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Virtual mid- to late-stage pipeline update at ASCO 2024

June 3, 2024

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Agenda

9:00 AM	Introduction	Dr. Jan van de Winkel, President & CEO
9:03 AM	Tisotumab vedotin at ASCO	Dr. Judith Klimovsky, EVP & CDO
9:08 AM	Epcoritamab at ASCO	Dr. Tahi Ahmadi, EVP & CMO
9:13 AM	Acasunlimab at ASCO	Dr. Tahi Ahmadi
9:18 AM	Further Advancing Our Differentiated Product Pipeline Towards The Market	Dr. Jan van de Winkel
9:20 PM	Q&A	All

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Tisotumab Vedotin at ASCO

Dr. Judith Klimovsky

Tisotumab vedotin in head and neck squamous cell carcinoma: updated analysis from innovaTV 207 Part C

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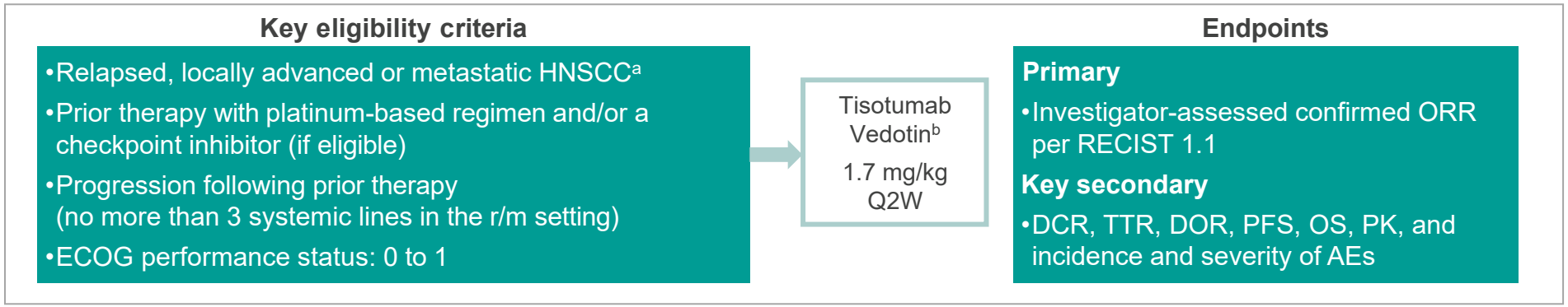
Background and innovaTV 207 study design

- An unmet need remains for patients with r/m HNSCC that progresses on modern 1L therapy, for whom subsequent treatment options and data are limited[1,2]
- Tisotumab vedotin is a TF-directed ADC and is approved for the treatment of adult patients with previously treated r/m cervical cancer
  - Tisotumab vedotin has shown encouraging activity in r/m HNSCC[3]
- Here, we present results from the full HNSCC cohort of innovaTV 207 Part C

innovaTV 207 Study Design: Part C (N=40)[3]



ADC, antibody–drug conjugate; TF, tissue factor.
[a]Patients with sqNSCLC were also included in Part C, but only HNSCC results are presented here. [b]With self-administered preventive eye care.
1. Ho AL. J Clin Oncol. 2023;41(4):736-741. 2. Borel C, et al. Cancers (Basel). 2020;12(9):2691. 3. Cirauqui B, et al. AACR 2023. Abstract CT164.

Patient and disease characteristics

Characteristic	Part C HNSCC (N=40)
Age, median (range), years	61.0 (29-74)
Male sex, n (%)	36 (90.0)
Race, n (%)	
Black or African American	1 (2.5)
White	30 (75.0)
Unknown/Not reportable	9 (22.5)
Ethnicity, n (%)	
Hispanic or Latino/a, or of Spanish origin	6 (15.0)
Not of Hispanic or Latino/a, or Spanish origin	28 (70.0)
Unknown/Not reportable	6 (15.0)
Baseline ECOG performance status, n (%)	
0	14 (35.0)
1	26 (65.0)

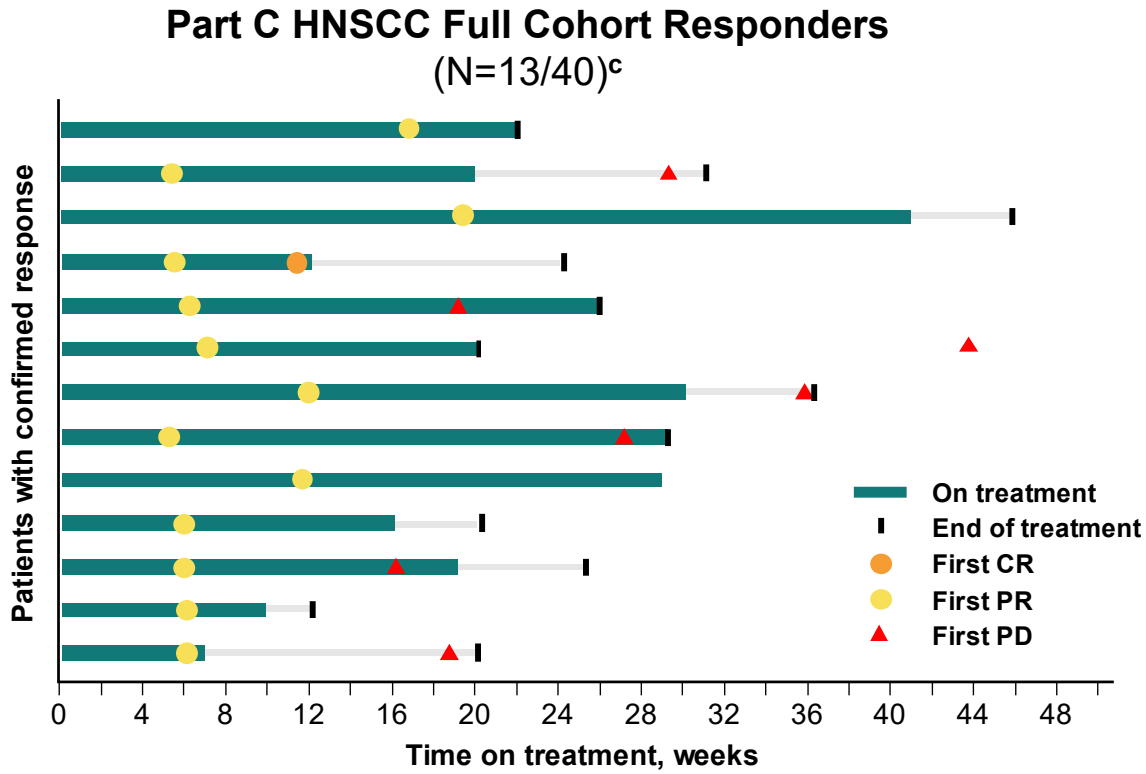
Characteristic	Part C HNSCC (N=40)
Diagnosis subtype, n (%)	
Oropharynx	16 (40.0)
P16 positive	12 (75.0)
P16 negative	4 (25.0)
Larynx/Hypopharynx	13 (32.5)
Oral cavity	9 (22.5)
Sinus/Nasopharynx	2 (5.0)
Highest line of prior systemic therapy in r/m setting, n (%)	
1	6 (15.0)
2	19 (47.5)
3	15 (37.5)
Prior systemic therapy in r/m setting, n (%)[a]	
Checkpoint inhibitor	40 (100)
Platinum-based therapy[b]	32 (80.0)
Cetuximab	27 (67.5)
Taxane	23 (57.5)
Methotrexate	1 (2.5)

[a]Other therapies (n=2) are not listed.
[b]39 of 40 (97.5%) of patients received prior platinum-based therapy in any setting.

Antitumor activity of tisotumab vedotin

	Part C HNSCC 2L-4L (N=40)	Subgroup 2L/3L (N=25)
Confirmed ORR, n (%) (95% CI)	13 (32.5) (18.6-49.1)	10 (40.0) (21.1-61.3)
Best overall response, n (%)[a]		
CR	1 (2.5)	0
PR	12 (30.0)	10 (40.0)
SD	13 (32.5)	6 (24.0)
PD	10 (25.0)	7 (28.0)
DCR, n (%) (95% CI)[b]	17 (42.5) (27.0-59.1)	13 (52.0) (31.3-72.2)
Median DOR, months (95% CI)	5.6 (2.4-NR)	5.6 (3.0-NR)

Median follow up (Part C HNSCC): 16.9 months (95% CI, 6.8-20.2)

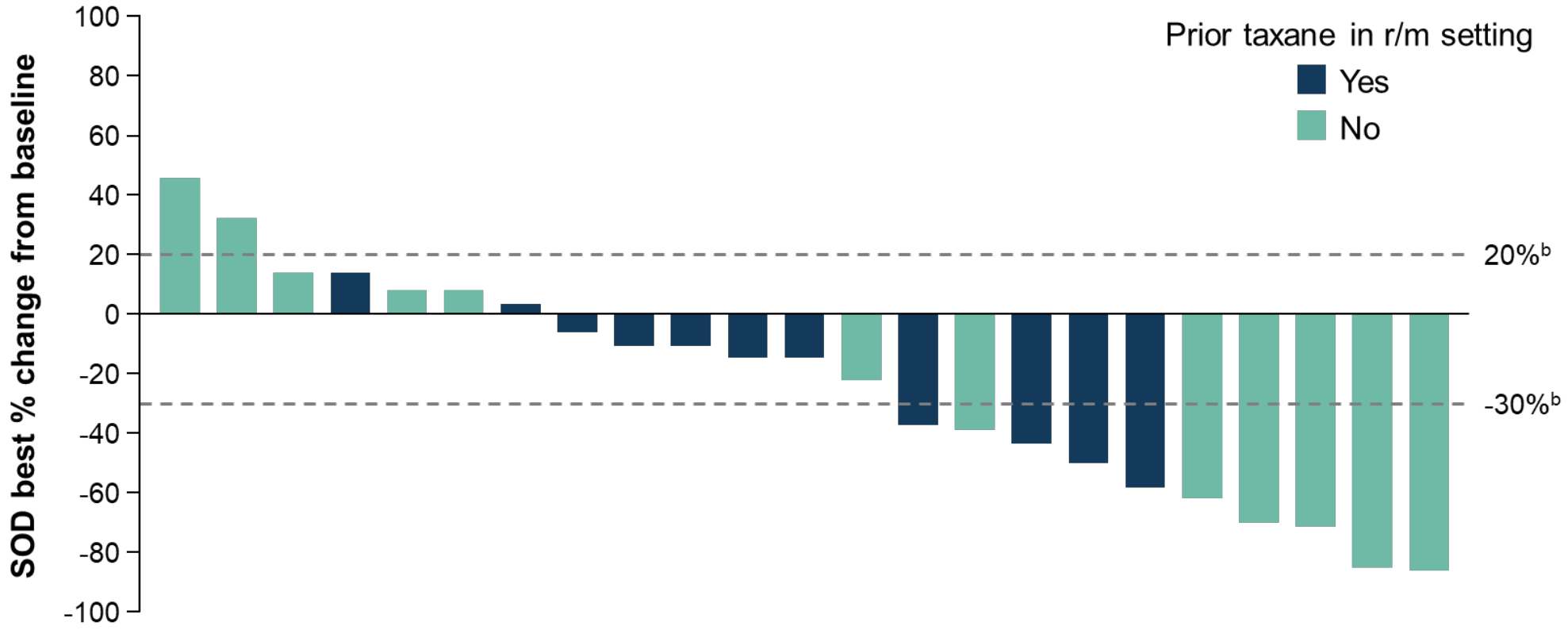


- A higher confirmed ORR was observed in the 2L/3L subgroup of patients

Data cutoff: December 4, 2023. Confirmed objective responses are reported per investigator.
[a]Four patients in Part C (HNSCC) and 2 patients in the 2L/3L subgroup were not evaluable. [b]DCR is cCR+cPR+SD (SD ≥12 wks). cMedian time to response (range) was 1.4 months (1.2-4.5) in Part C (HNSCC) and 1.5 (1.2-4.5) in the 2L/3L subgroup.

