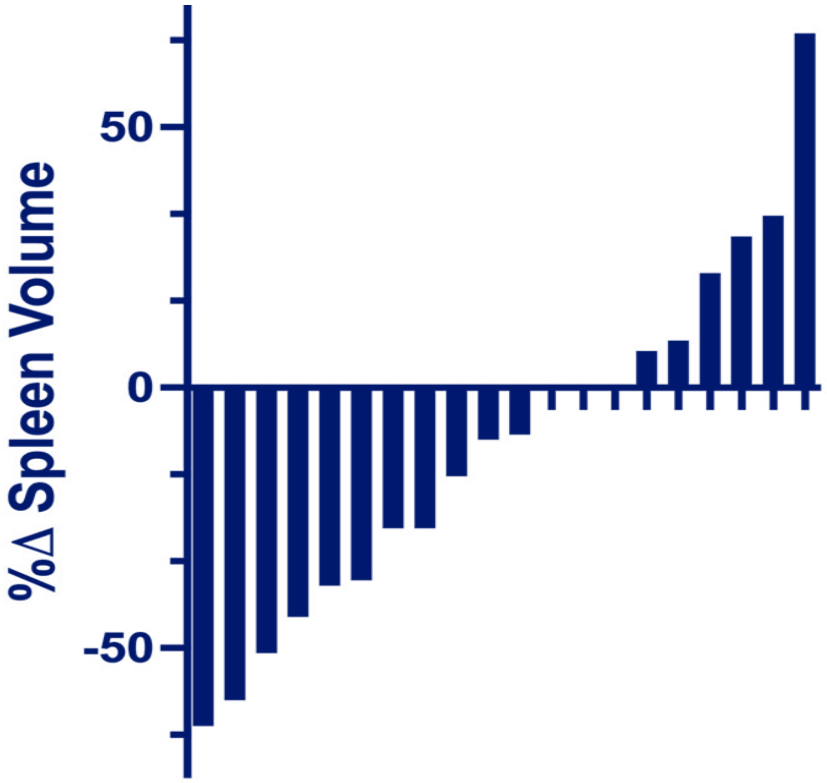
Padron ASH 2022 Abstract 457.

KEY DATA

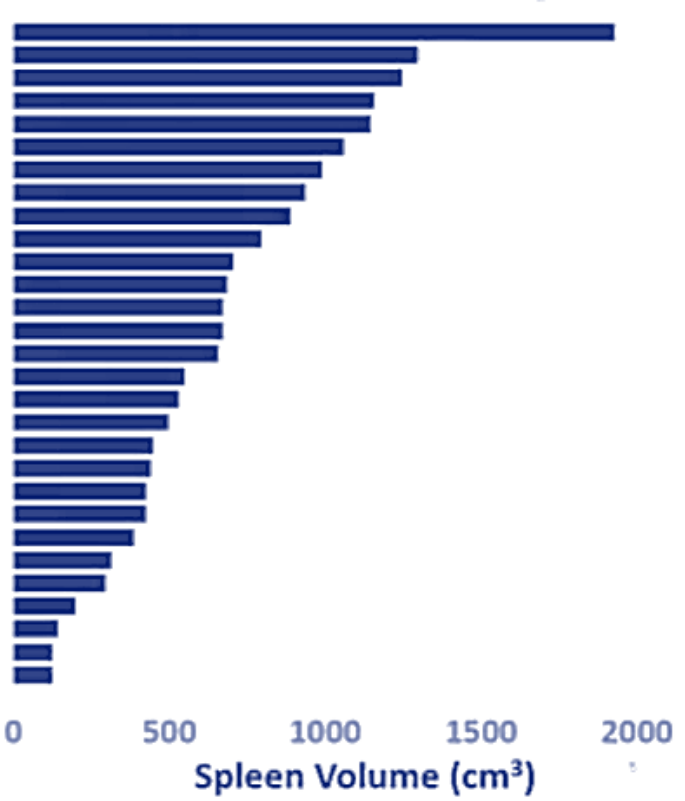
Ruxolitinib for CMML

Splenomegaly and Response

- 6/20 (30%) had ≥35% SVR measured by CT Scan
- 10/20 (50%) had 10% or more SVR



- Median spleen volume 681 cm^3 at baseline



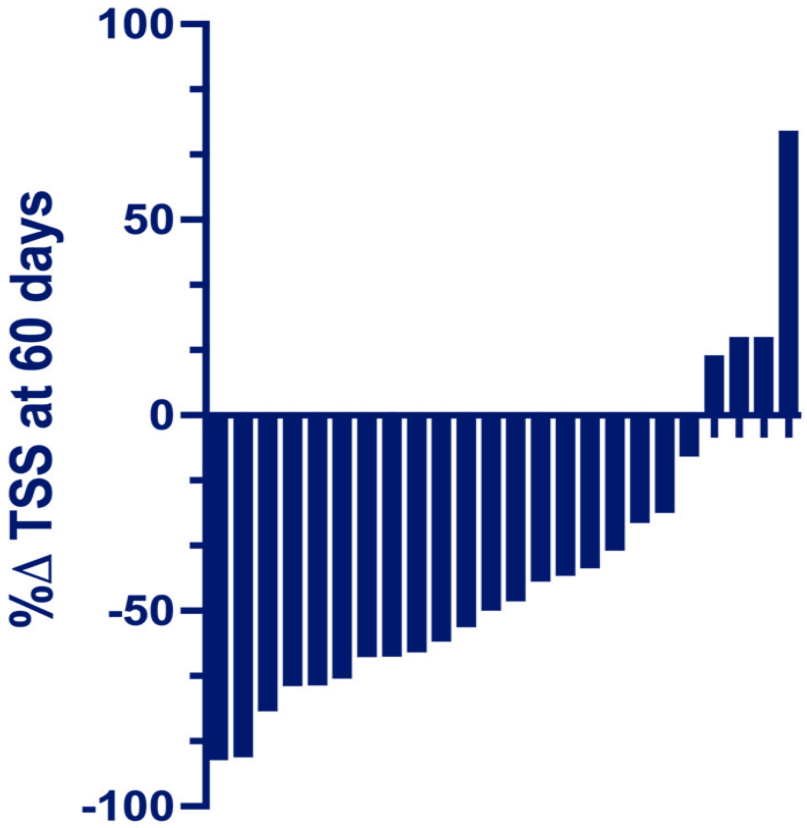
Padron ASH 2022 Abstract 457.

