



Singapore Lymphoma Scientific Symposium 2025

Navigating the Complexity of an Evolving Treatment Landscape in R/R Lymphomas



29 Aug 2025
(Friday)



12:00–13:00



National Cancer
Centre Singapore

For Healthcare Professionals Only.
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Gilead Sciences Singapore Pte. Ltd.,

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Speaker



Asst Prof Ahmad Alsaeed

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Deputy Chairman, Princess Noorah
Oncology Center Assistant Professor in
Hematology, COM-J- KSAU-HS King
Abdulaziz Medical City (NGHA) Jeddah*

Asst Prof Ahmad Alsaeed is a Consultant in Adult Hematology and Bone Marrow Transplantation at the Adult Stem Cell Transplant and Cellular Therapies Section, Princess Norah Oncology Center (PNOC), King Abdulaziz Medical City– Jeddah, Ministry of National Guard, Kingdom of Saudi Arabia. He also serves as Assistant Professor at King Saud bin Abdulaziz University for Health Sciences (KSAU-HS).

He leads the Acute Myeloid Leukemia Team and chairs the BMT Taskforce at PNOC. His areas of interest include transplantation and cellular therapies. Dr Alsaeed has contributed to over 35 peer-reviewed publications and conference abstracts.

Sharing Experiences from Saudi Arabia



Dr Ahmad Alsaeed

Consultant Adult Hematology/BMT

Deputy Chairman Princess Norah Oncology Centre PNOC

King Abdulaziz Medical City, Ministry of National Guard

Jeddah-Saudi Arabia

Disclosure

- Speaker/Honorarium:
 - Kite, Johnson and Johnson, Takeda, Novartis
- Consultancy/Advisory Boards:
 - Takeda, Pfizer, Roche, Menarini Stemline

Princess Noorah Oncology Center King Abdulaziz Medical City Ministry of National Guard Health Affairs (MNGHA) Jeddah, Kingdom of Saudi Arabia

- In the Kingdom of Saudi Arabia, CAR T-cell program started in May 2023, and the available products include:
 1. Axi-cel
 2. Brexu-cel
 3. Tisa-cel
 4. Cilta-cel
- Currently, four centers in the Kingdom of Saudi Arabia are performing CAR T-cell therapy
- Two more centers expected this year
- Around 70–100 cases done annually



Information and image provided by the Speaker.

Disclaimer: Some of the regimens mentioned in this slide may not be approved in Singapore. Please refer to your local prescribing information for details of the approved indications in your region.

axi-cel, axicabtagene ciloleucel; brexu-cel, brexucabtagene autoleucel; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleuce; tisa-cel, tisagenlecleucel.

A R/R DLBCL Patient Who is Responding to Bridging Therapy

Dr Ahmad Alsaeed

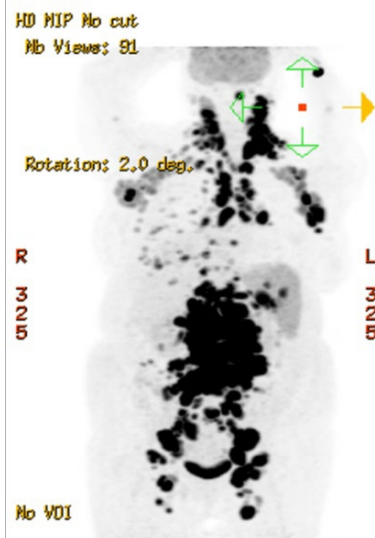
Consultant Adult Hematology/BMT
Deputy Chairman Princess Norah Oncology Centre PNOC
King Abdulaziz Medical City, Ministry of National Guard
Jeddah-Saudi Arabia

Navigating the Complexity of an
Evolving Treatment Landscape in R/R Lymphomas

Patient background

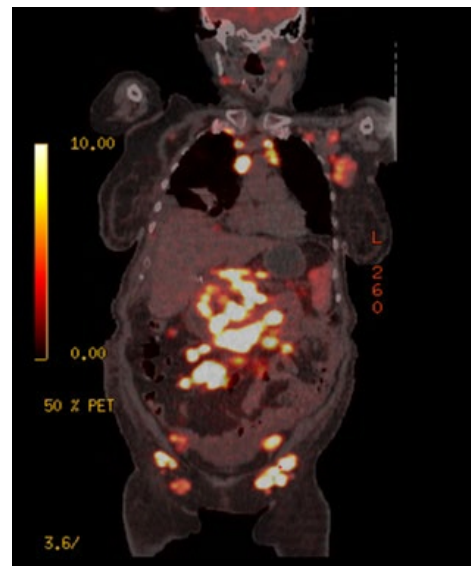
66-year-old Saudi woman

- Known to have DM, hypertension, hypothyroidism, HBV core positive on entecavir
- Initially diagnosed (at another hospital) on Nov 2022 as DLBCL
- Initial presentation with:
 - B symptoms
 - Generalized lymphadenopathy



PET/CT oncology CONCLUSION:

Significant extensive very avid disease with lymphadenopathy above and below the diaphragm at virtually all lymph node stations with pleural, splenic, peritoneal and bony involvement.



Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

CT, computed tomography; DLBCL, diffuse large B-cell lymphoma; DM, diabetes mellitus; HBV, hepatitis B virus; PET, positron emission tomography.

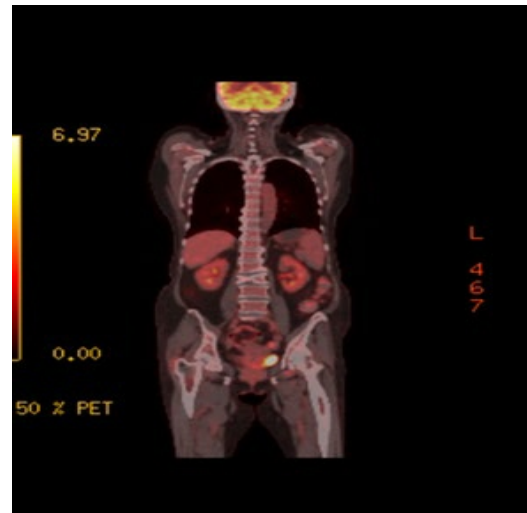
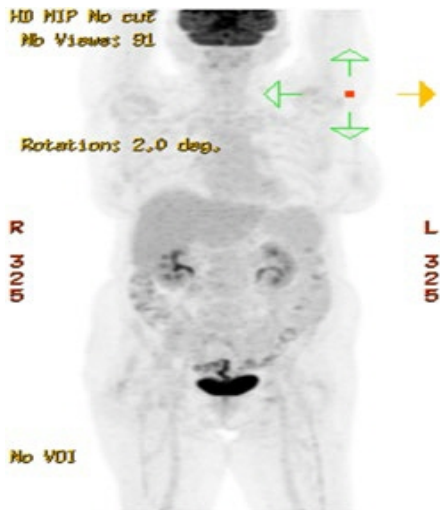
Diagnosis and 1L treatment

- Biopsy c/w LBCL, GCB subtype
- FISH positive for BCL-6 gene but negative for C-Myc and BCL2
- High KI67, 90%

- Treated with six cycles of R-CHOP, completed *April 2023*
- Required some dose adjustment for febrile neutropenia and cytopenias

Diagnosed with
advanced-stage
DLBCL

EOT PET scan showed CMR



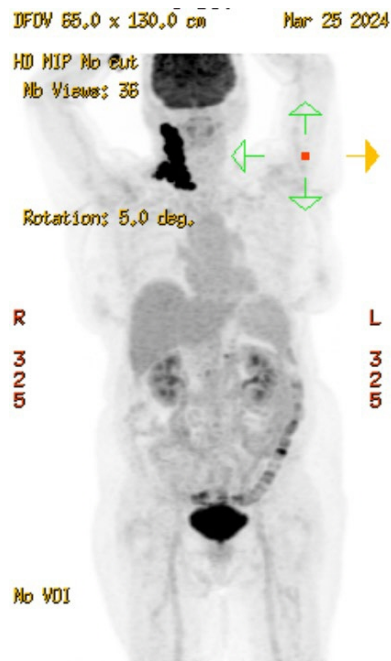
Diagnosis

1L therapy

Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

1L, first-line, therapy; CMR, complete metabolic response; c/w, consistent with; DLBCL, diffuse large B-cell lymphoma; EOT, end of treatment; FISH, fluorescence in situ hybridization; GCB, germinal center B-cell; LBCL, large B-cell lymphoma; PET, positron emission tomography; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone.

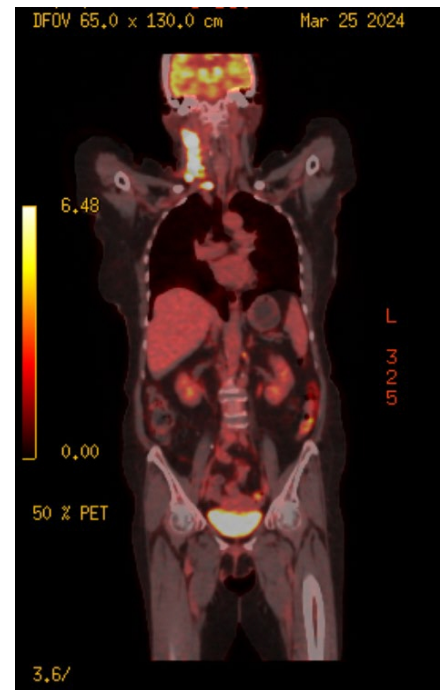
Presented with B symptoms and cervical LAP – Feb 2024



PET/CT Oncology

25/03/2024

Very avid lymphadenopathy in the right neck as described. There are also a couple of small avid upper abdominal nodes.



Right cervical LN biopsy on 4/03/2024 showed DLBCL, germinal center subtype

Diagnosis

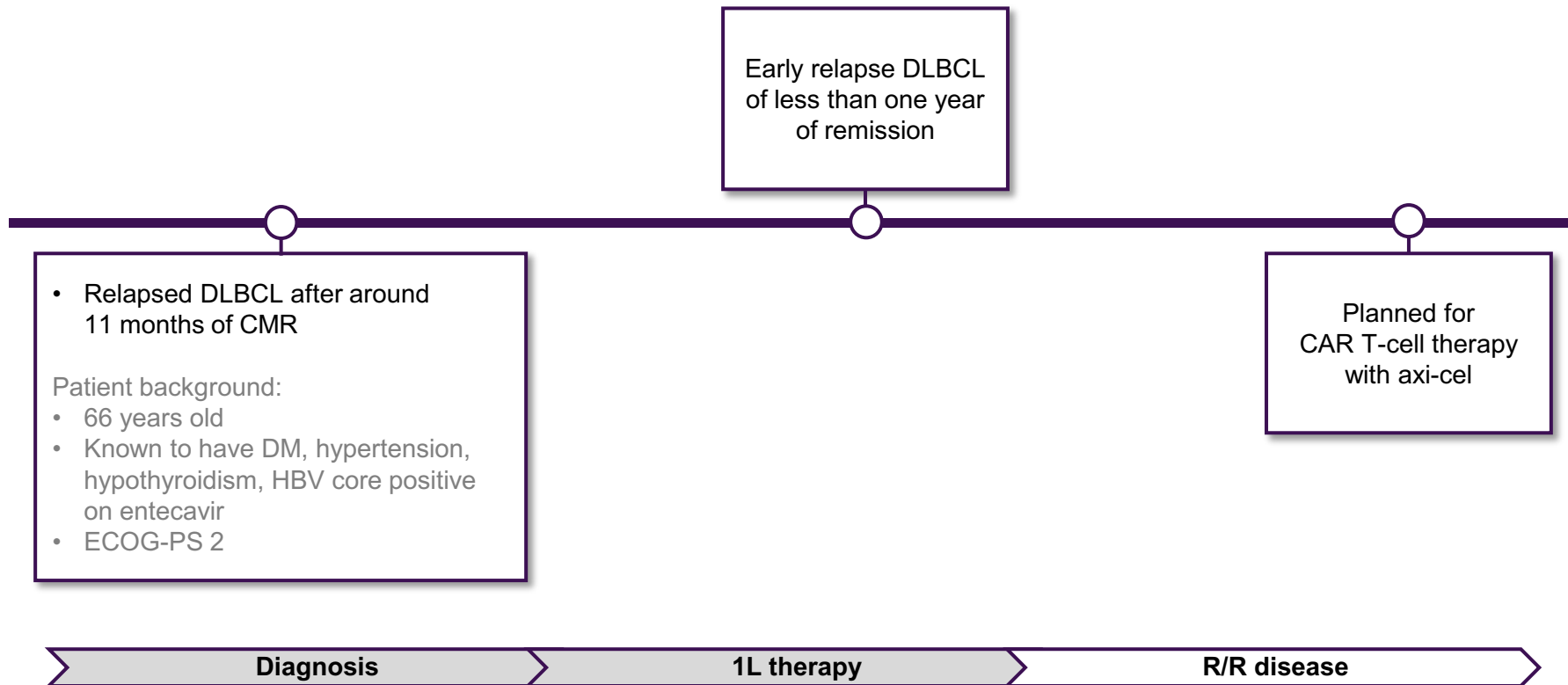
1L therapy

R/R disease

Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

1L, first-line, therapy; CT, computed tomography; DLBCL, diffuse large B-cell lymphoma; LAP, lymphadenopathy; LN, lymph node; PET, positron emission tomography; R/R, relapsed/refractory.

Early relapse DLBCL



Case study details, based on a real patient, are provided by the Speaker.

1L, first-line, therapy; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CT, computed tomography; CMR, complete metabolic response; DLBCL, diffuse large B-cell lymphoma; DM, diabetes mellitus; ECOG-PS, Eastern Cooperative Oncology Group Performance Status score; HBV, hepatitis B virus; PET, positron emission tomography; R/R, relapsed/refractory.

Bridging therapy

DFOV 65,0 x 130,0 cm Jun 04 2024

HD MIP No cut
Nb Views: 36

Rotation: 5,0 deg.

P

3
2
5

A

3
2
5

No VOI

Bridging therapy
with R-Pola

6/05/2024
CAR T-cell collected

PET/CT Oncology 04/06/2024

CONCLUSION

Deauville 2 complete metabolic response

DFOV 65,0 x 130,0 cm Jun 04 2024

52
0

50 % PET

R/R disease

Bridging therapy

Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

CAR, chimeric antigen receptor; CT, computed tomography; PET, positron emission tomography; R-Pola, rituximab, polatuzumab vedotin; R/R, relapsed/refractory.

