NAPISTAR 1-01: Results of phase 1 dose escalation of monotherapy with TUB-040, a novel NaPi2b-targeting exatecan ADC, in patients (pts) with platinum-resistant ovarian cancer (PROC)

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Key takeaways

- **NaPi2b** is sodium-phosphate transporter which is **expressed in > 95%** of **high grade serous ovarian cancer**
- In the cohorts of **1.67-3.3 mg/kg TUB-040** delivers **deep and durable responses** with **minimal grade ≥3 hematological toxicity**
- **Manageable adverse event profile with low discontinuation rates** due to a treatment emergent adverse event
- **Unconfirmed and confirmed ORR** of **67%** (95% CI 52.0%, 80.5%) and **61%** (95% CI 45.4%, 74.9%); respectively in the 1.67-3.3 mg/kg cohorts
- In the overall population, clinically meaningful **mPFS of 11.0 months,** with a **response duration > 6 months in 79%**
- **These encouraging results in PROC support rapid development of TUB-040 in non biomarker restricted ovarian cancer population**

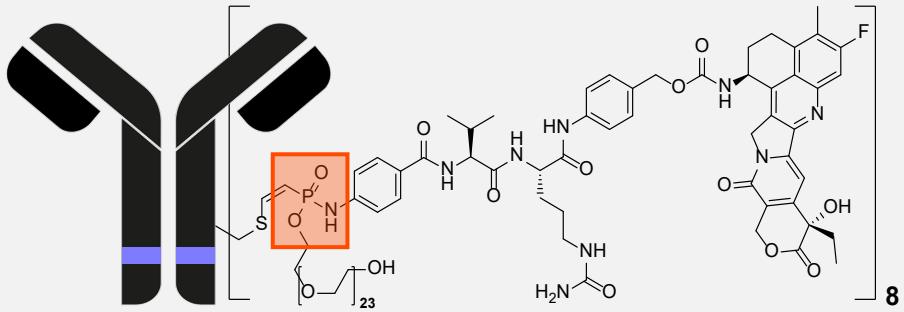
TUB-040 demonstrated significant durable efficacy and low rates of haematological toxicity, in heavily pre-treated PROC patients

N=66 evaluable patients who had at least 1 RECIST response assessment across doses from 0.5 – 5.3 mg/kg. There were no responses observed at doses below 1.67 mg/kg. Responses of PR/CR per RECIST at a minimum of 1 post-baseline assessment. Efficacy data in patients treated at 3.3 mg/kg continue to mature. CR, complete response; DCR, disease control rate; PR, partial response; SD, stable disease. Data Cut off: 05 April 2026.

Background

- Platinum-resistant ovarian cancer patients have an overall survival of 12-16 months. New, efficacious and well tolerated therapeutic options are needed
- NaPi2b is a rapidly internalizing sodium-phosphate transporter which is highly overexpressed in ovarian cancer
- TUB-040 is optimized to maximize efficacy and tolerability with innovative ADC design elements:
  - Fc-silencing to minimize off target toxicities
  - P5 mAB linkage with stable DAR; no premature payload loss and enhanced hydrophilicity
  - Peptide-cleavable linker for efficient intracellular release
  - Clinically validated, exatecan payload (TOP-1) with bystander activity

DESIGN ELEMENTS OF TUB-040



αNaPi2b - P5 mAb linkage - peptide-cleavable release - Exatecan

Here we report the updated safety and efficacy data from the dose escalation phase of the NAPISTAR 1-01 study in PROC, with a focus on dose levels 1.67-3.3 mg/kg

