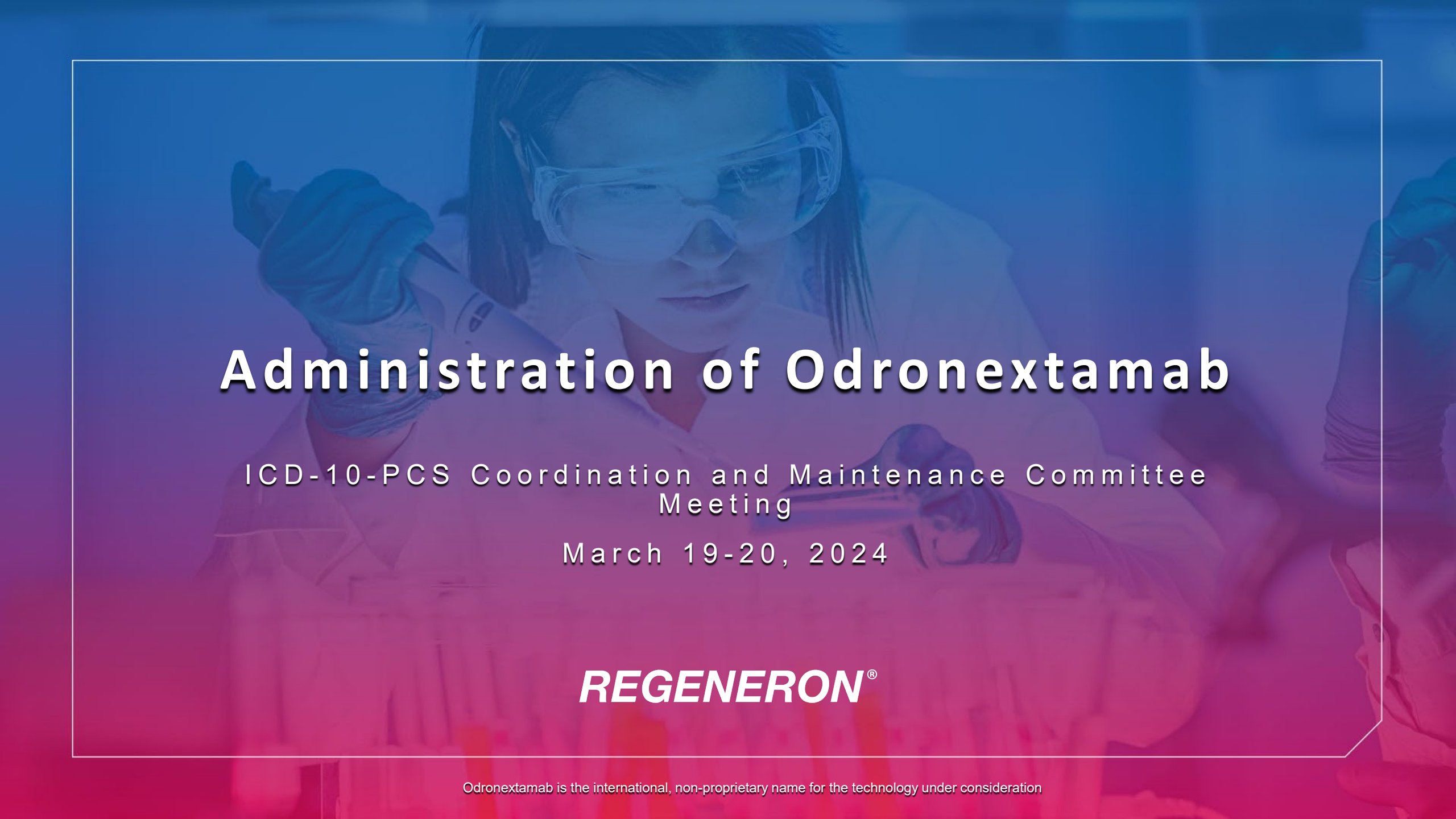

Administration of Odronextamab

ICD-10-PCS Coordination and Maintenance Committee Meeting

March 19-20, 2024

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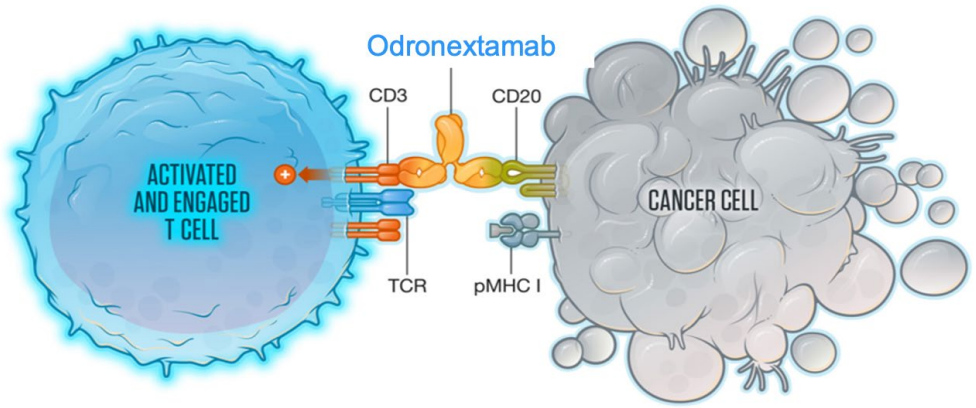
Odronextamab is the international, non-proprietary name for the technology under consideration

Odronextamab offers patients with R/R FL and R/R DLBCL a novel, off-the-shelf immunotherapy that has a generally manageable safety profile and demonstrates substantial clinical benefits

- Odronextamab is the international, non-proprietary name for the technology under consideration
- A **novel, fully human** CD20×CD3 bispecific antibody with an **IgG4-based structure** that will **simultaneously bind** to CD20 found on both healthy and cancerous B cells and CD3 found on T cells created using **Regeneron's proprietary *Veloci-Bi*® technology**
- **Two indications**, upon approval:
  - Adults with R/R FL after at least 2 prior systemic therapies
  - Adults with R/R DLBCL after at least 2 prior systemic therapies, including those with or without prior CAR T therapy
- Under consideration for **New Technology Add on Payment (NTAP) for FY2025**