Change in tumor size

2L/3L subgroup (N=25)[a]



- 10 out of 25 patients (40.0%) experienced a ≥30% reduction in target lesion diameters

Data cutoff: December 4, 2023. SOD, sum of diameters.
[a]Two patients are not displayed due to lack of postbaseline assessment that is eligible for the efficacy analysis. [b]Per RECIST 1.1 thresholds, PD is defined as a ≥20% increase in the SOD of target lesions from baseline and PR is defined as a ≥30% decrease in the SOD of target lesions from baseline.

Tisotumab vedotin exposure and safety

	Part C HNSCC (N=40) n (%)
TEAE any grade	38 (95.0)
TEAE grade ≥3	27 (67.5)
Treatment-emergent SAEs	19 (47.5)
TEAE leading to treatment discontinuation[a]	8 (20.0)
Any TEAE leading to death[b]	1 (2.5)

[a]Six (15.0%) patients had treatment-related discontinuations
[b]Pneumonia, not deemed related to the study drug by the investigator

- The median treatment duration was 2.2 months (range, 0.2-9.4) in Part C (HNSCC) and 2.3 months (range, 0.4-9.4) in the 2L/3L subgroup
- Patients had received a median of 2.5 cycles (range, 1-8)[c]
- The most common TEAEs were peripheral sensory neuropathy in 16 (40.0%) patients, constipation in 13 (32.5%), and conjunctivitis, decreased appetite, and fatigue in 12 (30.0%)

SAE, serious adverse event; TEAE, treatment-emergent adverse event.
[c]Refers to any cycle in which the patient had received any amount of the study drug; tisotumab vedotin was dosed on day 1 and day 15 of each 28-day cycle.

Conclusions: innovaTV 207[a] Part C

- Tisotumab vedotin monotherapy demonstrated encouraging antitumor activity in a pretreated population of patients with r/m HNSCC. Part C data are still evolving
  - Confirmed ORR was 32.5% in Part C HNSCC (2L-4L) and 40.0% in the 2L/3L subgroup
  - DCR was 42.5% (95% CI, 27.0-59.1) in Part C HNSCC and 52.0% (95% CI, 31.3-72.2) in the 2L/3L subgroup
- The safety profile was manageable and consistent with previous tisotumab vedotin monotherapy data
  - Most AESIs were low-grade and non-serious
- The innovaTV 207 (NCT03485209) study is ongoing and continues to enroll patients with r/m HNSCC in both the 1L (Part F) and 2L/3L (Part E) settings
- Tisotumab vedotin has potential for treatment of patients with r/m HNSCC that has progressed following immunotherapy and platinum-based chemotherapy

[a]Study in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

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Epcoritamab at ASCO

Dr. Tahi Ahmadi

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EPCORE NHL-1 Follicular Lymphoma (FL) Cycle (C) 1 Optimization (OPT) Cohort: Expanding the Clinical Utility of Epcoritamab in Relapsed or Refractory (R/R) FL

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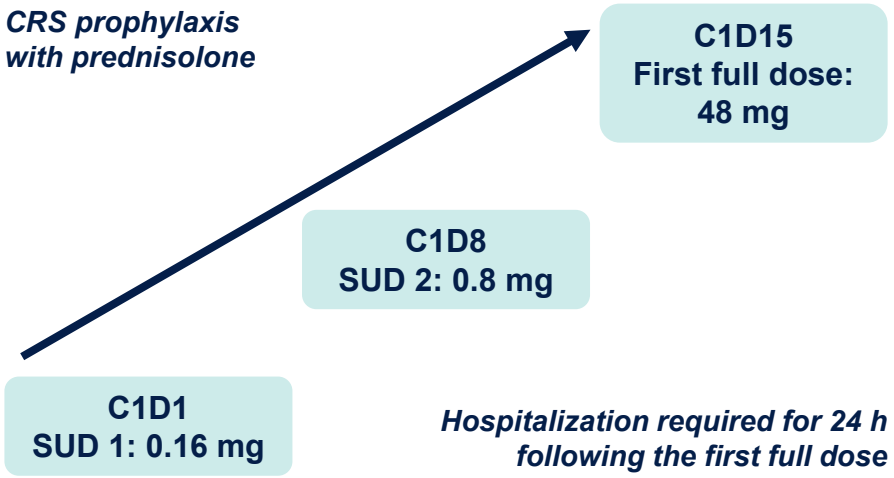
First C1 OPT–Focused Data Disclosure From EPCORE® NHL-1

Key inclusion criteria

- R/R CD20+ FL grade 1–3A
- ECOG PS 0–2
- ≥2 prior lines of therapy, including ≥1 ~~regimen with an~~ anti-CD20 mAb
- Prior alkylating agent or lenalidomide
- FDG-avid disease by PET/CT
- Prior CAR T allowed

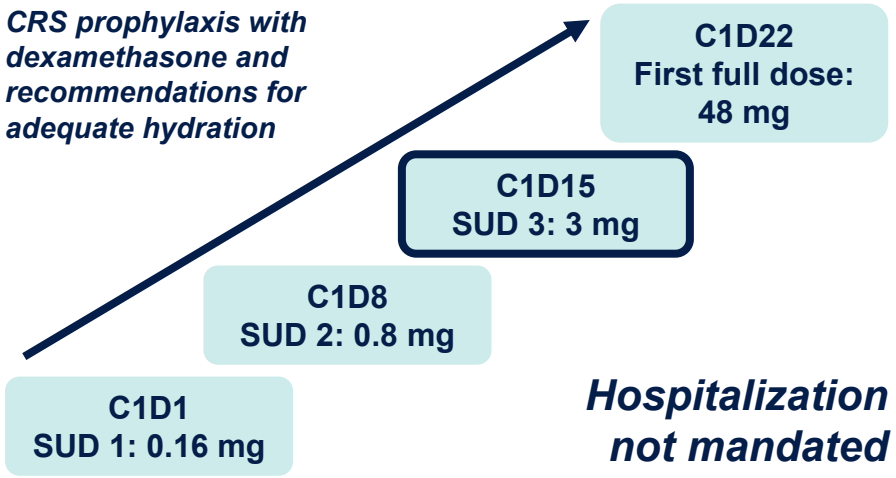
Pivotal[a]



Primary objective: ORR by independent review committee

Data cutoff: April 21, 2023
Median follow-up: 17.4 mo

C1 optimization[a]



Primary objective: CRS incidence and severity

Data cutoff: January 8, 2024
Median follow-up: 5.7 mo

Phase 1/2 trial. C, cycle; CAR T, chimeric antigen receptor T-cell therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; mAb, monoclonal antibody; MRD, minimum residual disease; OPT, optimization; ORR, overall response rate; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SUD, step-up dose. [a]Patients received subcutaneous epcoritamab QW C1–3, Q2W C4–9, and Q4W C≥10 until progressive disease (≥2 measurable [by CT/MRI] and FDG PET–positive lesions) or unacceptable toxicity. Radiographic disease evaluation was performed every 6 wk for the first 24 wk (6, 12, 18, and 24 wk), then every 12 wk (36 and 48 wk), and every 6 mo thereafter. MRD was assessed in peripheral blood using the clonoSEQ® (Adaptive Biotechnologies, Seattle, WA) next-generation sequencing assay. ClinicalTrials.gov: NCT03625037; EudraCT: 2017-001748-36.

Baseline Characteristics Consistent Across Cohorts

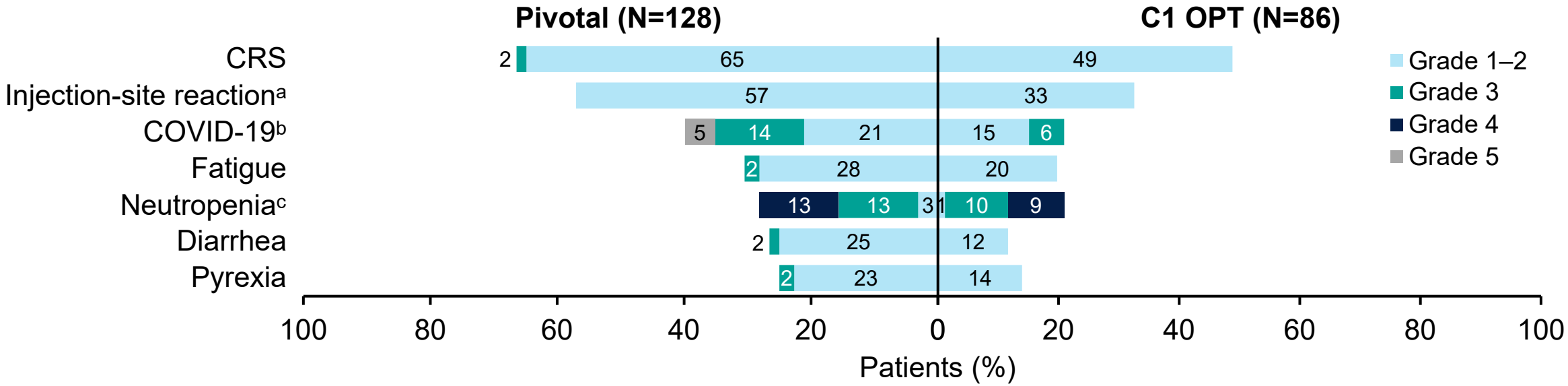
Demographics	Pivotal Cohort N=128	C1 OPT N=86
Median age, y (range)	65 (39–84)	63.5 (33–90)
Male, n (%)	79 (62)	49 (57)
Ann Arbor stage, n (%)[a]		
III–IV	109 (85)	79 (92)
FLIPI, n (%)[b]		
3–5	78 (61)	44 (51)

