2026 ASCO® ANNUAL MEETING

A phase 1/2 study of the next-generation Nectin-4-targeting antibody–drug conjugate CRB-701 (SYS6002) in patients with recurrent or metastatic cervical cancer

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Presented by: **Yohann Loriot, MD, PhD**

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Key takeaway points

1. CRB-701 is a next-generation Nectin-4-targeted ADC being investigated for treatment of advanced solid tumors

2. The most frequent TRAEs are ocular toxicities, which are largely manageable and reversible with dose modifications and prophylactic measures

3. CRB-701 monotherapy produces notable antitumor responses (cORR, DoR, PFS) in patients with cervical cancer

ADC, antibody–drug conjugate; cORR, confirmed objective response rate; DoR, duration of response; PFS, progression-free survival; TRAE, treatment-related adverse event

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Background

- **Cervical cancer** is the **fourth most common** cancer in women globally (approximately 660,000 cases/year) and has a disproportionate burden in low- and middle-income countries[1,2]
- Prognosis is strongly stage-dependent, with **5-year relative survival rates** of approximately **92%** and **21%** for **localized disease** and **distant metastatic disease**, respectively[3]
- **Nectin-4 (*PVRL4*) expression** has been detected in approximately **80–90% of cervical cancers**, particularly in advanced or recurrent lesions, making it a promising therapeutic target[4]

1. Sung H *et al*. *CA Cancer J Clin* 2021;71(3):209–49; 2. World Health Organization (WHO). 2025. www.who.int/news-room/fact-sheets/detail/cervical-cancer (Accessed April 21, 2026);
3. National Cancer Institute. https://seer.cancer.gov/statfacts/html/cervix.html (Accessed April 21, 2026); 4. Zhai C et al. *Front Oncol* 2024;14:1395784

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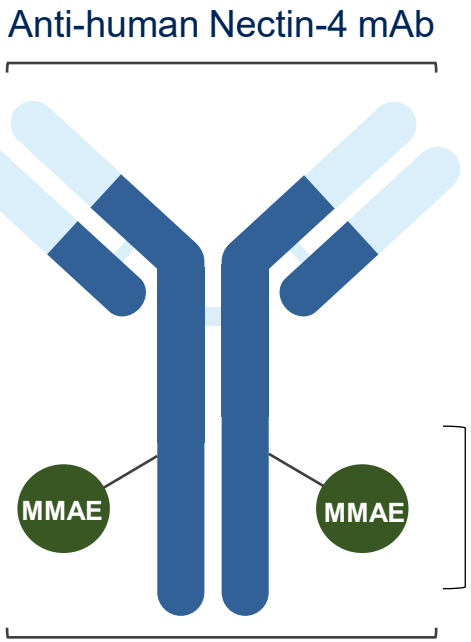
Background



Cathepsin-B-cleavable linker conjugated via site-specific mTGase technology, forming a stable isopeptide bond

CRB-701 is a **next-generation Nectin-4-targeted MMAE-based ADC**[1]

CRB-701 appears to have a **differentiated safety, efficacy and PK profile** compared with published data for other agents in the same class[1–5]

- Previously presented results from the **ongoing phase 1/2 CRB-701-01 study** (NCT06265727) of CRB-701 in patients from Europe and the USA who have advanced solid tumors have demonstrated:[1]
  - A **manageable safety profile** with keratitis, alopecia, fatigue, anemia and dysgeusia being the most commonly occurring TRAEs
  - **Antitumor responses** in patients with **high and low levels of Nectin-4** expression (measured by IHC), regardless of tumor type
  - **Encouraging efficacy** signals in a relatively small number of heavily **pretreated patients with cervical cancer** who were treated with CRB-701 2.7 mg/kg or 3.6 mg/kg Q3W (N = 37)

1. Perez C *et al*. European Society for Medical Oncology Congress, 2025. Poster; 2. Astellas Pharma. Summary of product characteristics, enfortumab vedotin. EMA, 2024. https://www.ema.europa.eu/en/documents/product-information/padcev-epar-product-information_en.pdf (Accessed May 8, 2026); 3. Zhang J *et al. Ann Oncol* 2025;36:934–43; 4. Swiecicki PL *et al. J Clin Oncol* 2025;43:578–88; 5. Powles T *et al. N Engl J Med* 2021;384:1125–35