- **Off-the-shelf**, monotherapy treatment administered as an **intravenous** (IV) infusion

R/R DBCL=relapsed/refractory diffuse large B-cell lymphoma; R/R FL=relapsed/refractory follicular lymphoma

Odronextamab is a CD20xCD3 bispecific antibody with a novel, fully human design based on IgG4, created using Regeneron's proprietary Veloci-Bi® technology



Odronextamab is designed to simultaneously engage **CD20 on cancer cells with CD3-expressing T cells**, resulting in local **T-cell activation and cytotoxicity**[1]

pMHC=peptide major histocompatibility complex; TCR=T-cell receptor.

1. Smith EJ et al. *Sci Rep*. 2015;5:1-12.

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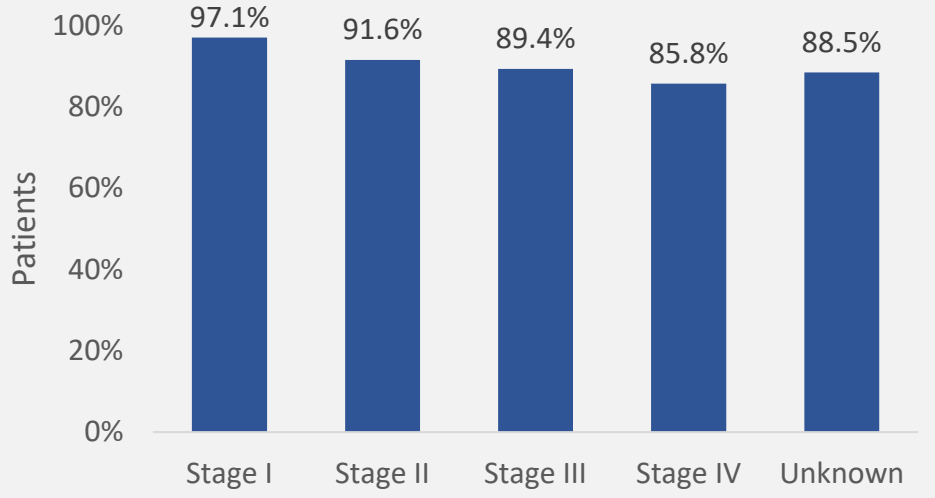
FL is the second most common lymphoma diagnosed in the US†

FL accounts for approximately 35% of all NHLs and 70% of indolent lymphomas[1]

- The median age at diagnosis is 64 years and the majority of patients with FL have advanced stage disease (Stage III/IV) at diagnosis[2]
- Overall, the 5-year relative survival rate for FL is 90.6%[2]
- Approximately 20% of patients experience early disease progression within 2 years of 1L treatment (POD24), which is associated with poor outcomes[3,4]