KEY DATA

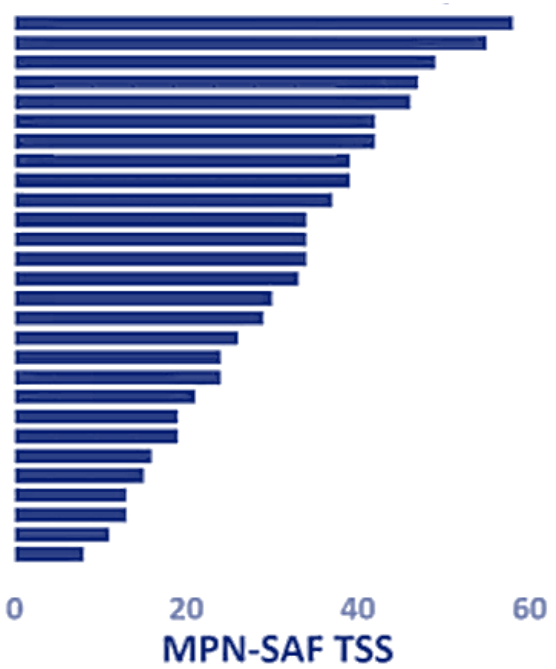
Ruxolitinib for CMML

MPN-SAF TSS and Response

- 54% achieved MPN-SAF TSS >50% reduction
- All but 4 had a TSS reduction



- Median MPN-SAF TSS of 31 at baseline

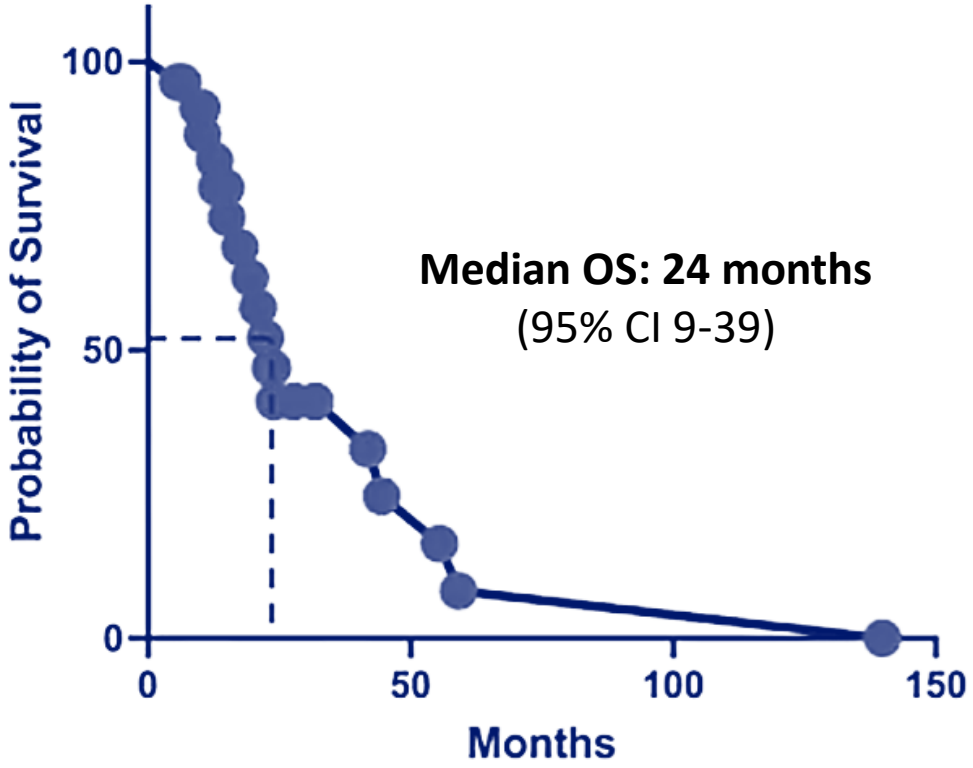


Padron ASH 2022 Abstract 457.

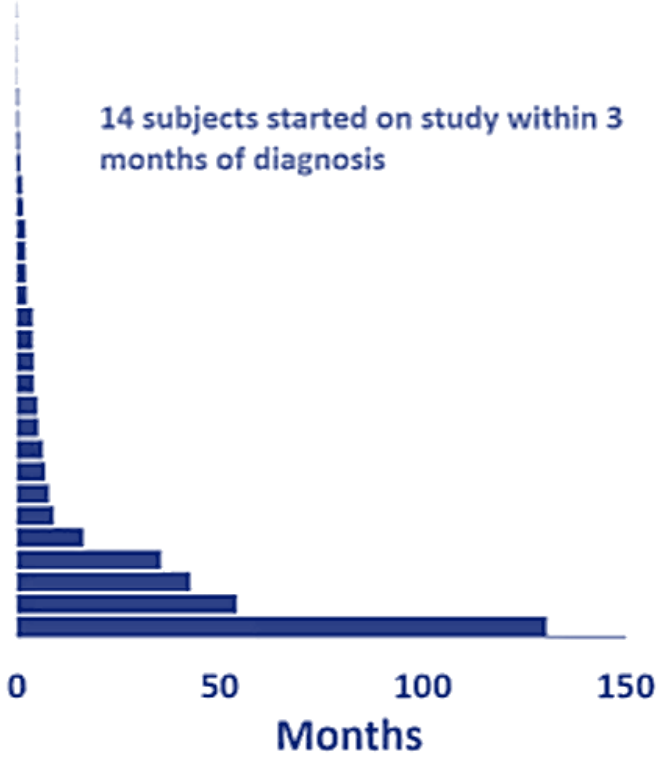
KEY DATA

Ruxolitinib for CMML

Overall survival



Median OS: 24 months
(95% CI 9-39)



Padron ASH 2022 Abstract 457.

SUMMARY

Ruxolitinib for CMML

- Clinically meaningful benefit with ruxolitinib for patients with CMML with splenomegaly and/or high disease symptom burden
  - 66% of patients achieved clinical benefit
  - 33% of patients achieved ≥35% spleen volume response
  - 54% had a reduction in TSS >50%
- Overall survival of 24 months
- No new safety concerns
  - Treatment-related adverse events and reasons for discontinuation similar to that reported in the initial phase 1/2 study

Padron ASH 2022 Abstract 457.

Ruxolitinib for CMML

Ruxolitinib is a potential therapeutic option for patients with symptomatic chronic myelomonocytic leukemia

More to come…

2022 ASH Key Studies

Lymphomas

- TRIANGLE
- BRUIN
- CAPTIVATE
- L-MIND/First-MIND
- Glofitamab/NP30179

Multiple Myeloma

- GEM-CESAR
- ASCENT
- IFM2017-03
- MajesTEC-1

Leukemias

- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
- MOMENTUM
- Study 2102-HEM-101