Bridging Therapy prior to CAR T Cell in LBCL

Characteristic	Axi-cel (ZUMA-1, ZUMA-7) ^{1,2}	Tisa-cel (JULIET) ³
Bridging therapy on clinical trials	None allowed in pivotal study*; often used in practice	92%

In patients with CMR,
CAR T-cell therapy vs auto-transplant?

Subgroup of R/R LBCL who achieve CMR to salvage treatment still could have good outcome to transplant (Fit patients who require only one salvage treatment)⁴

Potentially decreased efficacy, based on the theoretical possibility of suboptimal CAR T-cell expansion in the absence of an adequate number of CD19+ tumor cells⁵

Toxicity[†]

Disclaimer: Please refer to your local prescribing information for details of the approved indications in your region.

*In ZUMA-7, bridging therapy was restricted to glucocorticoids and the use of chemotherapy bridging was prohibited.

†Speaker's opinion from clinical experience.

1L, first line; axi-cel, axicabtagene ciloleucel; SOC, standard of care; tisa-cel, tisagenlecleucel.

1. Neelapu SS, et al. N Engl J Med 2017;377(26):2531-2544. 2. Locke FL, et al. N Engl J Med 2022;386:640-654. 3. Schuster SJ, et al. N Engl J Med 2019;380(1):45-56. 4. Tun AM, et al. Haematologica. 2024;109(7):2186-2195. 5. Cappell KM, Kochenderfer JN. Nat Rev Clin Oncol. 2023;20(6):359-371.

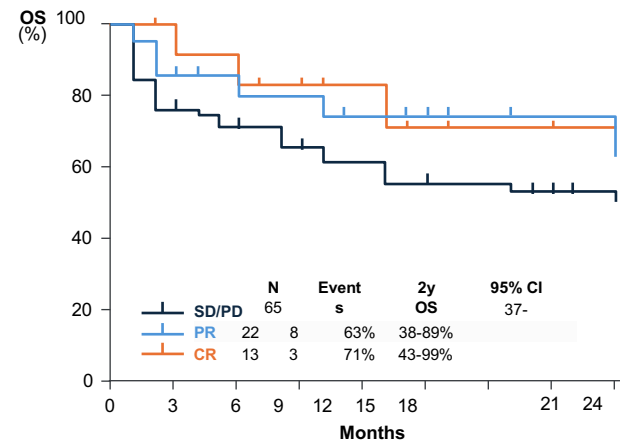
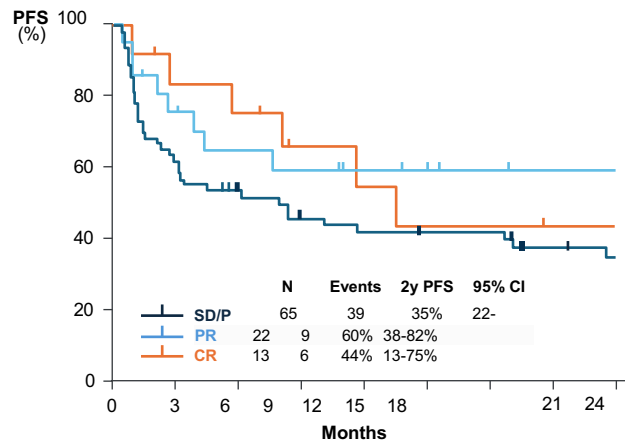
Response to bridging therapy and efficacy & safety outcomes with CAR T-cell therapy



2L+

RW axi-cel

- mFU: 26 months
- Outcomes from a retrospective, single centre study in 240 patients with R/R LBCL treated with axi-cel between January 2018 and December 2021
- 13 patients were in CMR at the time of axi-cel infusion^a



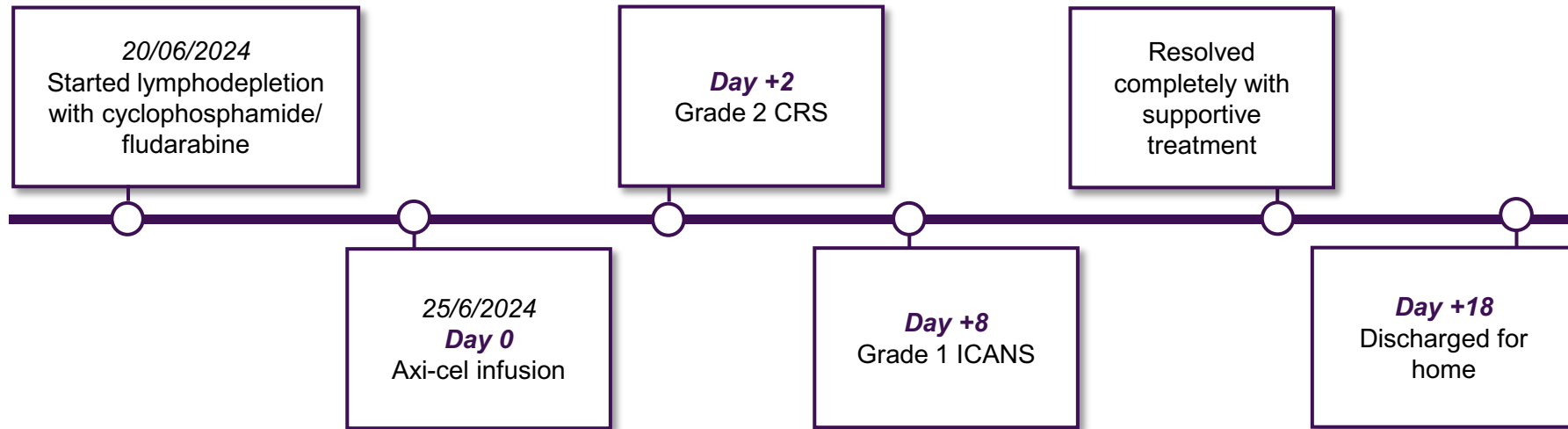
	CMR	PR	SD/PD
Grade ≥3 CRS, %	15	5	9
Grade ≥3 ICANS, %	23	36	39



Patients with pre-infusional CMR treated with axi-cel have comparable safety and efficacy profiles to those with pre-infusional active disease

a: A propensity score was calculated using logistic regression and patients in SD/PD were matched 5:1 with patients in CMR while patients in PR were matched 2:1 with patients in CMR. 2L+, second line or later; AE, adverse event; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CI, confidence interval; CMR, complete metabolic response; CR, complete response; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; mFU, median follow-up; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; R/R, relapsed/refractory; RW, real-world; SD, stable disease; y, year. Jallouk AP, et al. Haematologica 2023;108:1163-1167.

CAR T-cell treatment



Bridging therapy

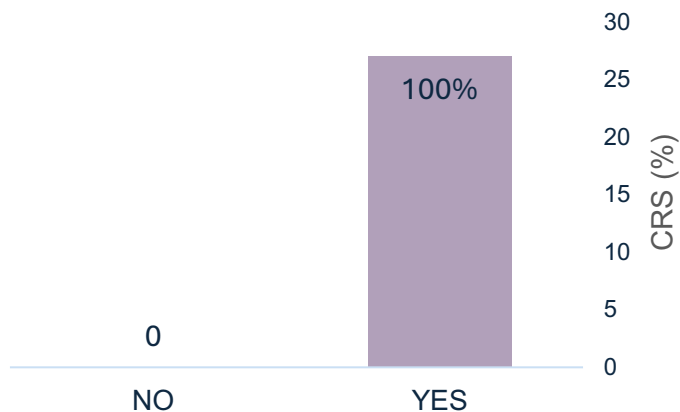
2L therapy

Case study details, based on a real patient, are provided by the Speaker.

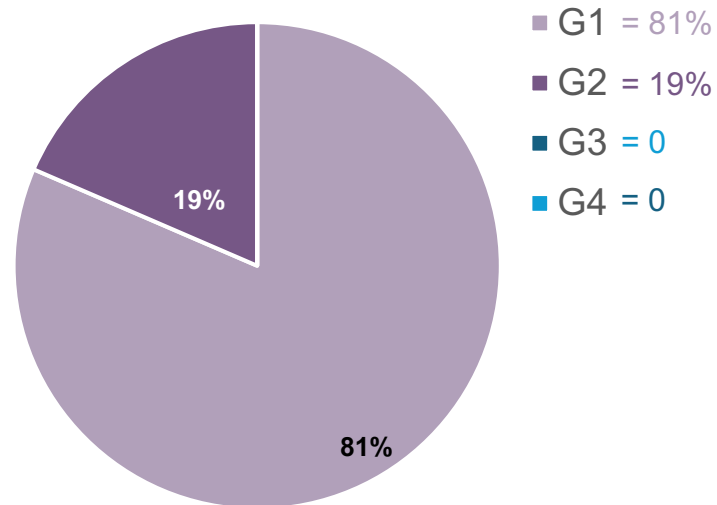
2L, second-line therapy; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

RWE – First 30 cases at Princess Noorah Oncology Center: Toxicities (CRS/ICANS)

CRS

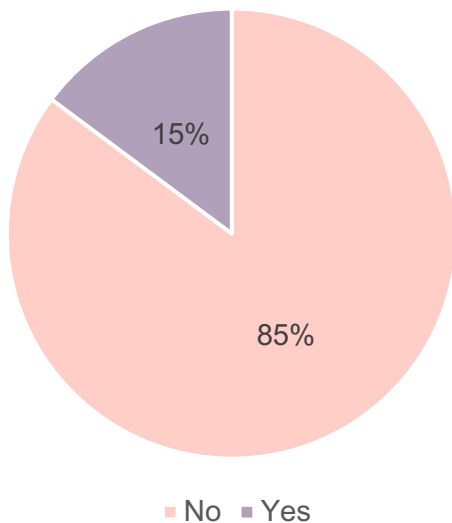


Grade of CRS

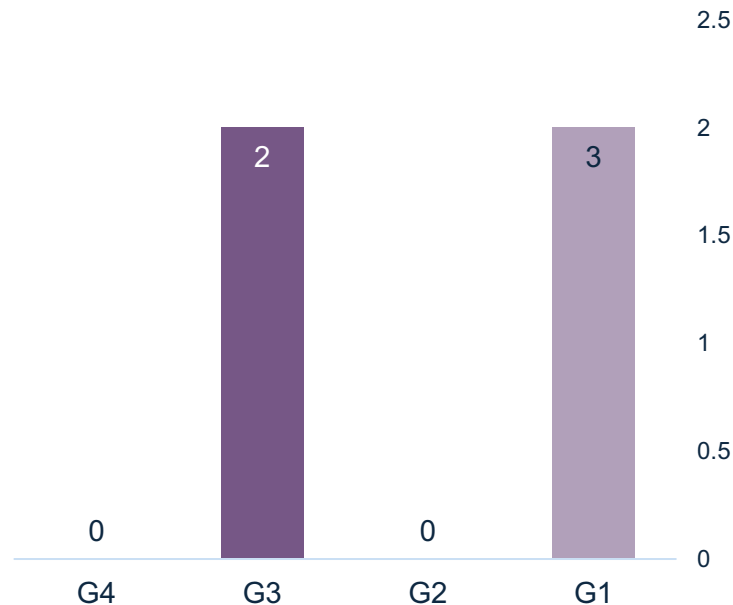


RWE – First 30 cases at Princess Noorah Oncology Center: Toxicities (CRS/ICANS)

ICANS



Grade of ICANS



King Faisal Specialist Hospital & Research Centre: Axi-cel experience in DLBCL/HGBCL

Non-Western Real-World Experience of Axi-Cel CAR-T in Refractory/Relapsed B-Cell Lymphoma from a Tertiary Center in Saudi Arabia

Khalid Alsuhaibani, MD^{1*}, Amal Hejab, MD^{1*}, Syed Osman Ahmed, BSc, FRCPath, MRCP^{1*}, Ali Alahmari, MD^{1*}, Amr Hanbali, MD^{1*}, Walid Rasheed, MD¹, Alfadel Alshaibani, MD^{1*}, Naeem A. Chaudhri, MD¹, Ayman Saad, MD¹, Shaykhah Alotaibi, MD^{1*}, Hanan Alkhalidi, MD^{1*}, Abdullah Alamer, MD^{1*}, Mansour Alfayez, MD¹, Saud Alhayli, MD^{1*}, Marwan Shaheen, MD^{1*}, Feras Abdulaziz Alfuraih, MD^{1*}, Ahmad S. Alotaibi, MD^{1*}, Hadeel Samarkandi^{2*}, Farhatullah Syed, PhD^{3*}, Fahad Alsharif, MD^{1*}, Fahad Almohareb, MD¹, Hazza Alzahrani, MD^{1*}, Mahmoud Aljurf, MD^{1*}, Riad Elfakih, MD^{1*} and Abdulwahab Albabtain, MD^{1*}

ASH 2024 Abstract. *Alsuhabani and Hejab et al.*

2L

AE (N=19)

n (%)

CRS

All grade

17 (89)

Grade ≥3

2 (6)

ICANS

All grade

7 (33)

Grade ≥3

3 (16)

3L+

AE (N=31)

n (%)

CRS

All grade

29 (92)

Grade ≥3

3 (4)

ICANS

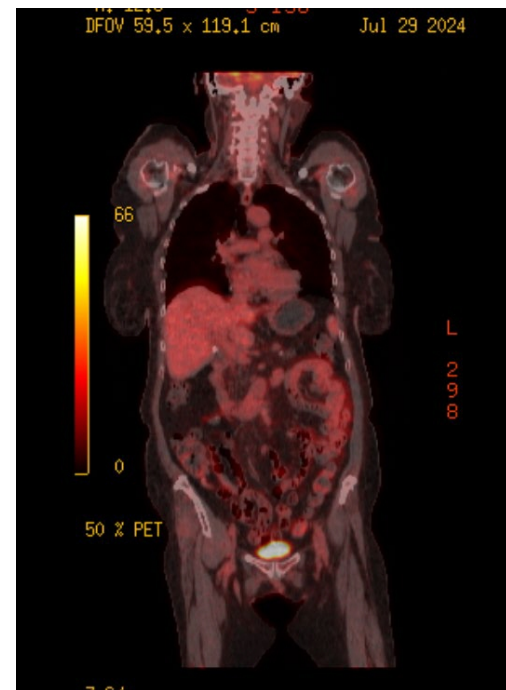
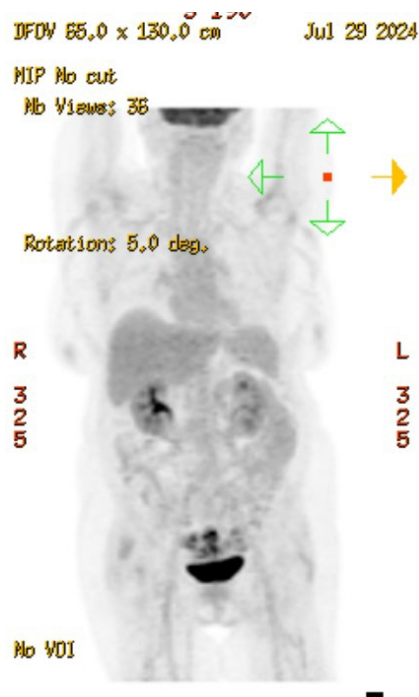
All grade

14 (45)

Grade ≥3

5 (16)

Day 30 PET-scan showed CMR



2L therapy

Follow-up

Safety of CAR T-cell therapy in patients with B-cell lymphoma and concomitant HBV or HCV infection?