5-year relative survival by stage at diagnosis: FL[2]



FL =follicular lymphoma; NHL=Non-Hodgkin's Lymphoma; POD24=Progression of disease within 2 years

1. Freedman A, Jacobsen E. *Am J Hematol.* 2020;95:316–27; **2**. National Cancer Institute. SEER cancer stat facts: NHL — follicular lymphoma. https://seer.cancer.gov/statfacts/html/follicular.html (accessed November 8, 2023). **3**. Casulo C, et al. *Blood*. 2022;139:1684–93. **4**. Casulo C, et al. *J Clin Oncol*. 2015;33:2516–22. †: The Leukemia and Lymphoma Society. Treatment For Indolent NHL Subtypes. https://www.lls.org/lymphoma/non-hodgkin-lymphoma/nhl-subtypes/treatment-indolent-nhl-subtypes (accessed November 30, 2023)

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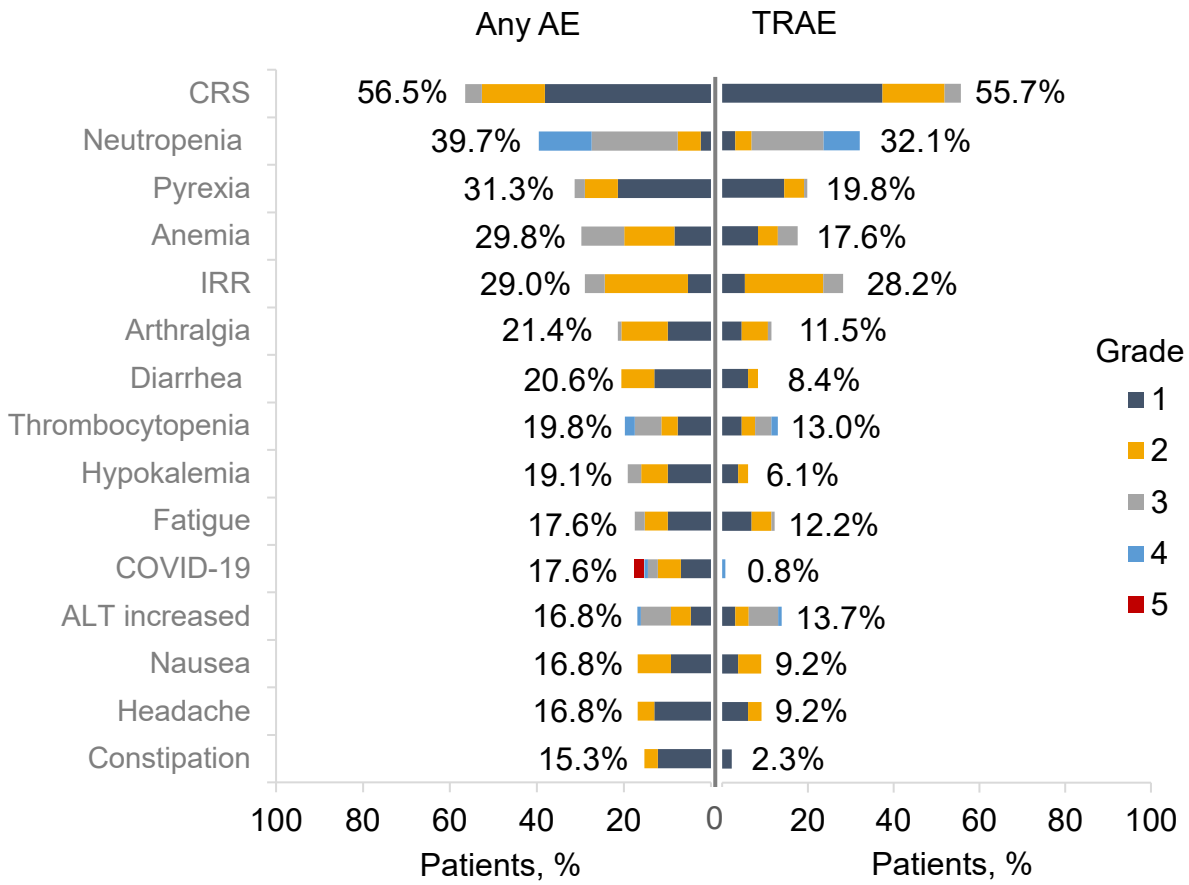
ELM-2: Odronextamab safety profile in patients with R/R FL