Treatment History	Pivotal Cohort N=128	C1 OPT N=86
Median number of prior lines of therapy (range)	3 (2–9)	2 (2–9)
≥3 prior lines, n (%)	81 (63)	41 (48)
≥4 prior lines, n (%)	40 (31)	17 (20)
POD24 (any 1L),[c] n (%)	67 (52)	42 (49)
Double refractory,[d,e] n (%)	90 (70)	54 (63)
Primary refractory,[d] n (%)	69 (54)	38 (44)
Refractory[d] to last prior systemic therapy, n (%)	88 (69)	49 (57)

- Like the pivotal cohort, the C1 OPT cohort included patients from a high-risk R/R FL population with a high unmet need
- All patients had ≥2 prior lines of therapy, including a regimen containing an anti-CD20 mAb

1L, first-line. [a]Ann Arbor stage was I–II in 19 patients in the pivotal cohort and 7 patients in C1 OPT. [b]FLIPI was 0–2 in 48 patients in the pivotal cohort (not available in 2 patients) and 42 patients in C1 OPT. FLIPI was prior to first dose on study. [c]Progression within 2 y of initiating any 1L therapy. [d]Refractory: No response or relapse within 6 mo after therapy. [e]Double refractory: Refractory to both anti-CD20 and an alkylating agent.

Common TEAEs (≥25%) Across Cohorts

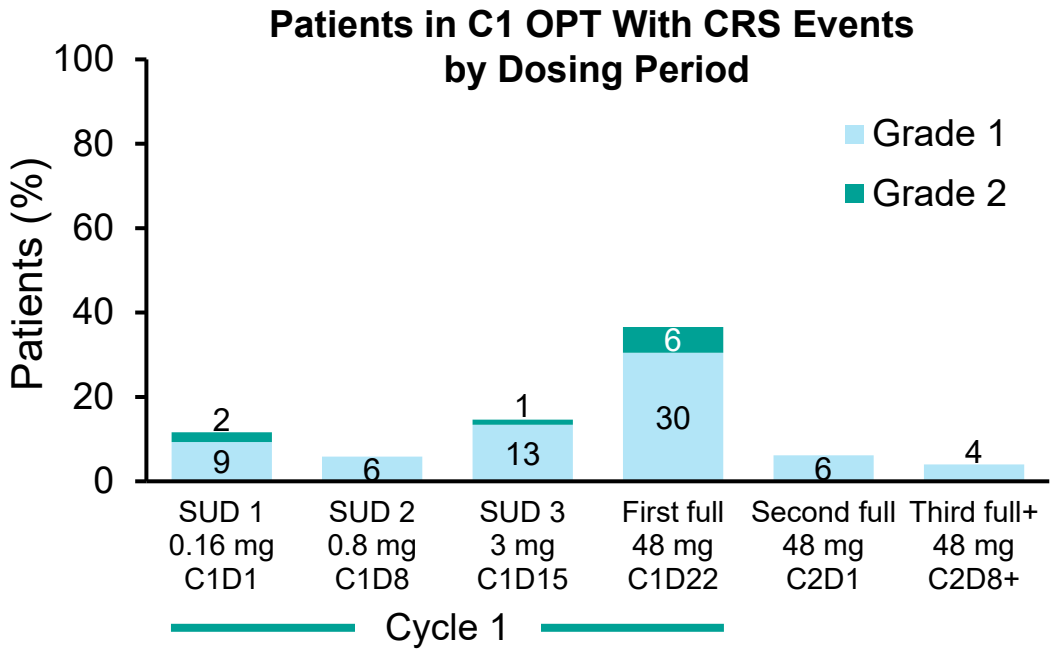


- In the C1 OPT cohort:
  - Grade ≥3 TEAEs occurred in 46 patients (53%)
  - TEAEs led to treatment discontinuation in 3 patients (3%; grade 2 bronchopulmonary aspergillosis [n=1] and pneumonitis [n=2])
  - No fatal TEAEs
- No clinical tumor lysis syndrome in either cohort

Graph shows TEAEs that occurred in ≥25% of patients in either cohort. TEAE, treatment-emergent AE. [a]Combined term includes injection-site reaction, erythema, rash, bruising, pruritus, inflammation, pain, edema, and nodule. [b]Combined term includes COVID-19 and COVID-19 pneumonia. [c]Combined term includes neutropenia and neutrophil count decreased. Four patients in the pivotal cohort and 1 patient in C1 OPT had febrile neutropenia (all grade 3).

C1 OPT Substantially Reduced Incidence and Severity of CRS and ICANS

	Pivotal N=128	C1 OPT N=86
CRS,[a] n (%)	85 (66)	42 (49)
Grade 1	51 (40)	34 (40)
Grade 2	32 (25)	8 (9)
Grade 3	2 (2)	0
Treated with tocilizumab, n (%)	31 (24)	10 (12)
Leading to epcoritamab discontinuation, n (%)	**0**	**0**
CRS resolution, n/n (%)	**85/85 (100)**	**42/42 (100)**
Median time to resolution, d (range)	2 (1–54)	2 (1–14)
ICANS, n (%)	8 (6)[b]	0

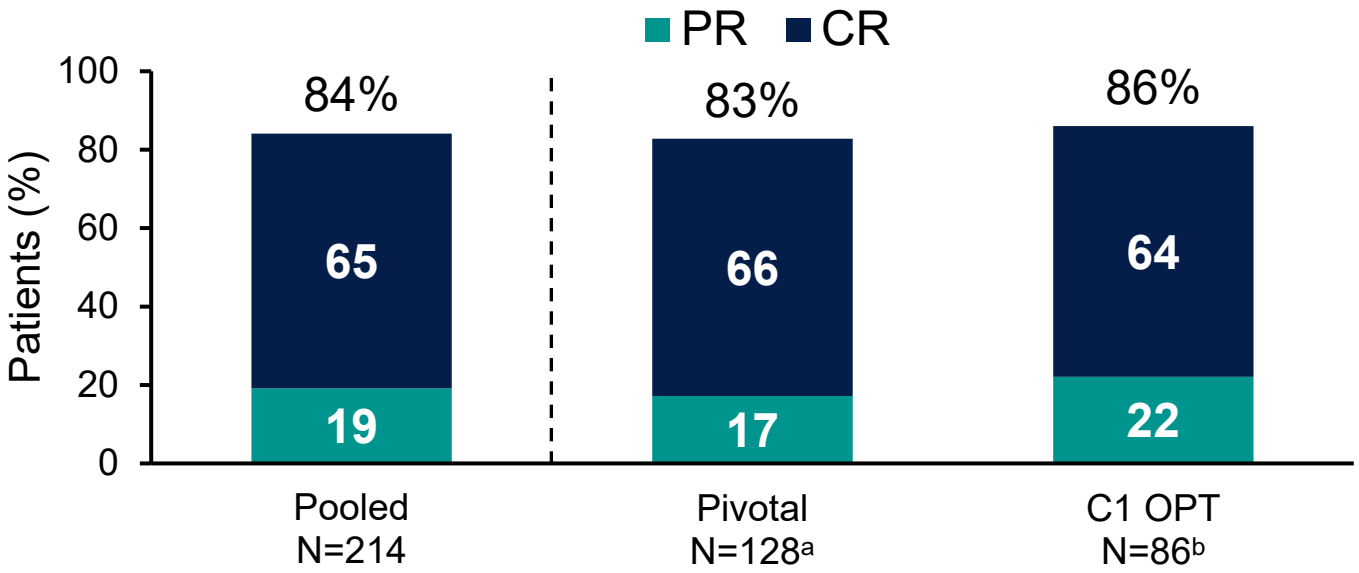


- In C1 OPT, with no mandatory hospitalization, 54% of patients who received the first full dose (44/82) had outpatient monitoring for CRS
  - Regardless of hospitalization status at the first full dose, 77% of patients with CRS following the first full dose (23/30) had CRS onset in the outpatient setting; all were able to identify CRS signs/symptoms in a timely manner and receive adequate treatment
- In both cohorts, most CRS occurred after the first full dose; median time to CRS onset after the first full dose was 2.5 days in C1 OPT

[a]Graded by Lee et al 2019 criteria.[1] [b]All grade 1–2; none leading to discontinuation.

1. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-38.

High Rates of Complete Response and MRD Negativity



MRD-Negativity Rate	n (%)
Pooled (n=135)	89 (66)
Pivotal (n=91)	61 (67)
C1 OPT (n=44)	28 (64)

Based on MRD-evaluable population per clonoSEQ® PBMC assay with 10^{-6} cutoff.

- At 6 mo in C1 OPT, an estimated 86% of patients with CR remained in CR
- No impact on time to response, for both cohorts:
  - Median time to response: 1.4 mo[c]
  - Median time to complete response: 1.5 mo[d]

CR was complete metabolic response (ie, PET negativity). CR, complete response; PBMC, peripheral blood mononuclear cell; PR, partial response. [a]Three patients (2%) were not evaluable. [b]Five patients (6%) were not evaluable. [c]Range: 1.2–4.4 in C1 OPT, 1.0–3.0 in pivotal. [d]Range: 1.2–4.7 in C1 OPT, 1.2–11.1 in pivotal.

Conclusions

- In the C1 OPT R/R FL cohort, the 3-SUD regimen and simple measures of prophylactic dexamethasone administration and hydration substantially reduced incidence and severity of CRS and ICANS with epcoritamab
  - No grade ≥3 CRS and no ICANS
  - With no mandatory hospitalization, most patients were monitored as outpatients at the first full dose, and regardless of hospitalization status at epcoritamab administration, CRS was managed effectively
- Epcoritamab demonstrated robust, clinically meaningful efficacy, including deep, durable responses and high rates of MRD negativity, in the largest R/R FL population treated with a T-cell–engaging therapy to date
- Responses incl MRD- were observed early, durable and correlated with long term outcomes
  - mPFS NR in pts with MRD-
- These encouraging data further support the feasibility and safety of epcoritamab as a potential outpatient treatment option for patients with R/R FL[1]
- FDA priority review for epcoritamab in R/R FL with target action date of June 28, 2024

1. Andorsky D, et al. Subcutaneous epcoritamab administered outpatient for relapsed or refractory diffuse large B-cell lymphoma and follicular lymphoma: Results from phase 2 EPCORE NHL-6. ASCO 2024. Abstract 7029.

