2022 ASCO® ANNUAL MEETING

GEMSTONE-201: pre-planned primary analysis of a multicenter, single-arm, phase 2 study of sugemalimab in patients with relapsed or refractory extranodal natural killer/T cell lymphoma (R/R ENKTL)

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Introduction

- Relapsed or refractory extranodal natural killer/T cell lymphoma (R/R ENKTL) is a rare and aggressive type of non-Hodgkin's lymphoma.
- After failing an asparaginase-based regimen, patients with R/R ENKTL usually have poor prognosis and continued risk of relapse but lack effective treatment.
  - Chidamide, a targeted therapy approved for R/R peripheral T-cell lymphoma (R/R ENKTL as its subtype) in China, showed an ORR of 18.8% (3/16)[1] in R/R ENKTL population.
  - R/R ENKTL patients responded to chemotherapy, however response was often not durable, with median overall survival (OS) < 7 months and 1-year OS rate < 20%.[2,3]
- Achieving complete response often correlates with longer duration of response and OS when treating an aggressive disease like ENKTL.
- Sugemalimab is a full-length, fully human PD-L1 targeted immunoglobin G4 (IgG4, s228p) monoclonal antibody (mAb), being investigated in a variety of solid tumors and hematological malignancies.
  - **Breakthrough Therapy Designation (BTD)** was granted in the US and China for sugemalimab to treat adult patients with R/R ENKTL.
  - PD-L1 expression was seen in 80% of ENKTL tumor cells[4], indicating that PD-1/PD-L1 blockade could become an effective treatment for ENKTL.
- We present the primary analysis from GEMSTONE-201, the largest registrational study reported to date to evaluate an anti-PD-1/L1 mAb in R/R ENKTL.

1. Shi. et al., Ann Oncol 2015; 2. Lim et al, Ann Oncol 2017; 3. Bellei et al, Haematologica 2018; 4. Jo, J.C., et al., Ann Hematol, 2017.

GEMSTONE-201 – Study Design

Screening Phase → **Treatment Phase** → **Follow-up**

Key Eligibility Criteria

- Histologically confirmed ENKTL
- R/R ENKTL patients previously treated with asparaginase-based systemic therapy
- ECOG PS 0-1
- At least one measurable or evaluable lesion per Lugano 2014[1]
- Adequate organ function

Study Treatment

Sugemalimab
1200 mg,
IV, Q3W,
up to 24 months

- Safety
- Survival
- Radiology (if needed)

Primary endpoint:

- ORR assessed by IRRC

Key secondary endpoints:

- ORR assessed by Investigators
- CR rate, PR rate, DoR assessed by IRRC and Investigators
- Safety

Key exploratory endpoint:

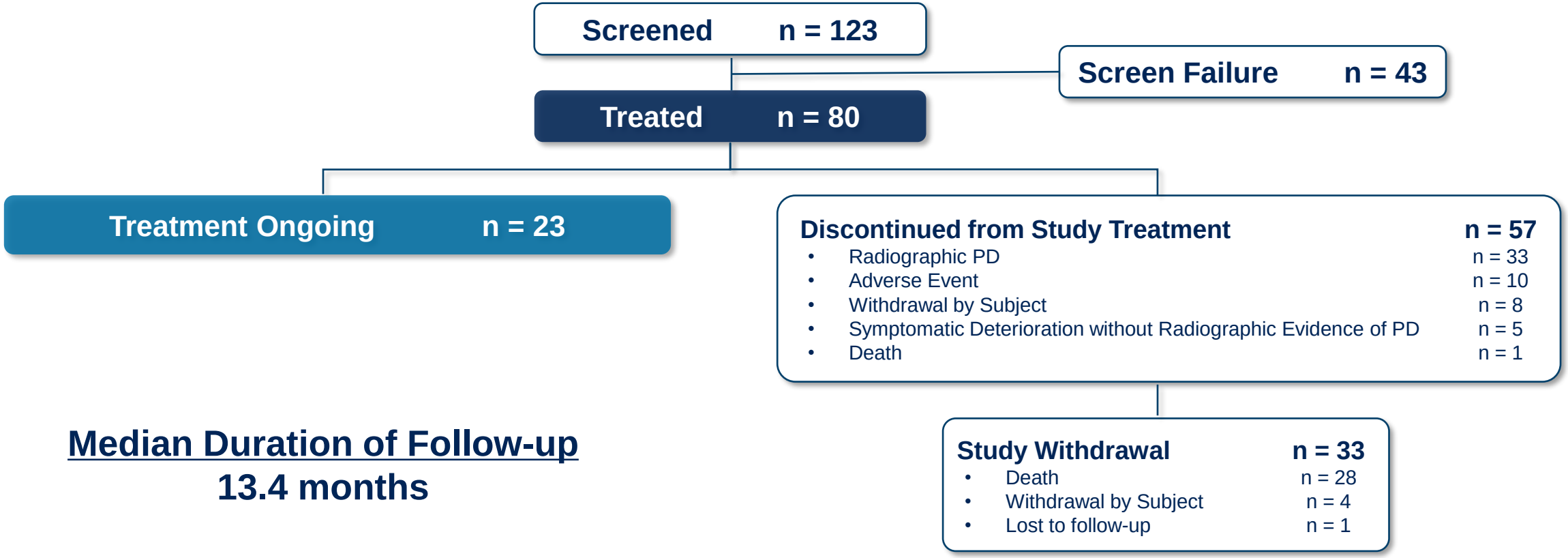
- 6-month OS rate

Statistical Method: IRRC-assessed ORR was tested at two-sided alpha of 0.05 with exact binomial test method.

1. Cheson BD, et al. J Clin Oncol 2014.

ECOG: Eastern Cooperative Oncology Group; PS: Performance Status; IV: Intravenous; Q3W: every three weeks; IRRC: Independent Radiological Review Committee; ORR: Objective Response Rate; CR: Compete Response; PR: Partial Response; DoR: Duration of Response; PK: Pharmacokinetics; PFS: Progression-free Survival; OS: Overall Survival

Patient Disposition



Median Duration of Follow-up
13.4 months

PD: Progressive Disease

Data cutoff date: Nov 10, 2021

Baseline Characteristics

	Sugemalimab (N = 80)
Sex, Male, n (%)	51 (63.8%)
Age, Median (range)	48.0 (29.0 – 74.0)
Baseline ECOG PS, n (%)	
0	21 (26.3%)
1	59 (73.8%)
Stage at Screening	
Stage I	9 (11.3%)
Stage II	17 (21.3%)
Stage III	0
Stage IV	54 (67.5%)

	Sugemalimab (N = 80)
Prior Systemic Therapy	
1 line	41 (51.3%)
2 lines	22 (27.5%)
≥ 3 lines	17 (21.3%)
Patient Status	
Relapsed	43 (53.8%)
Refractory	37 (46.3%)
Bone Marrow Involvement, Positive, n (%)	5 (6.3%)
Prior Autologous HSCT, Yes, n (%)	6 (7.5%)
Prior Radiotherapy, Yes, n (%)	49 (61.3%)

ECOG: Eastern Cooperative Oncology Group; Hematopoietic Stem Cell Transplantation; PS: Performance Status; HSCT

