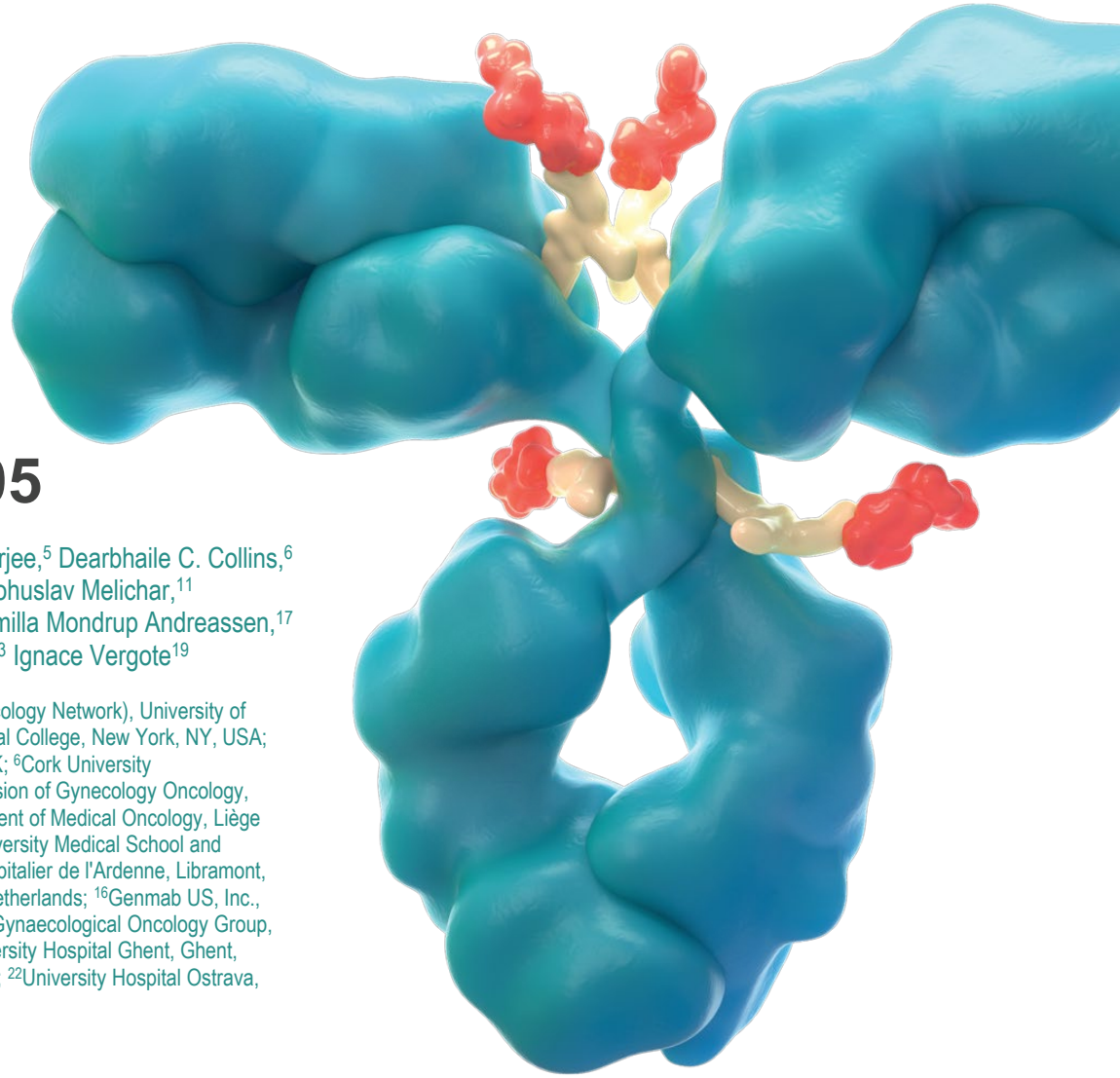
Tisotumab Vedotin + Carboplatin in First-Line or + Pembrolizumab in Previously Treated Recurrent/Metastatic Cervical Cancer: Interim Results of ENGOT-Cx8/GOG-3024/innovaTV 205