Excluded from clinical trials!!! So, RWE is important



LETTER ▶ [Blood](#). 2019 May 17;133(26):2800–2802. doi: [10.1182/blood.2019000888](#) 

Safety of CAR T-cell therapy in patients with B-cell lymphoma and chronic hepatitis B or C virus infection

[Paolo Strati](#)¹, [Loretta J Nastoupil](#)¹, [Luis E Fayad](#)¹, [Felipe Samaniego](#)¹, [Sherry Adkins](#)¹, [Sattva S Neelapu](#)^{1,✉}

▶ [Author information](#) ▶ [Article notes](#) ▶ [Copyright and License information](#)

PMCID: PMC7265784 PMID: [31101626](#)

- Chronic HBV with*
 - HBsAg, positive; anti-Hbc, positive; anti-Hbe, positive; HBe Ag, negative; HBc-IgM Ab, negative; antiHbs, 0.45; HBV viral load, 16
 - LFTs normal
 - No cirrhosis
- Treated with double coverage for three months starting with conditioning (entecavir & tenofovir) then continued on entecavir*
- No reactivation*

No fulminant hepatitis was observed in any of the 3 patients receiving axi-cel¹

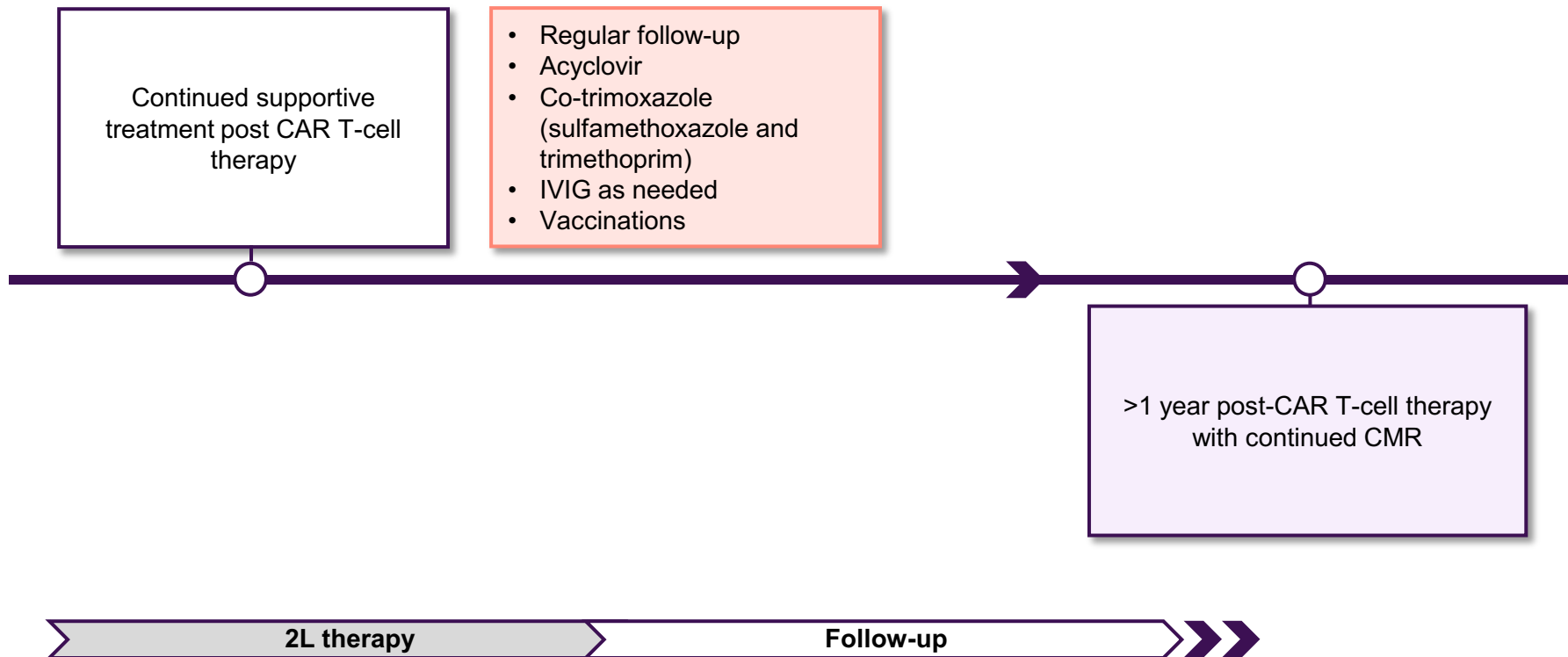


*Case study details, based on a real patient, are provided by the Speaker.

anti-HBc, anti-hepatitis B core antibody; anti-HBe, anti-hepatitis B e-antibody; anti-HBs, anti-hepatitis B surface antibody; CAR, chimeric antigen receptor; HBc-IgM Ab, hepatitis B core immunoglobulin M antibody; HBeAg, hepatitis B e-antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; LFT, liver function test; RWE, real-world evidence.

Strati P, et al. *Blood* 2019;133(26):2800-2802.

Follow-up post CAR T-cell therapy



Case study details, based on a real patient, are provided by the Speaker.

2L, second-line therapy; CAR, chimeric antigen receptor; CMR, complete metabolic response; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IVIG, intravenous immunoglobulin.

Thank you

Navigating the Complexity of an
Evolving Treatment Landscape in R/R Lymphomas

A R/R DLBCL Patient with High Tumor Volume

Dr Ahmad Alsaeed

Consultant Adult Hematology/BMT
Deputy Chairman Princess Norah Oncology Centre PNOC
King Abdulaziz Medical City, Ministry of National Guard
Jeddah-Saudi Arabia

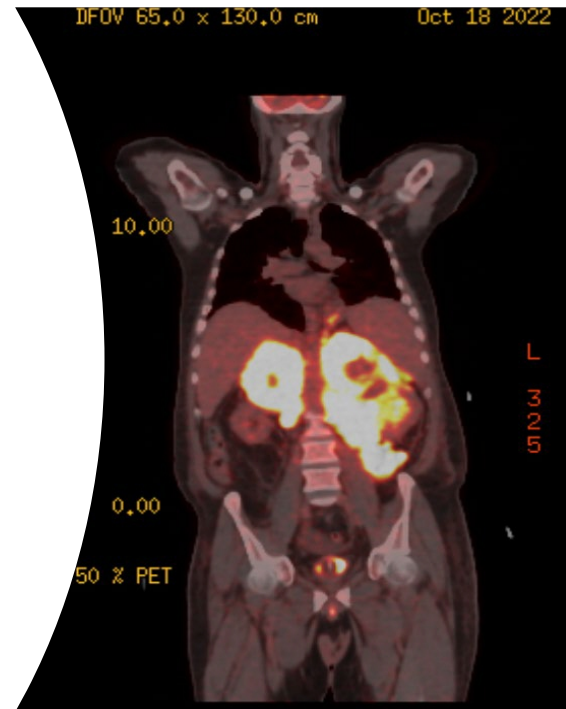
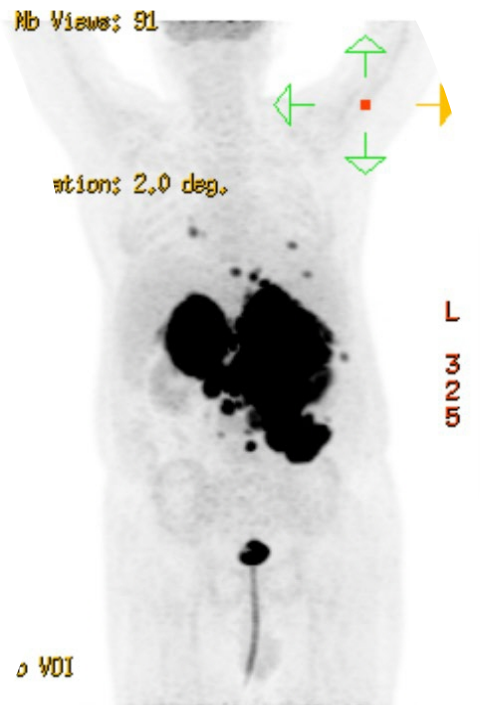
Navigating the Complexity of an
Evolving Treatment Landscape in R/R Lymphomas

Patient background

56-year-old man with unremarkable past medical history presented Oct 2022 with:

- B symptoms
- Abdominal masses
- AKI

- Biopsy confirmed DLBCL
- FISH negative for C-MYC and BCL2 and positive for BCL6
- No CNS or BM Involvement



Bilateral bulky adrenal masses (Left, 20×13×11 cm; Right, 10×8×8 cm)
Multiple abdominal LAP, largest 3.5 cm
Nodular peritoneal thickening and multiple deposits

Diagnosis

Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

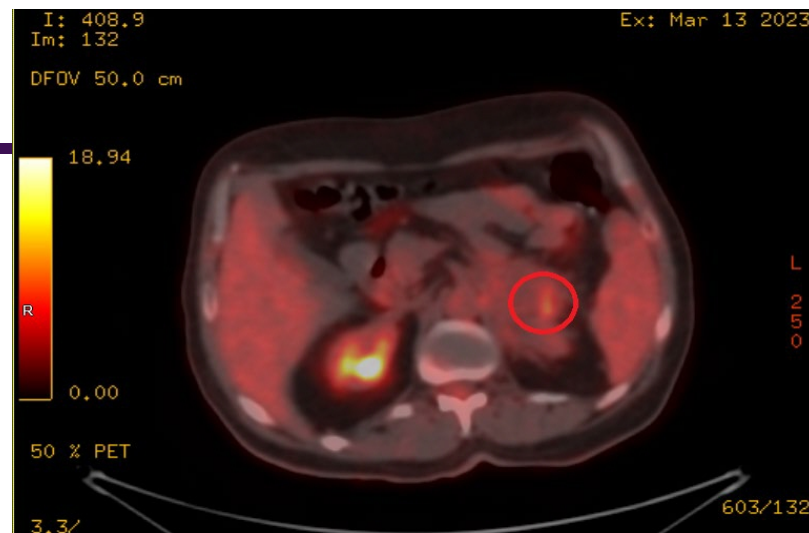
AKI, acute kidney injury; BM, bone marrow; CNS, central nervous system; CT, computed tomography; DLBCL, diffuse large B-cell lymphoma; DM, diabetes mellitus; FISH, fluorescence in situ hybridization; LAP, lymphadenopathy.

1L treatment

- Treated with 6 cycles of R-CHOP and prophylactic HDMTX, completed Feb 2023
- Interim CT-scan assessment showed PR

EOT PET-scan showed that disease within the abdomen and pelvis has markedly improved.

There is still residual tissue seen at the level of the left adrenal extending down to the level of the left kidney.



Left adrenal lesion core needle biopsy was **negative**

Diagnosis

1L therapy

Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

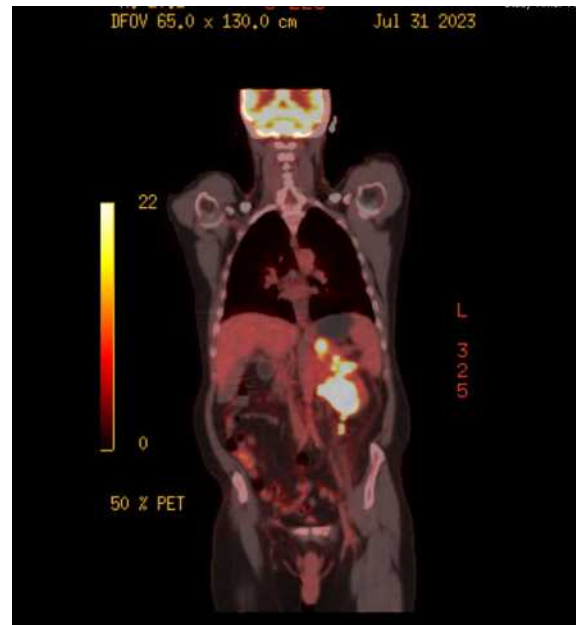
1L, first-line, therapy; CT, computed tomography; EOT, end of treatment; HDMTX, high-dose methotrexate; PET, positron emission tomography; PR, partial response; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone.