cornerstone specialty network™

MOMENTUM Clinical Trial

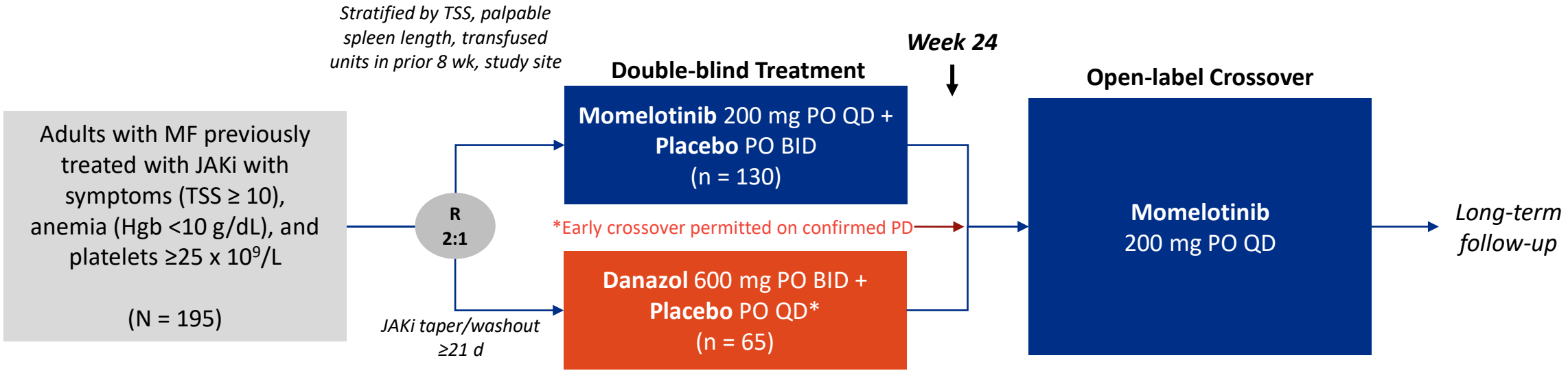
Does momelotinib provide benefit compared to danazol for symptomatic myelofibrosis patients with anemia previously treated with a JAK inhibitor?

Updated analysis

KEY DATA

MOMENTUM Clinical Trial

Study Design: international, randomized phase III trial



Primary endpoint: TSS response (≥50% reduction from baseline per MFASF v4.0) at Wk 24

Key secondary endpoints: transfusion independence (not requiring RBC transfusion within last 12 wk of 24-wk period with Hgb ≥12 g/dL), splenic response rate (≥25% or ≥35% reduction in spleen volume)

Current analysis: updated efficacy and safety analyses after all patients completed Wk 48 assessment, including subgroup with thrombocytopenia

Data cutoff: May 17, 2022

Gerds. ASH 2022. Abstr 627

KEY DATA

MOMENTUM Clinical Trial

Baseline Characteristics

Characteristic	Momelotinib (n = 130)	Danazol (n = 65)
Mean age, yr	69.85	71.46
Male, %	60.8	67.7
PMF/PPV-MF/PET-MF, %	60.0/20.8/19.2	70.8/16.9/12.3
DIPSS int-1/int-2/high, %	5.4/55.4/38.5	4.6/61.5/29.2
Mean prior JAKi therapy, yr	2.7	2.4
Mean Hgb, g/dL	8.1	7.9
Hgb <8 g/dL, %	47.7	49.2
Transfusion independence, %	13.1	15.4
Transfusion requiring,* %	38.5	32.3
Transfusion dependence,† %	48.5	52.3
Mean platelets, x 10^9/L	151.7	130.7

TI defined as not requiring RBC transfusion for ≥12 weeks, with Hgb levels ≥8 g/dL. *TR defined as patients who required transfusions but did not meet the criteria for TD. †TD defined as requiring RBC transfusion ≥4 units in the 8 weeks before randomization. DAN, danazol; DIPSS; Dynamic International Prognostic Scoring System; Hgb, hemoglobin; Int, intermediate; JAKi, Janus kinase inhibitor; MF, myelofibrosis; MMB, momelotinib; PET, post-essential thrombocythemia; PMF, primary myelofibrosis; PPV, post-polycythemia vera; RBC, red blood cell; RUX, ruxolitinib; TD, transfusion dependence; TI, transfusion independence; TR, transfusion-requiring.

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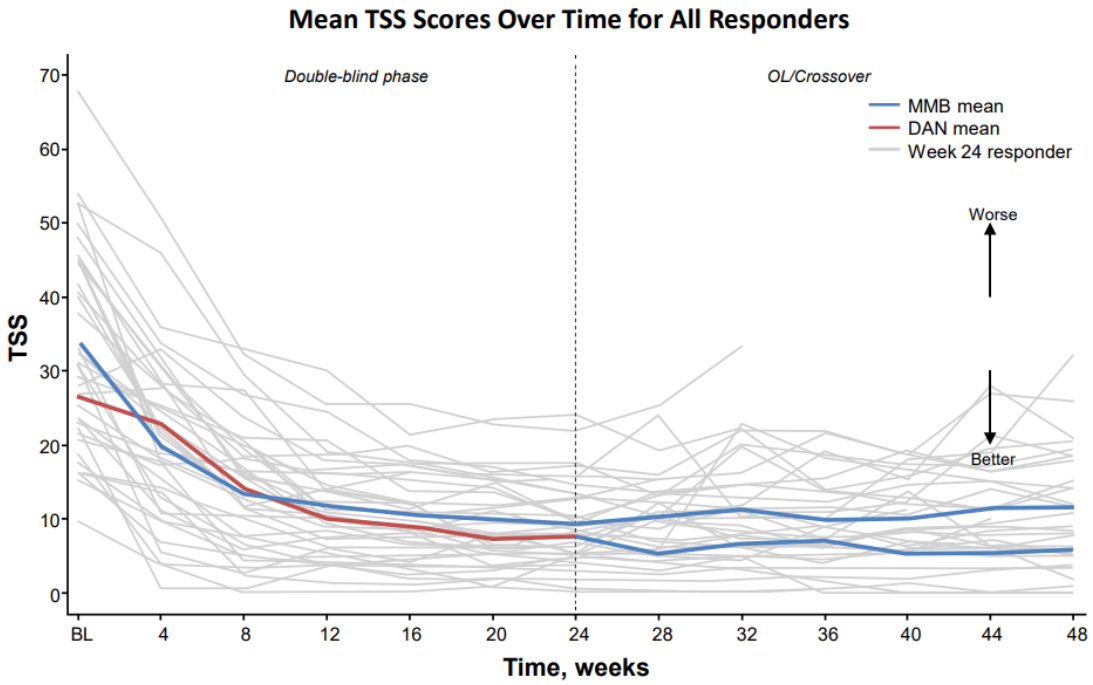
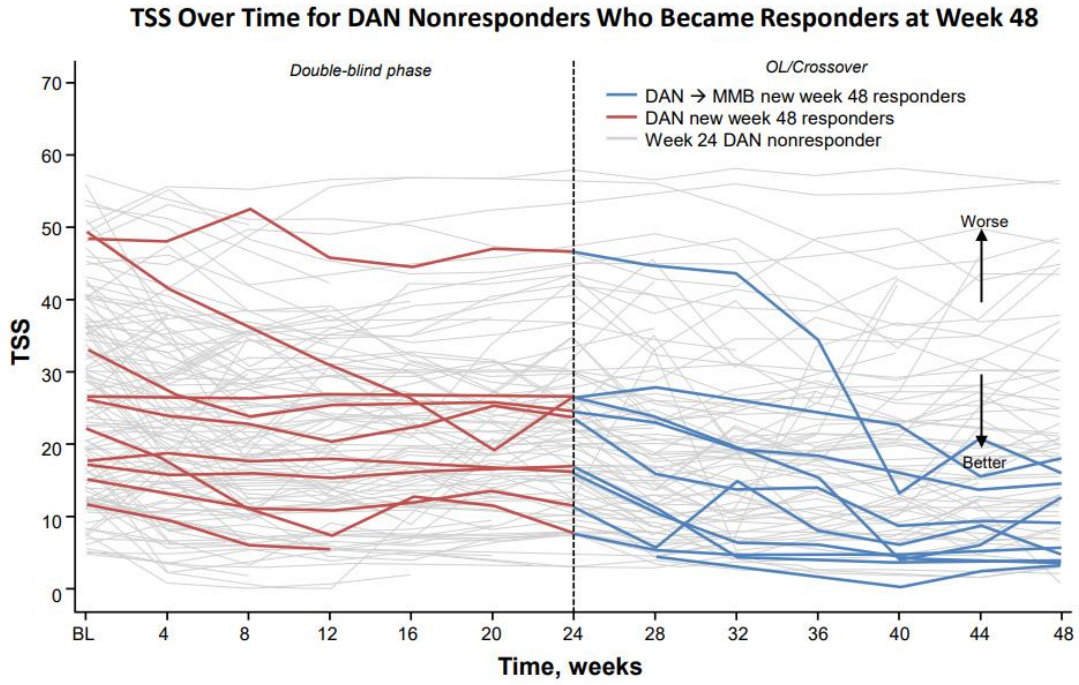
KEY DATA

