POST-NEW ORLEANS 2022
Novità dal Meeting della Società Americana di Ematologia

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Milano
Teatro Dal Verme
2-3-4 Febbraio 2023

Terapie di salvataggio con anticorpi monoclonali

Luigi Rigacci

DICHIARAZIONE

Luigi Rigacci

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(Menarini)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(Novartis, Astra Zeneca, Abbvie, Takeda, Gilead, Gentili)**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro

RELAPSED/REFRACTORY LYMPHOMAS

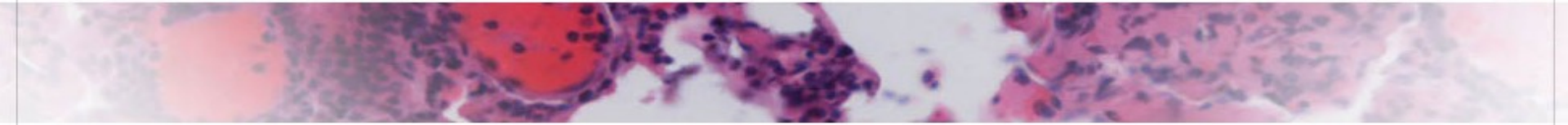
Selected 11 oral presentations and 29 posters

Only those potentially changing practice:

- Aggressive Lymphoma (DLBCL)
- Indolent Lymphoma (FL)

DIFFUSE LARGE B CELL LYMPHOMA

American Society of Hematology
Helping hematologists conquer blood diseases worldwide



Polatuzumab Vedotin Combined with R-ICE (PolaR-ICE) as Second-Line Therapy in Relapsed/Refractory Diffuse Large B-Cell Lymphoma

Alex F. Herrera[1], Lu Chen[2], Jennifer Crombie[3], Jonathon Cohen[4], Ranjana Advani[5], Ann LaCasce[3], Leslie Popplewell[1], Sandrine Puverel[1], Lacolle Peters[1], Shari Daniels[1], James Godfrey[1], Geoffrey Shouse[1], Matthew Mei[1], Swetha Kambhampati[1], Lihua E. Budde[1], Liana Nikolaenko[1], Steven Rosen[1], Larry Kwak[1], Stephen Forman[1], and Matthew Matasar[6]

1 Department of Hematology/HCT, City of Hope, Duarte, CA; 2 Department of Computational and Quantitative Medicine, City of Hope, Duarte, CA; 3 Dana-Farber Cancer Institute, Boston, MA; 4 Winship Cancer Institute of Emory University, Atlanta, GA; 5 Division of Oncology, Stanford Cancer Institute, Stanford, CA; 6 Memorial Sloan Kettering Cancer Center, New York, NY

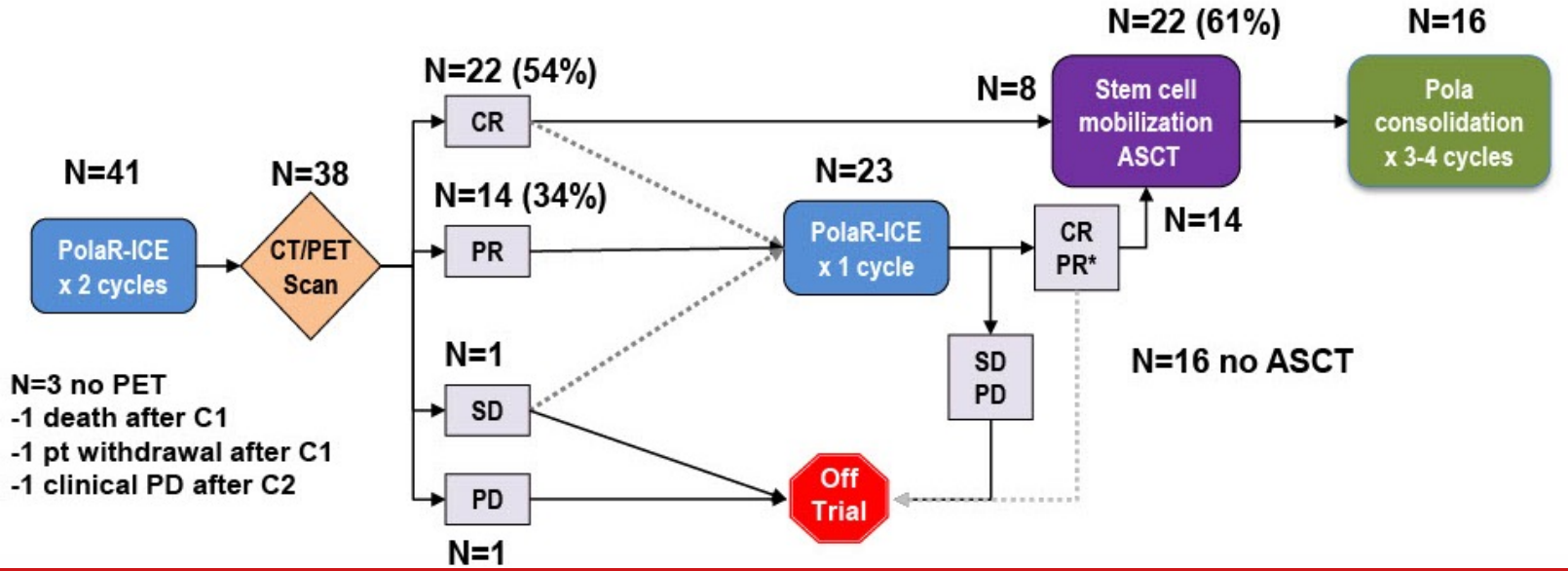
Study scheme and response to PolaR-ICE

Response after 2 cycles (all-treated)

- **ORR 88%, CR 54%**

Response at end of salvage (all-treated)

- **ORR 80%, CR 56%**

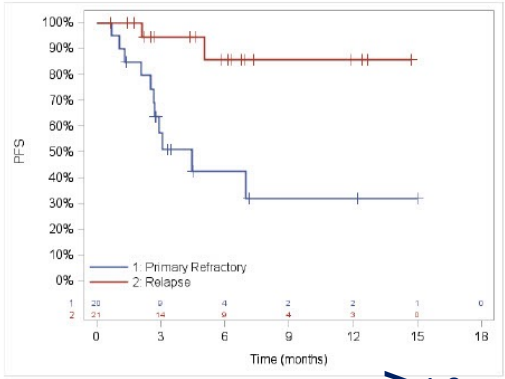


Response in Subgroups (end of salvage)

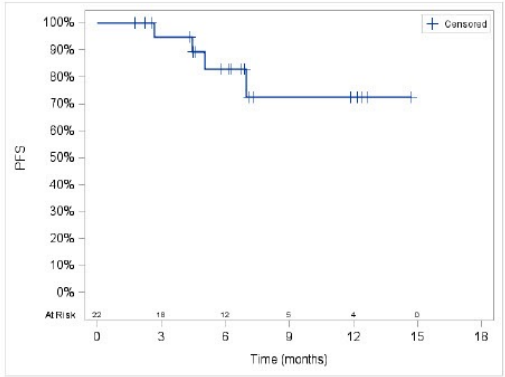
Response	Primary Refractory (n=20)	Relapsed (n=21)	Overall (n=41)
Overall	14 (70%)	19 (90%)	33 (80%)
Complete Response	7 (35%)	16 (76%)	23 (56%)
Partial Response	7 (35%)	3 (14%)	10 (24%)
Stable Disease	1 (5%)		1 (2%)
Progressive Disease	3 (15%)	1 (5%)	4 (10%)
Not assessed	2 (10%)	1 (5%)	3 (7%)