Planned and treated with consolidative radiotherapy with 36 Gy, completed 18 May 2023

Follow-up PET-Scan on 31/7/2023
Showed disease progression DS5
(left adrenal/renal mass)

Left renal lesion, biopsy: 14/8/2023

***LARGE B-CELL LYMPHOMA, CONSISTENT
WITH DIFFUSE LARGE B-CELL
LYMPHOMA, NOT OTHERWISE SPECIFIED,
NON-GERMINAL CENTER TYPE**



Refractory LBCL to R-CHOP/Radiotherapy

Diagnosis

1L therapy

R/R disease

Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

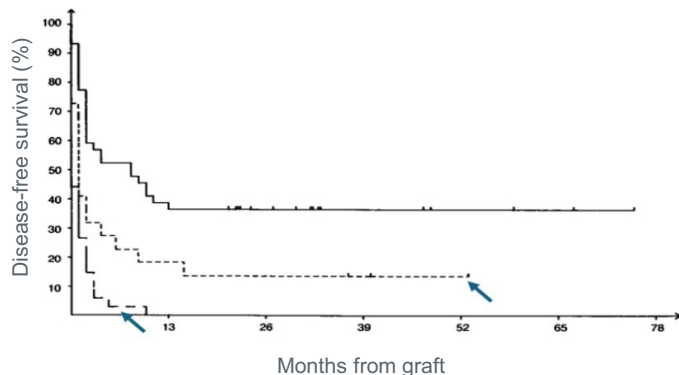
1L, first-line, therapy; PET, positron emission tomography; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone; R/R, relapsed/refractory.

Treatment/outcomes of R/R LBCL

- Until relatively recently, the prognosis of patients with R/R DLBCL was very poor, and treatment options were very limited¹
- The SOC therapy with potential for cure for this patient population is HDCT-ASCT if the lymphoma is chemosensitive²

No role of autologous HCT in chemorefractory disease

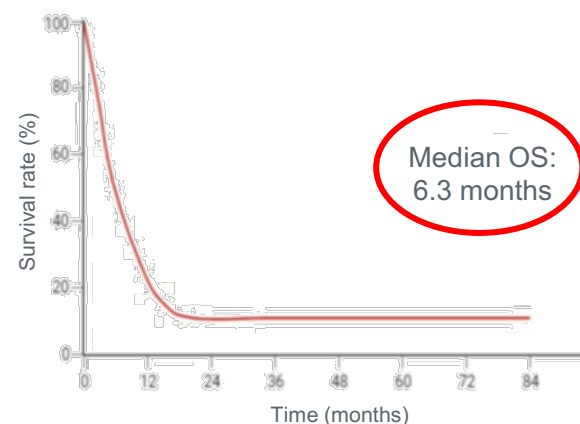
Actuarial three-year disease-free survival according to response to initial or salvage chemotherapy.^{3*}



Scholar-1: Pooled response rates to commencement of salvage therapy²

- Outcomes reported from a 2017 data analysis from two observational cohorts and two large phase 3 clinical trials in DLBCL
- Patients with progressive disease or stable disease as best response
- Response rates and OS estimated at time of initiation of salvage therapy
- Pooled ORR was 26% and CR was 7%

Scholar-1: Pooled OS after salvage therapy (N=603)¹



Adapted from: Crump M, et al. J Clin Oncol 2017;34:7516.

*The solid line indicates patients with sensitive relapses, the dashed line (---) patients with resistant relapse, and the broken line (— — —) patients with no complete remission. The small vertical marks indicate the survival of patients for the indicated period.

CR, complete response; DLBCL, diffuse large B cell lymphoma; HCT, hematopoietic cell transplantation; HDCT-ASCT, high-dose chemotherapy with autologous stem cell transplantation; NHL, non-Hodgkin lymphoma; ORR, objective response rate; OS, overall survival; PMBCL, peripheral mediastinal B cell lymphoma; R/R, relapsed/refractory; SOC, standard of care; TFL, transformed follicular lymphoma.

1. Crump M, et al. J Clin Oncol 2017;34:7516. 2. Bento L, et al. Blood Adv 2025;9(13):3281-3292. 3. Philip T, et al. N Engl J Med 1987;316:1493-8.

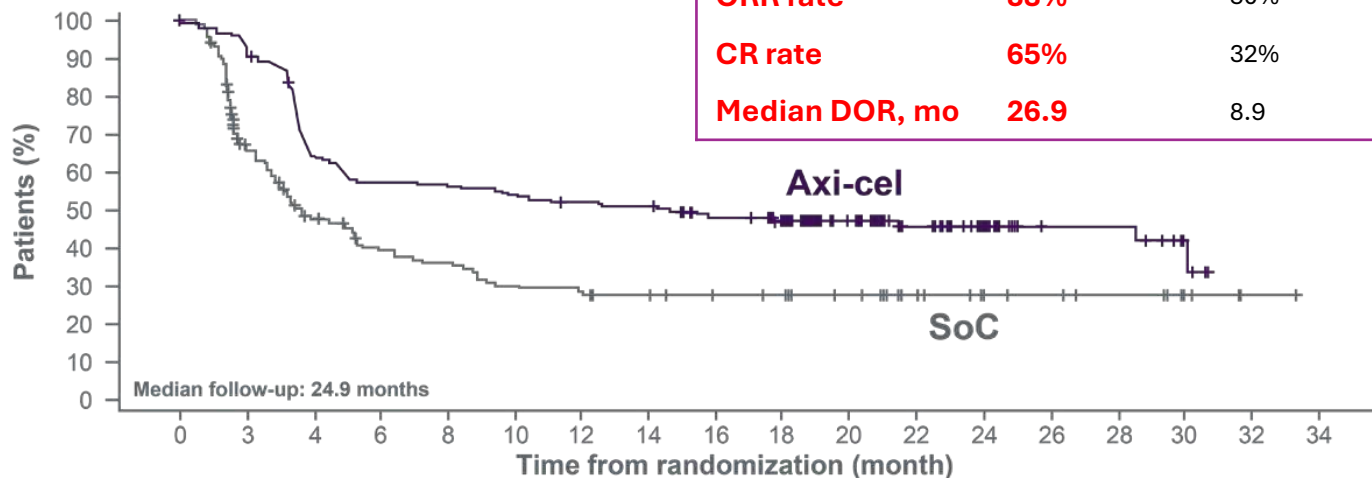
Role of CAR T-cells in R/R LBCL

- Clinical trials
- Real-world evidence

ZUMA 7: Significant improvement in efficacy with 2L axi-cel vs SoC

Adult patients with DLBCL refractory to or relapsed ≤ 12 months after CIT (N=359)¹

PFS by IRC (ITT population)



Endpoint	Axi-cel (n=180)	SoC* (n=179)
Median EFS, mo [†]	8.3	2
Estimated 24-mo EFS	41%	16%
ORR rate	83%	50%
CR rate	65%	32%
Median DOR, mo	26.9	8.9

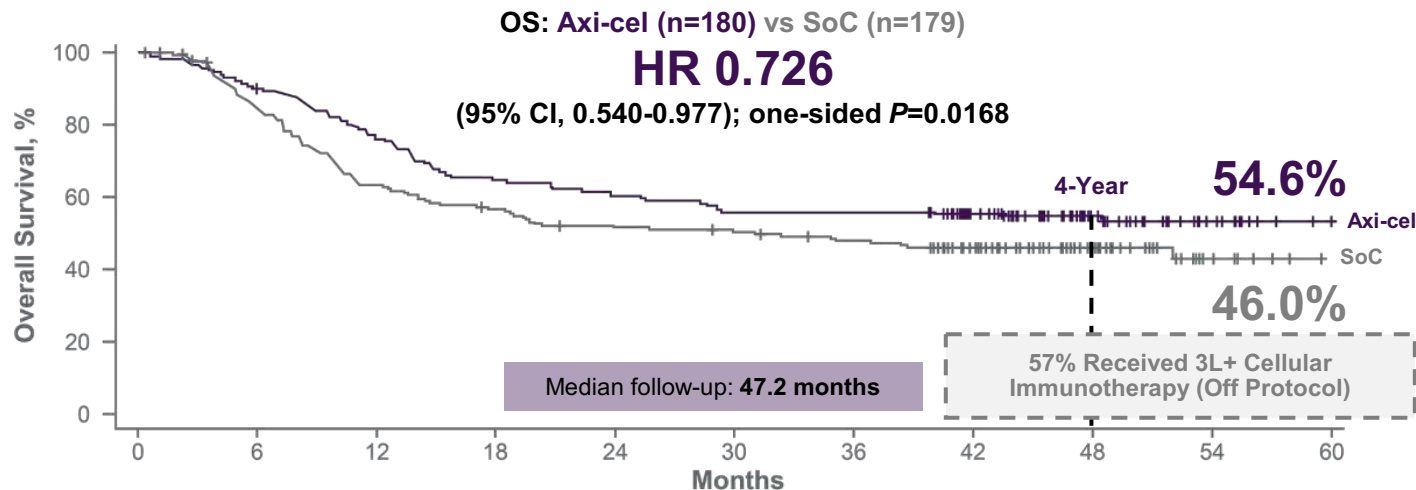
- Improvement in EFS with axi-cel was consistent in all pre-specified key subgroups²
- An expected level of high-grade AEs occurred, including CRS and NEs²
- Consistent outcomes were reported in patients aged ≥ 65 years²

*SoC included two or three cycles of investigator-selected, protocol-defined CIT, followed by HDC with ASCT in patients with a response to the CIT;

[†]EFS defined as the time from randomization to the earliest date of disease progression according to the Lugano classification, the commencement of new therapy for lymphoma, or death from any cause
2L, second line; AE, adverse event; axi-cel, axicabtagene ciloleucel; CIT, chemoimmunotherapy; CR, complete response; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; EFS, event-free survival; IRC, independent review committee; ITT, intention to treat; NE, neurologic event; ORR, objective response rate; PFS, progression-free survival; SoC, standard of care.

1. Locke FL, et al. N Engl J Med 2022; 386:640-654. 2. Westin JR, et al. N Engl J Med 2023; 389:148-157 (incl. Suppl.).

ZUMA 7: At the OS primary analysis, there was 27.4% reduction in the risk of death with axi-cel vs SoC



The reduction in risk of death with axi-cel was **27.4%**

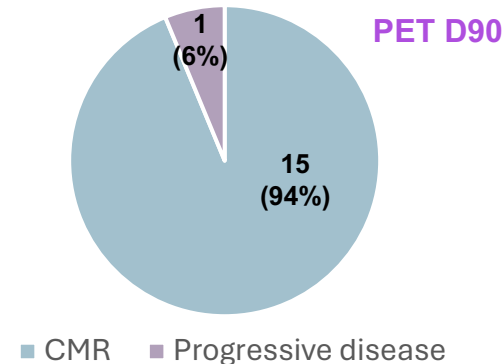
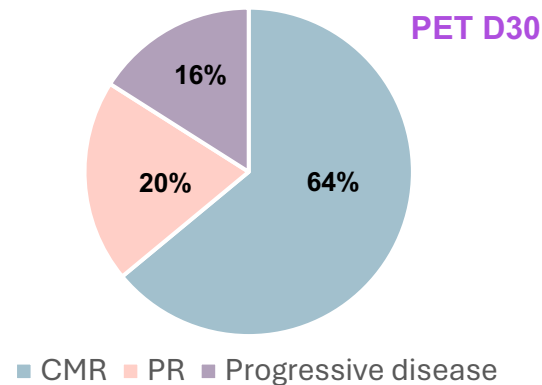
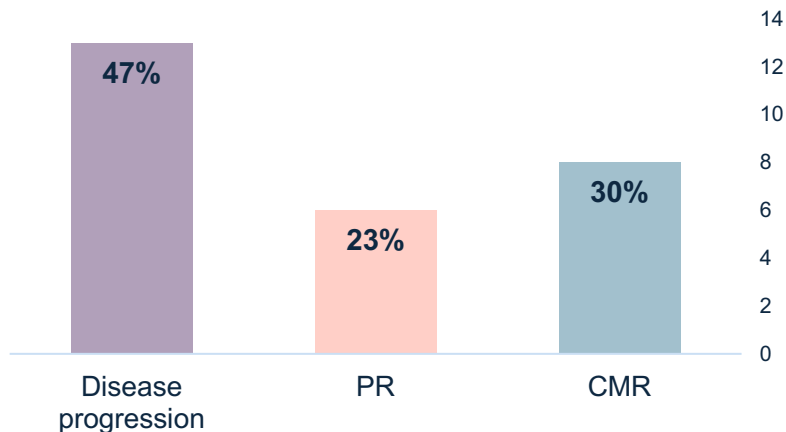
Axi-cel delivered high rates of survival, with **median OS not reached at 47.2 months'** median follow-up (vs 31.1 months in SoC)^{a,b}

a Approximately 30% for early R/R LBCL in ORCHARRD (van Imhoff GW, et al. J Clin Oncol. 2017;35:544-551). b <40% for those with prior rituximab and early R/R LBCL in CORAL (Gisselbrecht C, et al. J Clin Oncol. 2010;28:4184-4190).

3L, third line; axi-cel, axicabtagene ciloleucel; HR, hazard ratio; LBCL, large B-cell lymphoma; R/R, relapsed/refractory; SOC, standard of care.

1. Westin JR, et al. N Engl J Med 2023;389:148-157. 2. Westin JR, et al. ASCO 2023 (abstract 107).

RWE – First 30 cases at Princess Noorah Oncology Center: Outcomes by Disease status pre-CAR T-cell infusion (PET)



Real-world evidence data from the Speaker's Center provided by the Speaker.

CAR, CAR, chimeric antigen receptor; CMR, complete metabolic response; PET, positron emission tomography; PR, partial response; RWE, real-world evidence.