MOMENTUM Clinical Trial

Responses, TSS





Outcome at Wk 24, n (%)	Momelotinib (n = 130)	Danazol (n = 65)	P Value
TSS response	32 (24.6)	6 (9.2)	0.0095 (superior)

Outcome at Wk 48, n/N (%)	Momelotinib → Momelotinib (n = 93)	Danazol → Momelotinib (n = 41)
TSS response maintained from Wk 24 to Wk 48	31/32 (97)	6/6 (100)
TSS nonresponse at Wk 24 followed by new response at Wk 48	12/98 (12)	10/59 (17)

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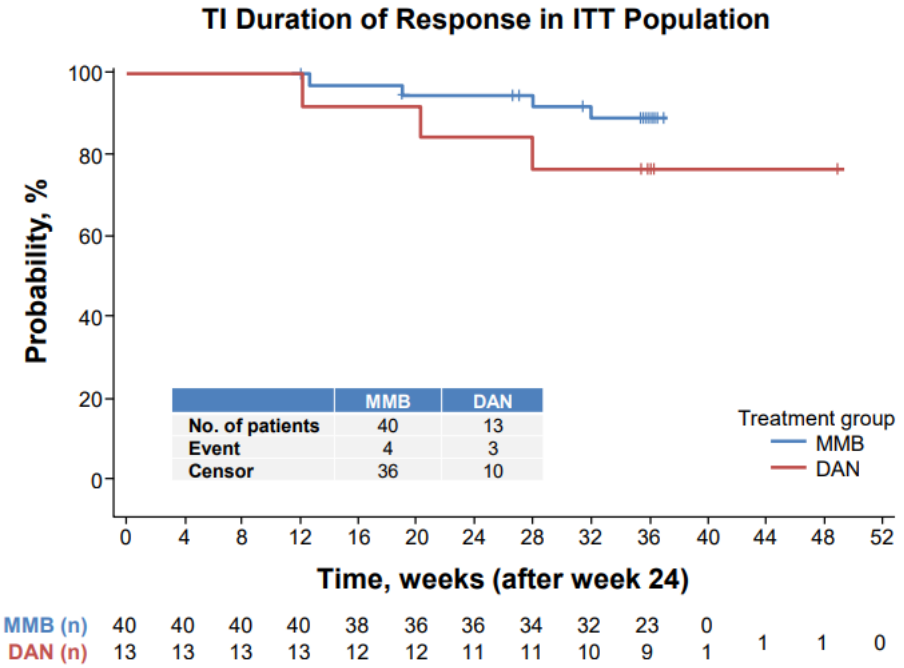
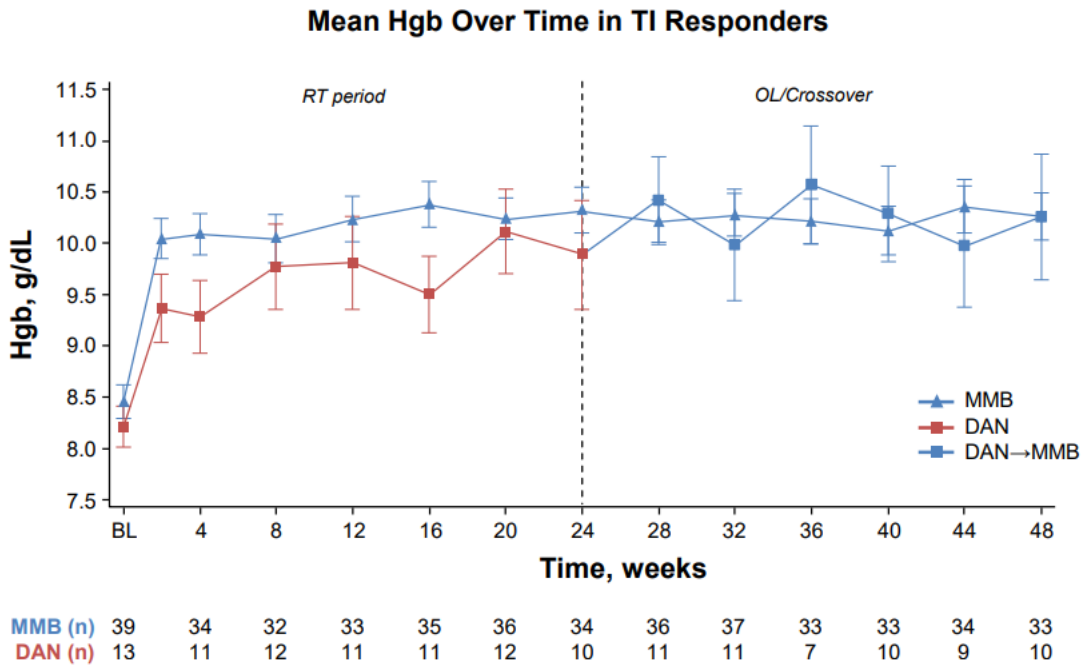
KEY DATA

MOMENTUM Clinical Trial

Responses, TI





TI Outcome at Wk 24, n (%)	Momelotinib (n = 130)	Danazol (n = 65)	P Value
Response	40 (30.8)	13 (20.0)	0.0064 (noninferior)

TI Maintained From Wk 24 to Wk 48, n/N (%)	Momelotinib → Momelotinib	Danazol → Momelotinib
Response maintained	36/40 (90)	10/13 (77)