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Study Rationale

- 1L **platinum-taxane doublets + bevacizumab** (if pt eligible) have improved survival outcomes in r/mCC;[1–4] more recently, single agent **pembrolizumab** or **pembrolizumab + chemotherapy ± bevacizumab** was approved for PD-L1-positive r/mCC tumors[4–6]
- **Tisotumab vedotin (TV)** is an antibody-drug conjugate which is directed to tissue factor[7]
- A **pivotal, single-arm, phase 2** study showed that TV monotherapy (2 mg/kg IV Q3W) had clinically meaningful activity (ORR=24%; mDOR=8.3 months) with a manageable safety profile in previously treated patients with r/mCC[8]
- In September 2021, TV received US accelerated approval for the treatment of r/mCC[7] with disease progression on or after chemotherapy and continues to be developed as a combination regimen for r/mCC and other solid tumors[8]
- The **RP2D** for TV (2.0 mg/kg Q3W) doublet combinations with pembrolizumab, carboplatin, or bevacizumab in r/mCC was recently reported.[10] Data from 2 expansion cohorts from that study (TV/carboplatin in 1L and TV/pembrolizumab in 2L+ r/mCC patients) are presented here

1L, first-line; 2L+, second-line and beyond; IV, intravenously; mDOR, median duration of response; ORR, objective response rate; PD-L1, programmed death-ligand 1; pt, patient; Q3W, every 3 weeks; RP2D, recommended phase 2 dose; r/mCC, recurrent/metastatic cervical cancer; TV, tisotumab vedotin.

[1]Minion LE, et al. *Gynecol Oncol*. 2018; 148: 609–621; [2]Tewari KS, et al. *N Engl J Med*. 2014;370:734–743; [3]Ebina Y, et al. *Int J Clin Oncol*. 2019;24:1–19;
[4]Abu-Rustum NR et al. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf; [5]Drugs@FDA: FDA-approved Drugs. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=125514;
[6]Colombo N, et al. *N Engl J Med*. 2021;385:1856–1867.
[7]Breij EC, et al. *Cancer Res*. 2014;74:1214–1226; [8]Coleman RL, et al. *Lancet Oncol*. 2021;22:609–619. [9]TIVDAK PI. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761208s000lbl.pdf; [10]Monk B, et al. Presented @ 2021 IGCS Annual Global Meeting, Aug 30–Sept 2, 2021.

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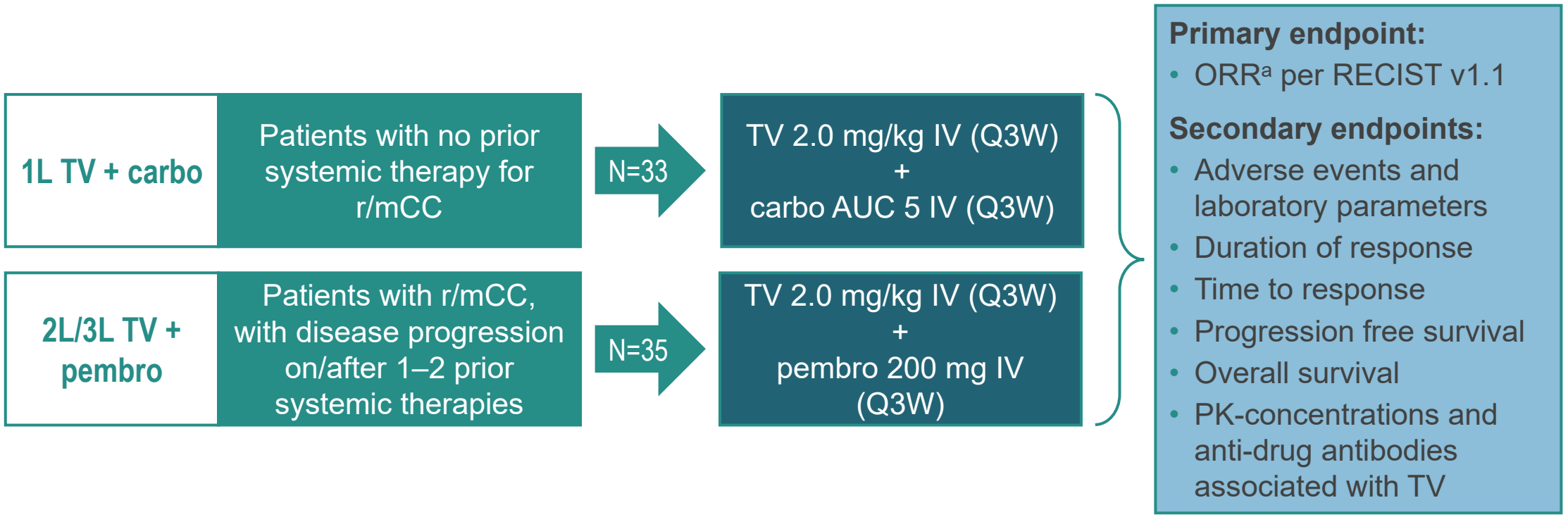
Dose-expansion phase: 1L TV + carbo and 2L/3L TV + pembro cohorts