PFS according in subgroups

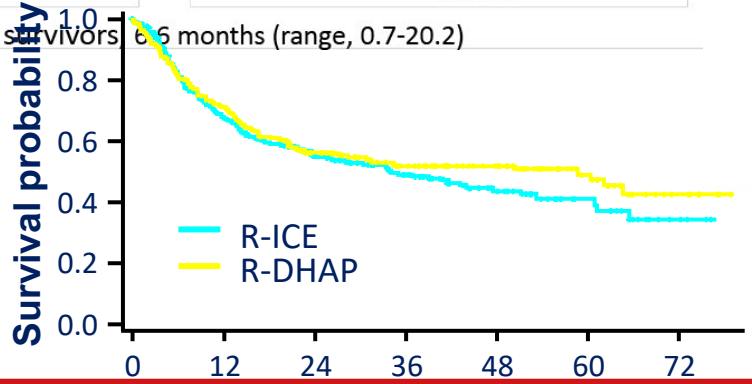
PFS by response to 1L tx (n=41)



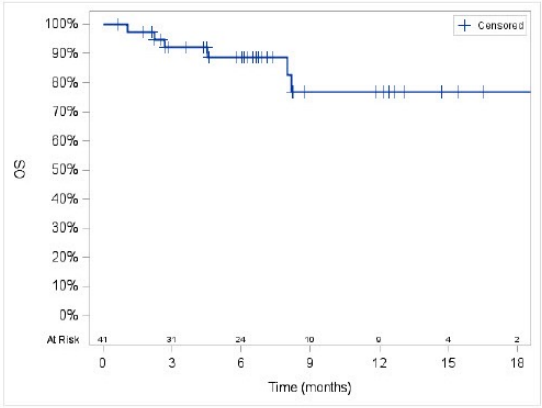
PFS in pts who went to ASCT (n=22)



Median follow-up in survivors, 6.6 months (range, 0.7-20.2)



Overall Survival with PolaR-ICE



Median follow-up in survivors, 6.6 months (range, 0.7-20.2)

CORAL Study

Abstract 443

Subcutaneous Epcoritamab + R-DHAX/C in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma Eligible for Autologous Stem Cell Transplant: Updated Phase 1/2 Results

Pau Abrisqueta, MD, PhD,[1] Raul Cordoba, MD, PhD,[2] Lorenzo Falchi, MD,[3] Sven de Vos, MD, PhD,[4] Marcel Nijland, MD, PhD,[5] Fritz Offner, MD, PhD,[6] Jun Wu, MD, MS,[7] Irina Bykhovski, PharmD,[8] Liwei Wang, PhD,[8] Ali Rana, MD, PhD,[8] Tycel Phillips, MD[9]

Study Design: EPCORE NHL-2 Arm 4

A phase 1b/2, open-label trial evaluating the safety and antitumor activity of epcoritamab + R-DHAX/C in adults with R/R DLBCL who are eligible for transplant

Key inclusion criteria

- R/R CD20+ DLBCL
  - DLBCL, NOS
  - "Double-hit" or "triple-hit" DLBCL[a]
  - FL grade 3B
  - T-cell/histiocyte-rich DLBCL
- Eligible for R-DHAX/C and HDT-ASCT
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Data cutoff: September 16, 2022
Median follow-up: 12.6 mo
ClinicalTrials.gov: NCT04663347

Dose escalation, n=8 → **Expansion, n=21**

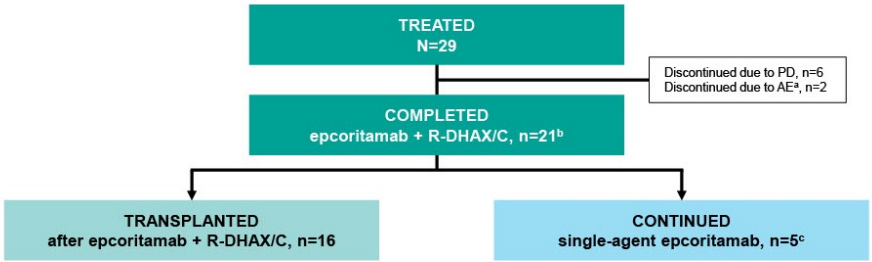
	Dose escalation, n=8	Expansion, n=21
Step-up dosing	**Epcoritamab (SC)** **24 mg (n=3) or** **48 mg (n=5)** QW C1–4, Q2W C5–9, Q4W C10+* **+ R-DHAX/C** C1–3	**Epcoritamab (SC)** **48 mg** QW C1–4, Q2W C5–9, Q4W C10+* **+ R-DHAX/C** C1–3

Primary objectives: DLT/Safety and tolerability
Key secondary objective: Antitumor activity[b]

Primary objective: Antitumor activity[b]
Primary endpoint: ORR per Lugano criteria
***Epcoritamab treatment until HDT-ASCT or PD (whichever is earlier)**

R-DHAX/C regimen in C1–3, 21 d each: rituximab 375 mg/m² IV Q3W; dexamethasone 40 mg/d IV or orally on days 1–4; cytarabine 2 g/m² IV repeated after 12 h Q3W; carboplatin AUC = 5 mg/mL x min (Calvert formula) or oxaliplatin 100 mg/m² IV Q3W. Cycle 4 was 21 d; cycles 5+ were 28 d each. [a]Classified as HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations. [b]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until disease progression.

Patient Disposition



The primary reason for patients not proceeding to transplant was patient and/or investigator choice

Median[d] (range) follow-up was 12.6 (2.0+ to 17.1) mo

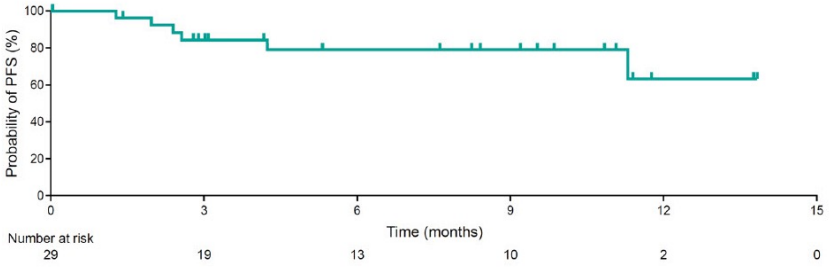
Overall and Complete Response Rates Were High

Response, n (%)[a]	Received ASCT n=16	Did not receive ASCT n=11[b]	Total efficacy evaluable n=27
Overall response	**16 (100)**	**7 (64)**	**23 (85)**
CMR	13 (81)	5 (45)	18 (67)
PMR	3 (19)	2 (18)	5 (19)
Stable disease	0	2 (18)	2 (7)
Progressive disease	0	1 (9)	1 (4)

Data cutoff: September 16, 2022. [a]Based on modified response-evaluable population, defined as patients with ≥1 target lesion at baseline and ≥1 postbaseline response evaluation and patients who died within 60 d of first dose. One patient died within 60 d of first dose without assessment. [b]Includes 5 patients who continued epcoritamab monotherapy and 6 patients who discontinued prior to reaching transplant.