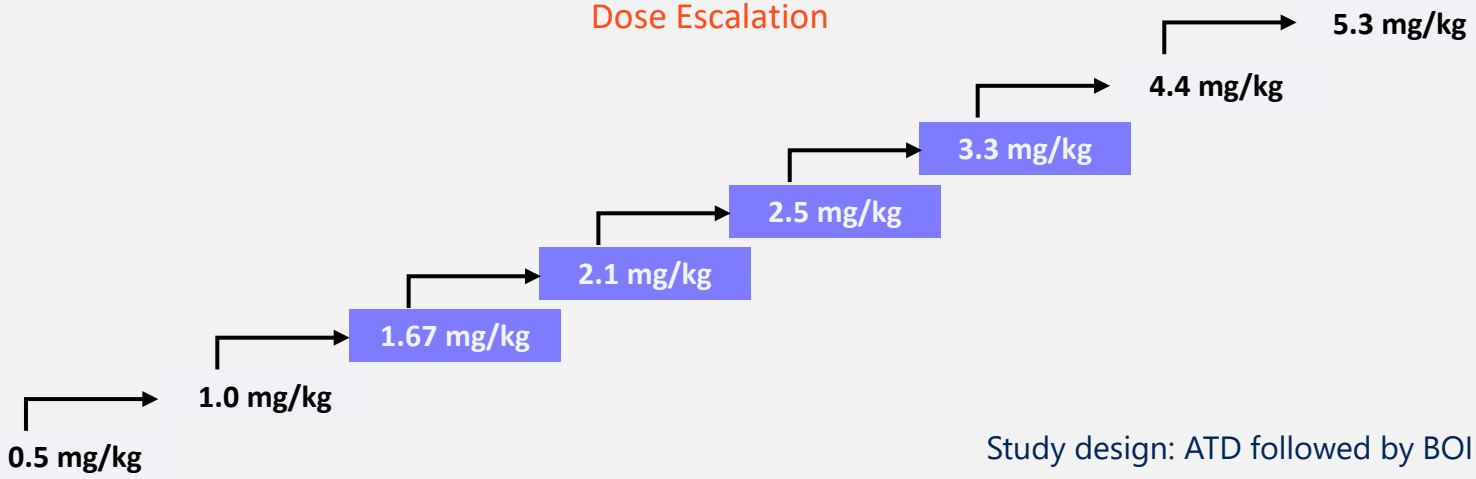
1. Richardson et al., 2023. (DOI:10.1001/jamaoncol.2023.0197)
2. Lin et al., 2015. (DOI:10.1158/1078-0432.CCR-14-3383)
3. Vogl et al., 2025. (DOI:10.1158/1535-7163.MCT-25-0254)
4. Taylor et al., 2024. (DOI:10.1182/blood.2024024442)
5. Wei et al., 2025. (DOI:10.1158/0008-5472.CAN-24)
6. Schmitt et al., 2024. (DOI:10.1158/1535-7163.MCT-23-0359)
7. Kasper et al., 2019. (DOI:10.1002/anie.201904193)
8. O'Reilly et al., 2004. (DOI:10.1200/jco.2004.22.90140.4006)
9. Khera et al., 2022. (DOI:10.1158/1535-7163.MCT-21-0580)
10. Mitsui et al., 1995. (DOI:10.1111/j.1349-7006.1995.tb02468)
11. Hsiang et al., 1985. (DOI:10.1016/S0021-

Data Cut off: 05April 2026. ADC, antibody drug conjugate; DAR8, drug-to-antibody ratio 8; Fc, fragment crystallizable; mAb, monoclonal antibody; IgG1, immunoglobulin NaPi2b, sodium-dependent phosphate transporter protein 2B; P5, phosphonamidate; TOPO-I, type 1 topoisomerase.

NAPISTAR 1-01: study design

A multicenter, FIH dose escalation and optimization Phase I/IIa Study (NCT06303505), investigating the NaPi2b ADC TUB-040 in PROC*

PHASE I
Dose Escalation



Study design: ATD followed by BOIN

PHASE IIa
Dose Optimization

- 2.1 mg/kg
- 2.5 mg/kg
- 3.3 mg/kg

Key Eligibility Criteria

- Histologically confirmed, platinum resistant, high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer
- A maximum of 5 platinum-based and 2 non-platinum prior lines of therapy
- ECOG 0-1
- No prior treatment with an ADC containing a TOPO-I inhibitor payload
- No biomarker selection based on NaPi2b expression

Objectives and Endpoints

- Safety and tolerability
- Determination of MTD
- ORR per RECIST 1.1, DCR, DoR, PFS and OS
- PK parameters of TUB-040
- Immunogenicity
- Quality of life

NAPISTAR 1-01 also includes an NSCLC arm, which is currently being explored independently from the PROC arm. Cut off: 05April 2026.
ADC, antibody-drug conjugate; ATD, accelerated titration dosing; BOIN, Bayesian optimal interval; DCR, disease control rate; DoR, duration of response; FIH, first-in-human; MTD, maximum tolerated dose; NaPi2b, sodium-dependent phosphate transporter protein 2B; ORR, overall response rate; OS, overall survival;; PFS, progression-free survival; PK, pharmacokinetics; PROC, platinum-resistant ovarian cancer.