ADC, antibody–drug conjugate; DAR, drug:antibody ratio; IHC, immunohistochemistry; mAb, monoclonal antibody; MMAE, monomethyl auristatin E; mTGase, microbial transglutaminase; PK, pharmacokinetics; TRAE, treatment-related adverse event; Q3W, every 3 weeks

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Objective

- This presentation provides **updated and expanded safety and efficacy data** from an additional 35 patients with cervical cancer (total N = 72) who were treated with CRB-701 at 2.7 mg/kg and 3.6 mg/kg Q3W in the CRB-701-01 study
- The updated analysis includes data from an additional **6 months of follow-up**, with cORR, DoR and PFS assessed

cORR, confirmed objective response rate; DoR, duration of response; PFS, progression-free survival; Q3W, every 3 weeks

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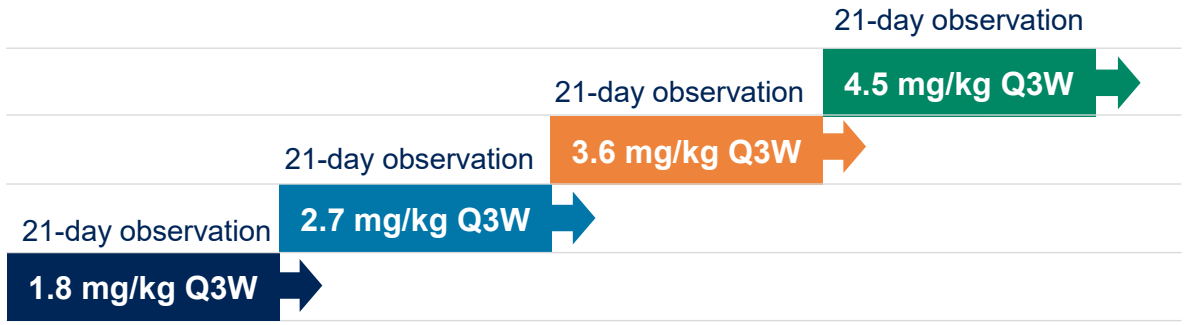
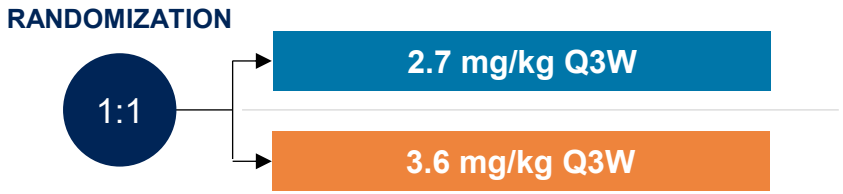
Methods

Dose escalation (part A): Bayesian Optimal Interval design



Dose escalation/de-escalation decisions were made based on the occurrence of DLTs

Dose optimization (part B): time-to-event Bayesian Optimal Phase 2 design



Dose levels in part B were defined by the pharmacologically active dose range identified in part A

Patient population

- Recurrent or metastatic cervical cancer
- Had received ≥ 1 line of therapy
- No previous exposure to Nectin-4-targeted or MMAE-based therapies
- All patients with cervical cancer treated with CRB-701 2.7 mg/kg and 3.6 mg/kg Q3W during dose escalation and optimization were included

Endpoints

- **Part A:** Occurrence of DLTs (primary endpoint)
  - Safety, cORR, DoR, PFS (secondary endpoints)
- **Part B:** cORR (primary endpoint)
  - DoR, PFS, safety (secondary endpoints)

cORR, confirmed objective response rate; DLT, dose-limiting toxicity; DoR, duration of response; MMAE, monomethyl auristatin E; PFS, progression-free survival; Q3W, every 3 weeks