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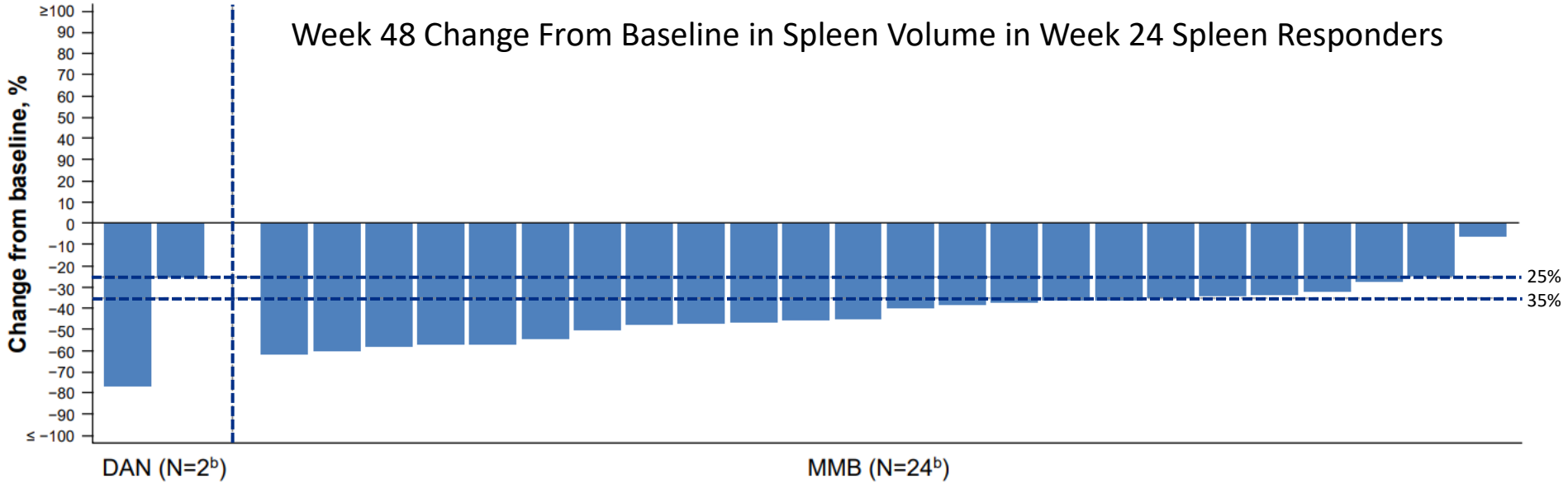
KEY DATA

MOMENTUM Clinical Trial

Responses, Spleen volume



SRR Outcome at Wk 24, n (%)	Momelotinib (n = 130)	Danazol (n = 65)	P Value
SRR (≥35% reduction)	30 (23.1)	2 (3.1)	0.0006 (superior)

SRR Maintained From Wk 24 to Wk 48, n/N (%)	Momelotinib → Momelotinib	Danazol → Momelotinib
SRR (≥35% reduction) maintained	24/24 (100)	2/2 (100)

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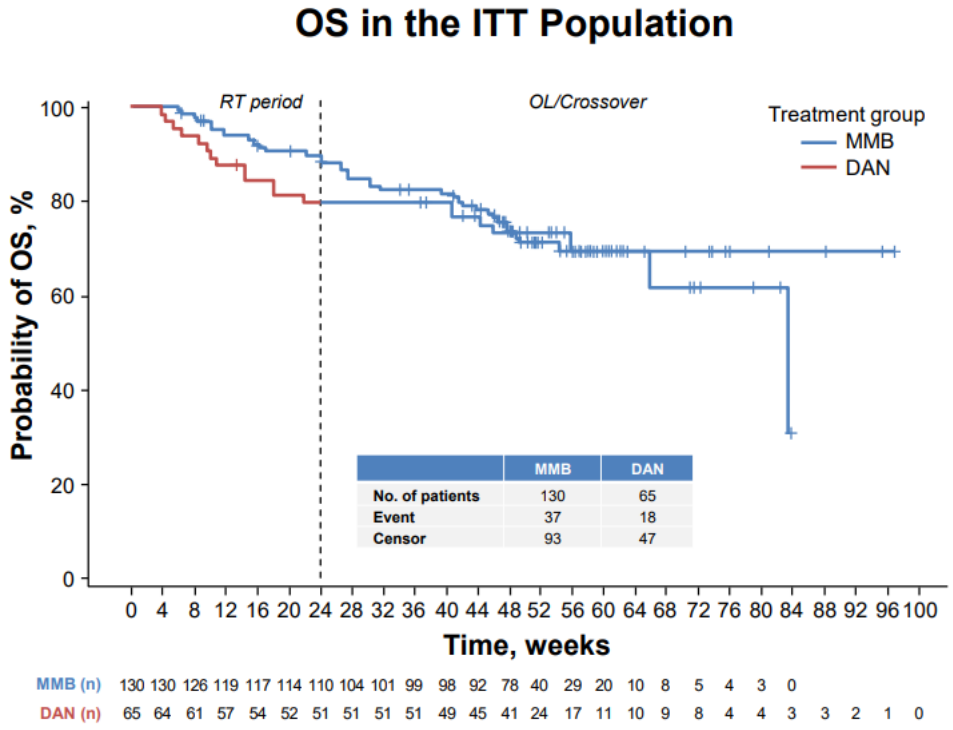
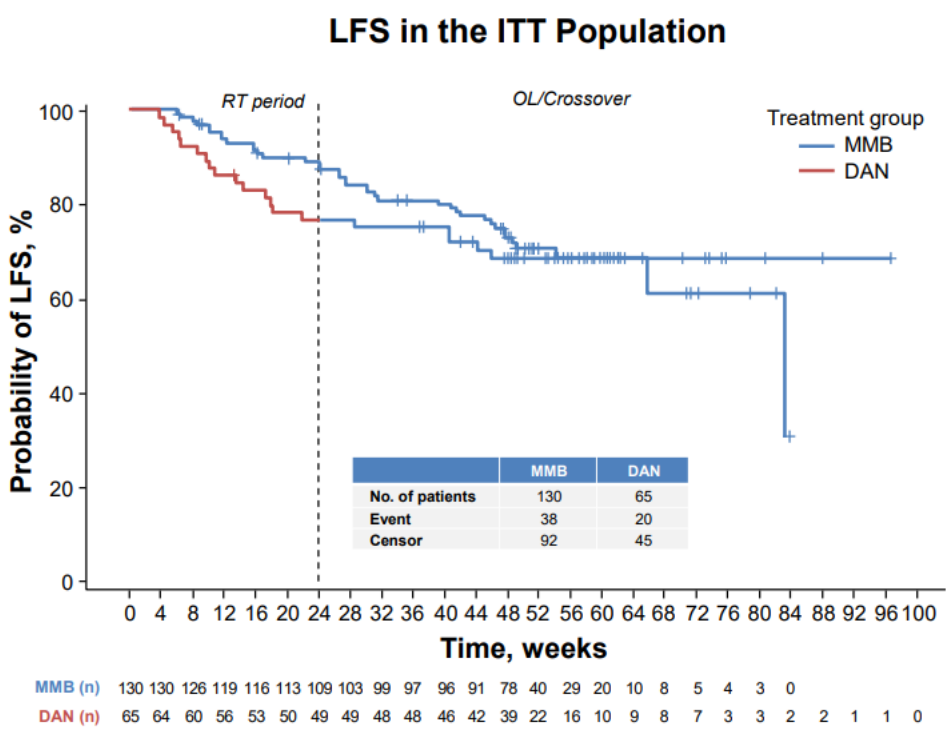
KEY DATA

MOMENTUM Clinical Trial

Overall Survival and Leukemia-Free Survival





Median follow-up for OS was 51 wks (range 6-84 wks) for MMB-randomized and 53 wks (range 4-97 wks) for DAN-randomized pts.