NAPISTAR 1-01: patient demographics and safety summary

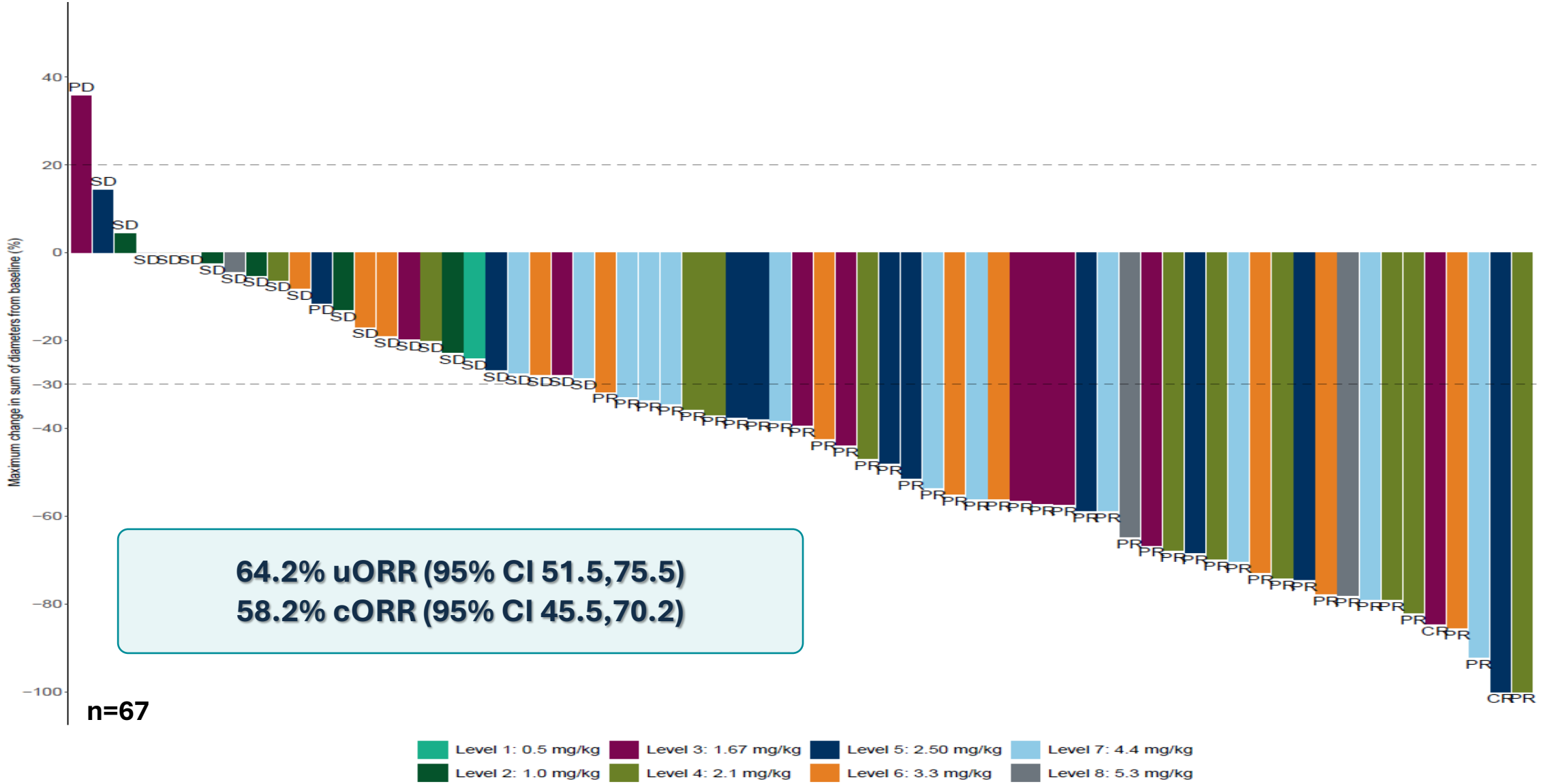
Baseline characteristic	Overall (N=67)
Age, years Median (range)	62.0 (34.0 - 81.0)
ECOG PS, n (%) 0 1	 37 (55.2) 30 (44.8)
Time from first diagnosis, years Median (range)	4.3 (0.9 -16.7)
Prior lines of therapy, n Median (range)	4 (1-7)
Prior bevacizumab, n (%)	56 (83.6)
Prior PARP inhibitor, n (%)	51 (76.1)
Prior IO therapy, n (%)	16 (23.9)
Prior mirvetuximab soravtansine, n (%)	10 (14.9)

Safety Summary	1.67-3.3 mg/kg (n=46)	0.5-5.3 mg/kg* (n=67)
Any TEAE[1], n (%) Grade >=3	46 (100) 19 (41)	67 (100) 36 (54)
Any Serious TEAE, n (%)	12 (26)	20 (30)
Dose modifications Dose reductions due to TEAE Treatment discontinuation due to TEAE	 12 (26) 0	 26 (39) 2 (3)
Nausea (all grades) Grade ≥ 3	36 (78) 2 (4)	51 (76) 2 (3)
Fatigue (all grades) Grade ≥ 3	26(57) 0	40 (60) 0
Neutropenia (all grades) Grade ≥ 3	21 (46) 13 (28)	36 (54) 28 (42)
Anemia (all grades) Grade ≥ 3	18 (39) 8 (17)	32 (48) 18 (27)
Thrombocytopenia (all grades) Grade ≥ 3	7 (15) 2 (4)	20 (30) 12 (18)
Pneumonitis (Grade 1) Grade ≥ 3	3 (7) 0	5 (8) 0