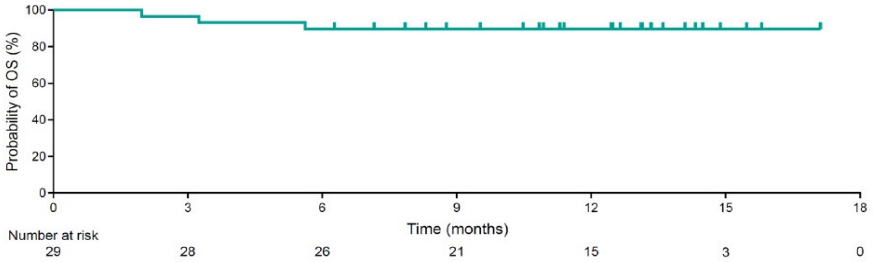
- Median* follow-up was 12.6 mo (range, 2.0+ to 17.1)
- Median duration of response and median duration of CMR were not reached
- Median time to response and complete response was 1.4 mo (range, 1.2–2.2 and 1.2–5.6, respectively)

Progression-Free Survival



mPFS not reached at a median follow-up of 12.6 mo

Overall Survival



An estimated 90% (95% CI, 71%–97%) of patients remained alive at 12 mo; mOS not reached at a median follow-up of 12.6 mo

Relapse is Uncommon in Patients with Large B-cell Lymphoma Who Are in Complete Remission at the End Of Fixed-course Glofitamab Treatment

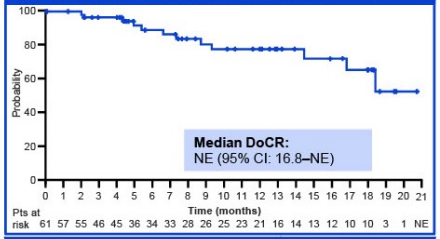
Martin Hutchings,[1] Carmelo Carlo-Stella,[2] Franck Morschhauser,[3] Emmanuel Bachy,[4] Paolo Corradini,[5] Gloria Iacoboni,[6] Cyrus Khan,[7] Krish Patel,[8] Mark Hertzberg,[9] Lorenzo Falchi,[10] Nancy L. Bartlett,[11] Joshua Brody,[12] Linda Lundberg,[13] Yuying Xie,[14] Estefania Mulvihill,[13] Pauline Baumlin,[13] James Relf,[15] Kathryn Humphrey,[15] Michael Dickinson[16]

Background: Glofitamab monotherapy at RP2D induces durable complete responses

Pivotal Phase II results presented at ASCO 2022

- DLBCL NOS, HGBCL, trFL or PMBCL; ≥2 prior therapies
- Glofitamab 2.5/10/30mg (**N=155**)
- Efficacy
  - **CR rate: 39.4%** (61/155)
  - **ORR: 51.6%** (80/155)
- Safety
  - Glofitamab was well tolerated with a low rate of discontinuation
  - CRS was mostly low grade

Pivotal Phase II cohort (ASCO 2022) – DoCR* by IRC



	N=61
Median DoCR follow-up, mo (range)	10.6 (0–21)
12-months DoCR, % (95% CI)	**77.6 (64.3–90.8)**
CRs ongoing at CCOD, n (%)	49 (80.3)

Outcomes in patients with R/R LBCL

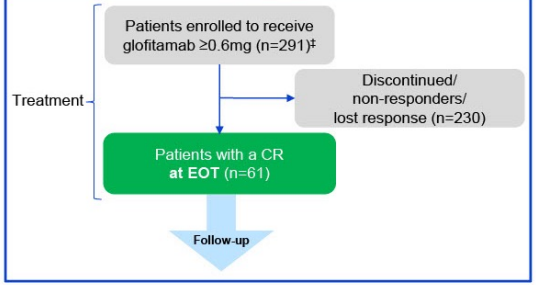
Best overall response*:

- CR: 35.4% (**103/291**)
- PR: 17.2% (50/291)
- ORR: 52.6% (153/291)

Median time to first CR (N=103)†:

- 43 days

Included patients with R/R LBCL had: DLBCL NOS, trFL, HGBCL or PMBCL

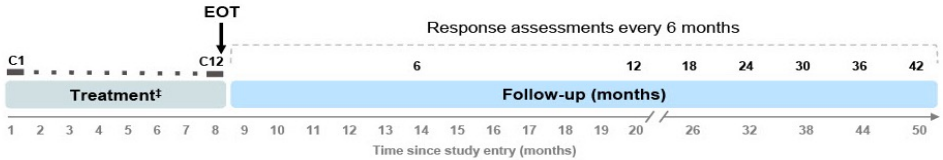


Complete remissions are achieved early in patients with R/R LBCL

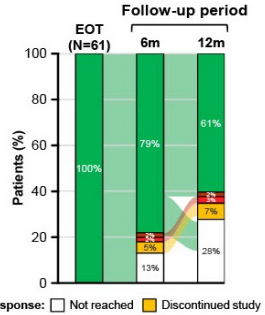
Study overview

Phase I/II dose escalation and expansion in patients with R/R LBCL

- **Glofitamab IV administration** fixed dose (0.6–25mg) or with step-up dosing during C1 (target dose: 16mg or 30mg) every three weeks, maximum 13 infusions
- **Obinutuzumab pretreatment** (1 x 1000mg) to mitigate CRS
- **Fixed duration treatment*** maximum 12 cycles† (8.3 months)
- **Optional re-treatment** in patients with PD after prior response



Remission at 12 months post-EOT in patients with CR at EOT



Response: Not reached | Discontinued study | Death | PD | Continued remission

Majority of patients remain in remission:

- 6 months follow-up: 79% (48/61)
- 12 months follow-up: 61% (37/61)

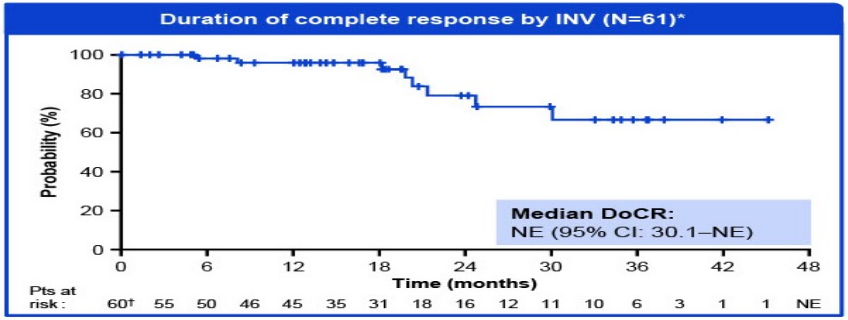
After 12 months follow-up, 7 patients had discontinued:

- 1 PD
- 2 deaths (due to lymphoma)
- 4 discontinued study (2 received allogeneic transplant, 1 due to physician decision, 1 lost to follow-up)