[a] Tumor response assessed every 6 weeks.

1L, first-line; 2L, second-line; 3L, third-line; AUC, area under the curve; carbo, carboplatin; IV, intravenously; ORR, objective response rate; pembro; pembrolizumab; PK, pharmacokinetic; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; r/mCC, recurrent/metastatic cervical cancer; TV, tisotumab vedotin.

Baseline Demographics and Clinical Characteristics

Parameter	TV + Carboplatin (N=33)	TV + Pembrolizumab (N=35)
Age, median (range), years	51 (25–78)	47 (31–73)
ECOG performance status, n (%)		
0	21 (64)	22 (63)
1	12 (36)	13 (37)
Histology, n (%)		
Squamous	24 (73)	19 (54)
Adenocarcinoma	8 (24)	15 (43)
Adenosquamous	1 (3)	0
Other	0	1 (3)
PD-L1-positive,[a] n (%)	Not evaluated	22 (82)[b]
Prior chemoradiation, n (%)	21 (64)	18 (51)
Prior lines of systemic regimen,[c] n (%)		
0	33 (100)	0
1	0	26 (74)
2	0	9 (26)[d,e]
Prior bevacizumab,[f] n (%)	N/A	18 (51)

Data cut-off: July 1, 2021.
[a]Prevalence of CPS PD-L1 ≥ 1.
[b]Based on evaluable biopsies, n=27.
[c]Systemic regimen administered in the metastatic or recurrent setting.
[d]Includes one patient receiving prior treatment with nivolumab + ipilimumab in the 1L setting.
[e]Includes one patient receiving prior treatment with pembrolizumab in the 2L setting.
[f]Adjuvant and neoadjuvant settings are excluded.
CPS, combined positive cells; ECOG, Eastern Cooperative Oncology Group; N/A, not applicable; PD-L1, programmed death-ligand 1; TV, tisotumab vedotin.