Epcoritamab With Rituximab + Lenalidomide (R^2) in Previously Untreated (1L) Follicular Lymphoma (FL) and Epcoritamab Maintenance in FL: EPCORE NHL-2 Arms 6 and 7

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Presented at the American Society of Clinical Oncology Annual Meeting; May 31–June 4, 2024; Chicago, IL

Study Design

Key inclusion criteria

- CD20⁺ FL
  - Grade 1, 2, or 3A
- 1L FL **(arm 6, 1L FL)**
- In CR or PR after 1–2 lines of SOC treatment **(arm 7, FL maintenance)**
- ECOG PS 0–2
- Measurable disease by CT or MRI **(arm 6, 1L FL)**
- Adequate organ function

Data cutoff: January 31, 2024

Step-up dosing[a]

Arm 6 (1L FL) expansion, N=41

Epcoritamab (SC)	Rituximab (IV)	Lenalidomide (oral)
48 mg	**375 mg/m²**	**20 mg**
QW C1–2, Q4W C3+ (28 d/C)	QW C1, Q4W C2–6	QD for 21 d in C1–12
Treatment up to 2 y		

Arm 7 (FL maintenance after SOC treatment) expansion, N=20

Epcoritamab (SC)
48 mg
QW C1 (28 d)
Q8W C2–13 (56 d/C)
Treatment up to 2 y

- **Primary objective:**
  - **Arm 6:** Antitumor activity (ORR)[b]
  - **Arm 7:** Safety/tolerability
- **Key secondary endpoints:**
  - **Arm 6:** Safety/tolerability, DOR, DOCR, PFS, OS
  - **Arm 7:** CR rate,[c] DOCR

1L, previously untreated; C, cycle; CR, complete response; CT, computed tomography; d, day(s); DOCR, duration of complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; mo, month(s); MRI, magnetic resonance imaging; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; QD, once daily; QW, once weekly; Q4W, once every 4 weeks; Q8W, once every 8 weeks; R², rituximab + lenalidomide; SC, subcutaneous; SOC, standard of care; SUD, step-up dose; wk, week(s); y, year(s). [a]SUD 1: priming, 0.16 mg; SUD 2: intermediate, 0.8 mg. [b]Radiographic disease evaluation was performed every 12 wk until CR, then every 24 wk until disease progression. [c]Radiographic disease evaluation was performed every 12 wk for the first 24 wk (12 and 24 wk), then every 24 wk until disease progression. ClinicalTrials.gov: NCT04663347. EudraCT: 2020-000845-15.

1L FL: Baseline Characteristics, Treatment Exposure, and Follow-Up

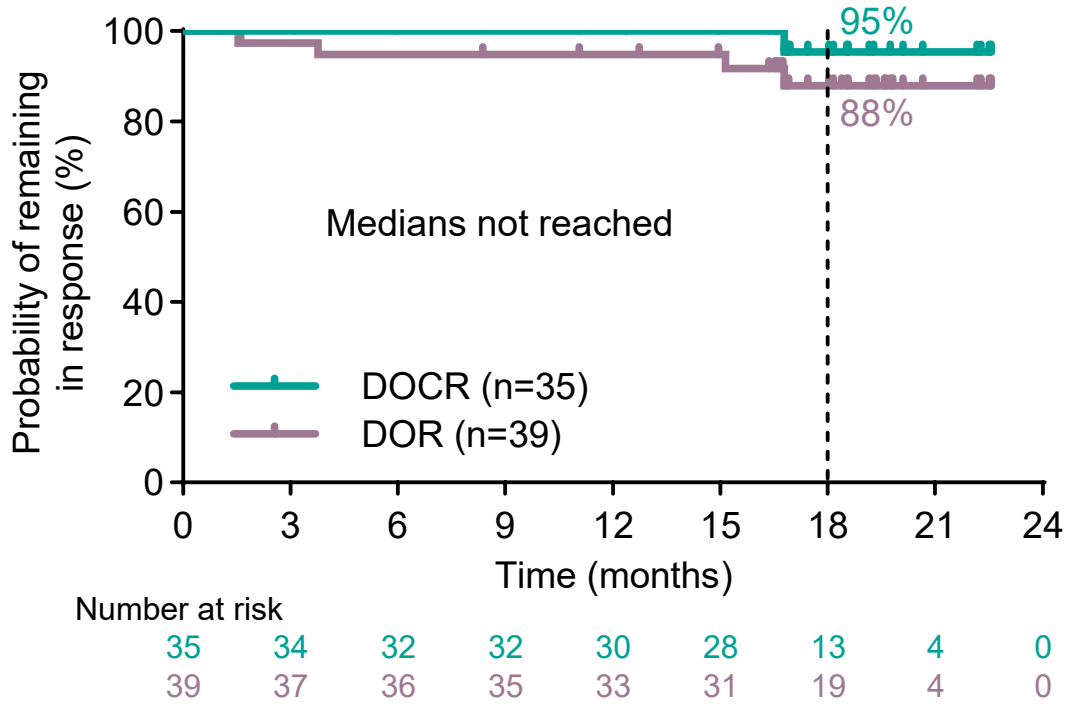
Characteristic	N=41
Median age, y (range)	57 (39–78)
Male, n (%)	21 (51)
Ann Arbor stage, n (%)[a]	
III	16 (39)
IV	22 (54)
FLIPI, n (%)[b]	
2	15 (37)
3–5	14 (34)
ECOG PS, n (%)	
0	34 (83)
1	6 (15)
2	1 (2)

Treatment Exposure and Follow-Up	N=41
Median follow-up, mo (range)	22.8 (1.4+ to 25.6)
Epcoritamab treatment exposure[c]	
Median number of treatment cycles initiated (range)[d]	23 (1–27)
Median duration of treatment, mo (range)	22.0 (0.5–24.2)
Ongoing treatment, n (%)	12 (29)
Completed treatment per protocol, n (%)	14 (34)
Discontinued treatment, n (%)	15 (37)
AE	9 (22)
Patient withdrawal	2 (5)
PD	1 (2)
Other[e]	3 (7)

1L, previously untreated; AE, adverse event; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; FLIPI, Follicular Lymphoma International Prognostic Index; mo, month(s); PD, progressive disease; wk, week(s); y, year(s). [a]Ann Arbor stage was I–II in 3 patients. [b]FLIPI was 0–1 in 12 patients. [c]Median time from diagnosis to first dose was 11.6 wk (range, 2.3–352). [d]Patients initiated a median of 6 cycles of rituximab (range, 1–6) and 12 cycles of lenalidomide (range, 1–12). [e]Other reasons for treatment discontinuation were maximum clinical benefit, complications from infection, and COVID-19 (n=1 each).

1L FL: Epcoritamab + R² Continued to Show Deep, Durable Responses

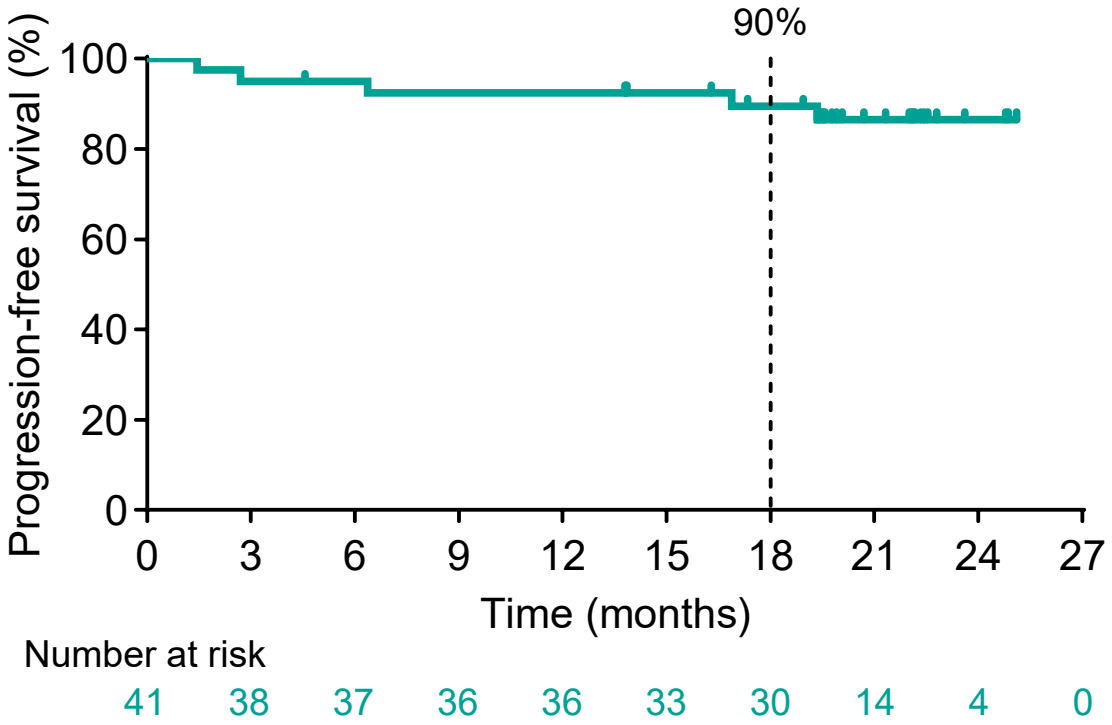
	N=41[a]
Overall response, n (%)	39 (95)
Complete response, n (%)	35 (85)
Partial response, n (%)	4 (10)
Progressive disease, n	0
Median time to response, mo (range)	2.7 (1.2–5.5)
Median time to complete response, mo (range)	2.8 (1.4–11.4)