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Patient disposition

Safety Population

All patients who have received ≥ 1 dose of CRB-701 (includes patients with a range of cytologically and/or histologically confirmed tumor types)

N = 317

Patients with cervical cancer

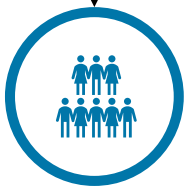
Patients with cytologically and/or histologically confirmed cervical cancer who received ≥ 1 dose of CRB-701

N = 72

Non-evaluable patients who did not have a post-baseline assessment scan[a]
n = 2

Efficacy Population

Patients with measurable disease at baseline who received CRB-701 2.7 mg/kg or 3.6 mg/kg Q3W and had ≥ 1 post-treatment assessment



n = 70

Q3W, every 3 weeks

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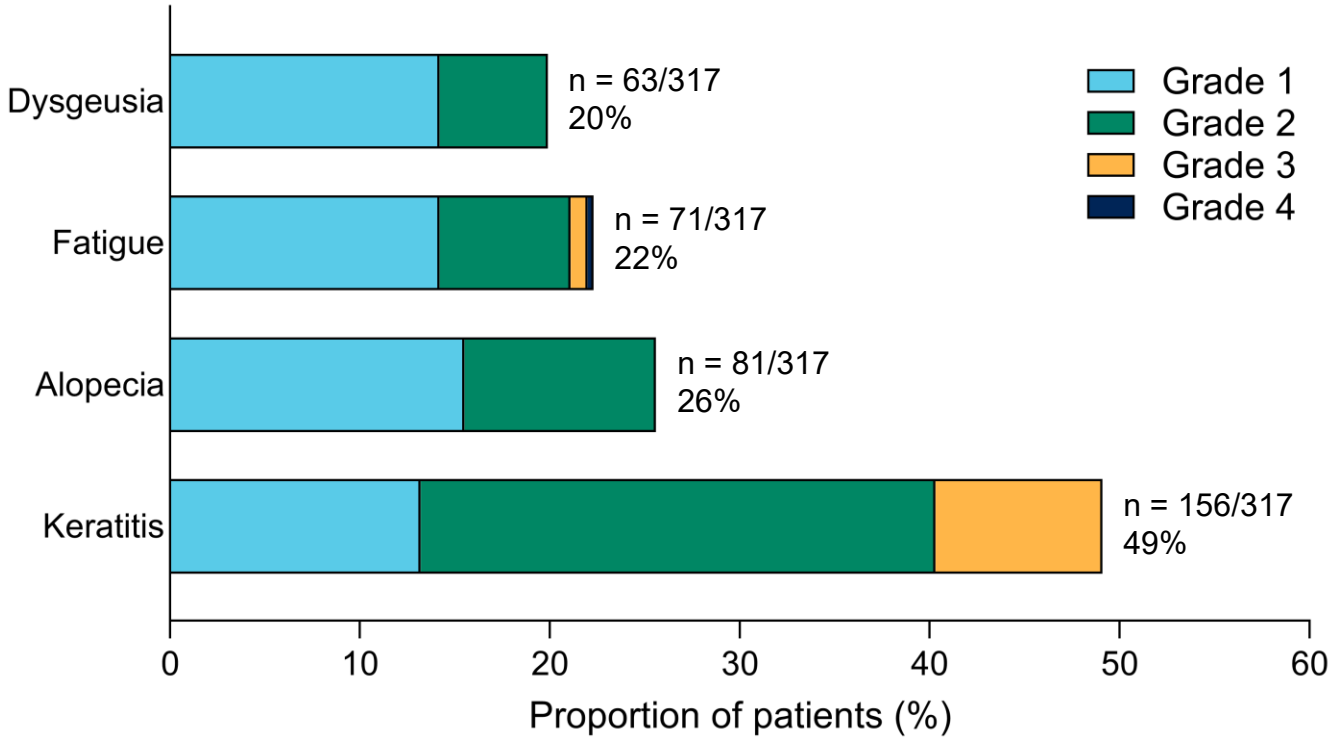
Overall safety profile