17 patients remained in follow-up but had not yet reached 12 months

Majority of patients remain in remission 12 months after cessation of therapy

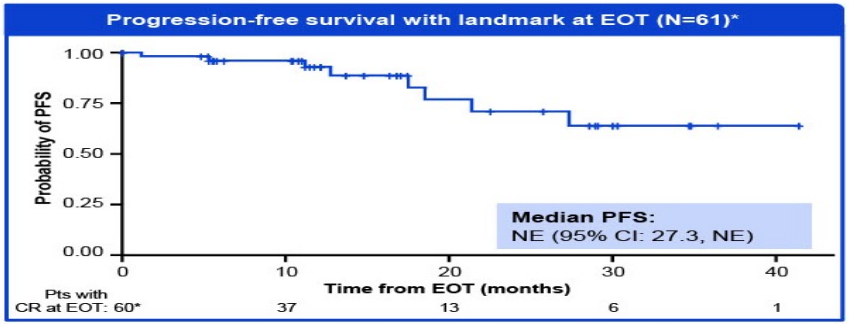
Durable responses after first CR



	N=61
Median DoCR follow-up from first CR, months (95% CI)	18.1 (14.8–20.7)
Median DoCR follow-up from EOT, months (95% CI)	11.5 (10.5–16.4)
Median DoCR, months (95% CI)	NE (30.1–NE)
24-months DoCR, % (95% CI)	79.1 (63.3–95.0)
CRs ongoing at CCOD, n (%)	52 (85.2)

CRs remain durable with significant follow up (11.5 months) post-EOT

PFS in patients with CR at EOT



	N=61
Median PFS follow-up from EOT, months (95% CI)	11.5 (10.5–16.4)
Median PFS, months (95% CI)	NE (27.3–NE)
12-month PFS, % (95% CI)	92.6 (84.3–100.0)

High proportion of patients (93%) remain progression free 12 months post-EOT

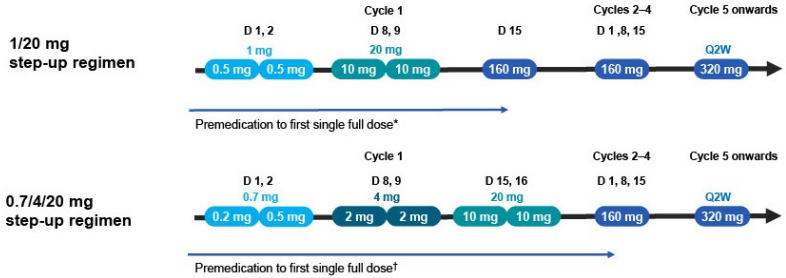
Odronextamab in Patients with Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL): Results from a Prespecified Analysis of the Phase 2 Study ELM-2

Won Seog Kim[1], Tae Min Kim[2], Seok-Goo Cho[3], Isidro Jarque[4], Elżbieta Iskierka[5], Michelle Poon[6], H. Miles Prince[7], Sung Yong Oh[8], Francesca Lim[9], Cecilia Carpio[10], Tran-Der Tan[11], Sabarish Ayyappan[12], Antonio Gutierrez[13], Jingjin Li[14], Melanie Ufkin[14], Min Zhu[14], Aafia Chaudhry[14], Hesham Mohamed[14], Srikanth Ambati[14], Jan Walewski[15], on behalf of ELM-2 Investigators

[1]Samsung Medical Center, Center for Hematologic Malignancy, Seoul, South Korea; [2]Seoul National University Hospital, Seoul, South Korea; [3]The Catholic University of Korea, Seoul St. Mary's Hospital Hematology, Seoul, South Korea; [4]Hospital Universitari i Politècnic La Fe, Valencia, Spain; [5]Copernicus Memorial Hospital, Department of Hematology, Medical University of Łódź, Łódź, Poland; [6]Hematology Oncology National University Hospital, Singapore; [7]Epworth Healthcare and University of Melbourne, East Melbourne, Australia; [8]Dong-A University Hospital, Busan, South Korea; [9]Singapore General Hospital, Singapore; [10]Department of Hematology, Vall d'Hebron Institute of Oncology (VHIO), University Hospital Vall d'Hebron, Autonomous University of Barcelona (UAB), Barcelona, Spain; [11]Hematology and Medical Oncology Koo Foundation Sun Yat Sen Cancer Center, Taipei City, Taiwan; [12]University of Iowa Hospital and Clinics, Iowa City, IA, USA; [13]Hospital Universitari Son Espases, IdISBa Palma, Spain; [14]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [15]Narodowy Instytut Onkologii im. Marii Skłodowskiej-Curie Państwowy Instytut Badawczy, Warszawa, Poland

Cycle 1 step-up regimen optimized to mitigate the risk for cytokine release syndrome

- The study initiated with a Cycle 1 step up regimen of 1/20 mg
- This was modified to 0.7/4/20 mg during Cycle 1 to further mitigate the risk of CRS



Patients disposition

	N=140
Cycle 1 step-up regimen (1/20 mg) / (0/7/4/20 mg)	47.9% / 52.1%
Median duration of exposure, weeks (range)	14.9 (0.9–118.9)
Median number of doses received, no. (range)	15 (1–52)
Median number of cycles completed, no. (range)	5 (0–57)
Completed Cycle 1	128 (91.4%)
≥4 cycles completed	82 (58.6%)
Treatment ongoing	34 (24.3%)
Treatment discontinued	75.7%
Disease progression	41.4%
Adverse event	9.3%
Death	12.9%
Patient or physician decision / withdrawal of consent	12.1%

Cytokine release syndrome

n, (%)	1/20 regimen N=67	0.7/4/20 regimen N=73
CRS any Grade	38 (56.7%)	39 (53.4%)
Grade 1	21 (31.3%)	28 (38.4%)
Grade 2	12 (17.9%)	10 (13.7%)
Grade 3	5 (7.5%)	1 (1.4%)
Grade 4	0	0
Grade 5	0	0
Received corticosteroids	13 (19.4%)	15 (20.5%)
Received tocilizumab	10 (14.9%)	19 (26.0%)
Received vasopressors	5 (7.5%)	1 (1.4%)

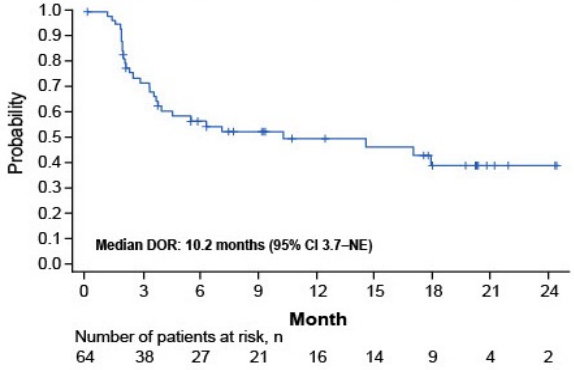
- 0.7/4/20 mg step-up regimen reduced the incidence of grade 2 and grade 3 CRS
- Approximately half of R/R DLBCL patients had CRS, mostly grade 1
- Only 1 case of grade 3 CRS with 0.7/4/20 mg step-up regimen (in the setting of acute pancreatitis at week 6) and no grade 4 or higher CRS events
- All CRS events resolved within a median time to resolution of 2 days (range 1–133)
- No patients required mechanical ventilation or ICU admission for the management of CRS