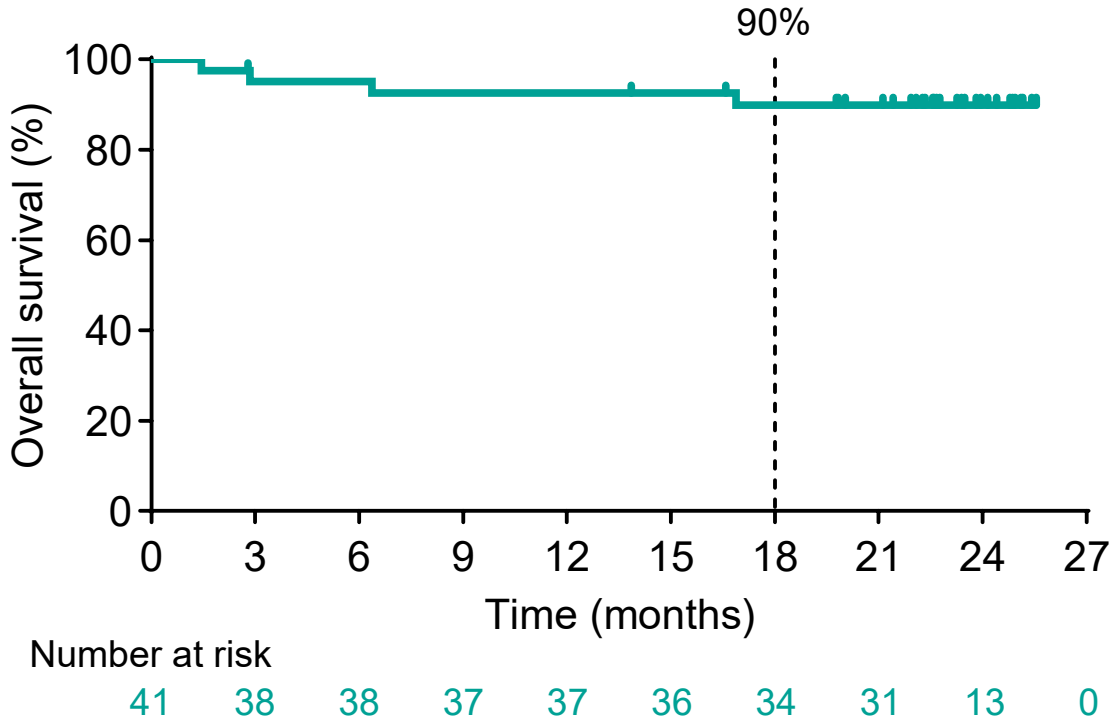


High rates of patients remaining in response and complete response were observed at 18 months

1L, previously untreated; DOCR, duration of complete response; DOR, duration of response; FL, follicular lymphoma; mo, month(s); R², rituximab + lenalidomide. Kaplan–Meier estimates of DOR and DOCR assessed by investigator. [a]A total of 2 patients were not evaluable.

1L FL: Progression-Free and Overall Survival

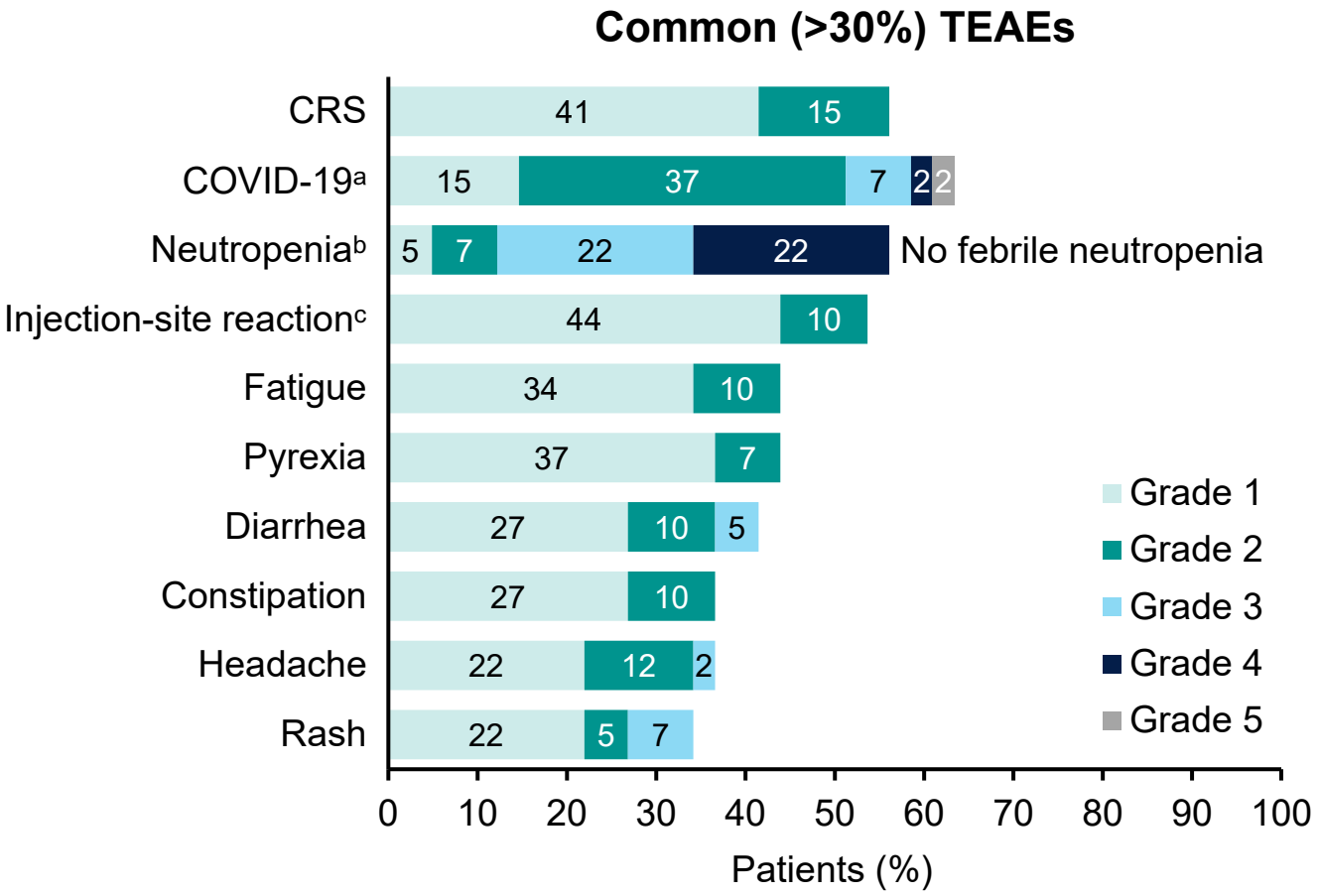




High rates of progression-free and overall survival were observed at 18 months

1L, previously untreated; FL, follicular lymphoma. Kaplan–Meier estimate of progression-free survival assessed by investigator.

1L FL: Safety Was Consistent With Prior Reports



- Common TEAEs were mostly low grade
- TEAEs leading to epcoritamab discontinuation were COVID-19 (n=5), CMV reactivation (n=1), ovarian epithelial cancer and pleural effusion (n=1), pneumonitis (n=1), and toxic skin eruption (n=1)
  - Pleural effusion and ovarian epithelial cancer were not deemed to be related to epcoritamab by the investigator
- Fatal TEAEs were COVID-19 pneumonia and septic shock (n=1 each)
- There is an increased risk of morbidity and mortality due to infections for patients with hematologic malignancies being treated with B-cell–depleting therapies

1L, previously untreated; CMV, cytomegalovirus; CRS, cytokine release syndrome; FL, follicular lymphoma; TEAE, treatment-emergent adverse event. [a]Combined term includes COVID-19, COVID-19 pneumonia, and post-acute COVID-19 syndrome. [b]Combined term includes neutropenia and decreased neutrophil count. [c]Combined term includes injection-site reaction, erythema, rash, pain, hypersensitivity, and swelling.

FL Maintenance After SOC: Baseline Characteristics, Treatment History, Exposure, and Follow-Up

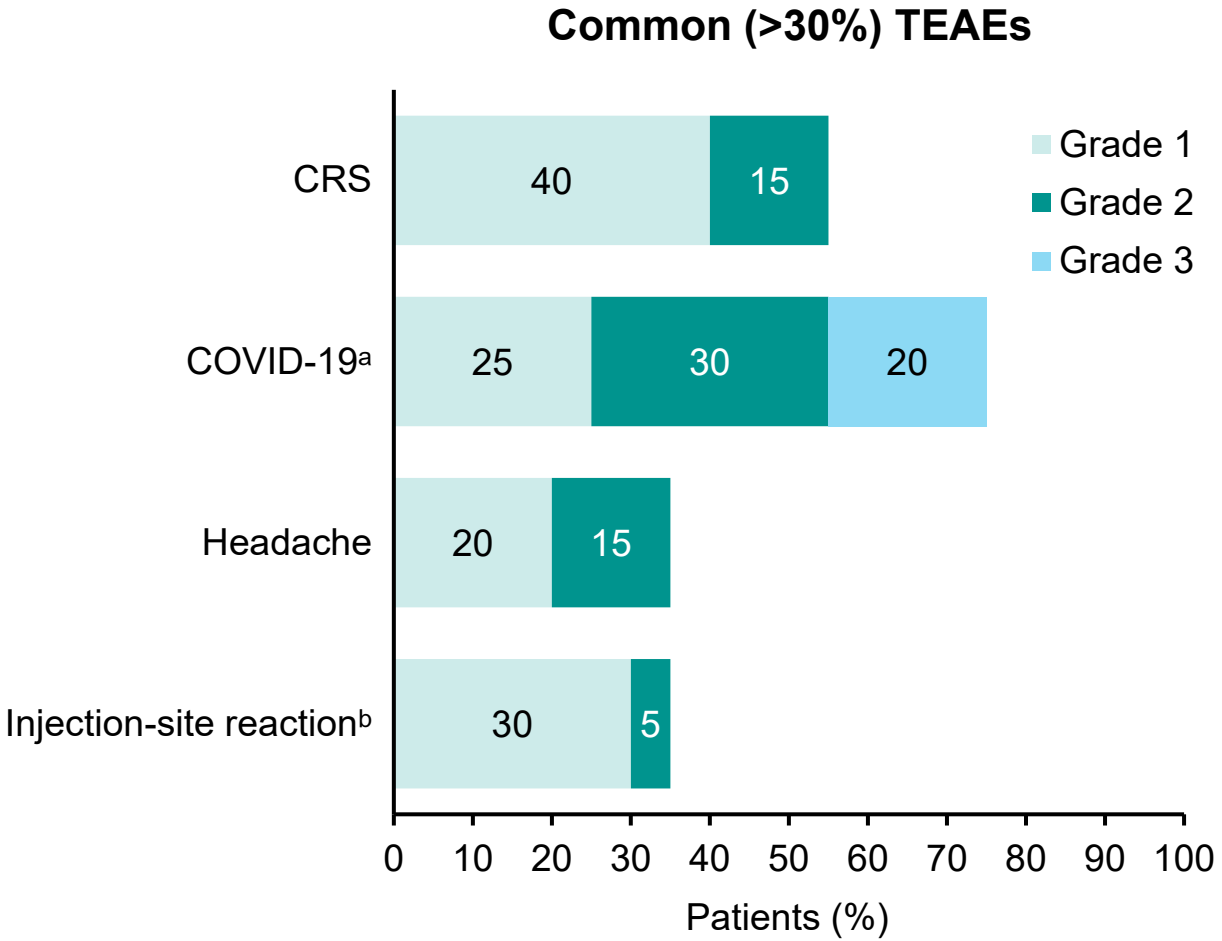
Characteristic	N=20
Median age, y (range)	54.5 (31–78)
Male, n (%)	11 (55)
FLIPI, n (%)[a]	
2	3 (15)
3–5	5 (25)
ECOG PS, n (%)	
0	17 (85)
1	3 (15)
Treatment History	**N=20**
Median time from end of SOC therapy to first dose, mo (range)	2.5 (0.7–6.0)
Median time from end of last anti-CD20 therapy to first dose, mo (range)	2.9 (1.2–9.7)
SOC line of therapy, n (%)[b]	
First line	16 (80)
Second line	3 (15)
Prior ASCT, n (%)	1 (5)
Best response to SOC therapy, n (%)	
Complete response	12 (60)
Partial response	8 (40)