Safety Population
N = 317

Treatment-related adverse events occurring in ≥ 20% of patients by maximum CTCAE grade (v5.0)[1]



- Keratitis was the most frequently reported TRAE, occurring in **49%** of patients
- Fewer than **10%** of patients experienced grade 3 keratitis; no grade 4 or 5 keratitis events were reported[a]
- The updated safety profile of CRB-701 remained consistent with previously reported data[2]
- The safety profile in patients with cervical cancer (N = 72) was similar to that observed in the overall Safety Population

Patients with multiple events of the same type are counted once at the highest grade. [a]Grade 1 = asymptomatic; clinical diagnostic observations only; intervention not indicated. Grade 2 = symptomatic; moderate decrease in visual acuity (best corrected visual acuity 20/40 and better or 3 lines or less decreased vision from known baseline). Grade 3 = symptomatic with marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or more than 3 lines of decreased vision from known baseline, up to 20/200); corneal ulcer; limiting self care activities of daily life. Grade 4 = perforation; best corrected visual acuity of 20/200 or worse in the affected eye. CTCAE, Common Terminology Criteria for Adverse Events; TRAE, treatment-related adverse event . 1. U.S. Department of Health and Human Services. 2017. https://dctd.cancer.gov/research/ctep-trials/for-sites/adverse-events/ctcae-v5-5x7.pdf (Accessed May 6, 2026); 2. Perez C *et al*. European Society for Medical Oncology Congress, 2025. Poster

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Ocular toxicity

Patients with cervical cancer
N = 72

Ocular toxicity, extent of drug exposure and dose modifications in patients with cervical cancer

Characteristic	2.7 mg/kg (n = 38)	3.6 mg/kg (n = 34)	Overall (N = 72)
Treatment-related keratitis, n (%)			
All grades[1,a]	15 (39.5)	27 (79.4)	42 (58.3)
Grade 1	5 (13.2)	3 (8.8)	8 (11.1)
Grade 2	8 (21.1)	21 (61.8)	29 (40.3)
Grade 3	2 (5.3)	3 (8.8)	5 (6.9)
Extent of drug exposure			
Duration of exposure,[b] days, median (range)	64.0 (23.0–178.0)	106.5 (23.03–189.0)	83.5 (23.0–185.0)
Relative dose intensity,[c] %, median (range)	97.7 (85.7–100.0)	86.2 (70.2–98.8)	96.1 (79.7–100.0)
Dose modification due to ocular toxicity, n (%)			
Discontinuation	0	3 (8.8)	3 (4.2)
Reduction	4 (10.5)	9 (26.5)	13 (18.1)
Interruption	15 (39.5)	21 (61.8)	36 (50.0)

Patients with multiple events of the same type are counted once at the highest grade. [a]Grade 1 = asymptomatic; clinical diagnostic observations only; intervention not indicated. Grade 2 = symptomatic; moderate decrease in visual acuity (best corrected visual acuity 20/40 and better or 3 lines or less decreased vision from known baseline). Grade 3 = symptomatic with marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or more than 3 lines of decreased vision from known baseline, up to 20/200); corneal ulcer; limiting self care activities of daily life. Grade 4 = perforation; best corrected visual acuity of 20/200 or worse in the affected eye. [b]Duration of exposure to CRB-701 is calculated using the date of last dose of CRB-701 – the date of first dose of CRB-701 + 1. [c]Relative dose intensity is defined as the ratio of the actual delivered dose to the planned dose, expressed as a percentage. 1. U.S. Department of Health and Human Services. 2017. https://dctd.cancer.gov/research/ctep-trials/for-sites/adverse-events/ctcae-v5-5x7.pdf (Accessed May 6, 2026)

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Baseline characteristics

Patients with cervical cancer
N = 72

Key baseline demographics and disease characteristics of patients with cervical cancer