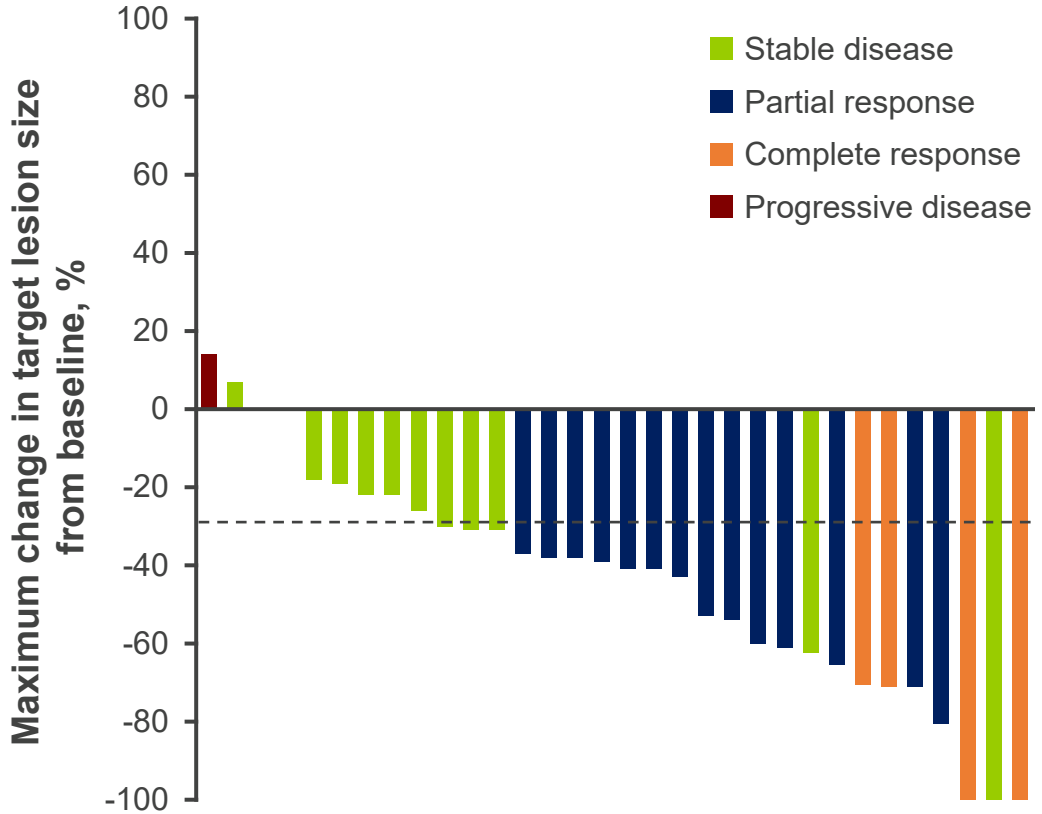
Summary of Efficacy for 1L TV + Carbo

Parameter	1L TV + Carbo (N=33) Median FU: 7.9 months
Median duration of exposure, months (range)	TV: 4.9 (1–9) Carbo: 4.1 (1–9)
Median number of cycles initiated (range)	TV: 6.0 (1–12) Carbo: 6.0 (1–12)
Confirmed response rate, n (%) [95% CI] Complete response, n (%) Partial response, n (%) **Stable disease, n (%)** **Progressive disease, n (%)** **Not evaluable, n (%)**	18 (55) [36–72] 4 (12) 14 (42) 12 (36) 2 (6) 1 (3)
Median duration of response, months (95% CI)	8.3 (4.2–NR)
Median time to response, months (range)	1.4 (1.1–4.4)
Median PFS, months (95% CI)	9.5 (4.0–NR)
Median OS, months (range)	NR (0.8+–14.1+)

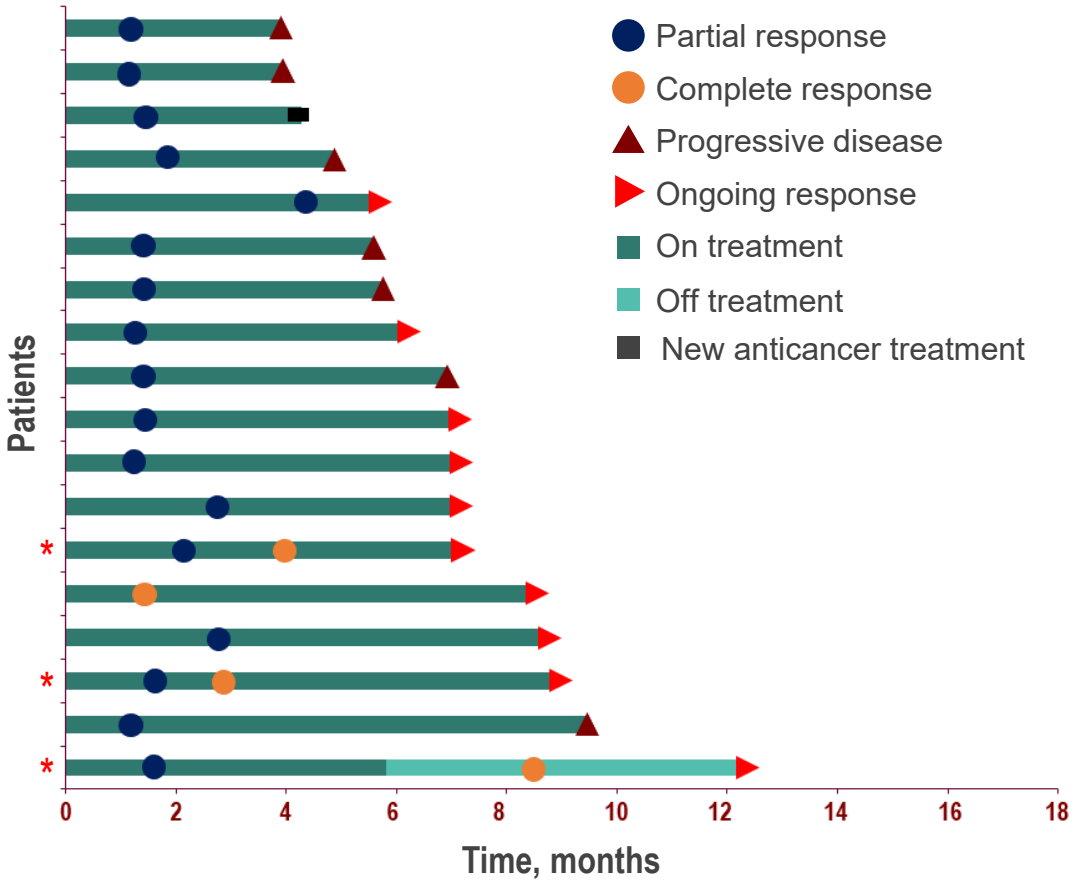
Data cut-off: July 1, 2021.
Treatment ongoing in 9 patients. +, censored.
1L, first-line; carbo, carboplatin; CI, confidence interval; FU, follow-up; NR, not reached; OS, overall survival; PFS, progression-free survival; TV, tisotumab vedotin.