Data cutoff date: Nov 10, 2021

Primary Endpoint – ORR by IRRC

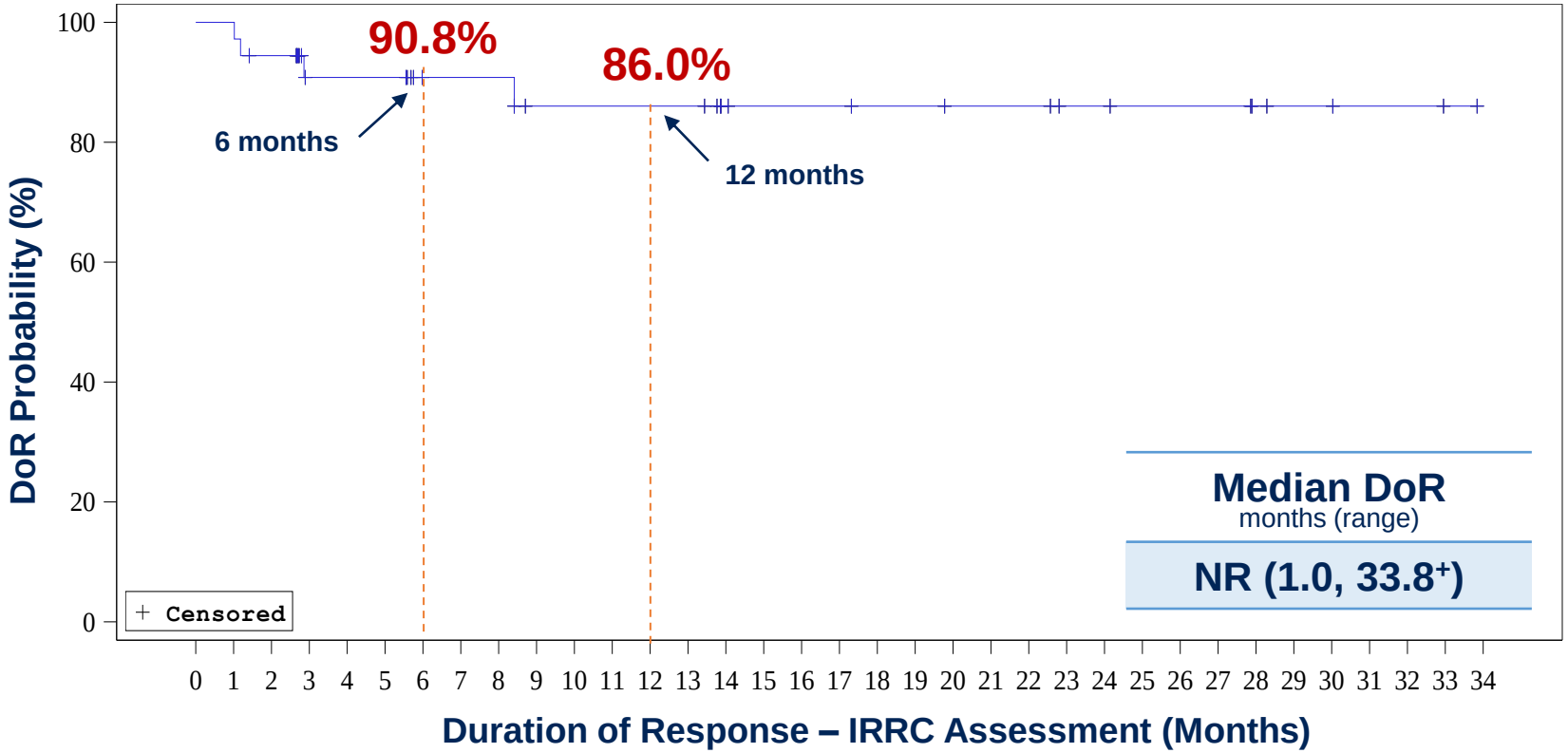
	Sugemalimab (N = 78[3])
ORR (CR+PR), n (%)	**36 (46.2%)**
95% CI	34.8%, 57.8%
P value	**< 0.0001**
Complete response	**29 (37.2%)**
Partial response	7 (9.0%)
Stable disease	8 (10.3%)
Progressive disease	24 (30.8%)
Unknown[1]	1 (1.3%)
NA[2]	9 (11.5%)

[1] The tumor assessment could not be completed by the investigator due to insufficient imaging evidence and this patient was therefore considered a non-responder.
[2] Nine patients had discontinued study treatment before the first post-baseline tumor assessment and were considered non-responders (recorded as "NA" in above table).
[3] Two patients were excluded from analysis for reasons that 1 patient was not confirmed as ENKTL by central pathology and the other patient was identified as no measurable or evaluable disease at baseline by IRRC.

ORR: Overall Response Rate; CR: Complete Response; PR: Partial Response; CI: Confidence Interval; NA: Not Applicable; IRRC: Independent Radiological Review Committee

Data cutoff date: Nov 10, 2021

Secondary Endpoint – DoR by IRRC



Subjects at risk

Sugemalimab	36	33	24	24	24	19	19	19	16	16	16	16	16	12	11	11	11	10	10	9	9	9	7	7	6	6	6	4	3	3	2	2	1	0

Analysis was performed on responders assessed by IRRC. "+" is for the minimum or maximum value from censored patients.
DoR: Duration of Response; IRRC: Independent Radiological Review Committee; NR: Not Reached; Q3W: every three weeks.