King Faisal Specialist Hospital & Research Centre: Axi-cel experience in DLBCL/HGBCL

Non-Western Real-World Experience of Axi-Cel CAR-T in Refractory/Relapsed B-Cell Lymphoma from a Tertiary Center in Saudi Arabia

Khalid Alsuhaibani, MD^{1*}, Amal Hejab, MD^{1*}, Syed Osman Ahmed, BSc, FRCPath, MRCP^{1*}, Ali Alahmari, MD^{1*}, Amr Hanbali, MD^{1*}, Walid Rasheed, MD¹, Alfadel Alshaibani, MD^{1*}, Naeem A. Chaudhri, MD¹, Ayman Saad, MD¹, Shaykhah Alotaibi, MD^{1*}, Hanan Alkhaldi, MD^{1*}, Abdullah Alamer, MD^{1*}, Mansour Alfayez, MD¹, Saud Alhayli, MD^{1*}, Marwan Shaheen, MD^{1*}, Feras Abdulaziz Alfraih, MD^{1*}, Ahmad S. Alotaibi, MD^{1*}, Hadeel Samarkandi^{2*}, Farhatullah Syed, PhD^{3*}, Fahad Alsharif, MD^{1*}, Fahad Almohareb, MD¹, Hazza Alzahrani, MD^{1*}, Mahmoud Aljurf, MD^{1*}, Riad Elfakih, MD^{1*} and Abdulwahab Albabtain, MD^{1*}

ASH 2024 Abstract. *Alsuhabani and Hejab et al.*

2L response rate

Response (N=19)	n (%)
ORR	15 (79)
CR	11 (58)
PR	4 (21)
PD	4 (21)

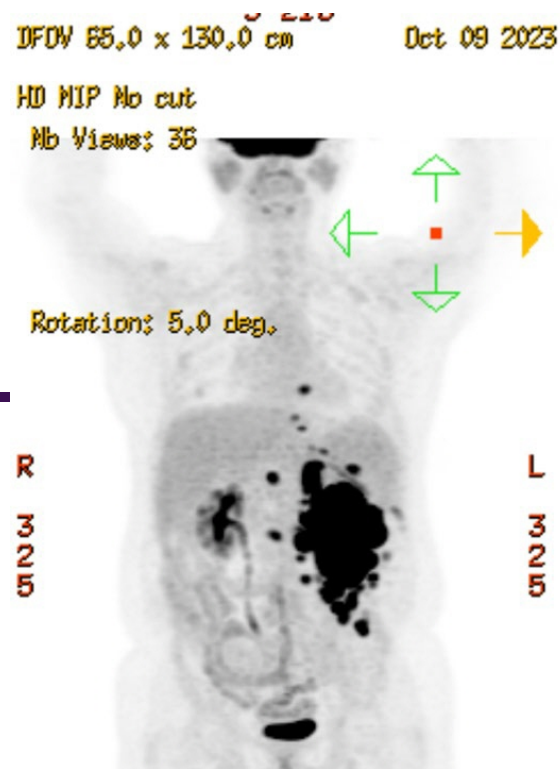
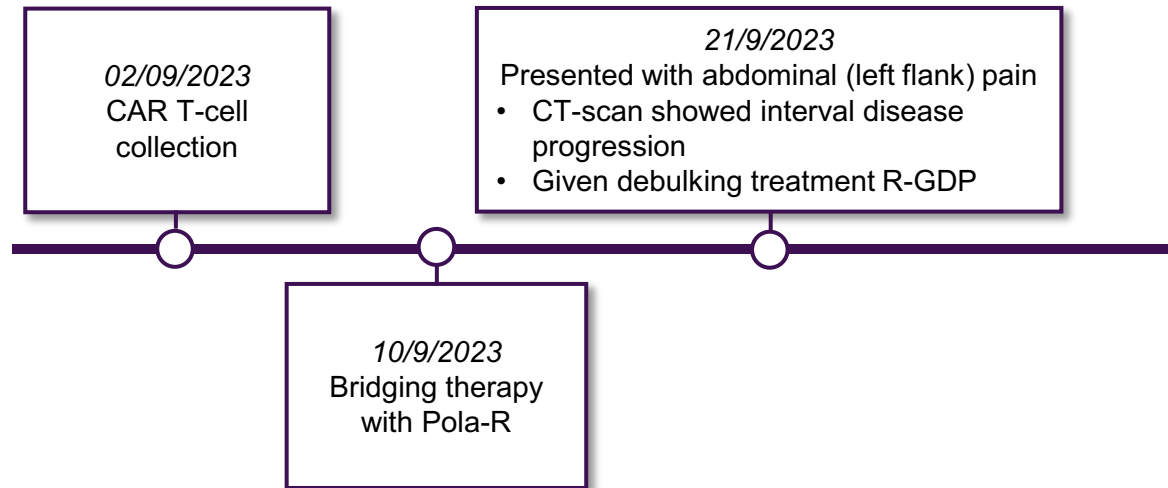
3L+ response rate

Response (N=31)	n (%)
ORR	25 (80)
CR	15 (48)
PR	10 (32)
PD	4 (13)
Died before assessment	2 (6)

At 12 months, **OS 2L 94.7%**, 3L 68.5%

At 12 months **PFS 2L 56.8%**, 3L 53.8%

Bridging therapy



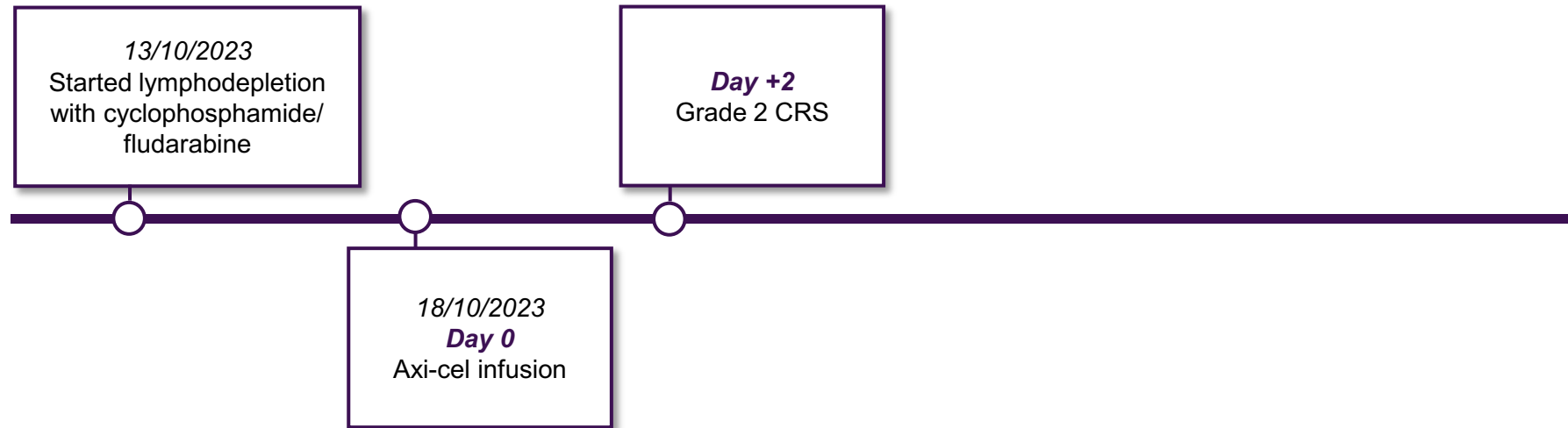
R/R disease

Bridging therapy

Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

2L, second-line therapy; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; Pola-R, polatuzumab vedotin plus rituximab; R-GDP, rituximab, gemcitabine, dexamethasone, cisplatin.

CAR T-cell treatment



Bridging therapy

2L therapy

Case study details, based on a real patient, are provided by the Speaker.

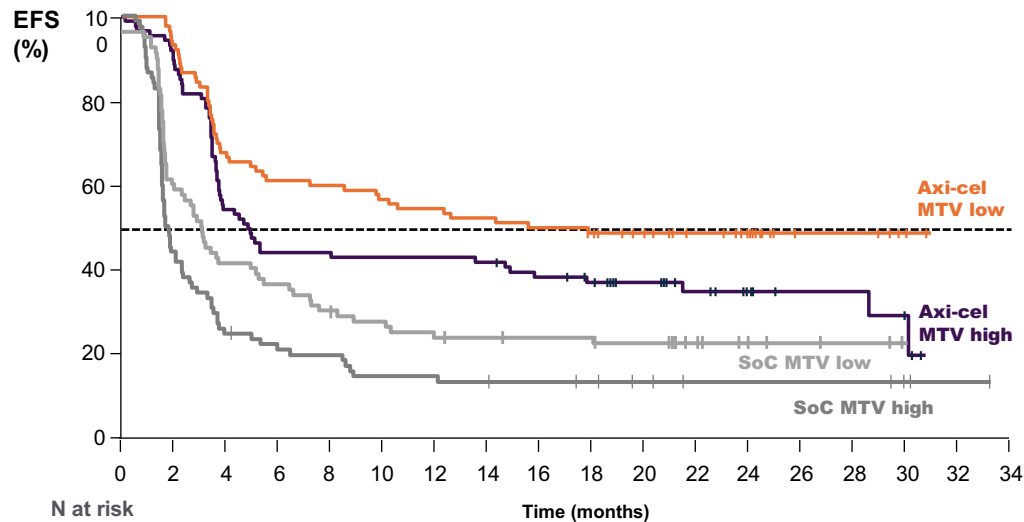
2L, second-line therapy; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CRS, cytokine release syndrome.

Tumor volume and efficacy of axi-cel vs SoC in 2L setting

ZUMA-7

2L

- mFU: 24.9 months
- Exploratory analysis of clinical outcomes in patients with R/R LBCL treated with axi-cel (n=175) vs SoC (chemo + HDCT ± ASCT; n=165) in the ZUMA-7 trial based on metabolic tumor volume



Axi-cel, MTV high	87	80	47	38	38	37	37	36	32	29	22	16	9	6	6	4
Axi-cel, MTV low	88	82	58	53	52	49	47	45	41	38	30	24	17	6	6	2
SoC MTV high	83	36	20	16	15	11	11	10	9	8	6	4	4	4	4	1
SoC MTV low	82	48	33	29	23	21	18	17	16	16	14	8	5	3	2	0

**Axi-cel MTV:
high vs low**
HR: 1.448
(95% CI=0.980-2.139,
p=0.06)

**Axi-cel MTV high
vs SoC MTV high**
HR: 0.417
(95% CI=0.293-0.592,
P<0.001)



Regardless of MTV, axi-cel has demonstrated superior EFS in the 2L setting compared to SoC^a

a: SoC 2L treatment in the curative setting for patients with R/R LBCL is high-dose chemotherapy with ASCT if the disease is responsive to salvage chemoimmunotherapy with ASCT if the disease is responsive to salvage chemoimmunotherapy. 2L, second line; ASCT, autologous stem cell transplantation; axi-cel, axicabtagene ciloleucel; CI, confidence interval; EFS, event-free survival; HDCT, high-dose chemotherapy; HR, hazard ratio; LBCL, large B-cell lymphoma; mFU, median follow-up; MTV, metabolic tumor volume; N, number; R/R, relapsed/refractory; SoC, standard of care. Locke FL, et al. Blood 2024;143:2464-2473.

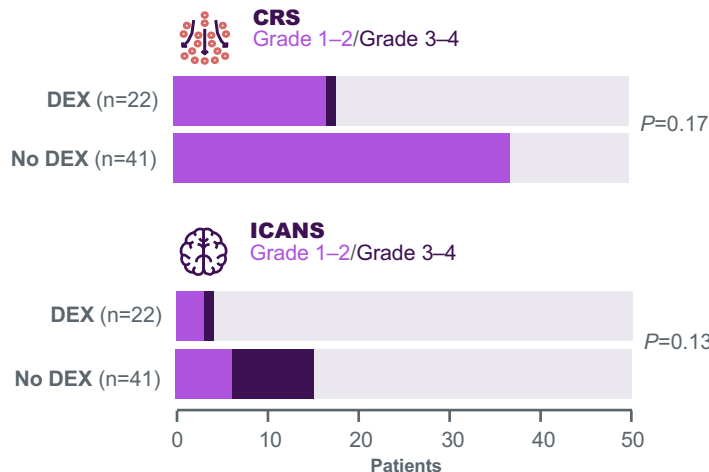
Prophylactic steroids for the management of CRS and ICANS with axi-cel



2L+

RW axi-cel

- University of Pennsylvania
- Real-world retrospective analysis of patients receiving axi-cel between Mar 2018 and Mar 2024 (N=63)



Prophylactic DEX (vs no DEX) reduced:

- Readmission length of hospital stay (3.5 vs 7 days, P=0.16)
- Admission to ICU for CRS/ICANS management (1 vs 6 patients, P=0.19)



Prophylactic management strategies may help mitigate the impact of AEs following CAR T-cell therapy

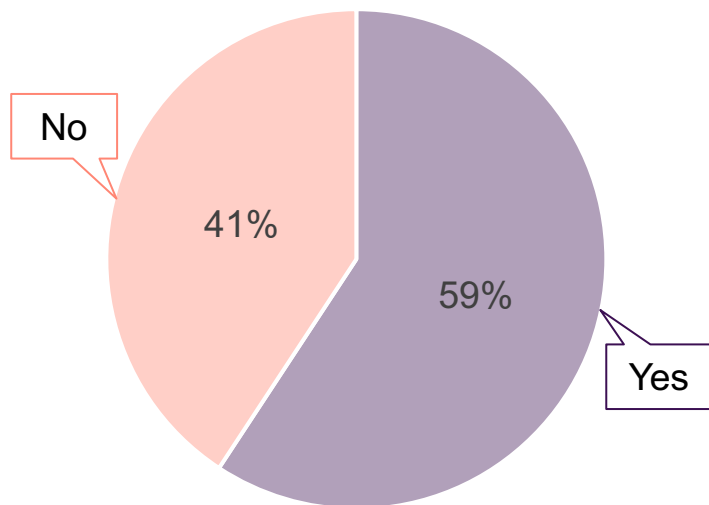
Please refer to your local prescribing information for details of the approved indications in your region.

2L+, second line or later; AE, adverse event; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; DEX, dexamethasone; ICANS, immune effector cell-associated neurotoxicity syndrome; ICU, intensive care unit; RW, real-world.

Adapted from Carulli A, et al. ASH 2024 (Abstract 2275, poster).