Other adverse event of interest

n (%)	1/20 regimen (N=67)	0.7/4/20 regimen (N=73)	All patients (N=140)
ICANS, any grade	3 (4.5%)	1 (1.4%)	4 (2.9%)
Grade ≥3	1 (1.5%)*	0	1 (0.7%)
Infusion related reaction, any grade	16 (23.9%)	8 (11.0%)	24 (17.1%)
Grade ≥3	0	0	0
Infection, any grade	40 (59.7%)	43 (58.9%)	83 (59.3%)
Grades 1–2	13 (19.4%)	24 (32.9%)	37 (26.4%)
Grades 3–4	21 (31.3%)	12 (16.4%)	33 (23.6%)
Grade 5	6 (9.0%)	7 (9.6%)	13 (9.3%)
Tumor lysis syndrome, any grade	1 (1.5%)	0	1 (0.7%)
Grade ≥3	1 (1.5%)		1 (0.7%)

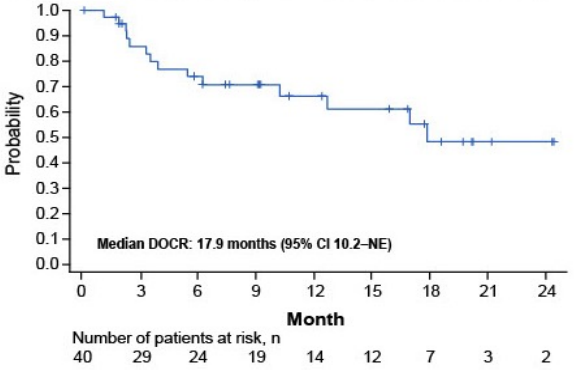
Response appears durable

Duration of response – Independent central review



- 12-month DOR: 49.4% (95% CI: 35.0–62.2)
- 18-month DOR: 38.9% (95% CI: 23.9–53.6)

Duration of complete response – Independent central review



- 12-month DOCR: 66.4% (95% CI: 47.1–80.1)
- 18-month DOCR: 48.3% (95% CI: 26.1–67.4)

- Odronextamab is an off-the-shelf investigational CD20xCD3 bispecific antibody
- First results from pivotal Phase 2 trial of odronextamab demonstrate clinically important antitumor activity in heavily pretreated, R/R DLBCL
  - ORR 49.2%; CR 30.8%
  - Reponses were deep and durable, mDOCR 17.9 months
- Consistent efficacy prior to and post-CAR T
- Odronextamab generally has a manageable safety profile with the optimized step-up regimen
  - CRS was mostly grade 1 and occurred mainly with Cycle 1 step-up
  - No cases of TLS and no grade 3 or higher ICANS or IRR reported
- Phase 3 randomized controlled studies will be initiating in earlier lines of therapy

FOLLICULAR LYMPHOMA

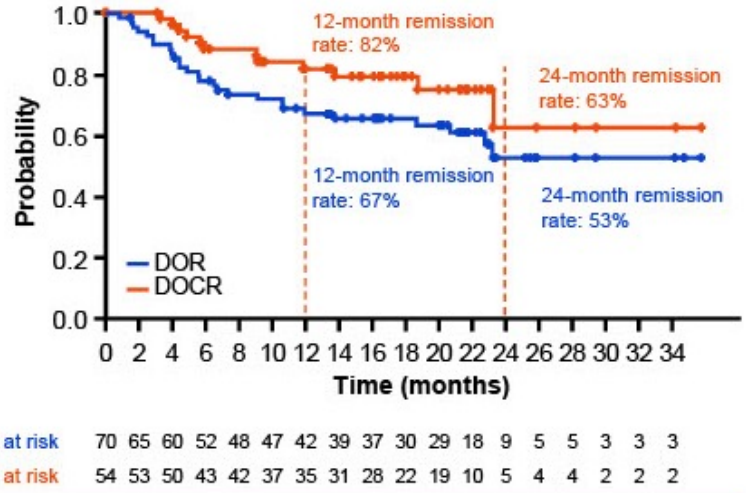
Mosunetuzumab Monotherapy Demonstrates Durable Efficacy with a Manageable Safety Profile in Patients with Relapsed/Refractory Follicular Lymphoma who Received ≥2 Prior Therapies: Updated Results from a Pivotal Phase II Study

Nancy L. Bartlett,[1] Laurie H. Sehn,[2] Matthew Matasar,[3] Stephen J. Schuster,[4] Sarit Assouline,[5] Pratyush Giri,[6] John Kuruvilla,[7] Miguel Canales,[8] Sascha Dietrich,[9] Keith Fay,[10] Matthew Ku,[11] Loretta Nastoupil,[12] Michael C. Wei,[13] Shen Yin,[13] Iris To,[13] Huang Huang,[14] Juliana Min,[15] Elicia Penuel,[13] Christopher R. Bolen,[13] L. Elizabeth Budde[16]

Durability of responses

Efficacy endpoint by investigator assessment	N=90
Median DOR, months (range), n=70	NR (21–NR)
24-month DOR (95% CI)	53% (38–68)
Median DOCR, months (range), n=54	NR (23–NR)
24-month DOCR (95% CI)	63% (38–88)
Median PFS, months (range)	24 (12–NR)
24-month PFS (95% CI)	48% (36–60)
Median TTNT, months (range)	NR (18–NR)
24-month TTNT (95% CI)	56% (45–67)
Median OS, months (range)	NR (NR–NR)
24-month OS (95% CI)	87% (80–94)

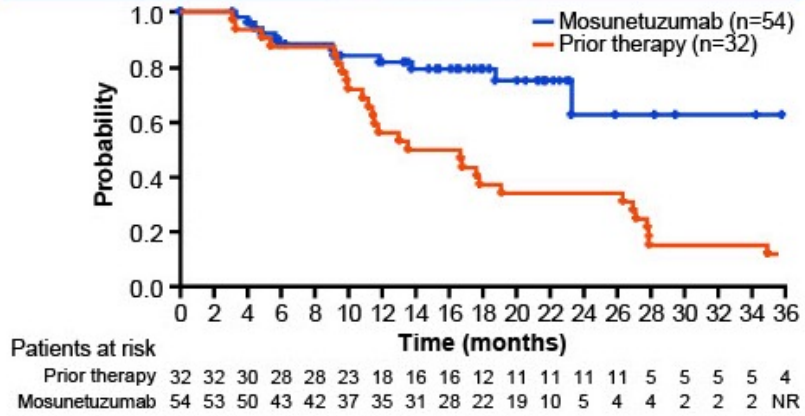
DOR and DOCR



Durable responses: majority of patients in remission after 2 years

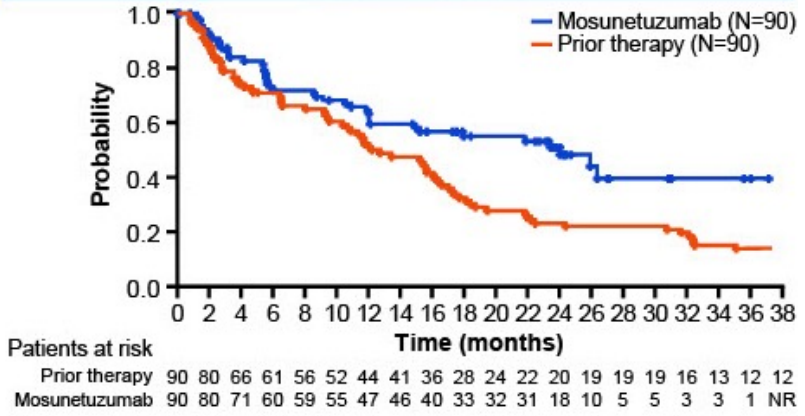
DOCR and PFS with mosunetuzumab versus last prior therapy