Data cutoff date: Nov 10, 2021

Secondary Endpoint – ORR by Investigator

Concordance rate between IRRC- and Investigator-assessed ORR = **97.1%**

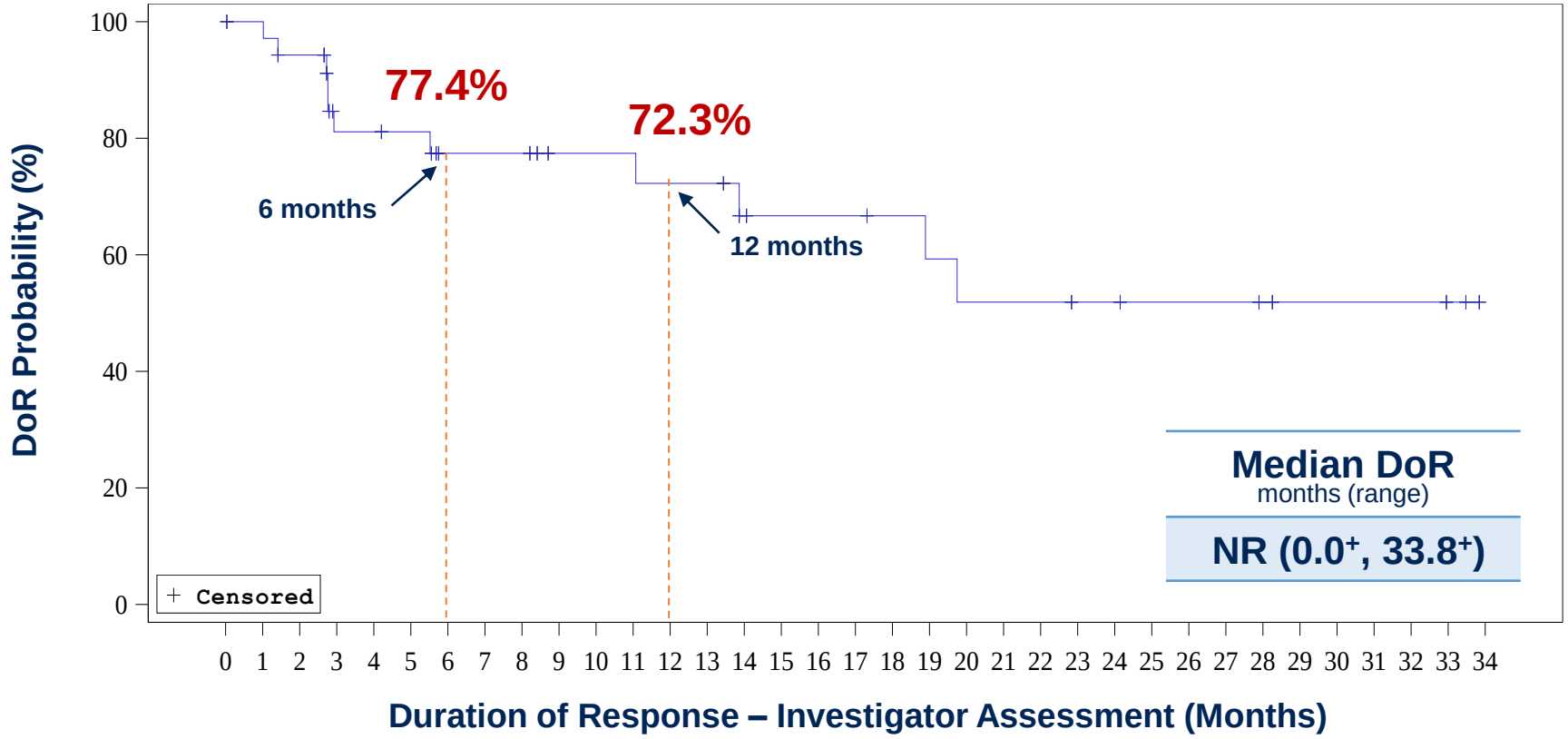
	Sugemalimab (N = 79[3])
ORR (CR+PR), n (%)	**36 (45.6%)**
95% CI	34.3%, 57.2%
Complete response	**24 (30.4%)**
Partial response	12 (15.2%)
Stable disease	4 (5.1%)
Progressive disease	28 (35.4%)
Unknown[1]	1 (1.3%)
NA[2]	10 (12.7%)