1L TV + Carbo: Tumor Response

Tumor Shrinkage:
Maximum Change in Target Lesion Size From Baseline



Time to Response and Duration of Response per RECIST 1.1



Data cut-off: July 1, 2021.
*Patients with an initial PR that later improved to confirmed CR.
1L, first-line; carbo, carboplatin; CR, complete response; PR, partial response; TV, tisotumab vedotin.

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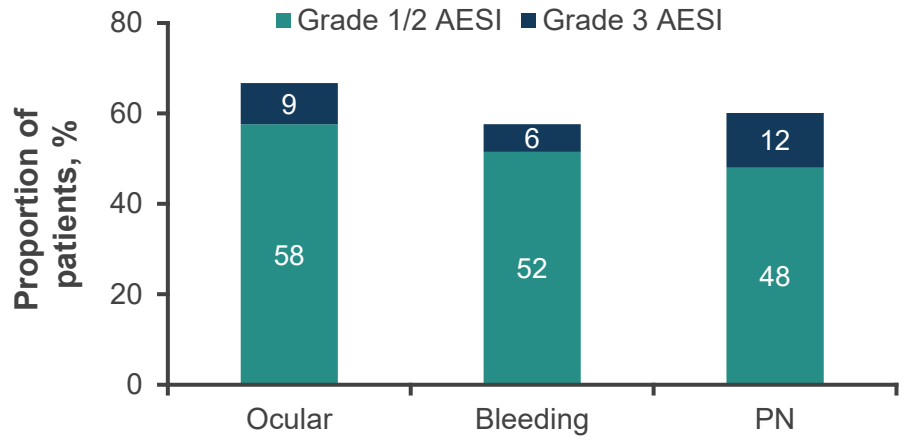
Summary of Safety for 1L TV + Carbo

Common AEs (>20% of patients)	TV + Carbo (N=33)	
Preferred terms	**Grade 1/2, n (%)**	**Grade 3+, n (%)**
Nausea	21 (64)	5 (15)
Alopecia	18 (55)	0
Anemia	6 (18)	12 (36)
Fatigue	15 (45)	3 (9)
Diarrhea	9 (27)	5 (15)
Epistaxis	14 (42)	0
Conjunctivitis	13 (39)	0
Dry eye	12 (36)	1 (3)
Constipation	12 (36)	0
Decreased appetite	10 (30)	2 (6)
Neutropenia	6 (18)	3 (9)
Neutrophil count decreased	5 (15)	4 (12)[a]
Peripheral sensory neuropathy	8 (24)	1 (3)
Vomiting	9 (27)	0
Dyspnea	8 (24)	0
Hypomagnesemia	7 (21)	1 (3)[a]
Dysgeusia	7 (21)	0
Platelet count decreased	2 (6)	5 (15)
Thrombocytopenia	3 (9)	4 (12)[a]