Treatment-emergent adverse events, n (%)	Patients N=131	
	All events	TRAEs
Grade ≥3 TEAE	102 (77.9%)	73 (55.7%)
Serious AE	81 (61.8%)	53 (40.5%)
Grade 5 TEAE	17 (13.0%)	3 (2.3%)
Related to COVID-19	7 (5.3%)	0
Other Grade 5 events	10 (7.6%)	3 (2.3%)
TEAE leading to treatment discontinuation	15 (11.5%)	10 (7.6%)

- Grade 5 TRAEs: pneumonia, PML, systemic mycosis (n=1 each)
- TRAEs leading to treatment discontinuation: IRR (n=2); IRR and tremor (n=1); ALT increase; arthralgia; CRS; epilepsy; PML; viral bronchitis; weight decrease (n=1 each)
- No cases of ICANS or TLS with the 0.7/4/20 recommended regimen

AEs (≥15% any grade) and TRAEs



Data cut-off date: Sep 15, 2022.
AEs per NCI-CTCAE v5.0. CRS per Lee 2019.
1. Kim TM, et al. 64th ASH Annual Meeting, New Orleans, LA, USA, December 10–13, 2022. Oral presentation #949.
AE=adverse event; ALT=alanine aminotransferase; CRS=cytokine release syndrome; ICANS=immune effector cell-associated neurotoxicity syndrome; IRR=infusion related reaction; PML=Progressive multifocal leukoencephalopathy; TEAE=treatment-emergent adverse event; TLS=tumor lysis syndrome; TRAE=treatment-related AE.
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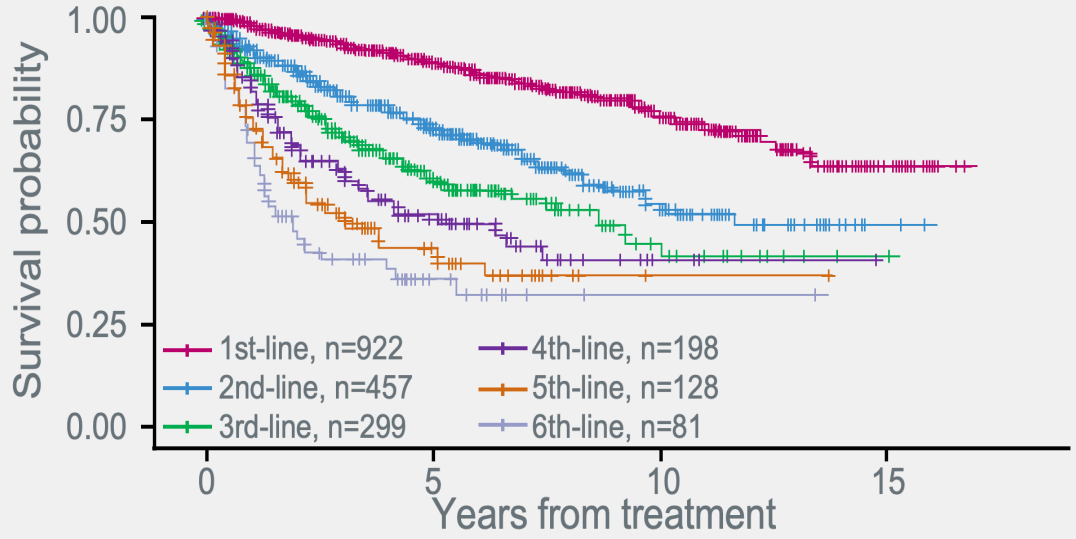
There is a need for additional treatment options in 3L FL

FL

- Despite current improvements in FL patient survival, **treating those with 3L+ becomes increasingly difficult**[1]
  - Patients with R/R FL face **diminishing durability of response** with each line of therapy[1]
  - Patients who **progress within 24 months** after initiating first-line therapy face a **poor prognosis**[2]
  - **Approximately 20%** of patients with 3L+ FL **achieve CR** with existing therapies[3]

OS by line of therapy in patients diagnosed with de novo FL between 1998 and 2009 managed at MSK



A study in the US showed the median OS decreased with each line of therapy, with median OS not reached in 1L, decreasing to 11.67 years in 2L and 3.13 years after 5L[4]

3L=third line; CAR-T=chimeric antigen receptor T-cell; CR=complete response; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; MSK=Memorial Sloan Kettering Cancer Center; NCCN=National Comprehensive Cancer Network; OS=overall survival; R/R=relapse/refractory; US=United States.