- **Heavily pre-treated patient population with a median of 4 prior lines of therapy; the majority of patients exposed to prior bevacizumab and/or a PARP inhibitor**
- **Manageable adverse event profile with low discontinuations due to treatment related AEs**

All subjects with a NaPi2b IHC evaluation at the time of the DCO are included. Data Cut off: 05 April 2026. ECOG, Eastern Cooperative Oncology Group; NaPi2b, sodium-dependent phosphate transporter protein 2B; PARP, poly ADP ribose polymerase; PS, performance score.

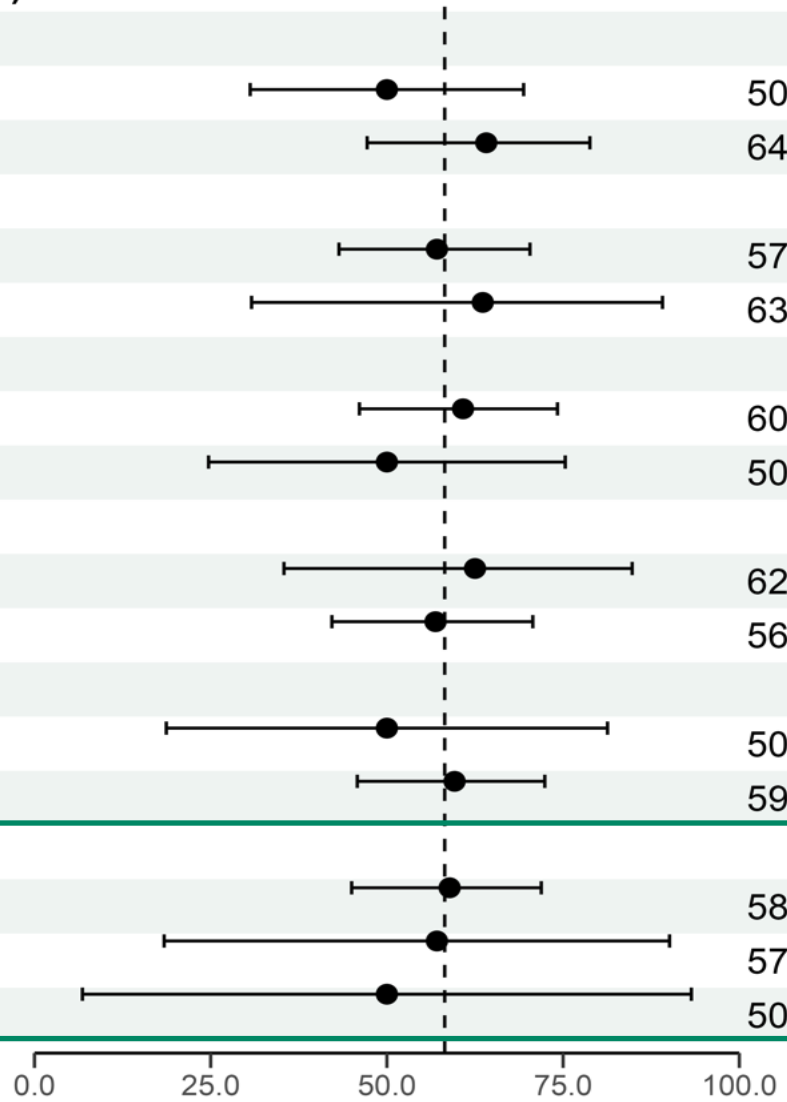
Efficacy across a wide therapeutic range with complete responses



N=66 evaluable patients who had at least 1 RECIST response assessment across doses from 0.5 – 5.3 mg/kg. There were no responses observed at doses below 1.67 mg/kg. Responses of PR/CR per RECIST at a minimum of 1 post-baseline assessment. CR, complete response; PR, partial response; SD, stable disease. Data Cut off: 05April 2026.