	TV + Carbo (N=33)
Patients with ≥1 TEAE, n (%)	33 (100)
AE related to TV	32 (97)
AEs leading to discontinuation of TV, n (%)	6 (18)
Grade ≥3 AE, n (%)	26 (79)
Grade ≥3 AE related to TV	19 (58)
SAE, n (%)	14 (42)
SAE related to TV	5 (15)
Fatal AE, n (%)	0
Fatal AE related to TV	0



Data cut-off: July 1, 2021.
Each AESI category consists of multiple AE preferred terms.
All Grade 3+ events listed are grade 3 unless otherwise indicated.
[a] Includes one grade 4 event.
1L, first-line; AE, adverse event; AESI, adverse event of special interest; carbo, carboplatin; PN, peripheral neuropathy; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

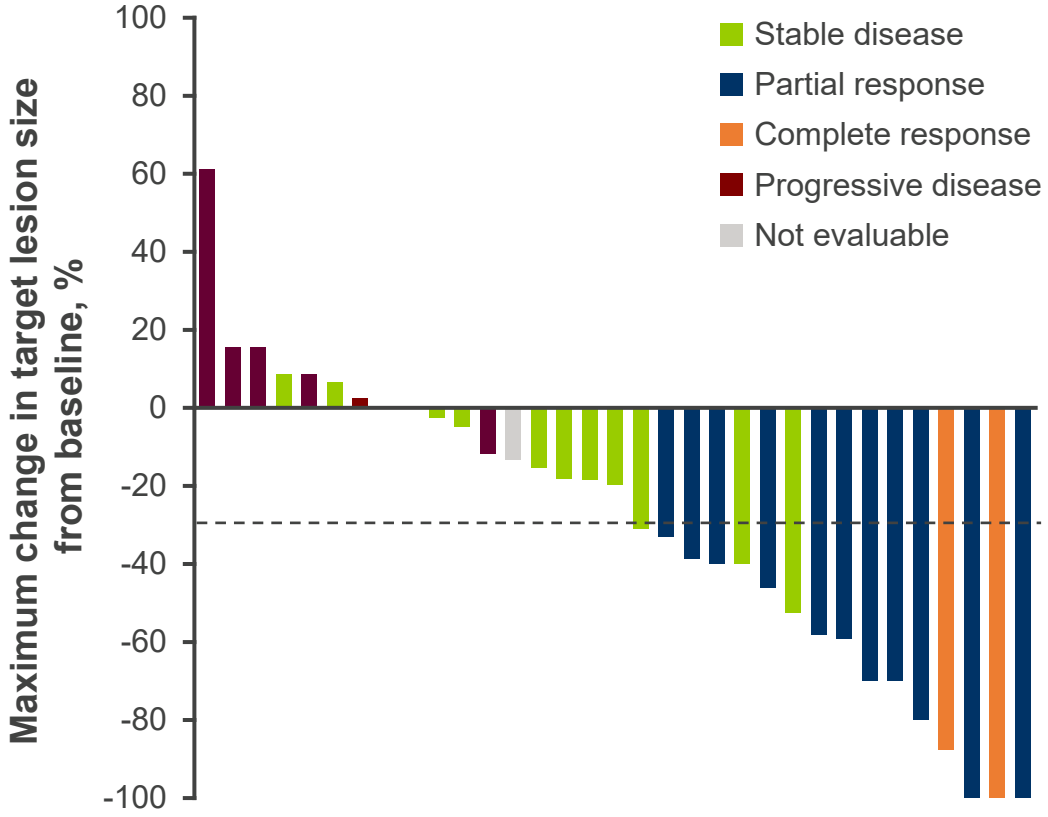
Summary of Efficacy for 2L/3L TV + Pembro