DOCR



	Mosunetuzumab (n=54)	Last prior therapy (n=32)
Median DOCR, months (95% CI)	NR (23–NR)	15 (11–26)

PFS



	Mosunetuzumab (N=90)	Last prior therapy (N=90)
Median PFS, months (95% CI)	24 (12–NR)	12 (10–16)

Extended DOCR and 12-month improvement in median PFS with mosunetuzumab compared with last prior therapy

- Pivotal Phase II study of mosunetuzumab continues to demonstrate:
  - Clinically meaningful outcomes in heavily pre-treated R/R FL patients, after more than 2 years of follow-up: **CR rate, 60%; 24-month DOCR, 63%**
  - A manageable safety profile with no new CRS events and no late-onset or chronic toxicities

Subcutaneous Epcoritamab with Rituximab + Lenalidomide in Patients with Relapsed or Refractory Follicular Lymphoma: Phase 1/2 Trial Update

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Study Design: EPCORE NHL-2, Arm 2b

A phase 1b/2, open-label trial evaluating the safety and antitumor activity of epcoritamab + R² in adults with R/R FL[a]

Key inclusion criteria

- R/R CD20+ FL
  - Grade 1, 2, or 3A
  - Stage II–IV
- Need for treatment based on symptoms or disease burden, as determined by GELF criteria[1]
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Data cutoff: September 16, 2022
Median follow-up: 6.4 mo

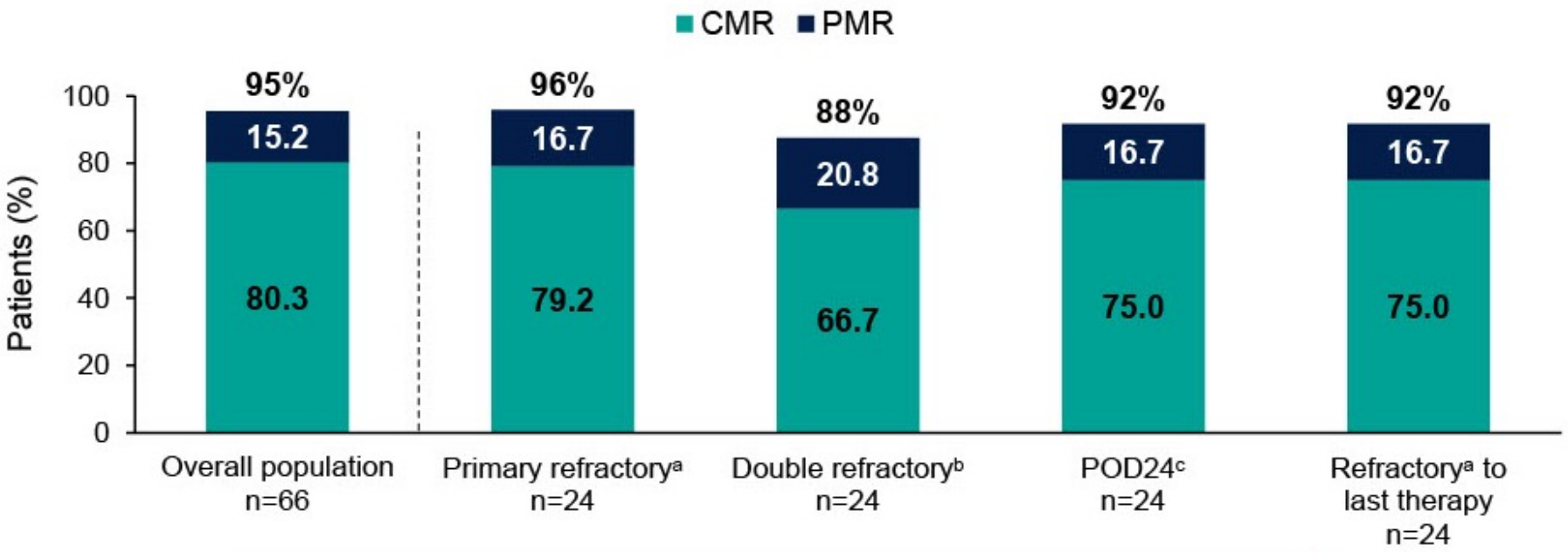
		Treatment Regimen Epcoritamab SC 48 mg + R²						
	Agent	**C1**	**C2**	**C3**	**C4**	**C5**	**C6–C12**	**C13+**
	Epcoritamab SC 48 mg	QW	QW	Q4W	Q4W	Q4W	Q4W	Q4W Up to 2 years
R²	Rituximab IV 375 mg/m²	QW	Q4W	Q4W	Q4W	Q4W		
R²	Lenalidomide oral 20 mg	Daily for 21 d (for 12 cycles)						

Primary objective: Safety and antitumor activity[b]

High Overall and Complete Metabolic Response Rates

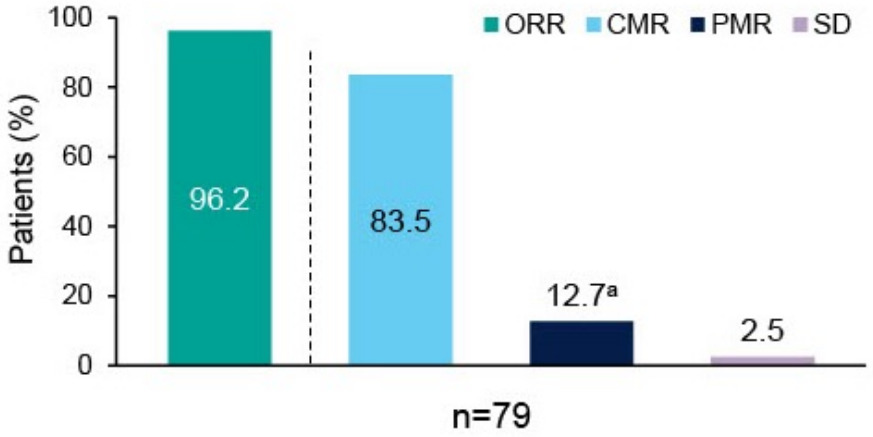
Response[a]	Efficacy Evaluable n=66
Overall response	**95%**
CMR	80%
PMR[b]	15%
Stable disease	3%
Progressive disease	2%