1. Rivas-Delgado A et al. *Br J Haematol*. 2019;184(5):753-759. **2.** Casulo C et al. *Lancet Haematol*. 2022;9(4):e289-e300. **3.** Kanters S et al. *BMC Cancer*. 2023;23(74):1-12. 4. Batlevi CL, et al. Blood Cancer J. 2020;10:74.

DLBCL is the most common B-NHL subtype, comprising 30–40% of all NHL cases in the US†

- DLBCL can be classified according to the cell of origin as germinal center B-cell-like (GCB), activated B-cell-like (ABC), or non-GCB DLBCL[1]
- The most common cytogenetic abnormalities in DLBCL involve the oncogenes BCL2, BCL6, and MYC, which are implicated in the development of high-grade B-cell lymphoma[2]

Response rates decrease with each subsequent LOT[3-5]

1L: 59% CR

2L: 30–40% CR

3L: 9–10% CR with CIT/TT — 60% with CAR T

4L: 6–15% CR with CIT/TT — 54% with CAR T

Survival decreases with each subsequent LOT[3,4]

- Patients who respond to 1L therapy have a 5-year survival of 78%
- Outcomes for patients with R/R DLBCL are poor
  - Median OS: **7.7 months after 3L therapy** and **4.4 months after 4L therapy**

1/2/3/4L, first/second/third/fourth-line; CIT=chemoimmunotherapy; CR=complete response; DLBCL=diffuse large B-cell lymphoma; LOT=lines of therapy; OS=overall survival; R/R= relapsed/refractory; TT=targeted therapy; CAR T=Chimeric Antigen Receptor T-cell

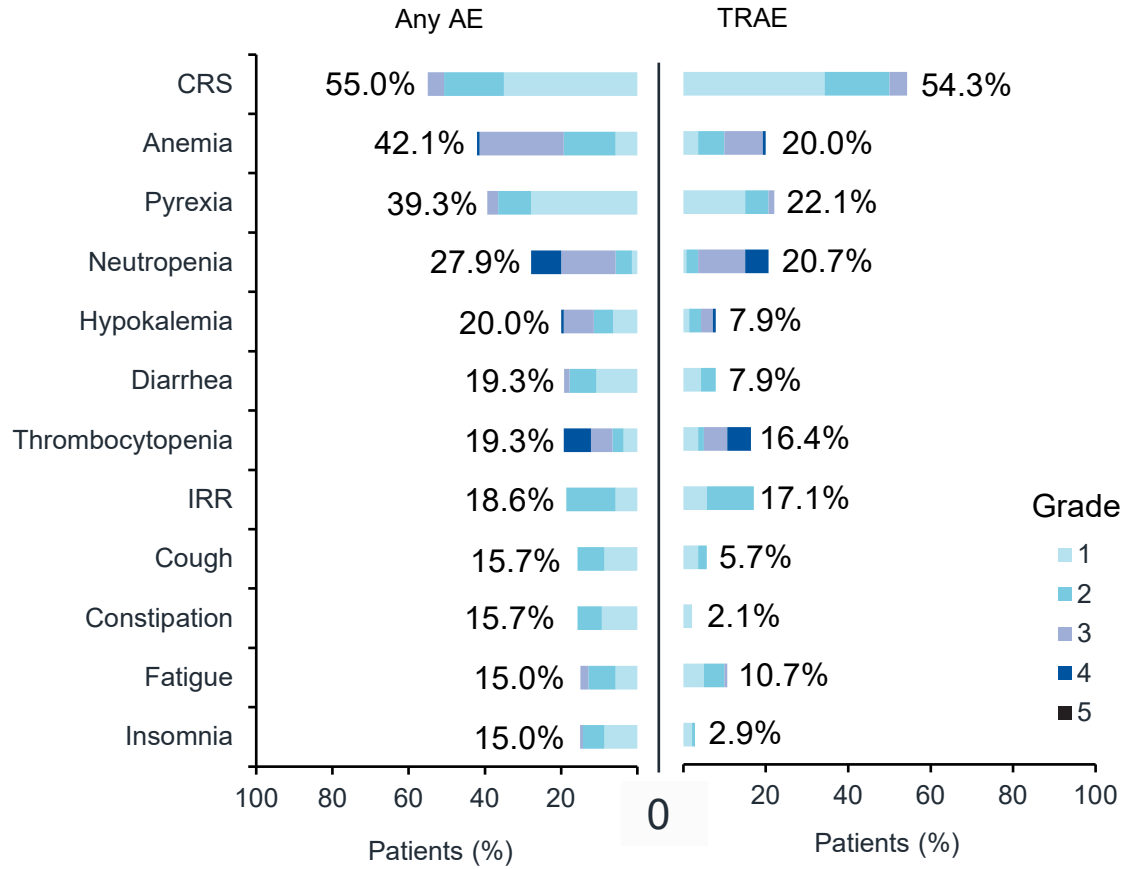
1. Singh R, et al. J Med Sci. 2018;38:137–43. **2**. Smith S. Clin Adv Hematol Oncol. 2017;15:40–2. **3**. Nuvvula S, et al. Clin Lymphoma Myeloma Leuk. 2022;22(6):362–72. **4**. Hamadani M, et al. Clin Lymphoma Myeloma Leuk. 2022;22(6):373–81. **5**. Crump M, et al. Blood. 2017;130(16):1800–8. †: National Cancer Institute. SEER cancer stat facts: NHL — Diffuse Large B-Cell Lymphoma. https://seer.cancer.gov/statfacts/html/dlbcl.html (accessed November 29, 2023)