[1] The tumor assessment could not be completed by the investigator due to insufficient imaging evidence and this patient was therefore considered a non-responder.
[2] Ten patients had discontinued study treatment before the first post-baseline tumor assessment and were considered non-responders (recorded as "NA" in above table).
[3] One patient was excluded from efficacy analysis set for reason that the patient was not confirmed as ENKTL by central pathology.

ORR: Objective Response Rate; CR: Complete Response; PR: Partial Response; IRRC: Independent Radiological Review Committee; CI: Confidence Interval; NA: Not Applicable

Data cutoff date: Nov 10, 2021

Secondary Endpoint – DoR by Investigator



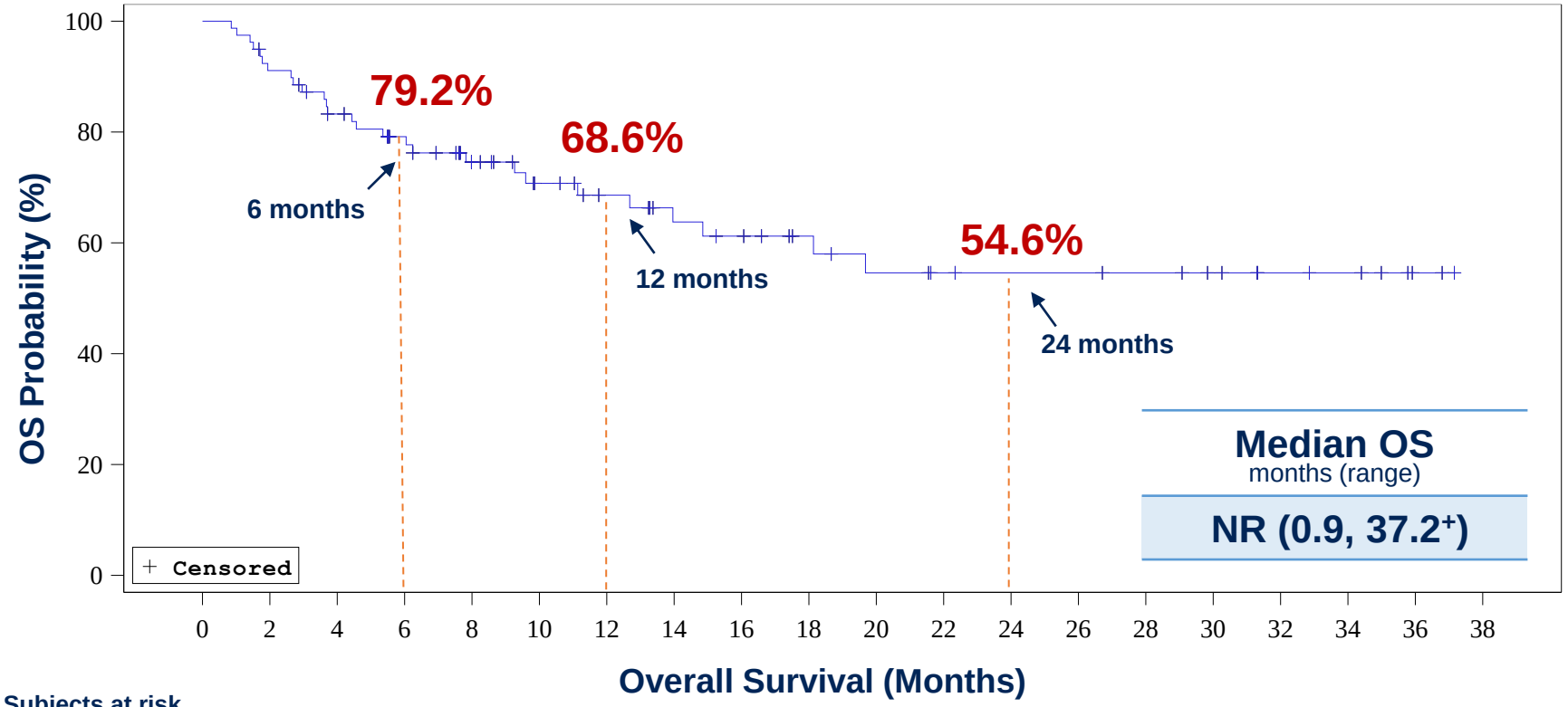
Subjects at risk

Sugemalimab	36	35	32	23	23	22	18	18	18	15	15	15	14	14	11	10	10	10	9	8	7	7	7	6	6	5	5	5	4	3	3	3	3	2	0

Analysis was performed on responders assessed by investigator. "+" is for the minimum or maximum value from censored patients.
DoR: Duration of Response; NR: Not Reached; Q3W: every three weeks.

Data cutoff date: Nov 10, 2021

Exploratory Endpoint – Overall Survival



Subjects at risk

Sugemalimab	79	78	71	67	62	59	54	50	43	40	35	34	30	29	25	24	23	21	19	17	16	16	14	13	13	13	13	12	12	12	10	9	7	6	6	4	2	1	0

Analysis was performed among patients in efficacy analysis set (n = 79). "+" is for the minimum or maximum value from censored patients.
OS: Overall Survival; NR: Not Reached; Q3W: every three weeks.