- OS At Week 24: MMB vs DAN (HR=0.506, p=0.0719)
- All pts crossed over to OL MMB at Week 24
- OS and LFS curves for MMB→MMB and DAN→MMB arms converged (HR=0.945, 95% CI=0.528, 1.693; HR=0.830, 95% CI=0.473, 1.4555, respectively)

Gerds. ASH 2022. Abstr 627

KEY DATA

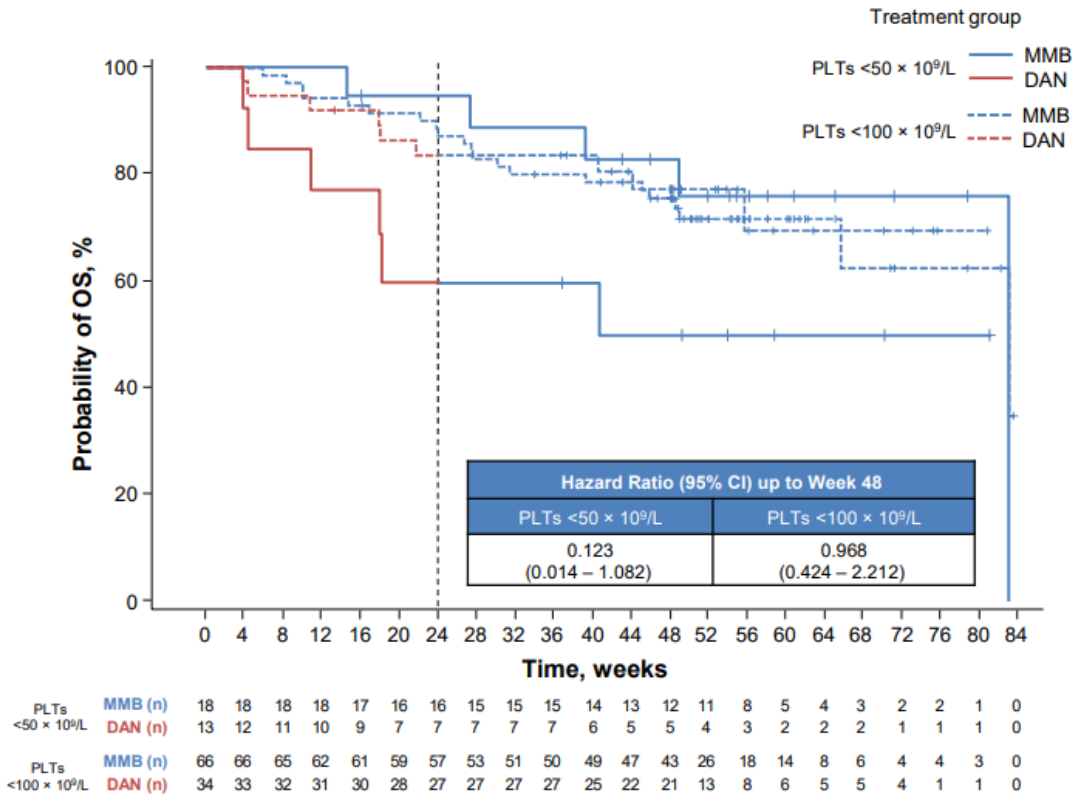
MOMENTUM Clinical Trial

Responses for Patients with Thrombocytopenia

Outcome at Wk 24, %	BL PLT <100 x 10^9/L		BL PLT <50 x 10^9/L	
	Momelotinib (n = 66)	Danazol (n = 34)	Momelotinib (n = 18)	Danazol (n = 13)
TSS50 response	29	15	22	8
TI response	27	21	17	15
SRR (≥ 35% reduction)	20	6	22	0

Maintenance of Response From Wk 24 to Wk 48, n/N (%)	BL PLT <100 x 10^9/L	
	Momelotinib → Momelotinib	Danazol → Momelotinib
TSS50 response	18/19 (95)	5/5 (100)
TI response	16/18 (89)	5/7 (71)
SRR (≥ 35% reduction)	13/13 (100)	2/2 (100)

OS in patients with baseline PLTs <50x10^9/L and <100x10^9/L



Gerds. ASH 2022. Abstr 627

KEY DATA

MOMENTUM Clinical Trial

Safety

TEAEs in ≥10% of Patients During OL Momelotinib, %	Momelotinib → Momelotinib (n = 93)		Danazol → Momelotinib (n = 41)	
Grade ≥3 AEs	49.5		46.3	
Serious AEs	31.2		29.3	
	Any Grade	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Nonhematologic events				
• Weight decreased	7.5	0	14.6	0
• Diarrhea	14.0	1.1	12.2	0
• Pyrexia	14.0	0	7.3	0
• Hypertension	3.2	0	12.2	2.4
• Asthenia	11.8	3.2	0	0
Hematologic events				
• Thrombocytopenia	14.0	8.6	17.1	14.6
• Anemia	10.8	8.6	7.3	2.4
• Neutropenia	5.4	5.4	4.9	0
Other events				
• COVID-19 (pneumonia)	10.8	5.4	0	0
• PSN	2.2	0	2.4	0

- Safety in Patients With Thrombocytopenia (PLTs <100x10^9/L) was consistent with the ITT population

Gerds. ASH 2022. Abstr 627

SUMMARY

MOMENTUM Clinical Trial

- With updated analysis at week 48, momelotinib maintained TSS, TI and splenic responses following crossover at week 24 from danazol
  - Efficacy in the thrombocytopenia subgroup were comparable to the ITT population

- No new safety concerns

Momelotinib: The FDA has set a Prescription Drug Use Fee Act action date of June 16, 2023, to decide on whether to approve the drug for the treatment of anemic myelofibrosis

Padron ASH 2022 Abstract 457.

MOMENTUM Clinical Trial

Momelotinib has impressive and durable spleen, symptom, and anemia responses in patients with myelofibrosis and anemia

More to come…

2022 ASH Key Studies

Lymphomas

- TRIANGLE
- BRUIN
- CAPTIVATE
- L-MIND/First-MIND
- Glofitamab/NP30179

Multiple Myeloma

- GEM-CESAR
- ASCENT
- IFM2017-03
- MajesTEC-1

Leukemias

- VIALE-A
- ECOG-ACRIN E1910
- Ruxolitinib for CMML
- MOMENTUM
- Study 2102-HEM-101

cornerstone specialty network™

Study 2102-HEM-101: Olutasidenib

Does olutasidenib provide benefit for patients with relapsed/refractory mIDH1 acute myeloid leukemia?