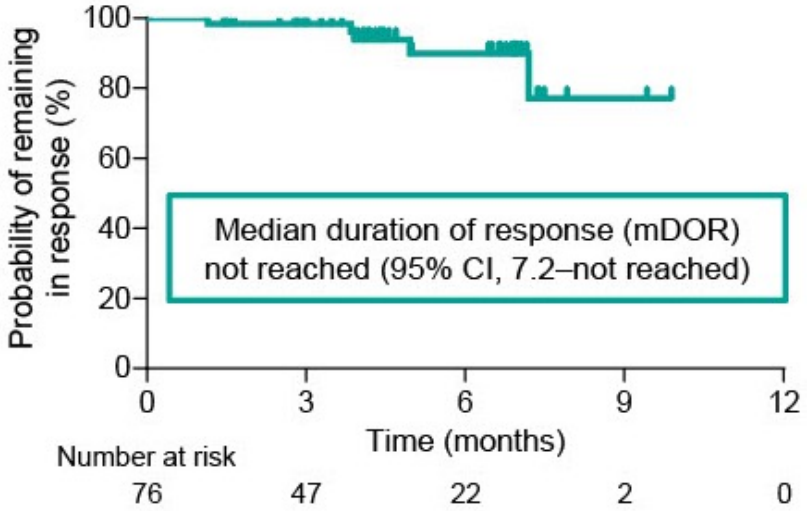
Responses Across High-risk Subgroups



Deep responses consistent across high-risk R/R FL subgroups

Updated Response Data

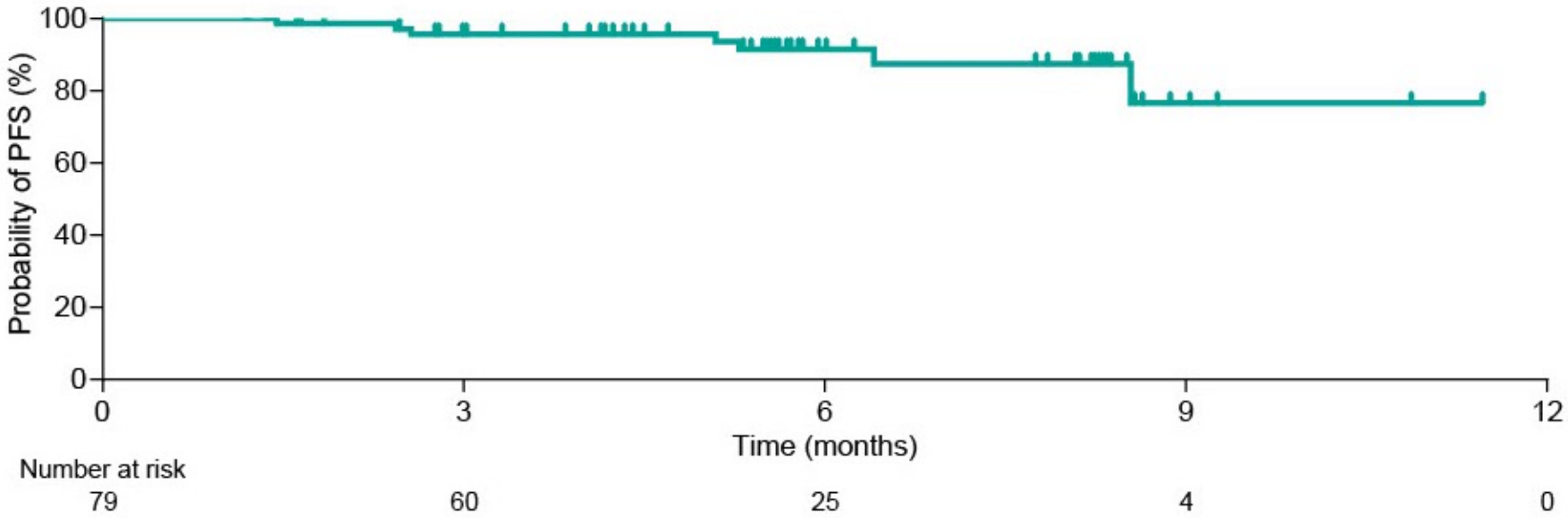




Data cutoff: October 31, 2022

Median follow-up: 5.6 mo (range, 1.2+ to 11.5+)

Progression-Free Survival



Median PFS not reached (95% CI, 8.5–not reached)

- **Epcoritamab + R^2 showed potent antitumor activity**
  - High response rates: ORR 96.2%, CMR 83.5%; majority achieved at first assessment
  - Deep responses observed across high-risk subgroups
  - Durable responses have been observed
- **Safety remained consistent with previous reports**
  - No grade ≥3 CRS observed; CRS events mostly occurred after the first full dose

Odronextamab in Patients with Relapsed/Refractory (R/R) Follicular Lymphoma (FL) Grade 1–3a: Results from a Prespecified Analysis of the Phase 2 Study ELM-2

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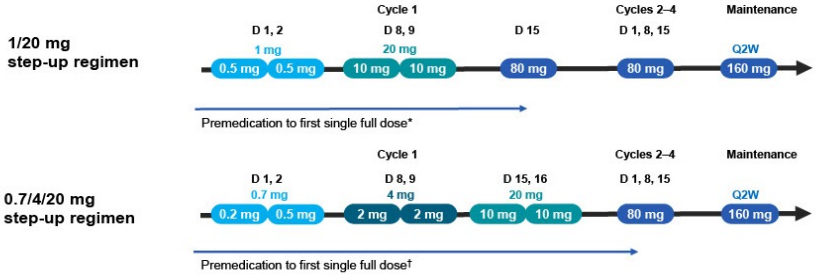
Cycle 1 step-up regimen optimized during the course of the study to further mitigate the risk for cytokine release syndrome

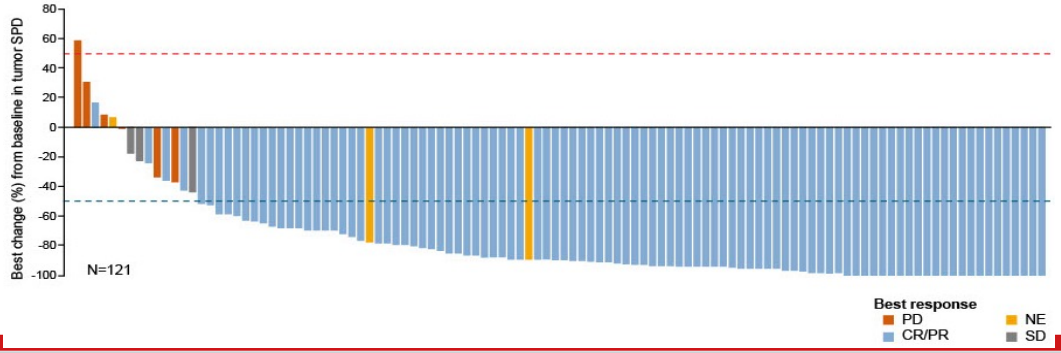
- The study initiated with a Cycle 1 step-up regimen of 1/20/80 mg
- This was modified to 0.7/4/20 mg during Cycle 1 to further mitigate the risk of CRS

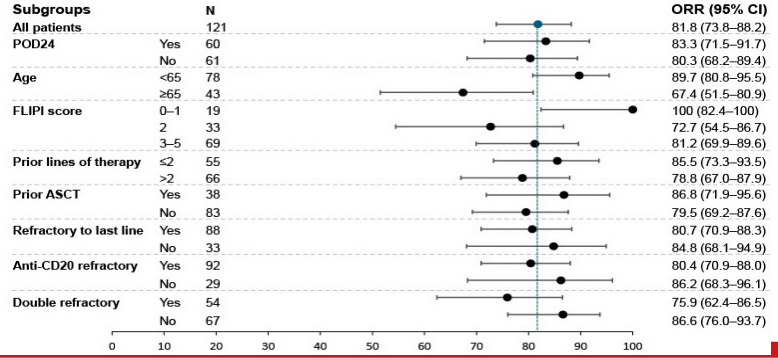


Patients disposition

	N=131
Cycle 1 step-up regimen (1/20 mg) / (0/7/4/20 mg)	51.9% / 48.1%
Median duration of exposure, weeks (range)	22.1 (0.4–137.0)
Median number of doses (range)	19 (1–61)
Median number of cycles (range)	9.1 (0.1–66.5)
Completed cycle 1	95.4%
Completed ≥4 cycles	80.9%
Treatment ongoing	42.7%
Treatment discontinued	57.3%
Disease progression	19.8%
Patient or physician decision / withdrawal of consent	17.6%
Adverse event	9.9%
Death	9.9%