ELM-2: Odronextamab safety profile in patients with R/R DLBCL

TEAE, n (%)	N=140	
	Any grade	Treatment-related
Grade ≥3 TEAE	110 (78.6%)	74 (52.9%)
Serious AE	85 (60.7%)	64 (45.7%)
Grade 5 TEAE	20 (14.3%)	5 (3.6%)
Related to COVID-19	5 (3.6%)	1 (0.7%)
Other Grade 5 events	15 (10.7%)	4 (2.9%)
TEAE leading to treatment discontinuation	14 (10.0%)	11 (7.9%)

- Grade 5 TRAEs: pneumonia (n=3), COVID-19 (n=1), and pseudomonal sepsis (n=1)
- No cases of TLS and no grade 3 or higher ICANS or IRR reported with the recommended regimen

AEs (≥15% any grade) and TRAEs



Data cut-off date: September 15, 2022.

AEs per NCI-CTCAE Version 5.0. CRS per Lee 2019 criteria.

1. Kim W-S, et al. 64th ASH Annual Meeting, New Orleans, LA, USA, December 10–13, 2022. Oral presentation #444.

AE=adverse event; CRS=cytokine release syndrome; DLBCL=diffuse large B-cell lymphoma; NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events; ICANS=immune effector cell-associated neurotoxicity syndrome; IRR=infusion-related reaction; R/R=relapsed/refractory; TEAE=treatment-emergent adverse event; TRAE=treatment-related adverse event.

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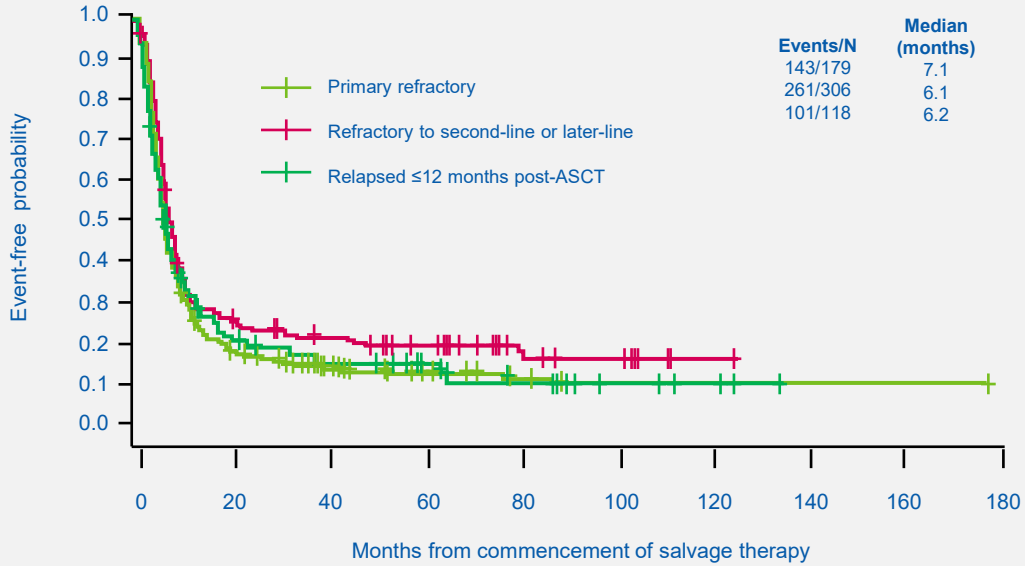
There is a need for additional treatment options in 3L DLBCL