Treatment Exposure and Follow-Up	N=20
Median follow-up, mo (range)	22.1 (5.8+ to 23.5)
Epcoritamab treatment exposure[c]	
Median number of treatment cycles initiated (range)	9.5 (2–13)
Median duration of treatment, mo (range)	19.7 (1.0–23.1)
Ongoing treatment, n (%)	8 (40)
Completed treatment per protocol, n (%)	4 (20)
Discontinued treatment, n (%)	8 (40)
AE	3 (15)
Patient withdrawal	3 (15)
PD	2 (10)

- Prior SOC treatments included anti-CD20 mAb–containing regimens (100%), alkylating agent–containing regimens (80%), anthracyclines (50%), and others (75%)

AE, adverse event; ASCT, autologous stem cell transplant; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; FLIPI, Follicular Lymphoma International Prognostic Index; mo, month(s); PD, progressive disease; SOC, standard of care; y, year(s). [a]FLIPI was 0–1 in 10 patients and unknown in 2 patients. [b]One patient came on to trial with SOC in the fourth-line, noted as a protocol deviation. [c]Median time from diagnosis to first dose was 10.1 mo (range, 5.3–260).

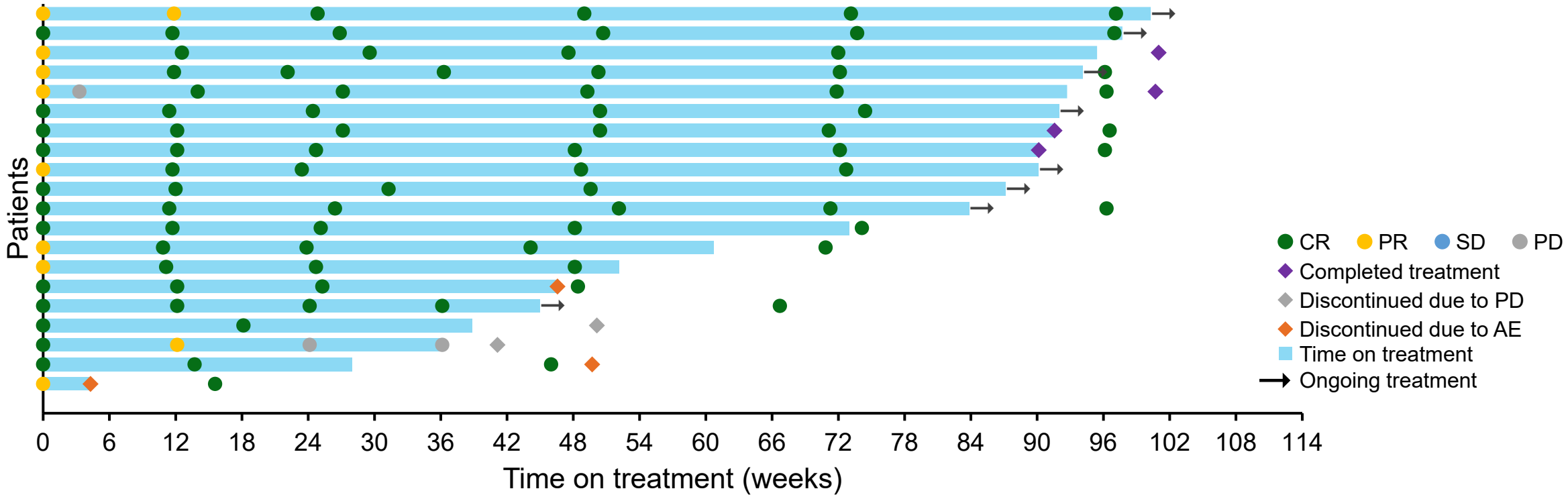
FL Maintenance After SOC: No New Safety Signals With Extended Q8W Dosing



- Common TEAEs were mostly low grade
- TEAEs leading to epcoritamab discontinuation were myelodysplastic syndrome and respiratory failure (n=1 each)
  - Myelodysplastic syndrome was not deemed to be related to epcoritamab by the investigator
- One fatal TEAE occurred (respiratory failure, post-acute COVID syndrome after 2 cycles of epcoritamab)

CRS, cytokine release syndrome; FL, follicular lymphoma; Q8W, once every 8 weeks; SOC, standard of care; TEAE, treatment-emergent adverse event. [a]Combined term includes COVID-19, COVID-19 pneumonia, and post-acute COVID-19 syndrome. [b]Combined term includes injection-site reaction, erythema, extravasation, and swelling.

FL Maintenance After SOC: Early Onset and Long Duration of Responses



All 8 patients enrolling with partial response (100%) converted to complete response

An estimated 83% of patients remained in response
and an estimated 90% of patients remained alive at 21 months

AE, adverse event; CR, complete response; FL, follicular lymphoma; PD, progressive disease; PR, partial response; SD, stable disease; SOC, standard of care. Per protocol, patients continued to receive scans if they discontinued treatment for reasons other than PD.

Conclusions

- Longer follow-up showed that fixed-duration epcoritamab + R^2 in previously untreated FL leads to deep and durable responses that translate to favorable long-term outcomes
  - ORR 95%, CR rate 85%
  - At 18 months, an estimated 90% of patients remained progression free and alive
- First disclosure of epcoritamab maintenance therapy given Q8W for up to 2 years after 1–2 lines of SOC treatment in patients with FL shows the regimen was well tolerated with no new safety signals and led to deepening responses
  - 100% of patients enrolling with partial response converted to complete response
- Results support the continued evaluation of epcoritamab-based, chemotherapy-free regimens in FL; two phase 3 trials are actively enrolling
  - EPCORE FL-1, epcoritamab + R^2 vs R^2 alone in relapsed or refractory FL (NCT05409066)
  - EPCORE FL-2, epcoritamab + R^2 vs chemoimmunotherapy or R^2 alone in previously untreated FL (NCT06191744)

Summary: Epcoritamab

- Six oral and poster presentations at ASCO 2024
- Data highlights the breadth of clinical program
  - Two first clinical data disclosures in Follicular Lymphoma
    - Novel C1 OPT data from pivotal R/R FL trial, expected PUDFA date June 28, 2024
    - First CD3XCD20 to show data as a FL maintenance therapy
  - Updated combination data across histologies and lines of therapy
    - Durable CRs observed across datasets including long term follow up from the pivotal monotherapy trial in R/R DLBCL, as well as for epcoritamab in combination with R-GemOx and R-DHAX/C
  - Outpatient administration
    - Underline the potential for epcor administration conducive of all practice settings
- These encouraging data speak to the potency, tolerability, combinability and versatility of epcoritamab
- In summary, data continues to give us confidence in epcoritamab being a potential future core therapy and “best in class and beyond”

Genmab

Genmab

Acasunlimab at ASCO

Dr. Tahi Ahmadi

Acasunlimab (DuoBody-PD-L1x4-1BB) Alone or in Combination With Pembrolizumab in Patients With Previously Treated Metastatic Non-Small Cell Lung Cancer: Initial Results of a Randomized, Open-Label, Phase 2 Trial

Joachim Aerts[1], Luis Paz-Ares[2], Carole Helissey[3], Frederico Cappuzzo[4], Gilles Quéré[5], Dariusz Kowalski[6], Jose Carlos Benitez[7], Florian Guisier[8], Benjamin Besse[9], Shirish Gadgeel[10], Thomas Wehler[11], Ignacio Gil-Bazo[12], Michael J. Chisamore[13], Cem Gorgun[14], Ilhan Celik[15], Marie Holst Mørch[16], Patricia Garrido Castro[17], Teng Jin Ong[18], Enriqueta Felip[19]

[1]Erasmus MC, Rotterdam, Netherlands; [2]Hospital Universitario 12 de Octubre, Madrid, Spain; [3]Military Hospital Begin, Saint-Mandé, France; [4]IFO Regina Elena, Rome, Italy; [5]Hopital Morvan CHU de Brest, Brest, France; [6]The Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [7]Medical Oncology Intercenter Unit, Regional and Virgen de la Victoria University Hospitals, Biomedical Research Institute of Málaga (IBIMA BIONAND Platform), Málaga, Spain; [8]Normandie Univ, UNIROUEN, LITIS Lab QuantIF team EA4108, CHU Rouen, Department of Pneumology and Inserm CIC-CRB 1404, F-76000 Rouen, France; [9]Gustave Roussy, Villejuif, France; [10]Henry Ford Cancer Institute, Detroit, MI, USA; [11]Universitatsklinik Gießen und Marburg, Standort Gießen, Marburg, Germany; [12]Fundacion Instituto Valenciano de Oncologia, Valencia, Spain; [13]Merck & Co., Inc., Rahway, NJ, USA; [14]BioNTech US Inc., Cambridge, MA, USA; [15]BioNTech SE, Mainz, Germany; [16]Genmab, Copenhagen, Denmark; [17]Genmab, Utrecht, Netherlands; [18]Genmab, Plainsboro, NJ, USA; [19]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain

Presented at the American Society of Clinical Oncology Annual Meeting; May 31–June 4, 2024; Chicago, IL
Poster Number 2533

GCT1046-04 Study Design

A phase 2, multicenter, randomized, open-label trial evaluating acasunlimab as monotherapy and in combination with pembro in patients with relapsed/refractory metastatic NSCLC after treatment with standard of care therapy with a CPI

Key inclusion criteria

- Age ≥18 years
- mNSCLC with disease progression after ≥1 prior anti-PD-L1 treatment
- Confirmed PD-L1 expression[a]
- ECOG PS 0–1
- Adequate hematologic and renal/hepatic function

Target N=126[b]

RANDOMIZED[c]

- **Acasunlimab 100 mg IV Q3W cycles 1–2, then 500 mg IV Q6W**
- **Acasunlimab 100 mg IV + pembro 200 mg IV Q3W**
- **Acasunlimab 100 mg IV + pembro 400 mg IV Q6W**

Treatment continued until:

- Progressive disease, unacceptable toxicity, or other reason for discontinuation; or
- ≤35 doses (Q3W) or ≤18 doses (Q6W) of pembro

Primary endpoint:
ORR by RECIST v1.1 per investigator

Key secondary endpoints:
DOR, PFS, OS, AEs, laboratory abnormalities

Selected exploratory endpoints:
PK, biomarkers

AEs, adverse events; CPI, immune checkpoint inhibitor; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry; IV, intravenous; ORR, overall response rate; OS overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PK, pharmacokinetics; RECIST, Response Evaluation Criteria in Solid Tumours; Q3W, once every 3 weeks; Q6W, once every 6 weeks.