Steroid need for CRS management

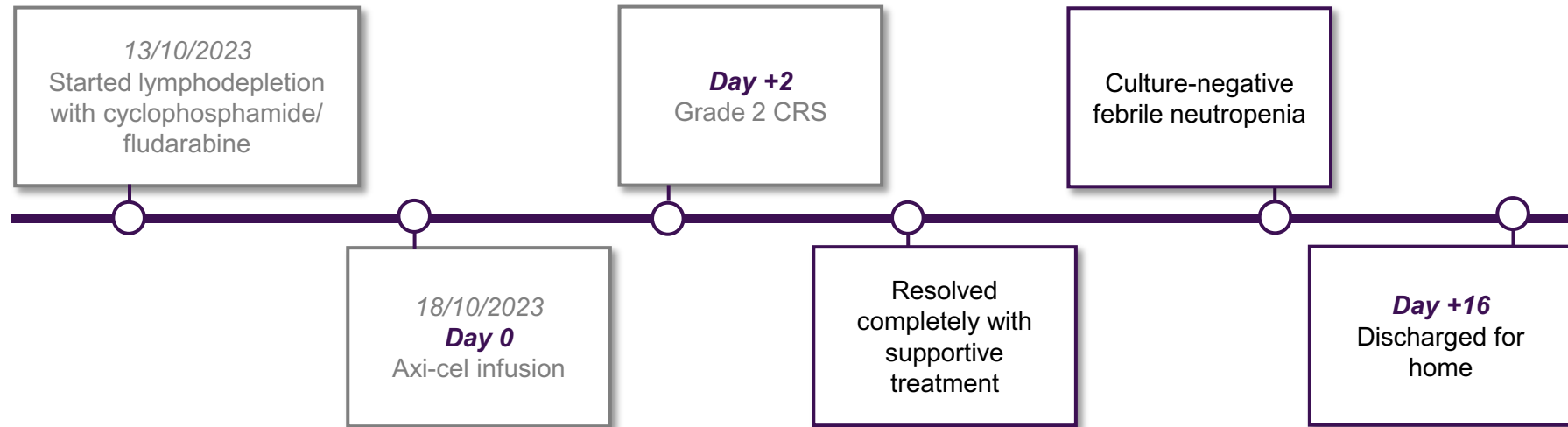
First 30 cases at Princess Noorah
Oncology Center¹



CRS in 100% of patients

- G1 in 81% of patients
- G2 in 19% of patients

CAR T-cell treatment



Bridging therapy

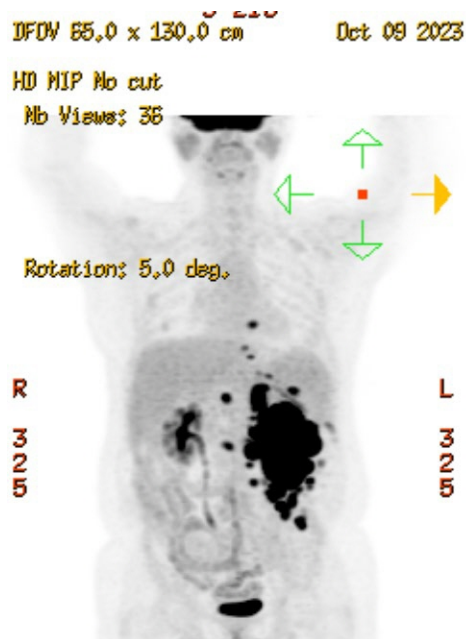
2L therapy

Case study details, based on a real patient, are provided by the Speaker.

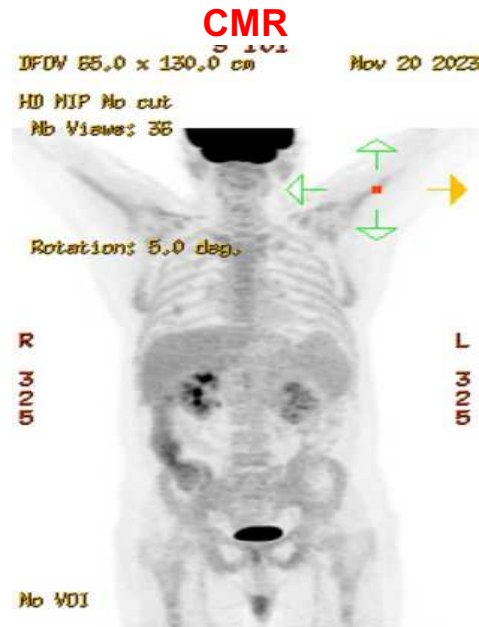
2L, second-line therapy; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CRS, cytokine release syndrome.

Treated with CAR T-cell therapy (axi-cel) in Oct 2023

Pre-CAR T-cell therapy



Day 30 post CAR T-cell therapy



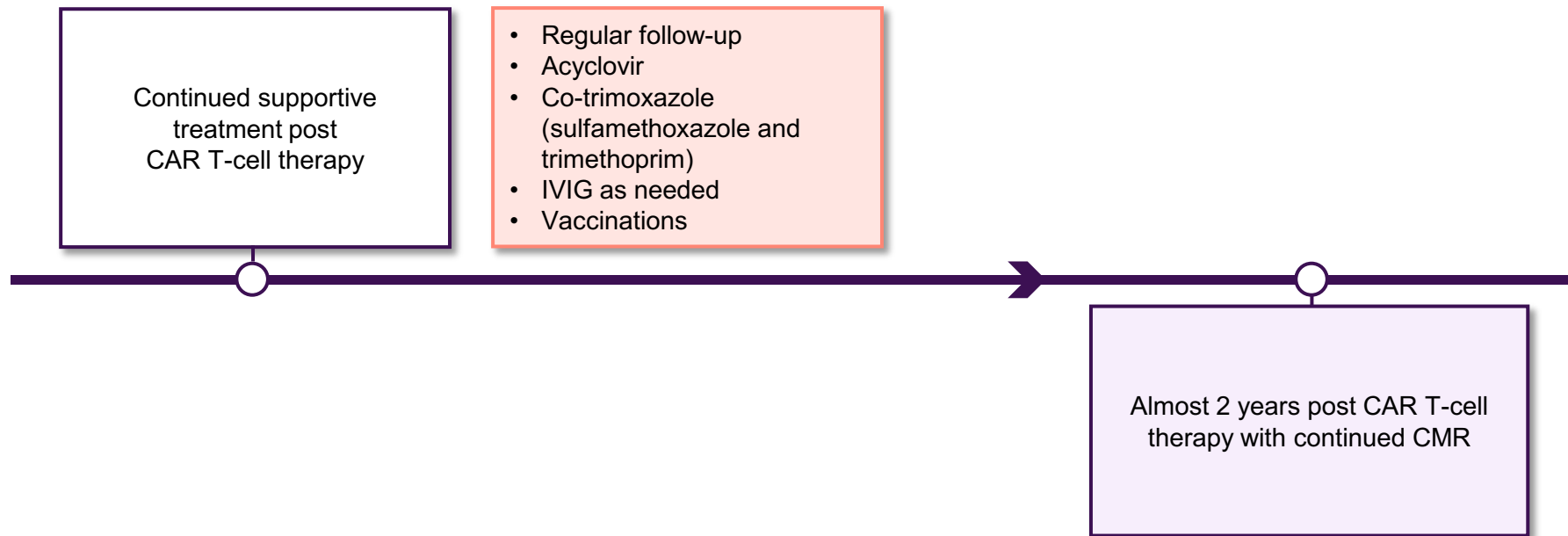
2L therapy

Follow-up

Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

2L, second-line therapy; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CMR, complete metabolic response.

Follow-up post CAR T-cell therapy



2L therapy

Follow-up

Case study details, based on a real patient, are provided by the Speaker.

2L, second-line therapy; CAR, chimeric antigen receptor; CMR, complete metabolic response; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IVIG, intravenous immunoglobulin.

Thank you

Navigating the Complexity of an
Evolving Treatment Landscape in R/R Lymphomas

A R/R DLBCL Patient with Comorbidities

Dr Ahmad Alsaeed

Consultant Adult Hematology/BMT
Deputy Chairman Princess Norah Oncology Centre PNOC
King Abdulaziz Medical City, Ministry of National Guard
Jeddah-Saudi Arabia

**Navigating the Complexity of an
Evolving Treatment Landscape in R/R Lymphomas**

Patient background

70-year-old Saudi man

- Known DM, hypertension, BPH, knee osteoarthritis on treatment
- Presented in *Oct 2023* with few months h/o B symptoms
- O/E lymphadenopathy
- ECOG PS 2
- CNS & BM assessment is negative

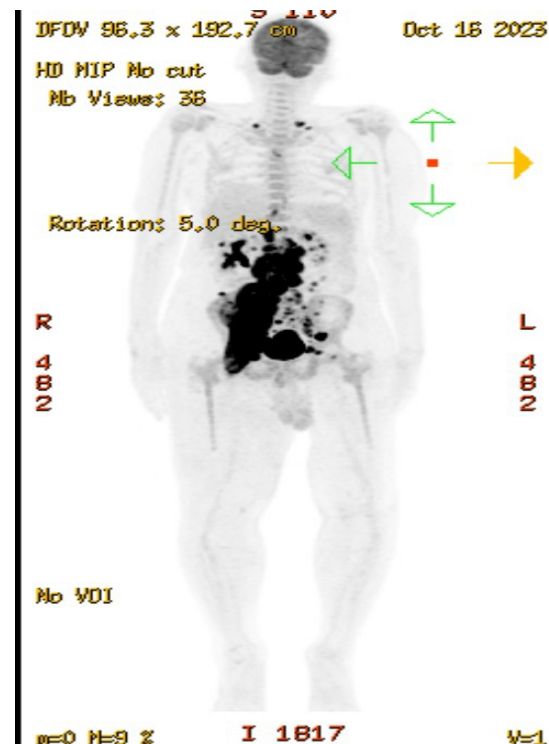
Right inguinal lymph node, biopsy:

- DLBCL, non-GCB
- FISH negative for C-MYC, BCL2, BCL6

Diagnosis

Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

BPH, benign prostatic hyperplasia; BM, bone marrow; CNS, central nervous system; CT, computed tomography; DLBCL, diffuse large B-cell lymphoma; DM, diabetes mellitus; ECOG-PS, Eastern Cooperative Oncology Group Performance Status score; FISH, fluorescence in situ hybridization; GCB, germinal center B-cell; h/o, history of; O/E, on examination; PET, positron emission tomography.

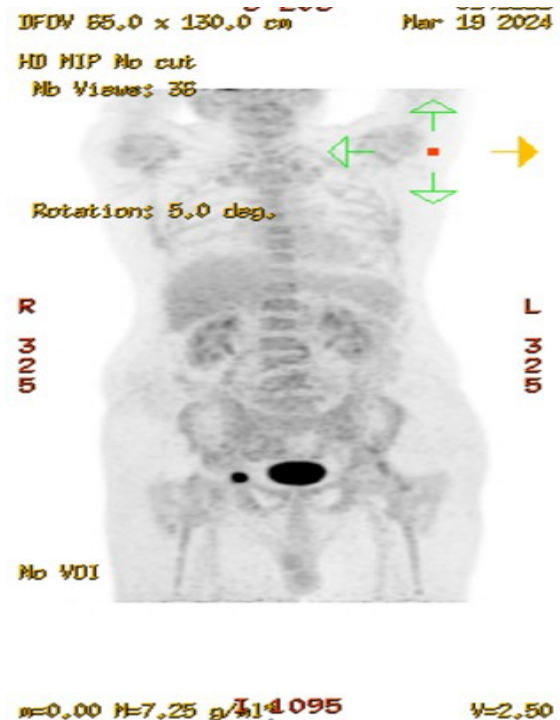


PET/CT Oncology 16/10/2023:

Markedly intense metabolically active bulky disease involving the right iliopsoas muscle, metabolically active lymphadenopathy above and below the diaphragm

1L treatment

- Treated with six cycles of R-CHOP
- Had FN and prolonged counts recovery required some dose adjustment and supportive treatment
- iPET-scan showed PR (DS4)



EOT PET/CT Oncology 19/03/2024 CONCLUSION:

Progressive disease with avid lesion seen in the right inguinal region anterior to the acetabulum SUV Max 17.3 (Deauville 5) which resolved on iPET-scan

Diagnosis

1L therapy

Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

1L, first-line, therapy; CT, computed tomography; DS4, Deauville score 4; FN, febrile neutropenia; iPET, interim PET; PET, positron emission tomography; PR, partial response; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone; SUV Max, maximum standardized uptake value.

Polling question:

A 70-year-old patient with multiple comorbidities has refractory DLBCL after first-line R-CHOP treatment. The patient has an ECOG PS of 2 and normal organ function.

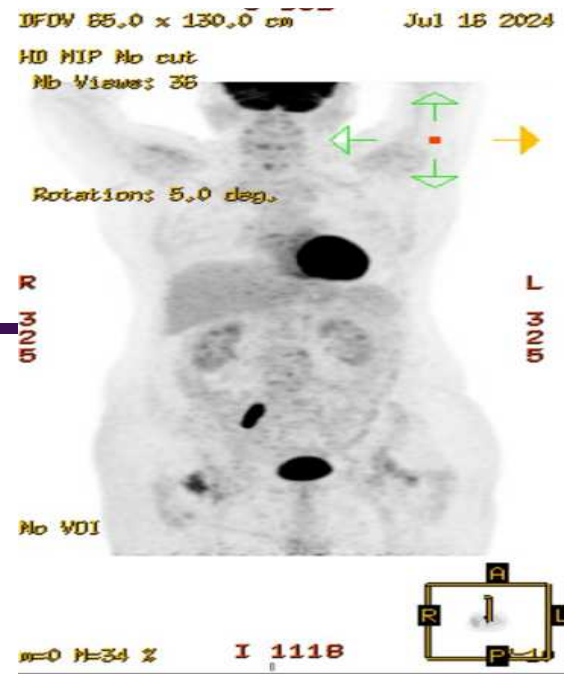
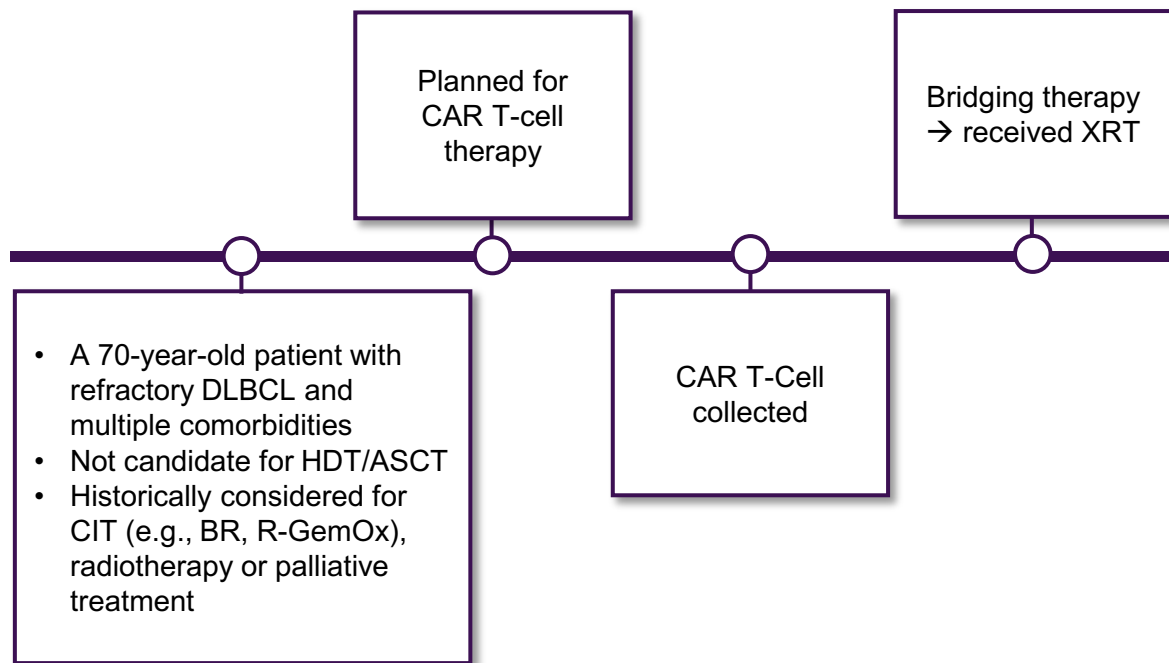
What would your favourable next treatment option be?