Planned interim analysis

*On **December 1, 2022**, the Food and Drug Administration (FDA) approved olutasidenib (Rezlidhia) capsules for adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test (Abbott RealTime IDH1 Assay)*

cornerstone specialty network™

KEY DATA

Study 2102-HEM-101: Olutasidenib

Study Design: open-label, multicenter, Phase 1/2 trial

Experimental: PH2 Cohort 1 FT-2102 (olutasidenib) Single Agent Relapsed or Refractory (R/R) AML

- IDH1 inhibitor-naïve pts with R/R m*IDH1*^{R132} AML
- Good performance status
- Good kidney and liver function

N=153

- Excluding symptomatic CNS mets and congestive heart failure

→ **Olutasidenib 150 mg BID monotherapy in continuous 28-day cycles**

Primary Endpoint: Rate of Complete Remission (CR) + Complete Remission with partial hematologic recovery (CRh) (modified IWG criteria 2003)

Secondary Endpoints: Overall Response Rate (ORR); Duration of CR+CRh; Duration of Overall Response (DOR); Rate of Transfusion Independence (TI), including red blood cells (RBC) and/or platelets; and Overall Survival (OS)

Data cut-off for the analysis was 18 June 2021

Cortes. ASH 2022. Abstr 2757.

KEY DATA

Study 2102-HEM-101: Olutasidenib

Patient Disposition

Patient Disposition as of Data Cut-off	
Safety Set, n	153
Efficacy Evaluable Set, n	147
Treatment ongoing, n (%)	21 (14)
Discontinued from treatment, n (%)	132 (86)
Primary reason for discontinuation, n (%)	
• Disease progression	62 (41)
• Adverse event	26 (17)
• HSCT	15 (10)
• Death	14 (9)
• Other*	15 (10)

*Includes investigator decision 7 (5%); permanent withdrawal of consent 5 (3%); patient decision, lack of response, and patient non-compliance / protocol violation each 1 (1%).

Patient Characteristics

Patient Characteristics in the EE Set (N=147)	
Men, n (%)	74 (50)
Median age (range)	71.0 years (32-87)
AML type, n (%)	
Primary de novo / Secondary	97 (66) / 50 (34)
Cytogenetics, n (%)*	
• Favorable	6 (4)
• Intermediate	107 (73)
• Poor	25 (17)
• Unknown	9 (6)
Prior therapy outcomes, n (%)	
Refractory / Relapsed**	51 (35) / 96 (65)
Median no. of prior treatments (range)	2.0 (1-7)
Prior Induction Therapy***	143 (97)
Prior HSCT, n (%)	17 (12)

*Data were not collected on which classification system of cytogenetic risk was used (either NCCN or ELN guidelines). **70% patients had remission duration ≤12 months. ***Data were not collected on the on the specific induction regimen used.

Cortes. ASH 2022. Abstr 2757.

KEY DATA

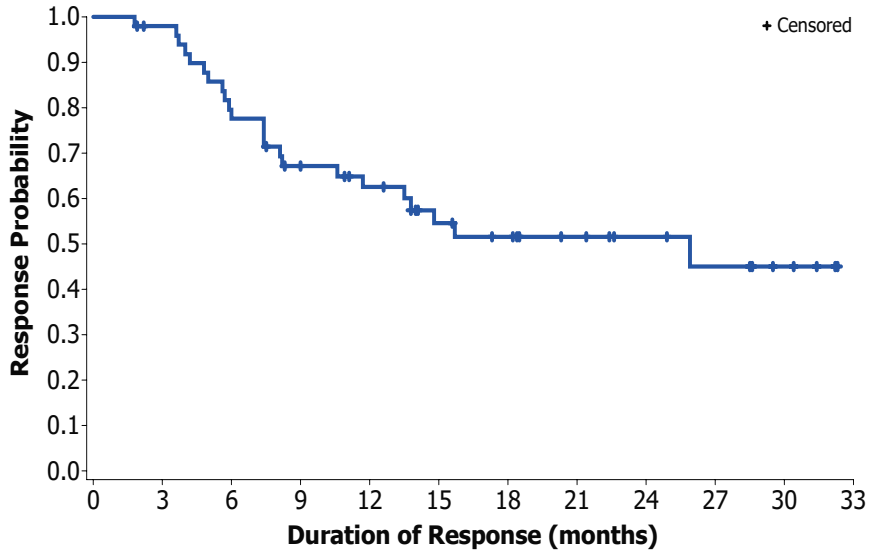
Study 2102-HEM-101: Olutasidenib

Response and Duration of Response

	Response Rate, n (%)	Median Time to Response (Range), Months
CR	**47** (32)	2.8 (0.9-7.4)
CRh	**4** (3)	N/A
CR+CRh	**51** (35)	**1.9** (0.9-5.6)
Other Responders		
• Cri*	15 (10)	N/A
• PR / MLFS**	3 (2) / 2 (1)	N/A
ORR, n (%)	71 (48)	1.9 (0.9-10.2)
Non-Responders	52 (35)	N/A

*CRi = CR with incomplete recovery
**MLFS = morphologic leukemia-free state; PR = partial remission.

- Median duration of CR+CRh was **25.9** months (95% CI, 13.5-NE)
- Median duration of CR was **28.1** months (95% CI, 13.8-NE)



CR/CRh Responders: 51 48 39 31 26 19 16 12 9 7 4 0

- Median duration of OR was **11.7** months (95% CI, 6.9-25.9)
- Response rates were similar for 12 pts who had received prior venetoclax:
  - CR+CRh rate was 33% (n=4; 95% CI, 9.9-65.1)
  - CR rate was 25% (n=3; 95% CI, 5.5-57.2).

Cortes. ASH 2022. Abstr 2757.

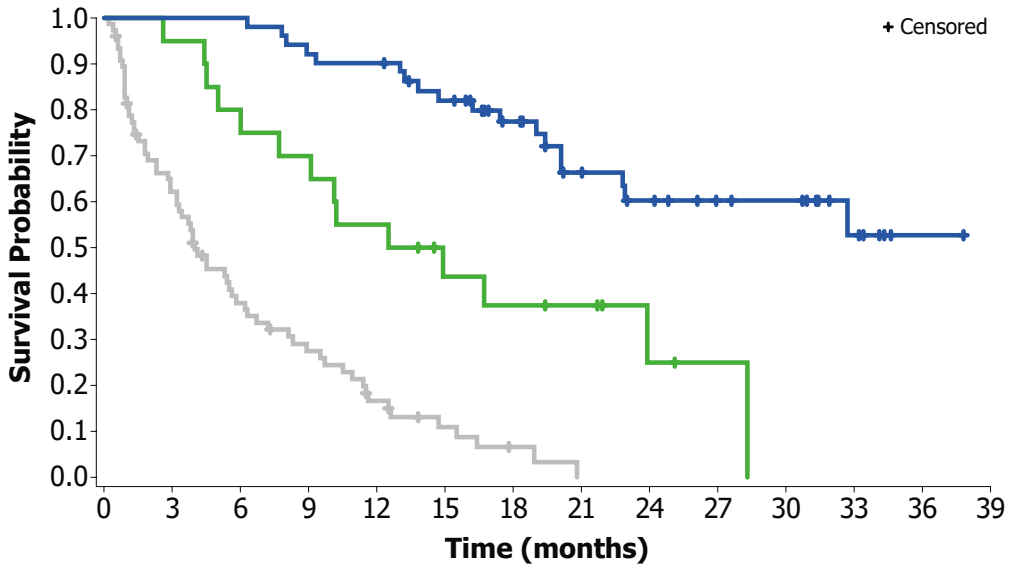
KEY DATA

Study 2102-HEM-101: Olutasidenib

Overall Survival

- Median overall survival (OS) was 11.6 months (95% CI, 8.9-15.5) in the overall population of 153 patients
- Estimated 18-month survival of patients with a CR+CRh was 78%.