NCT05117242.

Enrollment was discontinued in the acasunlimab monotherapy group in October 2023 and in the acasunlimab + pembro Q3W group in February 2024; enrollment is ongoing in acasunlimab + pembro Q6W group.

[a]Prior to cycle 1 day 1 with PD-L1 expression in ≥1% of tumor cells by a sponsor-designated central laboratory using the Dako PD-L1 IHC 22C3 pharmDx assay or per site local assessment. [b]Including safety run-in for combination regimen; up to 40 centrally PD-L1+ patients planned to randomized per arm. [c]Randomization stratified by PD-L1 expression (1–49% vs ≥50% PD-L1+ tumor cells) and histology (squamous vs nonsquamous).

Baseline Characteristics

	Acasunlimab Monotherapy[a] (n=22)	Acasunlimab + Pembro Q3W[a] (n=42)	Acasunlimab + Pembro Q6W[a] (n=49)
Median age (range), y	67.5 (36–87)	66.5 (40–79)	62.0 (39–82)
Age ≥65 y, n (%)	14 (63.6)	26 (61.9)	20 (40.8)
Male, n (%)	13 (59.1)	24 (57.1)	29 (59.2)
Histology, n (%)			
Squamous cell	4 (18.2)	10 (23.8)	14 (28.6)
Adenosquamous	3 (13.6)	0	0
Adenocarcinoma	14 (63.6)	29 (69.0)	34 (69.3)
Other[b]	1 (4.5)	3 (7.1)	1 (2.0)
PD-L1 status by central testing, n (%)			
≥1%	16 (72.7)	25 (59.5)	35 (71.4)
1–49%	11 (50.0)	18 (42.9)	26 (53.1)
≥50%	5 (22.7)	7 (16.7)	9 (18.4)
Negative	5 (22.7)	10 (23.8)	8 (16.3)
Not available	1 (4.5)	7 (16.7)	6 (12.2)

	Acasunlimab Monotherapy[a] (n=22)	Acasunlimab + Pembro Q3W[a] (n=42)	Acasunlimab + Pembro Q6W[a] (n=49)
Prior CPI (any combination), n (%)			
Pembro	20 (90.9)	35 (83.3)	42 (85.7)
Nivolumab	2 (9.1)	5 (11.9)	4 (8.2)
Durvalumab	2 (9.1)	1 (2.4)	3 (6.1)
Atezolizumab	0	2 (4.8)	2 (4.1)
Last prior CPI therapy, n (%)			
Monotherapy[c]	7 (31.8)	11 (26.2)	13 (26.5)
Combination with chemotherapy	15 (68.2)	30 (71.4)	35 (71.4)
Duration of prior CPI, n (%)			
<6 months	8 (36.4)	12 (28.6)	16 (32.7)
≥6 months	14 (63.6)	29 (69.0)	32 (65.3)
Missing	0	1 (2.4)	1 (2.0)
Number of prior systemic regimens			
1	15 (68.2)	25 (59.5)	32 (65.3)
2	6 (27.3)	13 (31.0)	11 (22.4)
3	0	3 (7.1)	4 (8.2)
≥4	1 (4.5)	1 (2.4)	1 (2.0)

Data cutoff: March 22, 2024.

[a]Patients who were PD-L1$^+$ by local testing were allowed to enroll; thus, some randomized patients were not PD-L1$^+$ by central testing. The population for efficacy analysis included only centrally confirmed PD-L1$^+$ patients. [b]Mixed-type NSCLC, large-cell NSCLC, NSCLC not otherwise specified, NSCLC with no additional information, and sarcomatoid carcinoma (n=1 each). [c]1 patient in the acasunlimab + pembro Q6W cohort received nivolumab and ipilimumab.

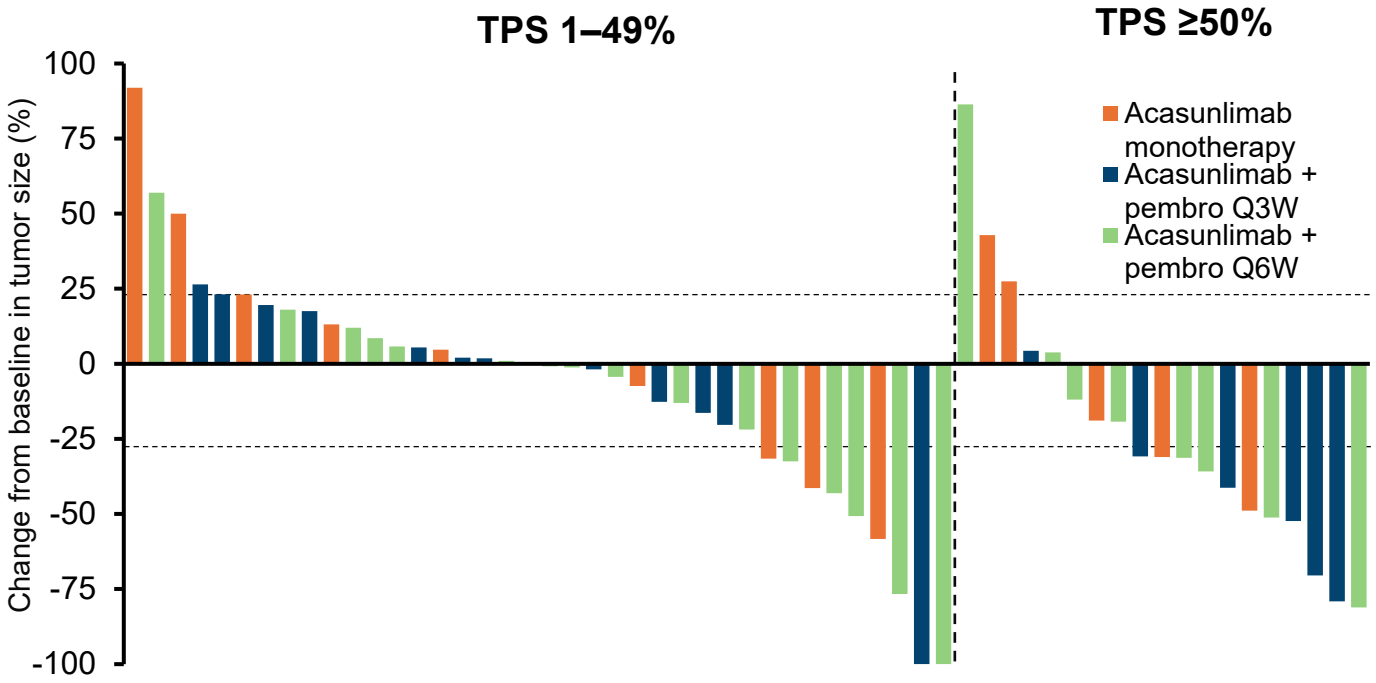
Patient Disposition

	Acasunlimab Monotherapy (n=22)	Acasunlimab + Pembro Q3W (n=42)	Acasunlimab + Pembro Q6W (n=49)
Ongoing treatment, n (%)	1 (4.5)	6 (14.3)	21 (42.9)
Discontinued treatment, n (%)	21 (95.5)	36 (85.7)	28 (57.1)
Documented radiographic disease progression	16 (72.7)	17 (40.5)	13 (26.5)
Clinical progression	1 (4.5)	3 (7.1)	3 (6.1)
AE[a]	4 (18.2)	14 (33.3)	12 (24.5)
Patient request	0	2 (4.8)	0

- Per study protocol, grade ≥3 immune-related AEs required discontinuation; the majority of AEs leading to discontinuation were asymptomatic liver-related events and resolved with corticosteroids
- Rate of discontinuation due to AEs was lower in the Q6W combination regimen than in Q3W

Data cutoff: March 22, 2024.
[a]AEs leading to discontinuation in ≥5% of patients in any treatment group included alanine aminotransferase increased and aspartate aminotransferase increased; note: the protocol mandated treatment discontinuation for grade 3 or higher transaminase elevations.