- A. HDT/ASCT
- B. CAR T-cell therapy
- C. Radiotherapy
- D. CIT (e.g., Pola-BR)



Scan to vote

Early relapse DLBCL and bridging therapy



PET/CT post-radiation
Deauville score 5

R/R disease

Bridging therapy

Case study details, based on a real patient, and accompanying imaging photos are provided by the Speaker.

BR, bendamustine and rituximab; CAR, chimeric antigen receptor; CIT, chemoimmunotherapy; CT, computed tomography; DLBCL, diffuse large B-cell lymphoma; HDT/ASCT, high-dose therapy / autologous stem cell transplant; PET, positron emission tomography; R-GemOx, rituximab, gemcitabine, and oxaliplatin; R/R, relapsed/refractory; XRT, radiotherapy.

Axi-cel demonstrates consistent outcomes in real-world populations versus clinical trials



2L

RW axi-cel

- mFU: 12 months
- CIBMTR: RW analysis of patients with R/R LBCL receiving axi-cel (Apr 2022– Jul 2023) N=446
- Main reasons for ZUMA-7 ineligibility:^b



Organ impairment, **34%**



Prior malignancy, **16%**

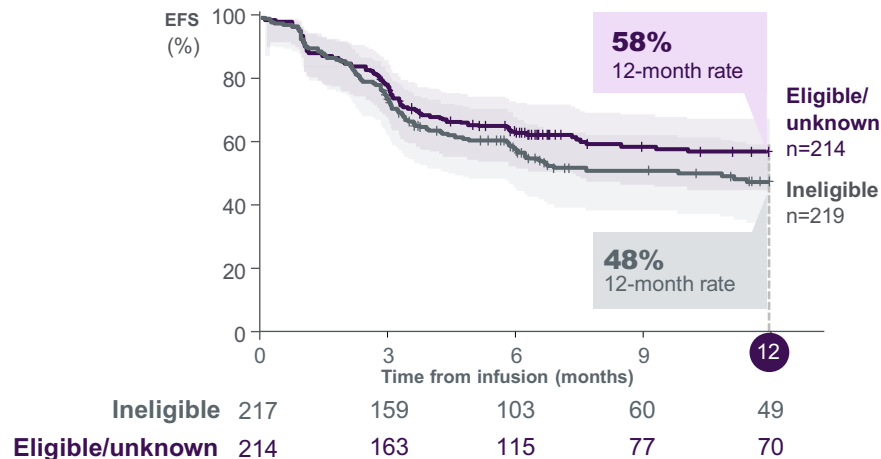


Infection, **4%**



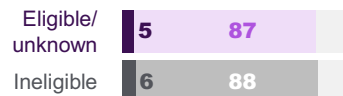
ECOG PS >1, **3%**

EFS by ZUMA-7 eligibility^a

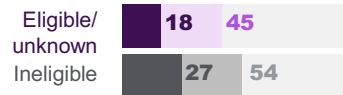


AEs of special interest

CRS (%)



ICANS (%)



Grade ≥3 All grade



Real-world evidence supports the benefits of axi-cel use in a broad patient population, including older patients with comorbidities

a: Analysis by ZUMA-7 eligibility was among patients with DLBCL, HGBCL, and FL Grade 3B; patients with PMBCL were analyzed separately; b: Patients with active central nervous system (CNS) disorder or inadequate renal, hepatic, pulmonary, or cardiac function are likely to be more vulnerable to the consequences of the adverse reactions and require special attention.

2L, second line; AE, adverse event; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CIBMTR, Center for International Blood and Marrow Transplant Research; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group Performance Status score; EFS, event-free survival; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; ICANS, immune effector cell-associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; mFU, median follow-up; PMBCL, primary mediastinal B-cell lymphoma; R/R, relapsed/refractory RW, real-world.

Adapted from Lee DC, et al. ASH 2024 (Abstract 526, oral).

CAR T-cell therapy

12/11/2024

Day 0

Axi-cel infusion

Post CAR T-cell Flu/Cy
conditioning

Bridging therapy

2L therapy

Case study details, based on a real patient, are provided by the Speaker.

2L, second-line therapy; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; Flu/Cy, fludarabine and cyclophosphamide.

At 21:00 hours, spiked fever (**CRS G1**); started on antibiotics

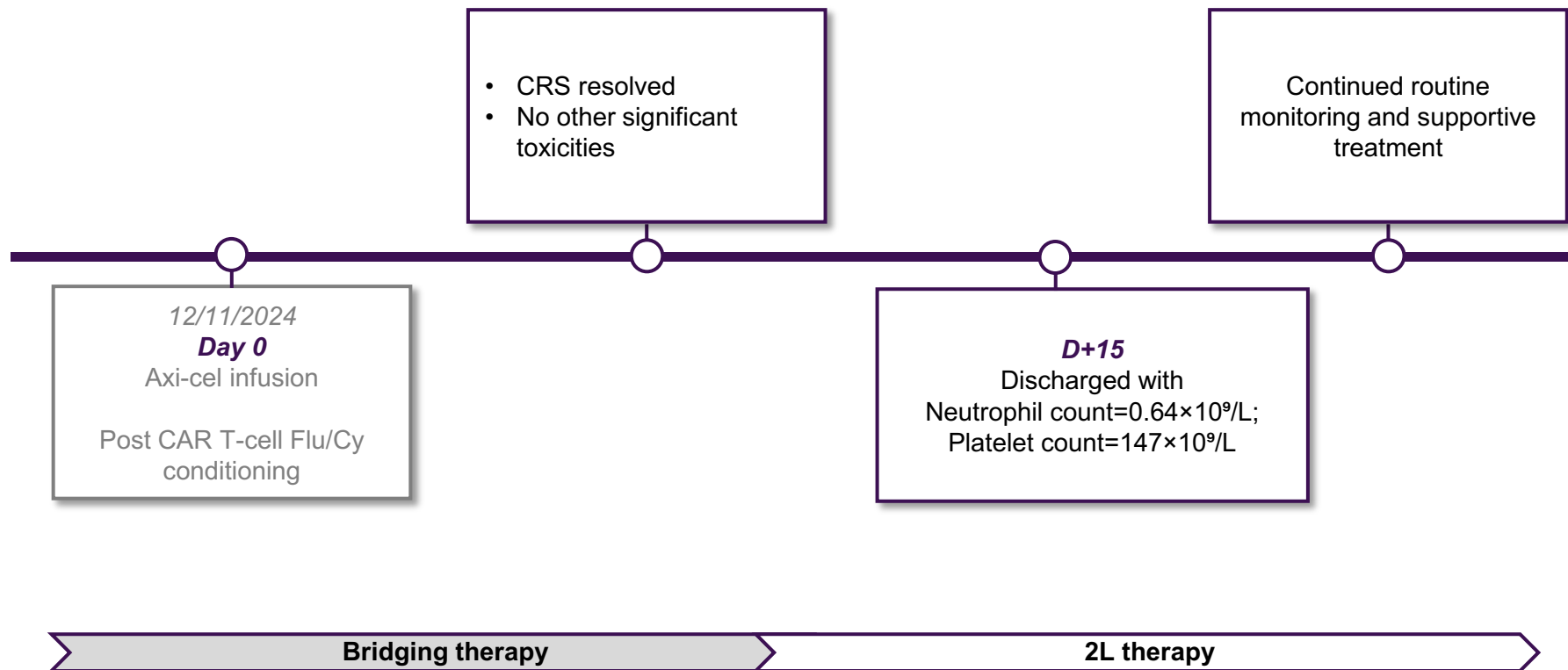


At 04:00 hours, the patient developed a fever of 39.4°C and oxygen saturation of 89% (**Grade 2 CRS**).
Tocilizumab was initiated.

Bridging therapy

2L therapy

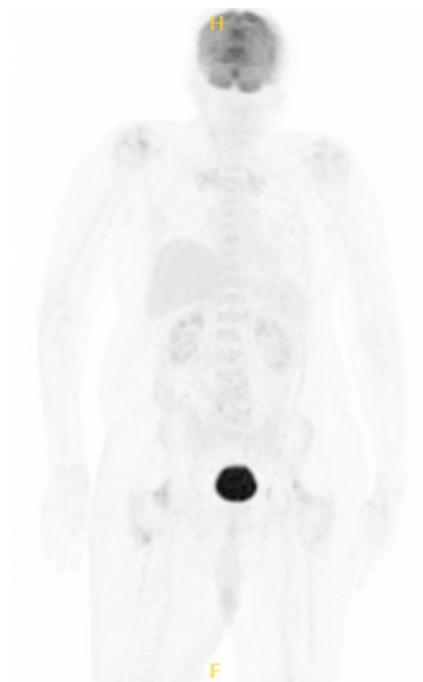
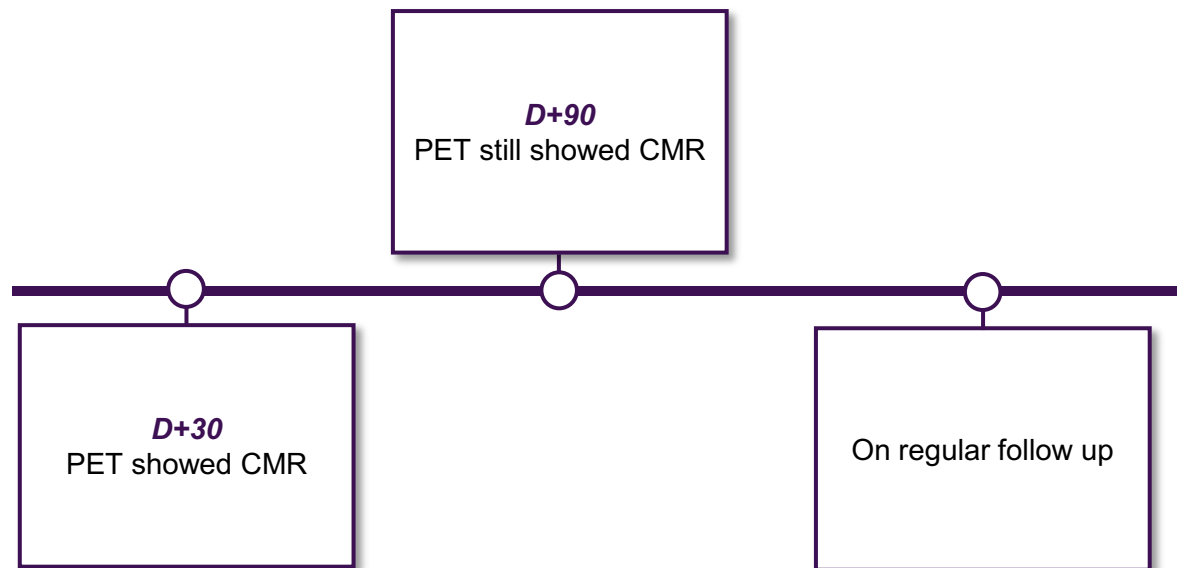
CAR T-cell therapy



Case study details, based on a real patient, are provided by the Speaker.

2L, second-line therapy; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; Flu/Cy, fludarabine and cyclophosphamide.