Characteristic	2.7 mg/kg (n = 38)	3.6 mg/kg (n = 34)	Overall (N = 72)
Age, years, median (range)	54 (32–76)	54 (33–78)	54 (32–78)
ECOG PS, n (%)			
0	18 (47.4)	14 (41.2)	32 (44.4)
1	20 (52.6)	20 (58.8)	40 (55.6)
Number of previous therapies, median (range)	3.0 (1–6)	3.5 (1–7)	3.0 (1–7)
Prior therapy type, n (%)			
Platinum-based chemotherapy	38 (100.0)	34 (100.0)	72 (100.0)
PD-1/PD-L1 inhibitor	28 (73.7)	22 (64.7)	50 (69.4)
Platinum-based chemotherapy plus PD-1/PD-L1 inhibitor	28 (73.7)	22 (64.7)	50 (69.4)
Bevacizumab	27 (71.1)	25 (73.5)	52 (72.2)
Disease extent, n (%)			
Locally recurrent	3 (7.9)	3 (8.8)	6 (8.3)
Metastatic	35 (92.1)	31 (91.2)	66 (91.7)

ECOG PS, Eastern Cooperative Oncology Group Performance Status; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1

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cORR, DoR and PFS

Efficacy Population
n = 70

cORR, DoR and PFS in patients with cervical cancer

Endpoint	2.7 mg/kg (n = 38)	3.6 mg/kg (n = 32)
cORR, n (%)	7 (18.4)	11 (34.4)
90% CI	9.0–31.8	20.6–50.4
DoR, months, median	6.8	8.0
95% CI	4.4–NE	4.2–NE
PFS, months, median	2.8	4.3
95% CI	1.4–5.7	2.9–9.5

- Notable cORR, DoR and PFS were observed in patients treated with CRB-701 3.6 mg/kg
- Of the 32 patients in the 3.6 mg/kg group:
  - **62.5%** had been exposed to **prior platinum-based chemotherapy** and **≥ 1 PD-1/PD-L1 inhibitor therapy**
  - Only two patients had **locally recurrent disease** (one patient had a **PR** and one had a **CR**)

- Similar efficacy was observed across subgroups stratified by prior lines of therapy (≤ 3 vs > 3)
- Four patients (5.7%) had a confirmed CR

CI, confidence interval; cORR, confirmed objective response rate; CR, complete response; DoR, duration of response; NE, not estimable; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PR, partial response

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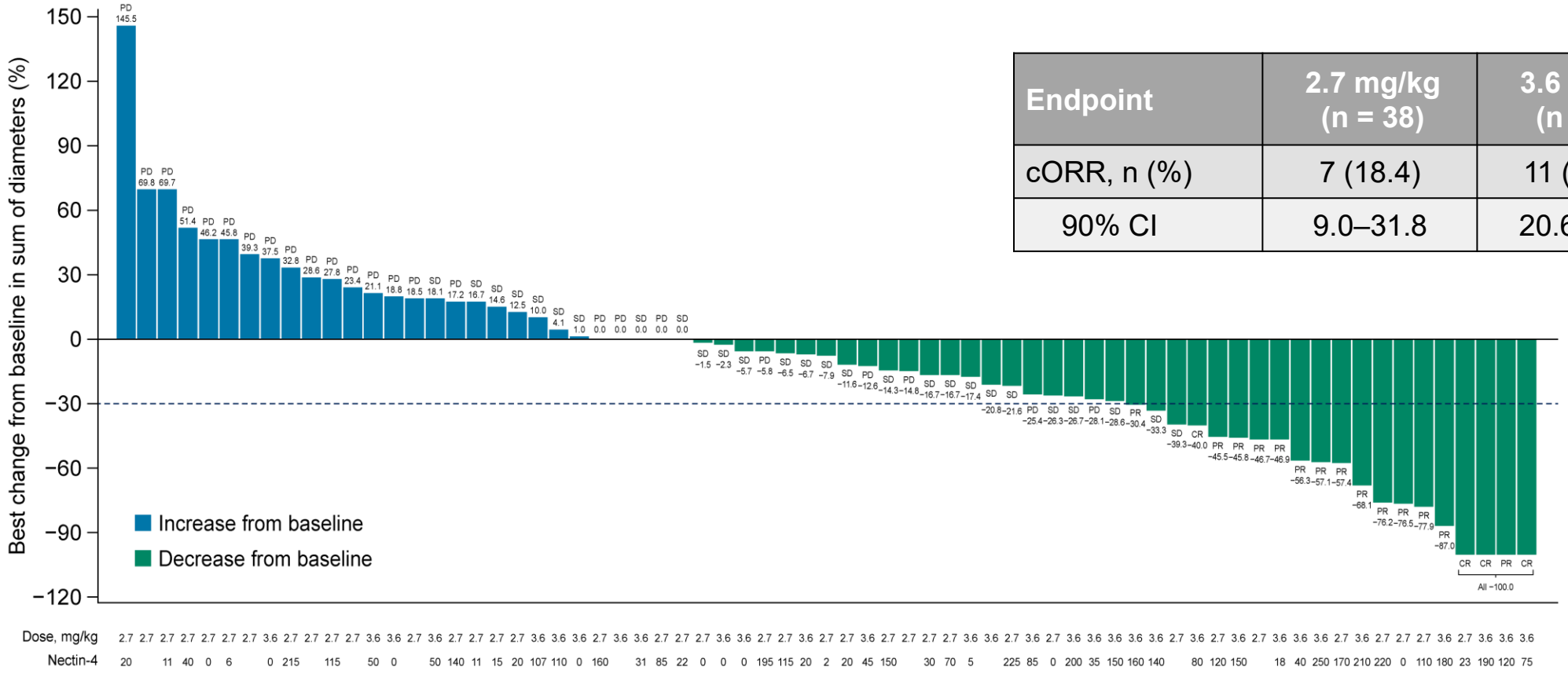
Best overall response (1/2)