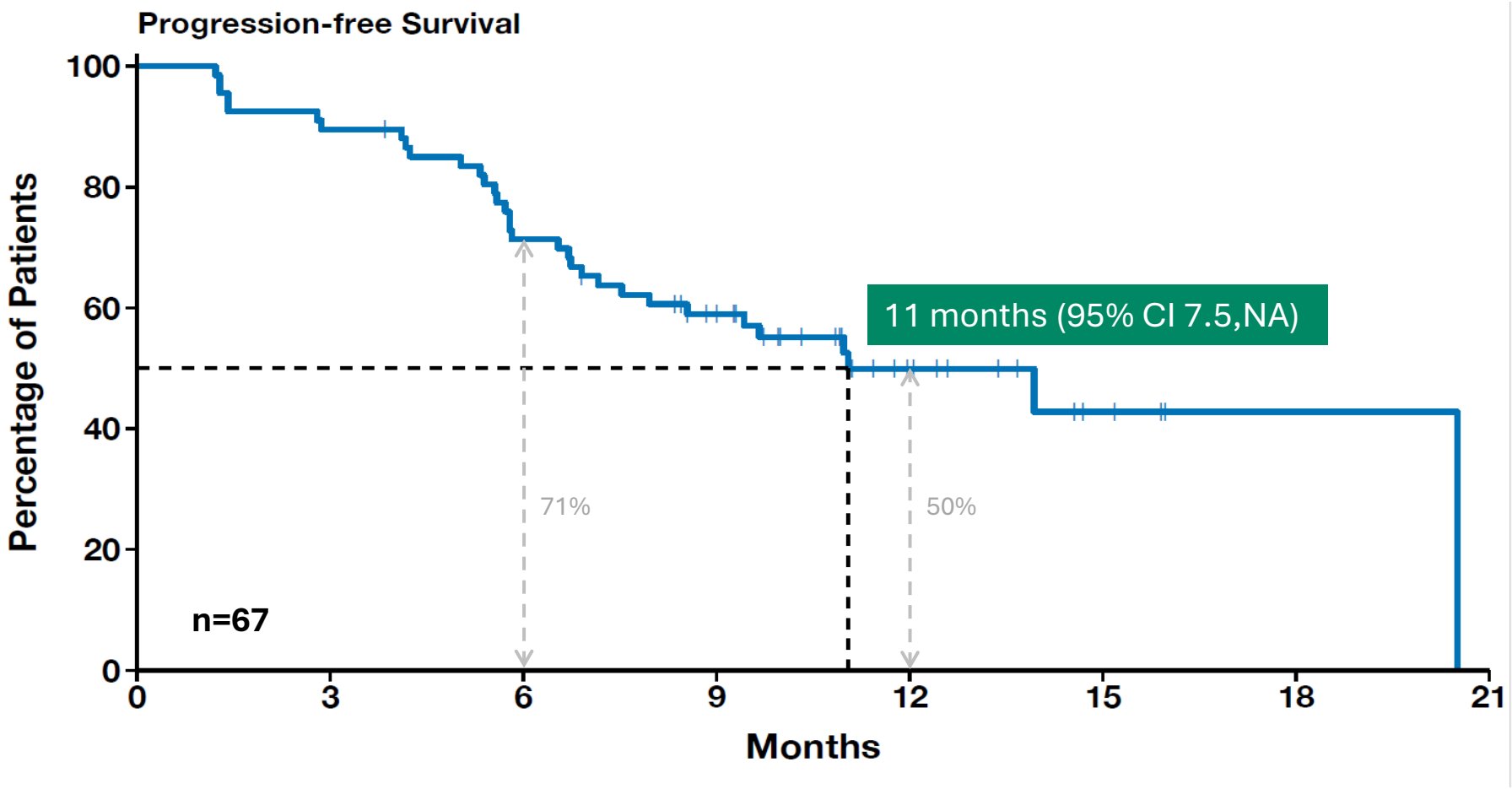
Consistent responses across multiple subgroups – all dose levels

Subgroup	Responders	Total (N)	ORR (95% CI)
Number of prior therapy lines			
< 4	14	28	50.0 (30.6 to 69.4)
≥ 4	25	39	64.1 (47.2 to 78.8)
Prior Exposure to Bevacizumab			
Yes	32	56	57.1 (43.2 to 70.3)
No	7	11	63.6 (30.8 to 89.1)
Prior Exposure to PARP inhibitors			
Yes	31	51	60.8 (46.1 to 74.2)
No	8	16	50.0 (24.7 to 75.3)
Prior Exposure to Immunotherapy			
Yes	10	16	62.5 (35.4 to 84.8)
No	29	51	56.9 (42.2 to 70.7)
Prior Exposure to Mirvetuximab			
Yes	5	10	50.0 (18.7 to 81.3)
No	34	57	59.6 (45.8 to 72.4)
Napi2B IHC			
High	33	56	58.9 (45.0 to 71.9)
Low	4	7	57.1 (18.4 to 90.1)
Missing	2	4	50.0 (6.8 to 93.2)



Data cut-off 05 April 2026.