Data cutoff date: Nov 10, 2021

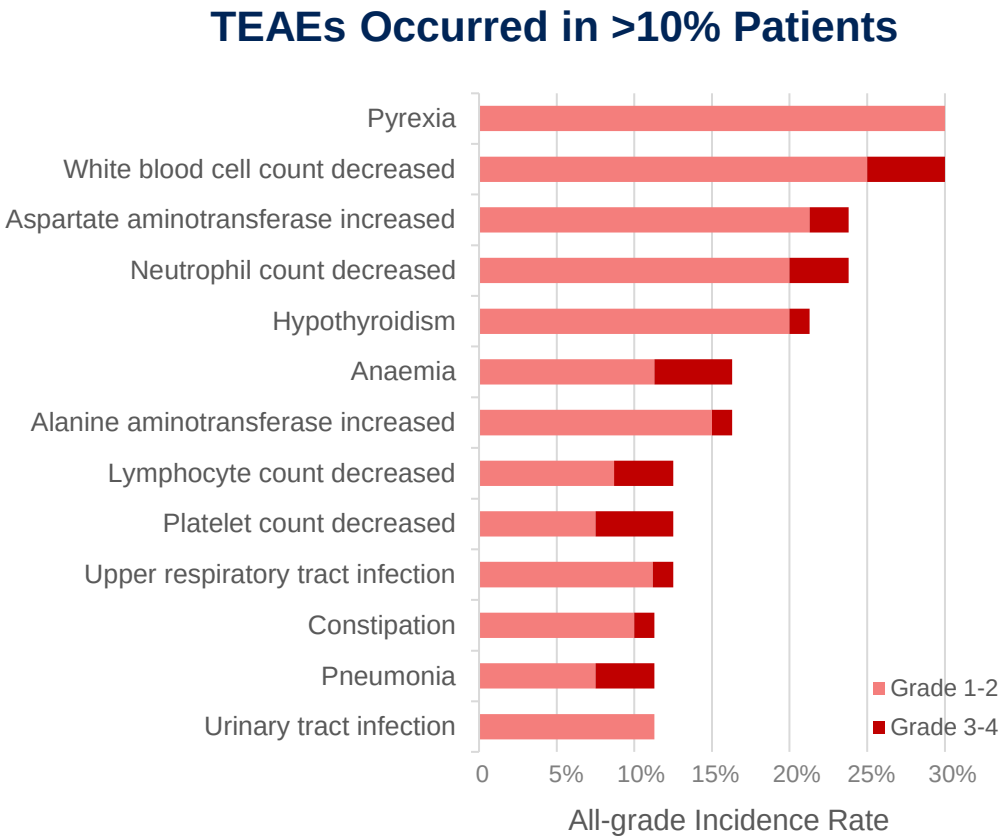
Safety Overview

	Sugemalimab (N = 80)
Treatment emergent adverse events (TEAE)	77 (96.3%)
Grade 3-5 TEAE	31 (38.8%)
Treatment-related adverse events (TRAE)	61 (76.3%)
Grade 3-5 TRAE	13 (16.3%)
Serious adverse events (SAE)	18 (22.5%)
Treatment-related SAE	5 (6.3%)
Immune-related adverse events (irAE)	21 (26.3%)
Infusion-related reaction TEAE	4 (5.0%)
TEAE leading to sugemalimab withdrawn	10 (12.5%)
TEAE leading to infusion interrupted	4 (5.0%)