Efficacy Population
n = 70

Percentage change from baseline in sum of diameters with confirmed best overall response for CRB-701 Q3W



Endpoint	2.7 mg/kg (n = 38)	3.6 mg/kg (n = 32)
cORR, n (%)	7 (18.4)	11 (34.4)
90% CI	9.0–31.8	20.6–50.4

Data are summarized based on the dose group assigned at enrollment. Each bar represents one participant. Best overall response is indicated at the end of each bar. Dotted line indicates the threshold for PR according to RECIST v1.1 criteria[1] (> 30% reduction in the sum of diameters). CI, confidence interval; cORR, confirmed objective response rate; CR, complete response; PD, progressive disease; PR, partial response; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease. 1. Eisenhauer EA *et al. Eur J Cancer* 2009;45:228–47

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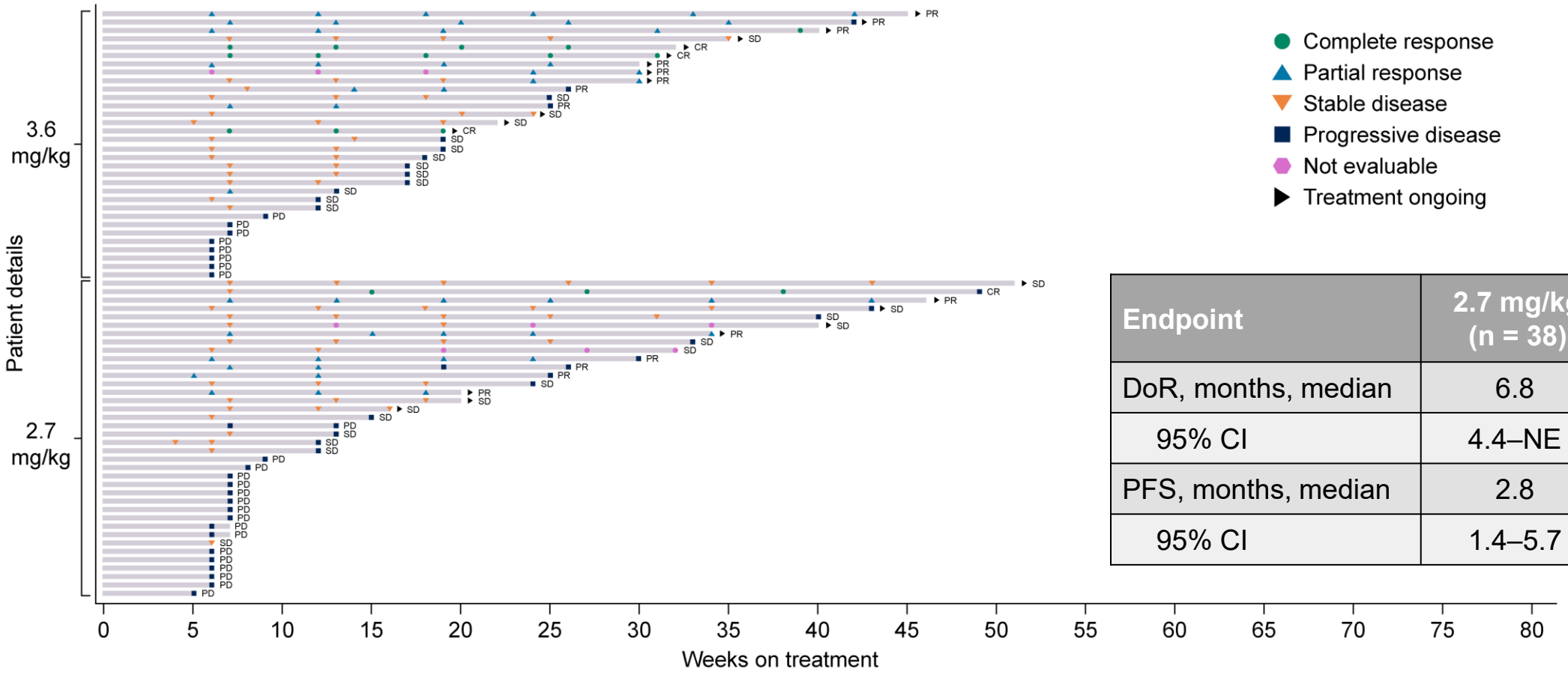
Best overall response (2/2)

Efficacy Population
n = 70

Patient-level best overall response by dose for CRB-701 Q3W



Endpoint	2.7 mg/kg (n = 38)	3.6 mg/kg (n = 32)
DoR, months, median	6.8	8.0
95% CI	4.4–NE	4.2–NE
PFS, months, median	2.8	4.3
95% CI	1.4–5.7	2.9–9.5

Data are summarized based on the dose group assigned at enrollment. Each bar represents one participant. Best overall response is indicated at the end of each bar. CI, confidence interval; CR, complete response; DoR, duration of response; NE, not evaluable; PD, progressive disease; PFS, progression-free survival; PR, partial response; Q3W, every 3 weeks; SD, stable disease

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Conclusions

- CRB-701 is a **next-generation Nectin-4-targeted ADC** being investigated for treatment of advanced solid tumors
- CRB-701 has a **manageable safety profile** in patients with advanced solid tumors
  - Ocular toxicities were the most frequent TRAE, which were **reversible** with dose interruptions or reductions and prophylactic measures
- CRB-701 monotherapy produces notable **antitumor responses** (cORR, DoR, PFS) in patients with **cervical cancer**
- These data demonstrate that CRB-701 is a **promising new therapeutic option** for second- and third-line treatment for patients with **cervical cancer** and support its continued development in a pivotal study

ADC, antibody–drug conjugate; cORR, confirmed objective response rate; DoR, duration of response; PFS, progression-free survival; TRAE, treatment-related adverse event

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Lay summary

What did this research tell us?

- This study looked at CRB-701, a new targeted cancer treatment, in people with advanced cervical cancer who had already received other treatments
- The results showed that CRB-701 could help shrink tumors in some patients. Most side effects were reversible eye-related problems, which were manageable with dose adjustments and preventive eye drops

Who does this research impact?

- This research is most relevant for patients with recurrent or metastatic cervical cancer who have limited treatment options after standard therapies

What does this mean for patients right now?

- These findings suggest that CRB-701 may offer a promising new treatment option for patients with advanced cervical cancer. Further studies are ongoing to better understand its long-term benefits and safety

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