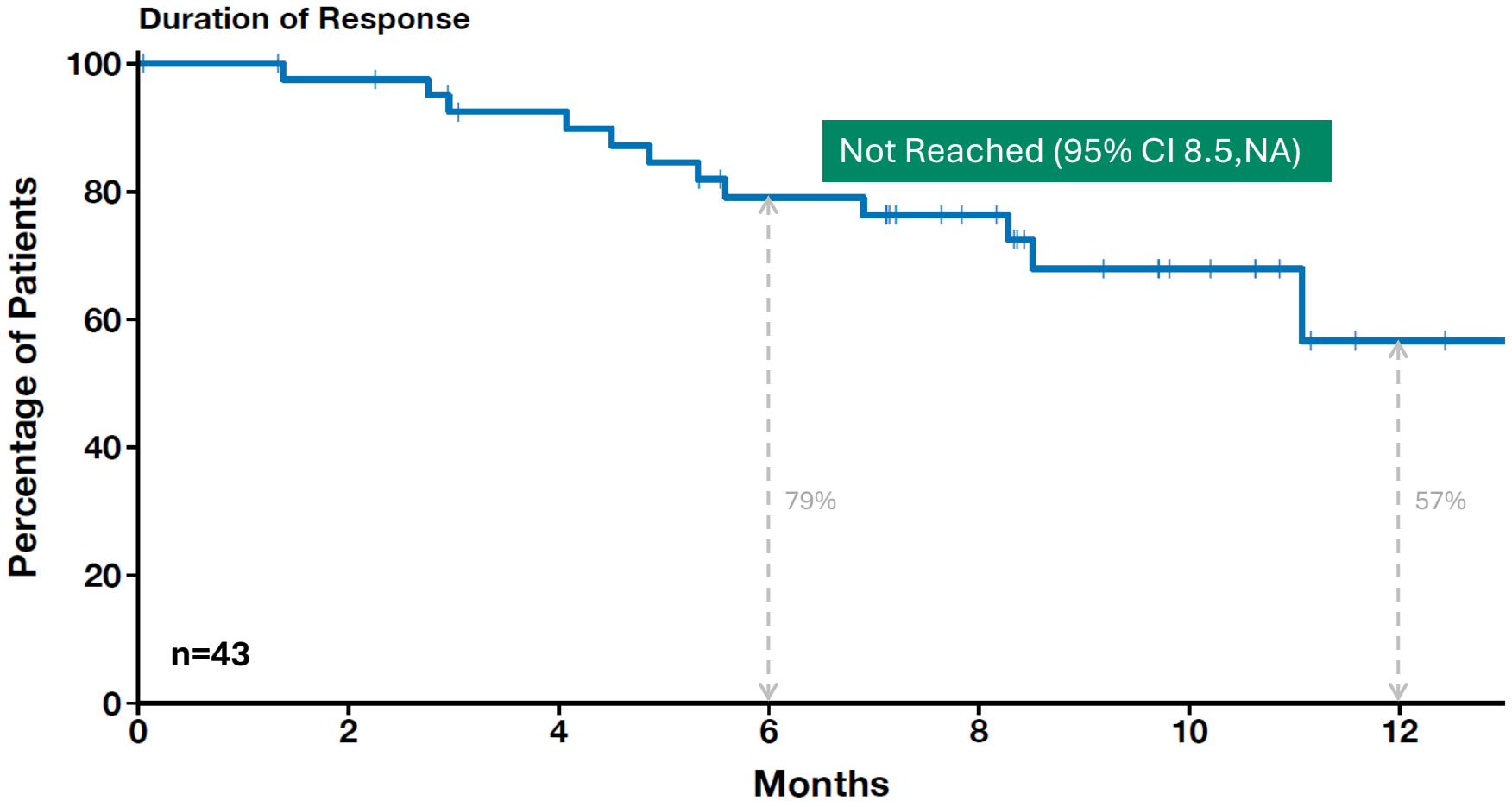
Clinically meaningful progression free survival – all dose levels



mPFS of 11 months with 71% and 50% progression free at 6 months and 12 months, respectively

Data cut-off 05 April 2026 . Median duration of follow-up 12 months.