DLBCL

- DLBCL patients have demonstrated **poor prognosis in the 3L+ setting despite available therapies**[1]
  - Outcomes are poor in patients with high-risk features[1]
- CAR-T therapies are associated with **sustained complete remissions and long-term survival**. However, many patients are still unable to receive intensive treatment options such as SCT and CAR-T therapy[2]
  - CAR-T therapy was administered in **19% of patients aged 65-69**, **22% of those aged 70-74**, and **13% of those aged over 75**[3]
  - **More than 50%** of patients who receive CAR T **will either fail or relapse** after achieving a response[4]
  - **Survival** for patients who fail CAR-T therapy is particularly **poor**[5]

Overall survival from the start of salvage therapy, according to refractoriness[2]



Median overall survival is slightly lower among patients who are refractory to second-line or later-line therapy than among those who are primary refractory[2]

1. Crump M et al. Blood. 2017;130(16):1800-1808. 2. Di Rocco A et al. Leuk & Lymph. 2020;62(4):828-836. 3. Chihara D et al. Blood. 2023;1:1-19. 4. Caballero AC et al. Front Immunol. 2022;13(904497):1-19. 5. Chow VA et al. J Hematol. 2019;94(8):E209-E213.

3L=third line; CAR-T=chimeric antigen receptor T-cell; CR=complete response; DLBCL=diffuse large B-cell lymphoma; NCCN=National Comprehensive Cancer Network; OS=overall survival; R/R=relapse/refractory.

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Odronextamab may be administered in the inpatient or outpatient settings of care

- Odronextamab is administered **intravenously** using a split- and step-up dosing design for four 21-day cycles, followed by maintenance treatment every 2 weeks until disease progression or unacceptable toxicity
- Inpatient usage of odronextamab could occur due to **a physician's order** or as a result of an adverse event, such as **cytokine release syndrome (CRS)**
- 0.7/4/20 mg step-up regimen reduced the incidence of grade 2 and grade 3 CRS
- In the inpatient setting, odronextamab will be documented in the **"medication administration" section** of the medical record

	FL		DLBCL	
n, (%)	1/20 regimen (N=68)	0.7/4/20 regimen (N=63)	1/20 regimen N=67	0.7/4/20 regimen (N=73)
CRS any Grade	38 (55.9%)	36 (57.1%)	38 (56.7%)	39 (53.4%)
Grade 1	22 (32.4%)	28 (44.4%)	21 (31.3%)	28 (38.4%)
Grade 2	12 (17.6%)	7 (11.1%)	12 (17.9%)	10 (13.7%)
Grade 3	4 (5.9%)	1 (1.6%)	5 (7.5%)	1 (1.4%)
Grade 4	0	0	0	0
Grade 5	0	0	0	0
Received corticosteroids	11 (16.2%)	17 (27.0%)	13 (19.4%)	15 (20.5%)
Received tocilizumab	9 (13.2%)	12 (19.0%)	10 (14.9%)	19 (26.0%)
Received vasopressors	4 (5.9%)	1 (1.6%)	5 (7.5%)	1 (1.4%)

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Odronextamab is administered using a split- and step-up dosing design for four 21-day cycles, followed by maintenance treatment every 2 weeks until disease progression or unacceptable toxicity

Day of Treatment		r/r DLBCL	r/r FL
		Dose of Odronextamab	Dose of Odronextamab
Cycle 1 (Step Up Dosing)	Day 1	0.2 mg	0.2 mg
	Day 2	0.5 mg	0.5 mg
	Day 8	2 mg	2 mg
	Day 9	2 mg	2 mg
	Day 15	10 mg	10 mg
	Day 16	10 mg	10 mg
Cycles 2 to 4	Day 1	160 mg	80 mg
	Day 8	160 mg	80 mg
	Day 15	160 mg	80 mg
Maintenance (Every 2 weeks)	Begin 1 week after the end of Cycle 4	320 mg	160 mg

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