Odronextamab efficacy





Cytokine release syndrome

n, (%)	1/20 regimen (N=68)	0.7/4/20 regimen (N=63)
CRS any Grade	38 (55.9%)	36 (57.1%)
Grade 1	22 (32.4%)	28 (44.4%)
Grade 2	12 (17.6%)	7 (11.1%)
Grade 3	4 (5.9%)	1 (1.6%)
Grade 4	0	0
Grade 5	0	0
Received corticosteroids	11 (16.2%)	17 (27.0%)
Received tocilizumab	9 (13.2%)	12 (19.0%)
Received vasopressors	4 (5.9%)	1 (1.6%)

- 0.7/4/20 mg step-up regimen reduced the incidence of grade 2 and grade 3 CRS
- Approximately half of patients with R/R FL had CRS, mostly grade 1
- Only 1 case of grade 3 CRS with 0.7/4/20 mg step-up regimen and no grade 4 or higher CRS events
- All CRS events resolved with a median time to resolution of 2 days (range 1–51)
- No patients required mechanical ventilation or ICU admission for the management of CRS

Adverse event of interest

n (%)	1/20 regimen (N=68)	0.7/4/20 regimen (N=63)	All patients (N=131)
ICANS, any grade	1 (1.5%)	0	1 (0.8%)
Grade ≥3	0		0
Infusion related reaction, any grade	21 (30.9%)	16 (25.4%)	37 (28.2%)
Grade ≥3	4 (5.9%)	2 (3.2%)	6 (4.6%)
Infection, any grade	51 (75.0%)	35 (55.6%)	86 (65.6%)
Grades 1–2	23 (33.8%)	21 (33.3%)	44 (33.6%)
Grades 3–4	19 (27.9%)	11 (17.5%)	30 (22.9%)
Grade 5	9 (13.2%)	3 (4.8%)	12 (9.2%)
Tumor lysis syndrome, any grade	1 (1.5%)	0	1 (0.8%)
Grade ≥3	1 (1.5%)		1 (0.8%)

- Odronextamab is an off-the-shelf, investigational CD20×CD3 bispecific antibody
- First results from the pivotal Phase 2 trial of odronextamab demonstrate a new benchmark for efficacy in heavily pretreated, R/R FL
  - ORR 81.8%, CR 75.2%; 92% of responders were complete responders
  - Reponses were deep and durable with a mPFS of 20.2 months
- Odronextamab has a generally manageable safety profile with the optimized step-up regimen
  - CRS was mostly grade 1 and generally occurred with Cycle 1 step-up
  - No cases of ICANS or TLS
  - Treatment-related adverse events leading to treatment discontinuation occurred infrequently (7.6%)
- Phase 3 randomized controlled studies will be initiating in follicular lymphoma in earlier lines of therapy

POSTERS

1351 NNV024 a humanized anti-CD37 antibody with enhanced ADCC and extended plasma half-life for the treatment of B-cell malignancies
1357 IKS03 a next generation CD-19 targeted antibody drug conjugated shows potente activity in preclinical models of aggressive B-cell lymphoma
1363 PIT 565, a first in class anti-CD19, anti-CD3, anti-CD2 trispecific antibody for the treatment of B-cell malignancies
1613 Phase I study of the anti-BTLA antibody Tifcemalimab as a single agent or in combination with Tporipalimab in R/R lymphomas
1618 Magrolimab in combination with Rituximab+Chemotherapy in patients wth R/R DLBCL
1625 A first in Human phase I study of ABBV-319, an antibody drug conjugated composed of a CD19 antobody linked to a potent proprietary gucocorticoid receptor modulator, in patients with R/R B-cell malignancies
1630 Mosunetuzumab with Polatuzimab Vedotin is effective and has a manageable safety profile in patients aged <65 years and >65 years with R/R diffuse large B-cell lymphoma and >=1 prior therapy: subgroup analysis of a phase Ib/II study
1637 SUNMO: a phase III trial evaluating the efficacy and safety of Mosunetuzumab in combination with Polatuzumab Vedotin versus Rituximan in combination with Gemcitabine plus Oxaliplatin in patients with R/R aggressive B-cell non Hodgkin Lymphoma
1659 Phase I study of CD-19 targeted CD-28 costimulatory agonist in combination with Glofitamab to enhance T cell effector function in R/R B-cell lymphoma
2938 First in Human (FIH) study of the fully-human Kappa-Lambda CD19/CD47 bisecific antibody TG-1801 in patients with B-cell lymphoma
2955 A phase II open label study of Loncastuximab Tesirine in combination with Rituximab in previously untreated unfit/frail patients with diffuse large B-cell lymphoma (LOTIS-9)
2983 Glofitamab in R/R diffuse large B-cell lymphoma: real world data
4200 Preliminary safety and efficacy evaluation of IMM0306, a CD20 bispecific monoclonal antibody-TRAP (mAB-Trap) from an ongoing phase I dose escalation study in patients with R/R B-cell non Hodgkin's lymphoma
4206 Phase III trial of subcutaneous Epcoritamab in combination with Rituximab and Lenalidomide (R2) vs R2 among patients with R/R follicular lymphoma (EPCORE FL-1)
4259 CD19 4-1BBL (RO7227166) a novel costimulatory bispecific antibody can be safely combined with the T-cell engaging bispecific antibody Glofitamab in R/R B-cell non Hodgkin Lymphoma
4262 A phase I study of Plamatomab an anti CD20 x anti CD3 bispecific antibody, in patients with R/R non Hodgkin's lymphoma: recommended dose safety/efficacy update and escalation exposure response analyisis
4267 The type II Glycoenginnred humanized anti CD20 monoclonal antibody MIL62 combined with Orelabrutinib in Chinese patients with relapsed or refractory B-cell non Hodgkin lymphoma: updated results of a multcenter phase I/IIa trial
4277 Phase II trial to evaluate safety of subcutaneous Epcoritamab monotherapy in the outpatients setting among patients with R/R diffuse grade 1-3° large B-cell and follicular lymphoma (Epcore NHL-6)

CONCLUSIONI

- Polatuzumab si dimostra una importante risorsa per migliorare l'efficacia dei regimi chemioterapici di salvataggio.
- Gli anticorpi bispecifici stanno sempre più confermando la loro efficacia sia da soli che in associazione.
- I risultati di questi anticorpi in seconda linea sono veramente importanti e soprattutto, aumentando il follow-up, di lunga durata.
- Il loro ruolo dopo le CAR-T si sta sempre più definendo.
- Gli effetti collaterali (CIRS e ICANS) con aggiustamento di dosi, scheduling ad incrementare, sono sempre meglio gestibili aprendo ad un utilizzo in regimi non di ricovero.