Clinically meaningful and durable responses – all dose levels

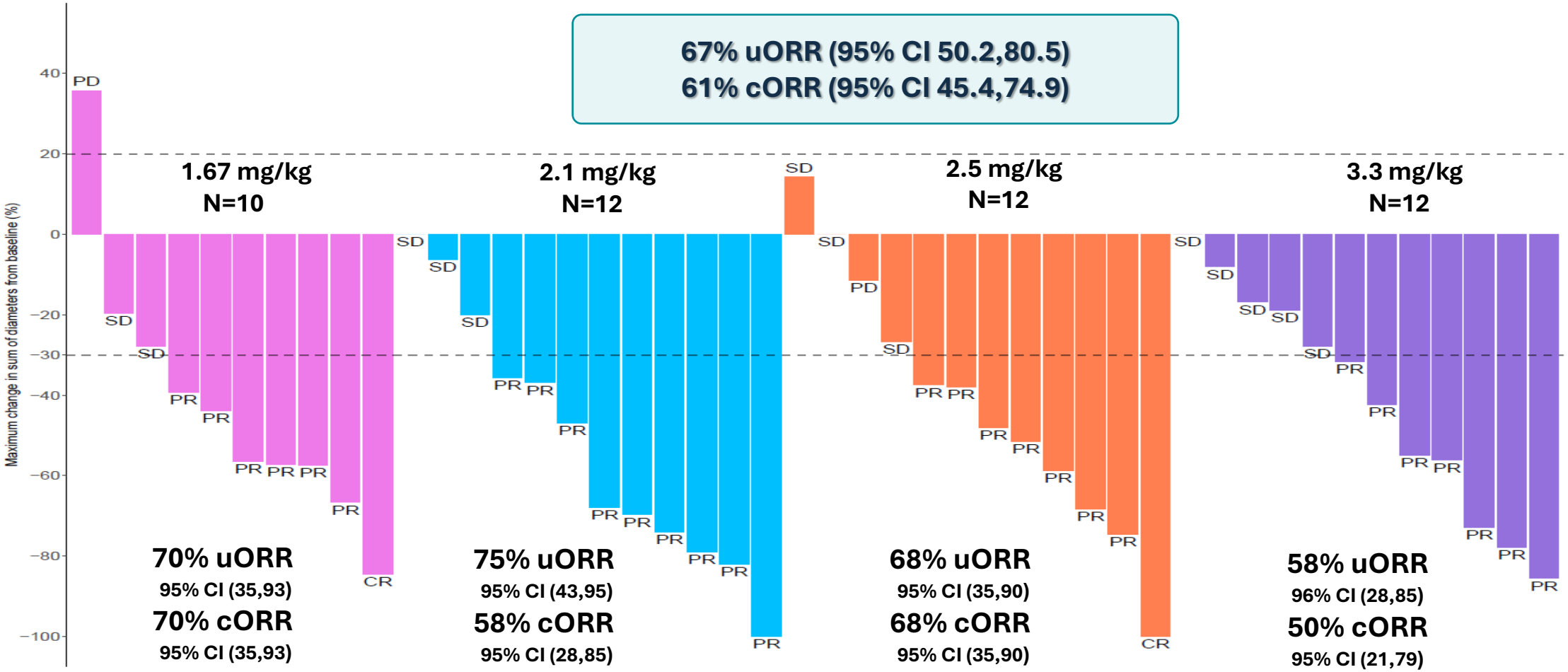


mDOR not reached with 79% and 57% of responders with a duration > 6 months and > 12 months, respectively

Data cut-off 05 April 2026. Median duration of follow-up 8.7 months.

Clinically meaningful responses across doses 1.67-3.3 mg/kg

67% uORR (95% CI 50.2,80.5)
61% cORR (95% CI 45.4,74.9)



Consistent durable high response rate and deep responses across the dose levels of 1.67-3.3 mg/kg with 74% of responders ongoing treatment