TEAE leading to treatment cycle delay	13 (16.3%)
TEAE leading to death	5 (6.3%)

1. Safety in ENKTL was consistent with the known safety profile of sugemalimab in other studies.
2. Most TRAEs were Grade 1/2 events.
3. The majority of sponsor-assessed irAEs were Grade 1/2; no Grade 4/5 irAEs were observed.
4. No deaths were attributed to sugemalimab as assessed by the Investigator.

Data cutoff date: Nov 10, 2021

Treatment Emergent Adverse Events (TEAEs)

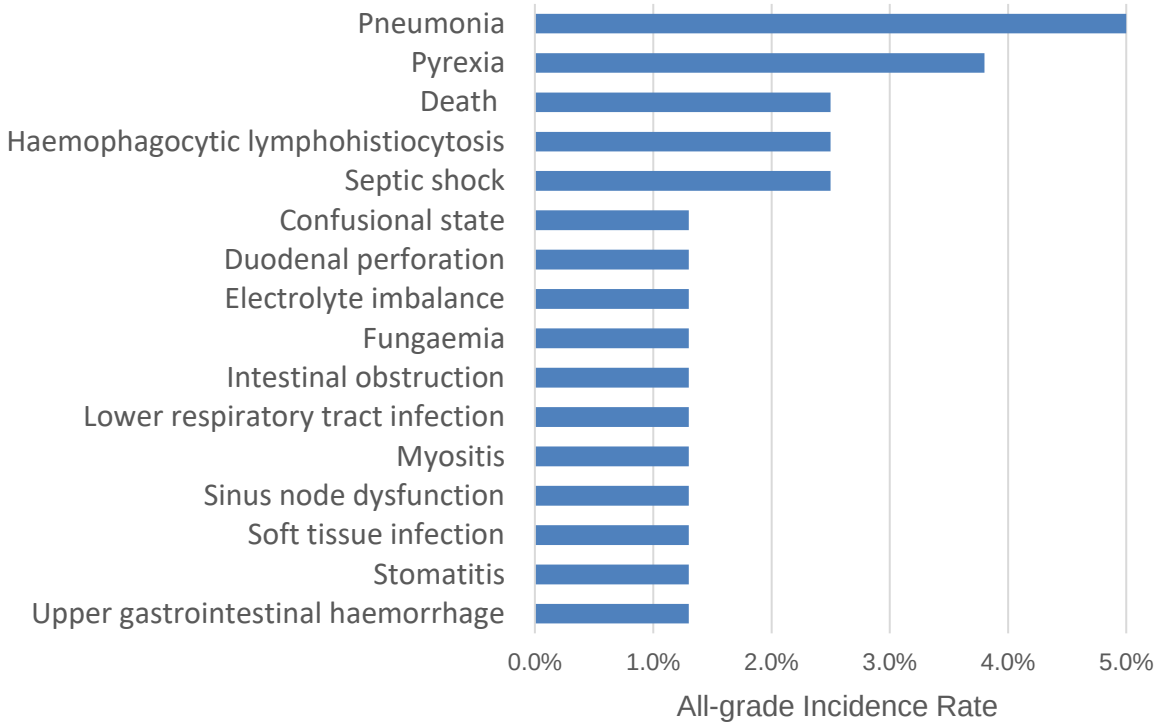


Most commonly reported TEAEs (>20%):