Follow-up PET-scan



Institution: Neuro

Stu

A

2L therapy

Follow-up

Subgroup analysis of ZUMA-7: Improved overall survival with axi-cel vs SOC in 2L DLBCL among the elderly

Baseline patient and disease characteristics among elderly patients^a

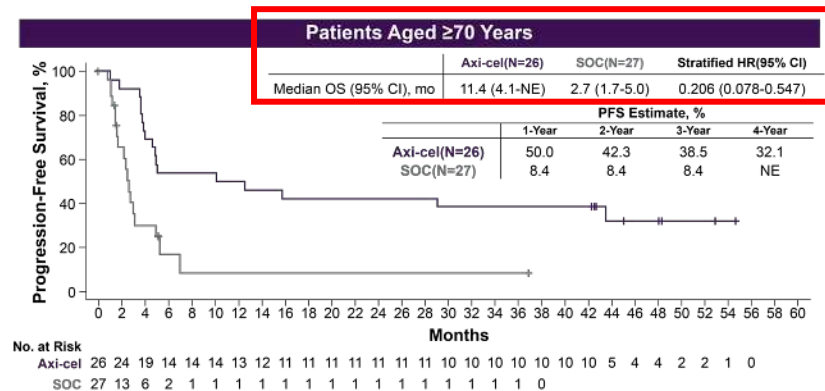
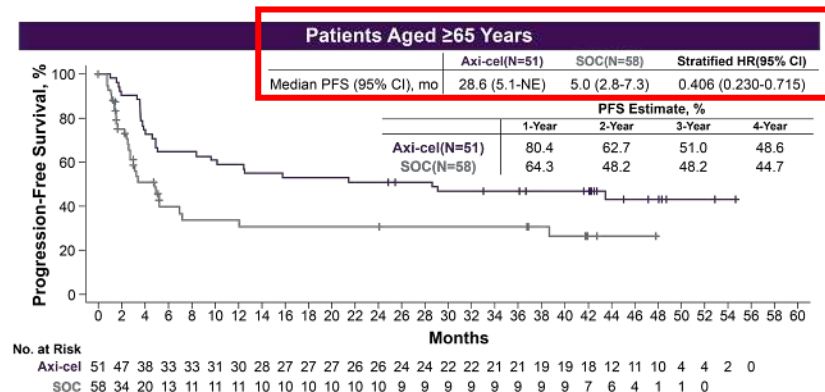
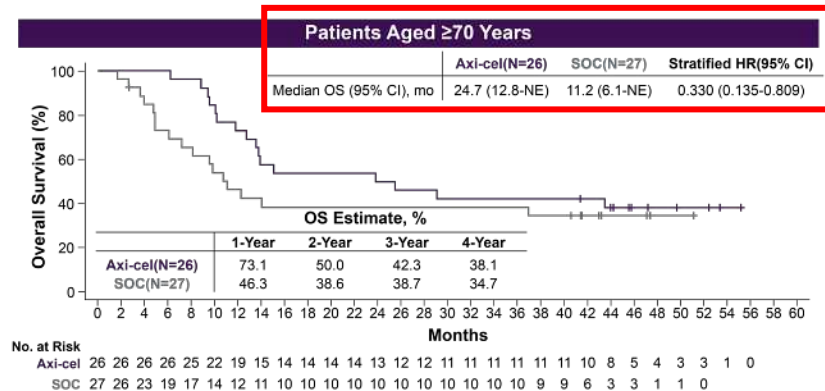
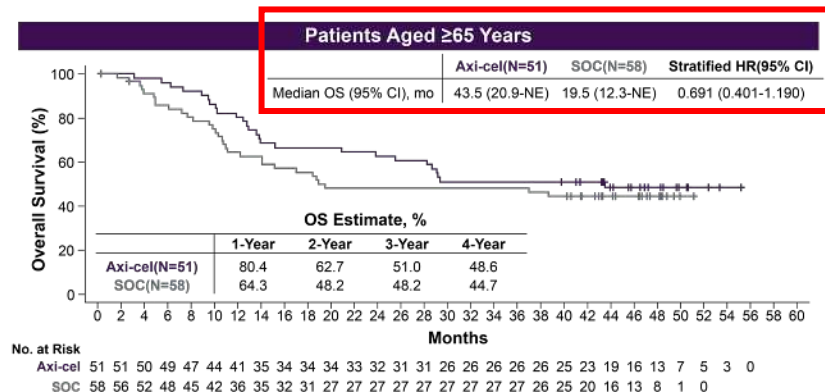
Characteristic	Axi-cel, ≥65 years (n=51)	SoC, ≥65 years (n=58)	Overall, ≥65 years (n=109)
Median age, years (range)	70 (65–80)	69 (65–81)	69 (65–81)
Sex, male, n (%)	28 (55)	39 (67)	67 (61)
Disease stage III–IV, n (%)	42 (82)	44 (76)	86 (79)
Derived sAAIPI total score of 2, n (%)	27 (53)	18 (31)	45 (41)
Response to 1L therapy, n (%)			
- Primary refractory	37 (73)	39 (67)	76 (70)
- Relapse ≤12 months of 1L therapy	14 (27)	19 (33)	33 (30)
Aged ≥70 years	26 patients	27 patients	53 patients

a: Patients were randomly assigned to receive axi-cel or SOC. Percentages may not total 100 because of rounding.

1L, first-line; axi-cel, axicabtagene ciloleucel; DLBCL, diffuse large B-cell lymphoma; ECOG, sAAIPI, second-line age-adjusted International Prognostic Index; SOC, standard of care.

Westin JR, et al. Clin Cancer Res 2023;29(10):1894-1905.

Subgroup analysis of ZUMA-7: Outcomes in elderly patients

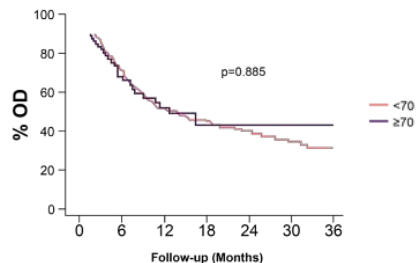
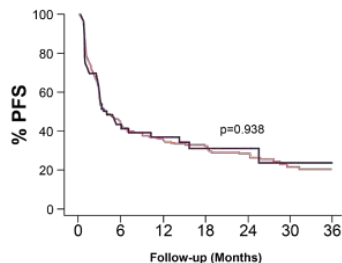


GETH-TC/GELTAMO Registry: Results of anti-CD19 CAR T-cell therapy in elderly patients

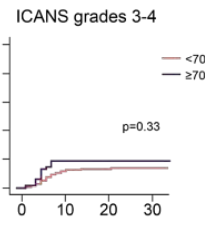
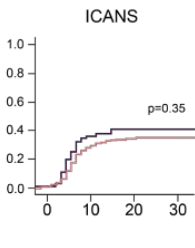
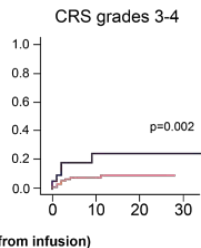
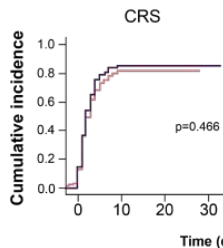
Patients with R/R aggressive LBCL underwent apheresis for CAR T-cell therapy as third or subsequent line (N=442)*

Patients <70 years
(n=341)

Patients ≥70 years
(n=71)



- CAR T-cell therapy was safe and effective in elderly patients.
- Response, OS and EFS in patients older and younger than 70 years were comparable.



- Age ≥ 70 years was an independent risk factor for grade ≥3 CRS.
- No differences were observed in terms of NRM.

Disclaimer: Please refer to your local prescribing information for details of the approved indications in your region.

*Patients with R/R aggressive LBCL who received commercial CAR T-cell therapy with either axi-cel or tisa-cel within Spanish GETH-TC/GELTAMO centers between 2019 and 2023.

axi-cel, axicabtagene ciloleucel; CRS, cytokine release syndrome; EFS, event-free survival; ICANS, immune effector cell-associated neurotoxicity syndrome; GETH-TC/GELTAMO registry: Spanish Group of Hematopoietic Transplant and Cell Therapy/Spanish Group of Lymphomas and Autologous Transplant; LBCL, large B cell lymphoma; OS, overall survival; NRM, non-relapse mortality; R/R, relapsed/refractory tisa-cel, tisagenlecleucel.

Bailén R, et al. Transplant Cell Ther. 2024;30(10):988.e1-988.e11.

CAR T-cell therapy in elderly DLBCL patients



Several real-world studies support the use of CAR T-cell therapy in elderly patients with DLBCL, demonstrating comparable efficacy and safety across age groups



Elderly patients should be equally considered for CAR T-cell therapy

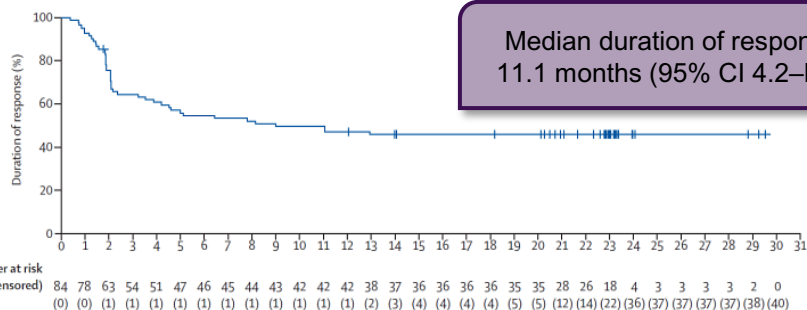


CAR T-cell therapy is cost-effective in both 2L and 3L, supporting its use in earlier lines of treatment

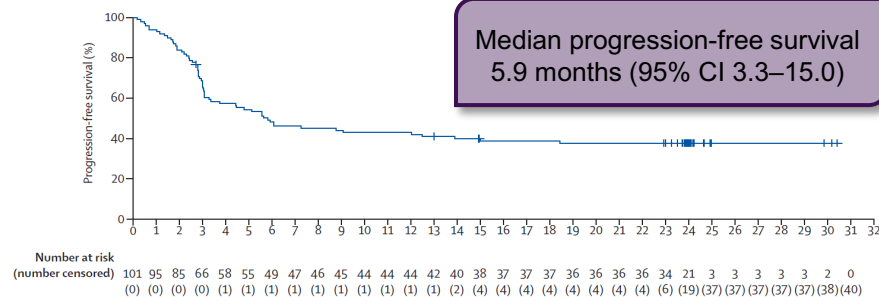
ZUMA-1 phase 2 trial: Clinical outcomes in 3L LBCL

2-year follow-up data

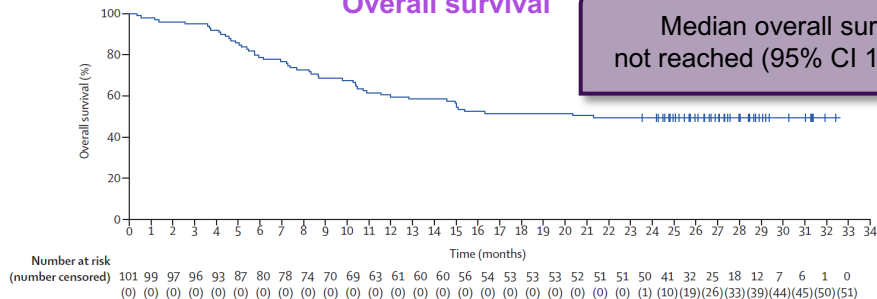
Duration of response



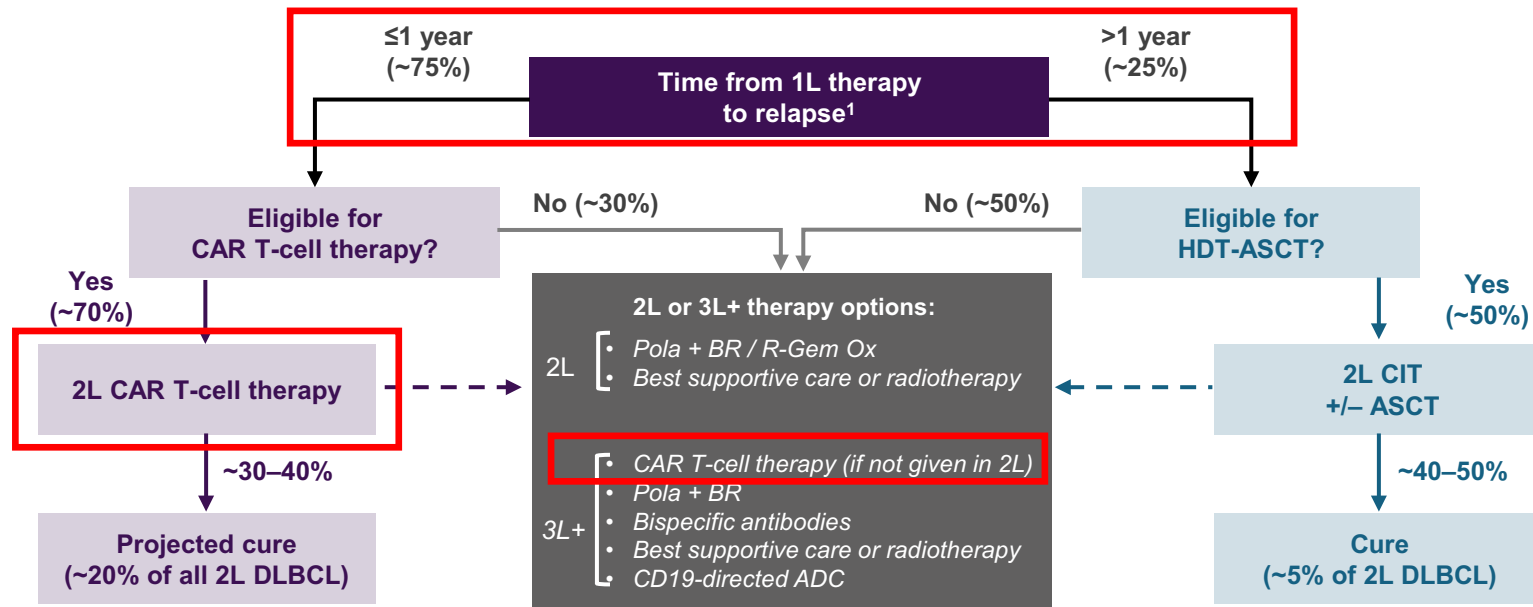
Progression-free survival



Overall survival



Treatment algorithm for R/R DLBCL



Real-world retrospective studies of axi-cel in 3L have shown efficacy and safety outcomes consistent with the ZUMA-1 clinical trial, reinforcing its outcomes across settings. CAR T-cell therapy is also considered cost-effective in both 2L and 3L settings. **Therefore, if not administered in 2L, CAR T-cell therapy should be offered in 3L.**^{1,2}

This is a proposed treatment guideline from one review article and should not replace local clinical guidelines and recommendations.

Disclaimer: Please refer to your local prescribing information for details of the approved indications in your region.

1L, first line; 2L, second line; 3L, third line; ADC, antibody-drug conjugate; ASCT, autologous stem cell transplant; BR, bendamustine; CAR, chimeric antigen receptor; CIT, chemoimmunotherapy; DLBCL, diffuse large B-cell lymphoma; HDT, high-dose therapy; pola, polatuzumab vedotin; R-Gem Ox, rituximab gemcitabine oxaliplatin; R/R, relapsed/refractory.

Figure adapted from: Westin J, Sehn LH. Blood. 2022;139(18):2737-2746.

1. Westin J, Sehn LH. Blood. 2022;139(18):2737-2746. 2. Hoffmann MS, et al. Transplant Cell Ther 2023;29:440-448.

Conclusions



CAR T-cell therapy is effective for patients with R/R LBCL



It is effective and with acceptable safety profile for elderly and patients with multiple comorbidities



Real-world evidence is comparable to clinical trials data

Thank you

Navigating the Complexity of an
Evolving Treatment Landscape in R/R Lymphomas