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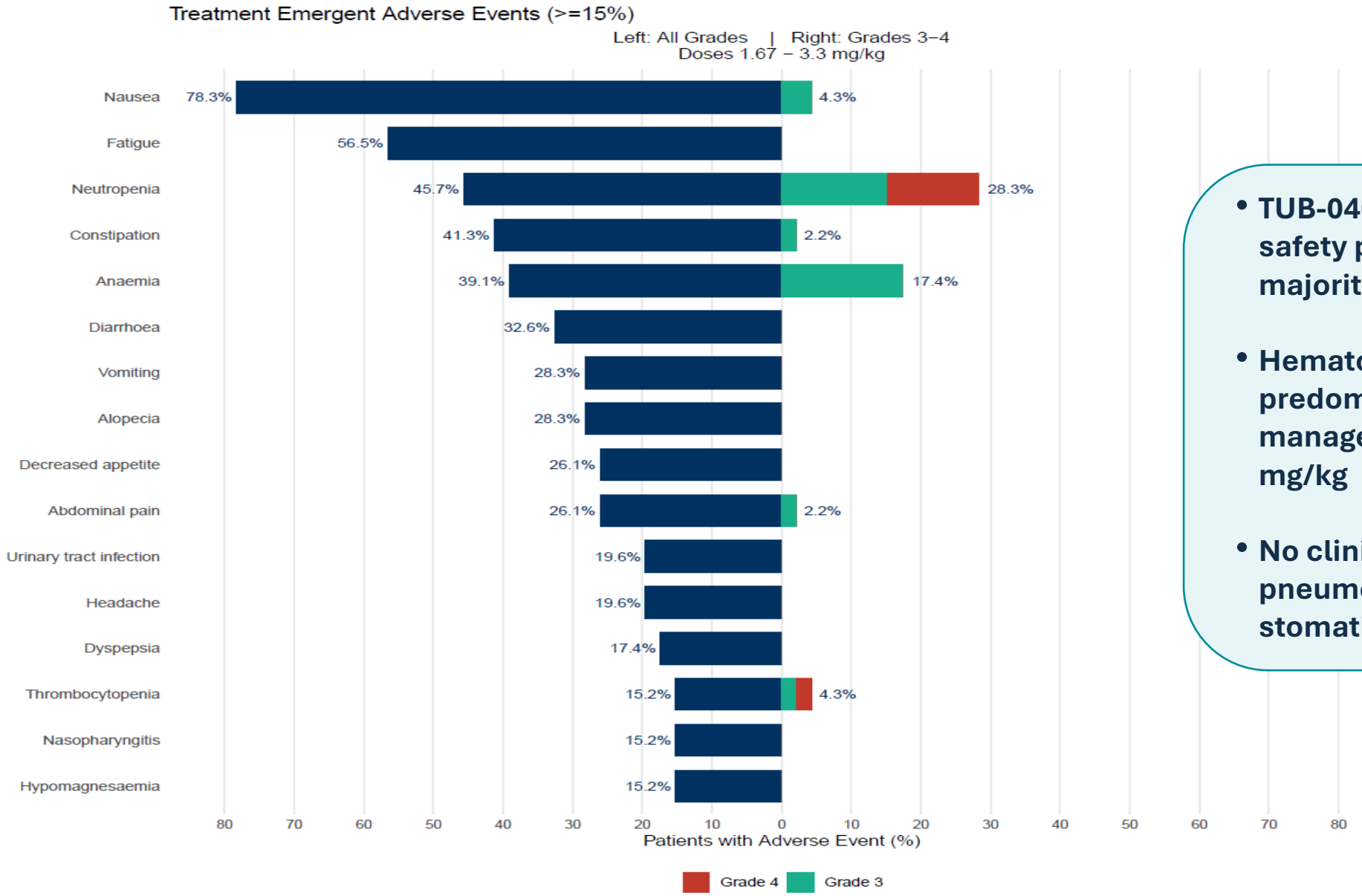
Responses of PR/CR per RECIST at a minimum of 1 post-baseline assessment. . Efficacy data in patients treated at 3.3 mg/kg continue to mature. CR, complete response; PR, partial response; SD, stable disease. Data Cut off: 05 April 2026.

TUB-040 is well tolerated across doses 1.67-3.3 mg/kg



- TUB-040 demonstrates a tolerable safety profile in PROC with the majority of events being low grade
- Hematologic toxicity was predominately low-grade and manageable at doses of 1.67 – 3.3 mg/kg
- No clinically relevant bleeding, pneumonitis, ocular toxicity, stomatitis, or neuropathy

Data cut-off 05 April 2026.

Limited grade ≥3 hematological toxicity across doses 1.67-3.3 mg/kg

Blood & lymphatic system disorders	1.67 mg/kg N=10 n (%)	2.1 mg/kg N=12 n (%)	2.5 mg/kg N=12 n (%)	3.3 mg/kg N=12 n (%)	Total N=46 n (%)
Anaemia	0 (0%)	0 (0%)	3 (25.0%)	5 (41.7%)	8 (17.4%)
Neutropenia	0 (0%)	2 (16.7%)	5 (41.7%)	6 (50.0%)	13 (28.2%)
Thrombocytopenia	0 (0%)	0 (0%)	1 (8.3%)	1 (8.3%)	2 (4.3%)
Febrile neutropenia	0 (0%)	0 (0%)	0 (0%)	1 (8.3%)	1 (2.2%)
Leukopenia	0 (0%)	0 (0%)	1 (8.3%)	0 (0%)	1 (2.2%)

Prophylactic/supportive therapy with G-CSF was not mandated per protocol but could be used per investigator discretion/institutional guidance after cycle 1

Data cut-off 05 April 2026.

Conclusions

- **NaPi2b** is sodium-phosphate transporter which is **expressed in > 95%** of **high grade serous ovarian cancer**
- In the cohorts of **1.67-3.3 mg/kg TUB-040** delivers **deep and durable responses** with **minimal grade ≥3 hematological toxicity**
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