1. Pyrexia (30.0%)
2. White blood cell count decreased (30.0%)
3. Aspartate aminotransferase increased (23.8%)
4. Neutrophil count decreased (23.8%)
5. Hypothyroidism (21.3%)

Data cutoff date: Nov 10, 2021

Serious Adverse Events (SAEs)



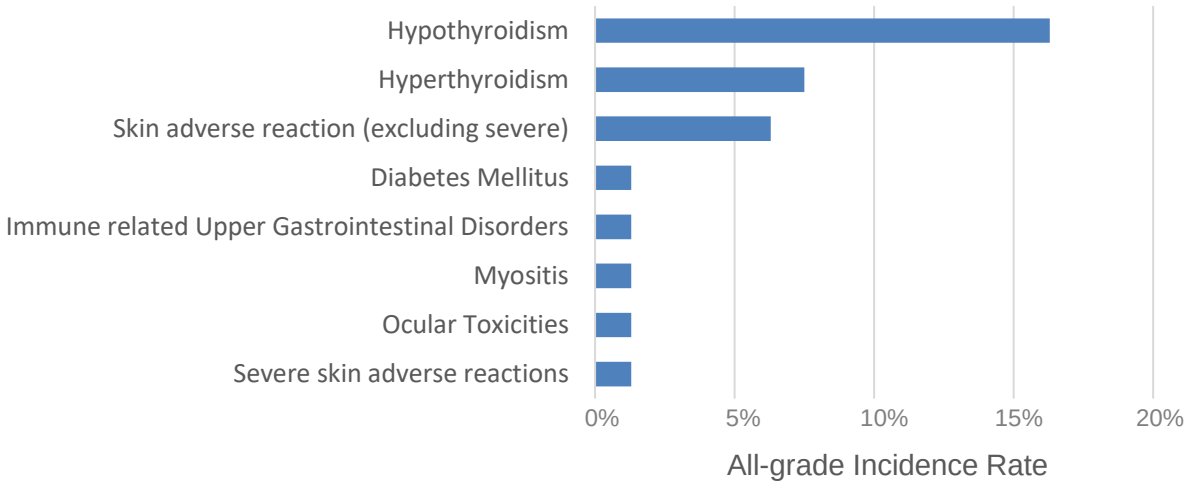
1. **Five SAEs were considered treatment-related by the Investigator.**
   - Pyrexia, n = 2
   - Sinus node dysfunction, n = 1
   - Pneumonia, n = 1
   - Myositis, n = 1

2. **All above SAEs resolved without sequelae except sinus node dysfunction.**

Data cutoff date: Nov 10, 2021

Sponsor-assessed irAEs

irAE Categories[1]



1. **Most commonly reported irAE categories (>5%):**
   - Hypothyroidism (16.3%)
   - Hyperthyroidism (7.5%)
   - Skin adverse reaction (excluding severe) (6.3%)
2. **Two patients experienced Grade 3 events.**
   (hypothyroidism and rash, n = 1 each)
3. **No Grade 4/5 irAEs were observed.**
4. **Grade 1 myositis (also reported as an SAE) resolved.**

[1] The Sponsor developed a query list of 24 categories of Medical Dictionary for Regulatory Activities (MedDRA) preferred terms (PTs) to identify irAEs based on the characteristics of immune-related adverse reactions of similar products, as well as the characteristics of immune-related adverse reactions in guidelines and literature.

irAE: Immune-related Adverse Event

Data cutoff date: Nov 10, 2021

Conclusions

1. GEMSTONE-201 is the largest registrational study (N = 80) reported to date to evaluate an anti-PD-1/L1 mAb in patients with R/R ENKTL.
2. Sugemalimab has demonstrated deep and durable anti-tumor activity in R/R ENKTL patients.
   - IRRC-assessed ORR 46.2%, CR rate 37.2%, median DoR not reached yet, 1-year DoR rate 86%
   - Investigator assessments highly consistent with IRRC results; concordance rate 97.1%
   - 1-year OS rate 68.6%, median OS not reached yet
3. Sugemalimab monotherapy was well-tolerated; safety in ENKTL was consistent with the known safety profile of sugemalimab in other studies.
4. Sugemalimab could potentially provide a new and effective treatment option for R/R ENKTL patients.

Acknowledgement

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