Anti-tumor Activity by Confirmed Best Overall Response



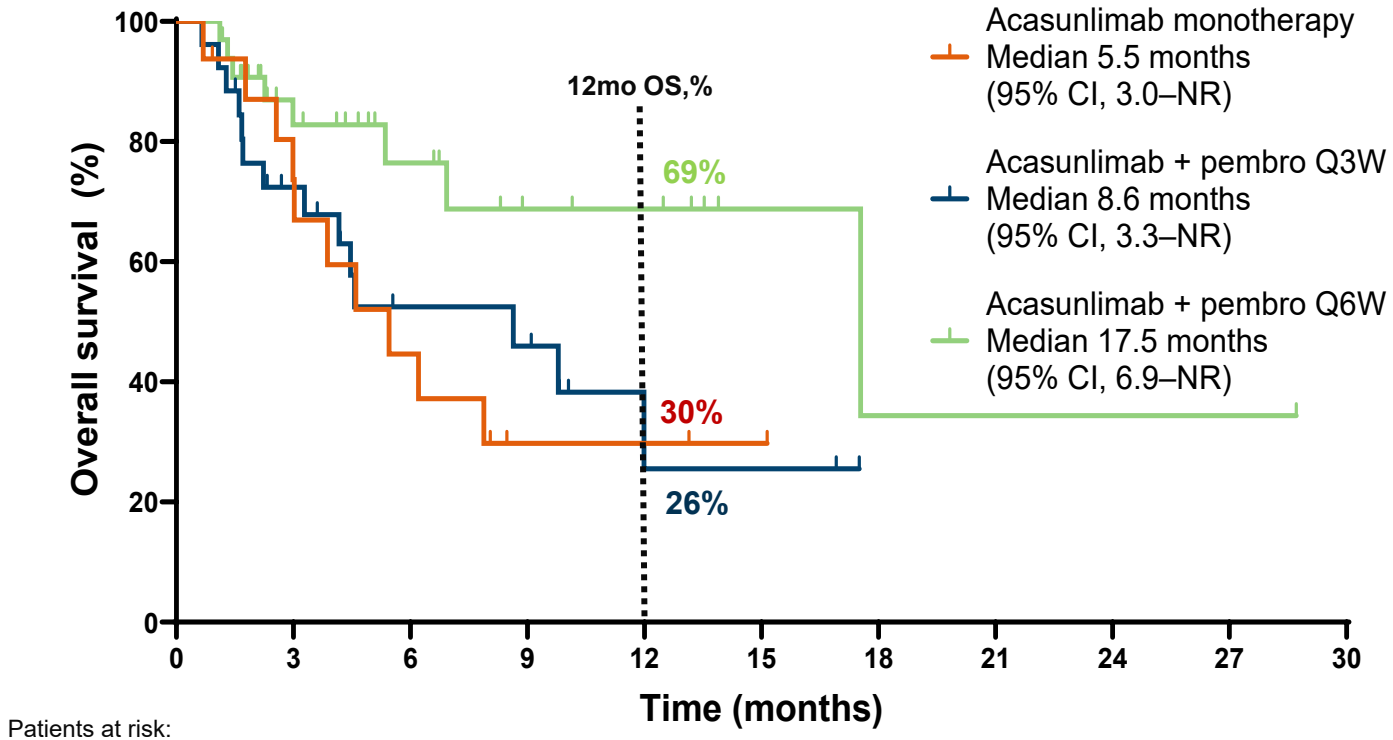
	Mono (n=16)	Combo Q3W (n=22)[a]	Combo Q6W (n=24)[b]
Unconfirmed ORR, % (95% CI)	31.3 (11.0–58.7)	20.8 (7.1–42.2)	29.6 (13.8–50.2)
Confirmed ORR, % (95% CI)	12.5 (1.6–38.3)	18.2 (5.2–40.3)	16.7 (4.7–37.4)
Confirmed DCR, % (95% CI)	50.0 (24.7–75.3)	59.1 (36.4–79.3)	75.0 (53.3–90.2)
Median DOR, mo (95% CI)	2.0 (1.6–NR)	5.2 (3.5–NR)	NR (NR–NR)
6-month PFS rate, %	0 (NA)	14 (3–31)	34 (13–56)

DCR, disease control rate; NA, not applicable; NR, not reported; TPS, tumor proportion score.
Data cutoff: March 22, 2024. Centrally confirmed PD-L1+ patients with post-baseline scans are shown.
Dashed lines indicate 20% and −30%. [a]n=24 for unconfirmed ORR. [b]n=27 for unconfirmed ORR.

- Acasunlimab + pembro demonstrated encouraging anti-tumor activity, with greater benefit seen in patients treated with the Q6W regimen:
  - Responses were deep and durable (mDOR, NR)
  - 30% ucORR and 75% disease control rate
- Anti-tumor activity was observed in:
  - Patients with TPS 1–49% and ≥50%
  - Patients with <6 mo and ≥6 mo of previous CPI treatment
  - Patients with squamous and non-squamous histology

Overall Survival (PD-L1+ Subset)

Kaplan–Meier Plot of OS in Patients With PD-L1+ mNSCLC



Patients at risk:

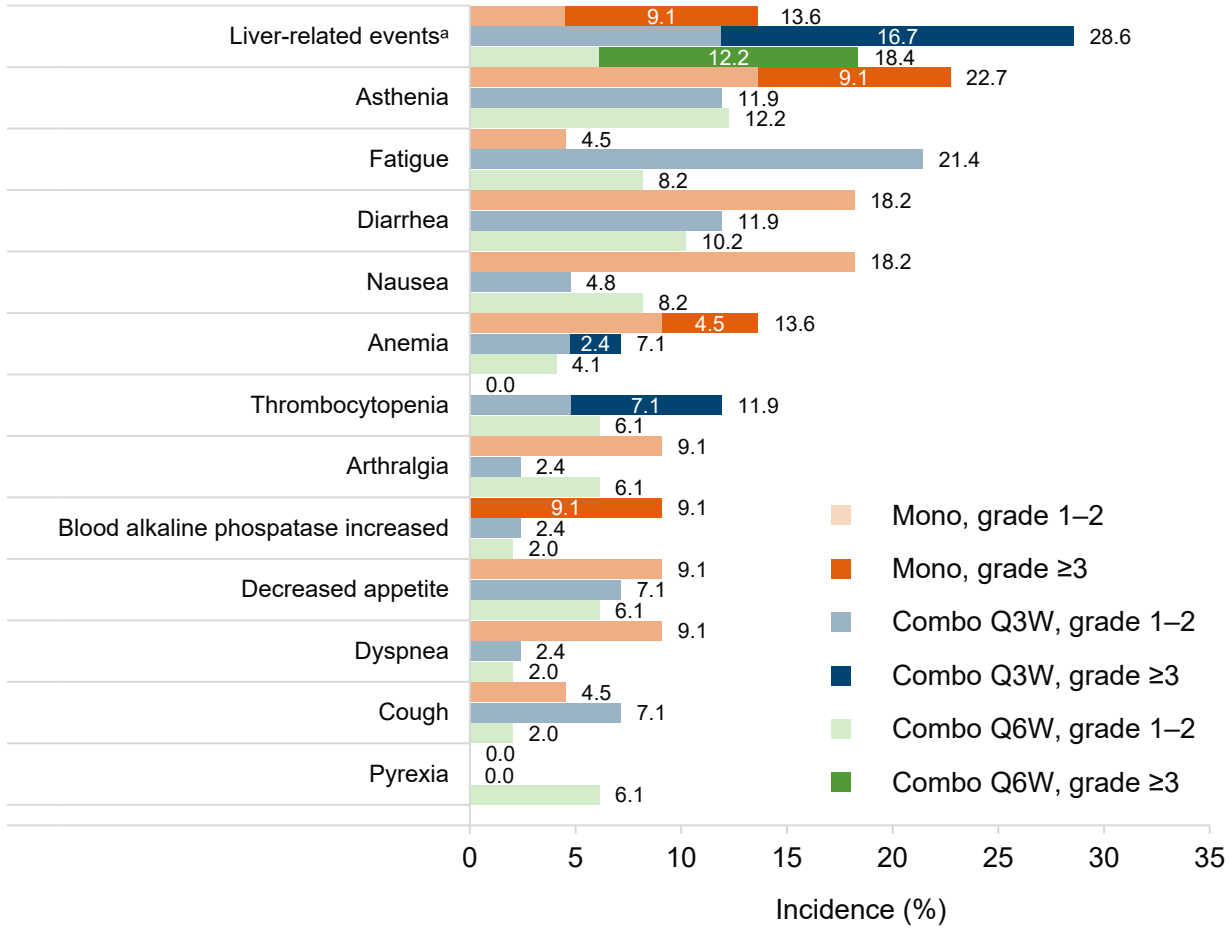
Acasunlimab monotherapy	16	11	6	2	2	1	0	0	0	0
Acasunlimab + pembro Q3W	26	16	8	7	2	2	0	0	0	0
Acasunlimab + pembro Q6W	38	20	12	7	6	2	1	1	1	1

- In patients with centrally confirmed PD-L1+ mNSCLC, acasunlimab + pembro administered Q6W showed a median OS of 17.5 months and a 12-month OS rate of 69%
- PD analyses corroborate the observed clinical benefit in the acasunlimab + pembro Q6W regimen through intermittent engagement and activation of 4-1BB that maintains long-term T-cell functionality and mitigates T-cell exhaustion vs the Q3W regimen*

Data cutoff: May 1, 2024. Centrally confirmed PD-L1+ patients are shown. * More date will be presented at an upcoming congress

Safety

TRAEs Reported in ≥5% of Patients in Any Treatment Group



- TRAEs observed with combination therapy were primarily grade 1/2
- Acasunlimab + pembro combination Q6W was associated with a lower incidence of grade ≥3 TRAEs (Q6W, 18.4%; Q3W, 28.6%), a lower incidence of treatment-related liver-related events (all grades: Q6W, 18.4%; Q3W, 28.6%)
- Majority of transaminase elevations were asymptomatic and reversible with corticosteroids and/or dose delay per protocol, and resolved more rapidly in patients treated with combination therapy Q6W vs Q3W

Data Cutoff: March 22, 2024. One grade 5 TRAE (immune-mediated hepatitis) was observed in the acasunlimab + pembro Q3W arm.

[a]Includes alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyltransferase increased, hypertransaminasemia, hepatitis, and immune-mediated hepatitis. Combo Q3W, acasunlimab + pembro Q3W; Combo Q6W, acasunlimab + pembro Q6W; CRS, cytokine release syndrome; Mono, acasunlimab monotherapy; TRAEs, treatment-related adverse events.

Conclusions

- Acasunlimab + pembro combination showed encouraging efficacy in patients with PD-L1$^+$ mNSCLC who had disease progression following ≥1 prior anti-PD-L1 treatment, with greater benefit observed with the Q6W regimen
  - Acasunlimab + pembro Q6W resulted in a 12-month OS rate of 69% and a median OS of 17.5 months
  - Adverse events were manageable, and a lower incidence of grade ≥3 TRAEs, transaminase elevations, and lower discontinuation rates were observed with the Q6W combination regimen
- These results support further evaluation of acasunlimab + pembro Q6W in patients with PD-L1$^+$ mNSCLC and will serve the basis for our late phase development plans in this indication

Further Advancing Our Differentiated Product Pipeline Towards The Market

Tivdak[1]

- Highly encouraging data in H&N
- Actively engaging with health authorities
- Working to generate additional data

EPKINLY[2]

- Promising data in both 1L and R/R FL
- Supports potential for EPKINLY as best-in-class in FL
- 1L FL study actively enrolling

Acasunlimab[3]

- Extraordinary Q6W OS data
- Manageable safety profile
- Supports Phase 3 trial start before end of year

Genmab 1. Co-development w/ Pfizer; 2. Co-development w/ AbbVie; 3. Co-development w/ BioNTech

Genmab

Q&A