Median OS (95% CI) by Response Category	
CR+CRh Responders	Not Reached (22.8-NR)
Other Responders	13.7 months (6.0-NR)
Non-Responders	4.0 months (3.2-5.8)



CR/CRh Responders:	51	51	51	47	46	40	31	23	18	14	13	7	1	0
Other Responders:	20	19	16	14	11	7	6	5	2	1	0	0	0	0
Non-Responders:	76	45	26	18	10	5	2	0	0	0	0	0	0	0

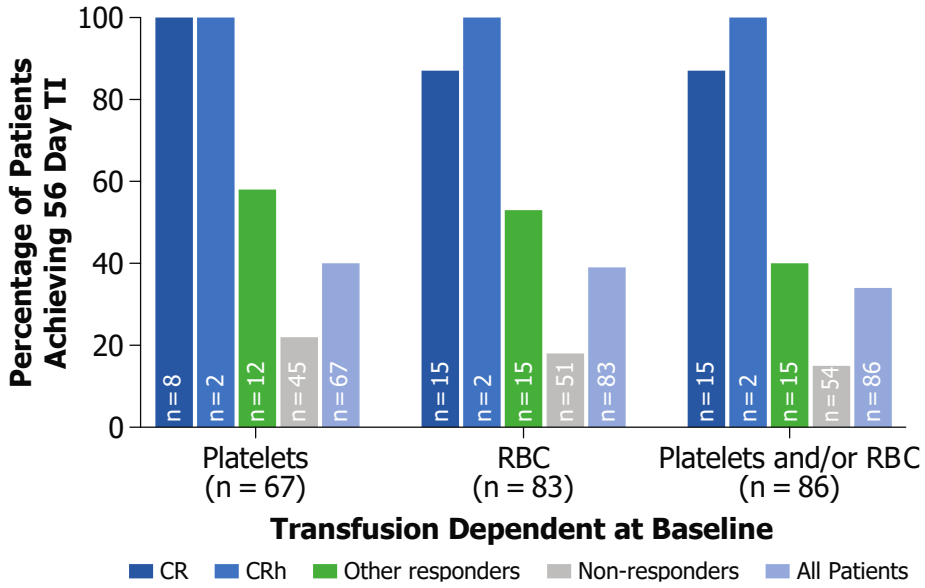
Cortes. ASH 2022. Abstr 2757.

KEY DATA

Study 2102-HEM-101: Olutasidenib

Transfusion Independence

- Among 86 patients who were platelet and/or RBC transfusion dependent at baseline, a 56-day TI was achieved in 29 (34%), across all response groups.
- Higher rates of TI were observed among transfusion dependent patients at baseline who achieved CR+CRh than for Other Responders.



Stem Cell Transplant

- In total, 16 (11%) patients were able to proceed to HSCT following Olutasidenib treatment (includes 1 patient who discontinued for an AE prior to HSCT).
- Of 15 patients who discontinued Olutasidenib to receive HSCT, 11 were in CR/CRh, 3 in CRi and 1 had SD.

Cortes. ASH 2022. Abstr 2757.

KEY DATA

Study 2102-HEM-101: Olutasidenib

Safety

Treatment-Related TEAEs (N=153)		
Adverse Events, n (%)	**All Grades (>5%)**	**Grade 3 or 4 (>2%)**
Patients with any AE	111 (73)	59 (39)
Nausea	35 (23)	0 (0)
Differentiation syndrome	22 (14)	13 (8)
Leukocytosis	20 (13)	7 (5)
ALT increased	13 (8)	4 (3)
Constipation	12 (8)	0 (0)
Fatigue	11 (7)	1 (1)
Vomiting	11 (7)	0 (0)
Anemia	9 (6)	7 (5)
AST increased	9 (6)	3 (2)
Thrombocytopenia	8 (5)	6 (4)
Neutropenia	8 (5)	8 (5)
GGT increased	8 (5)	7 (5)
Hepatic enzyme increased	6 (4)	5 (3)

- Differentiation syndrome (DS) occurred in 22 (14%) patients, with Grade ≥3 events in 14 (9%) and 1 fatal case; most cases resolved with treatment interruption, dexamethasone and/or supportive care.
- Hepatic AEs occurred in 38 (25%) patients, with Grade 3 events in 19 (12%) and Grade 4 events in 4 (3%); Grade 3/4 events (>1%) were increases in laboratory liver function parameters. Hepatic AEs were manageable with dose modifications and concomitant medications.
- QTc prolongation occurred in 12 (8%) patients with 1 (1%) Grade 3 event. None led to discontinuation.
- TEAEs leading to treatment discontinuation occurred in 48 (31%) patients including (>1%) disease progression (14%), and DS, febrile neutropenia, and pneumonia (2% each).
- Deaths were reported in 48 (31%) patients, with the majority related to progression of AML or its complications. Events leading to death in >1 patient were disease progression (14%), pneumonia (2%), and pneumonia fungal, cerebral hemorrhage, respiratory failure, sepsis, and other (1% each).

Cortes. ASH 2022. Abstr 2757.

SUMMARY

Study 2102-HEM-101: Olutasidenib

- Olutasidenib induced durable remissions and transfusion independence
- Some patients were able to proceed to HSCT following olutasidenib
- Well-characterized and manageable side-effect profile

January 18, 2023: REZLIDHIA™ (olutasidenib) has been added by the National Comprehensive Cancer Network® (NCCN®) to the latest NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for acute myeloid leukemia (AML). REZLIDHIA (olutasidenib) is now included as a recommended targeted therapy for adult patients with relapsed/refractory (R/R) AML with isocitrate dehydrogenase-1 (IDH1) mutation.

Cortes. ASH 2022. Abstr 2757.

Study 2102-HEM-101: Olutasidenib

Olutasidenib provides benefit for patients with R/R mIDH1 acute myeloid leukemia and should be considered as a treatment option

IDH1 mutation testing required

ALPINE

Does zanubrutinib provide benefit to patients with relapsed or refractory chronic lymphocytic leukemia and small lymphocytic lymphoma?

On **January 19, 2023**, the Food and Drug Administration (FDA) approved zanubrutinib (Brukinsa, BeiGene USA, Inc.) for chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)

Brukinsa is also indicated for the treatment of adult patients with:

- Nov 14, 2019: **Mantle cell lymphoma (MCL)** who have received at least one prior therapy
- Sept 1, 2021: **Waldenström's macroglobulinemia (WM)**
- Sept 15, 2021: **Marginal zone lymphoma (MZL)** (relapsed or refractory) who have received at least one anti-CD20-based regimen