Parameter	2L/3L TV + Pembro (N=34)[a] Median FU: 13.0 months
Median duration of exposure, months (range)	TV: 4.1 (1–16) Pembro: 4.3 (1–17)
Median number of cycles initiated (range)	TV: 6.0 (1–21) Pembro: 6.0 (1–25)
Confirmed response rate, n (%) [95% CI] Complete response, n (%) Partial response, n (%) Stable disease, n (%) Progressive disease, n (%) Not evaluable, n (%)	13 (38) [22–56] 2 (6) 11 (32) 12 (35) 7 (21) 2 (6)
Median duration of response, months (95% CI)	13.8 (2.8–NR)
Median time to response, months (range)	1.4 (1.3–5.8)
Median PFS, months (95% CI)	5.6 (2.7–13.7)
Median OS, months (range)	NR (1.3–17.5+)

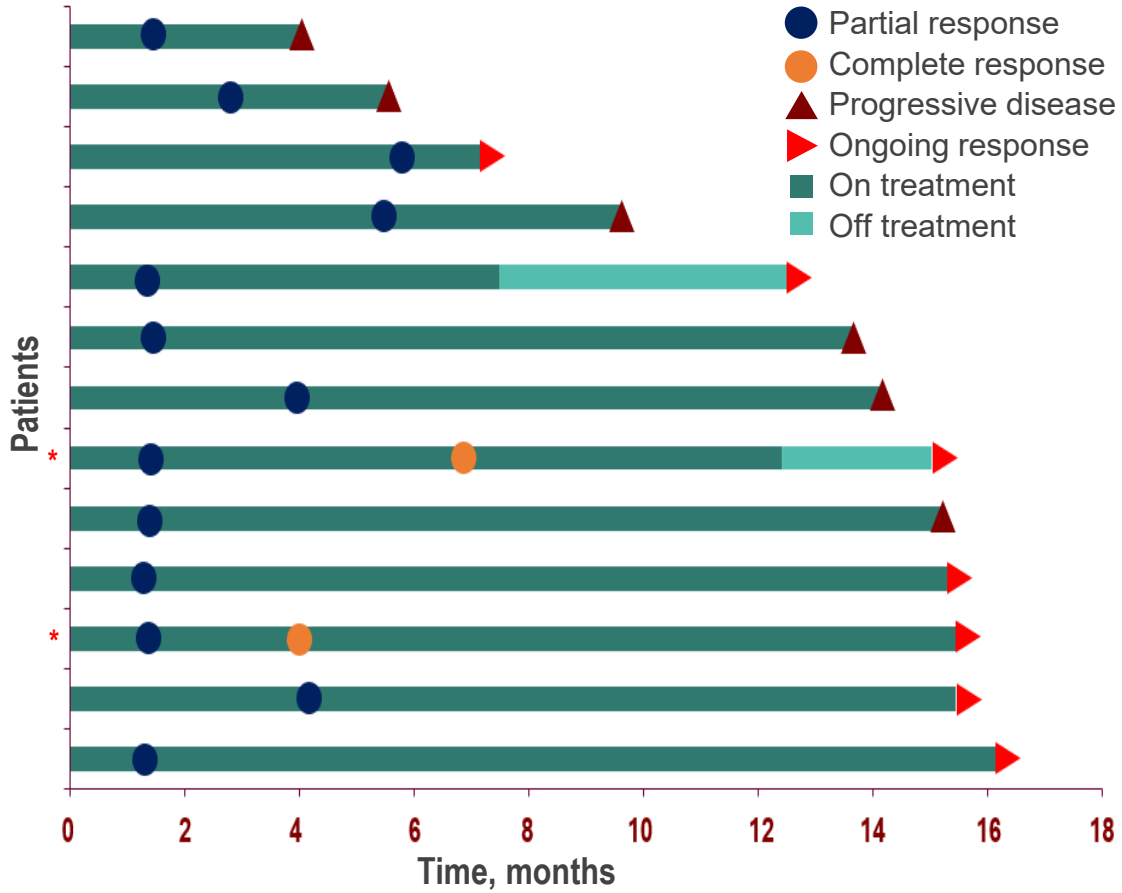
Data cut-off: July 1, 2021.
[a]1 pt was excluded from the full analysis set as they didn't have any target or non-target lesions at baseline.
Treatment ongoing in 4 patients. +, censored
2L/3L, second-/third-line; CI, confidence interval; FU, follow-up; NR, not reached; OS, overall survival; pembro, pembrolizumab; PFS, progression-free survival; pt, patient; TV, tisotumab vedotin.

2L/3L TV + Pembro: Tumor Response

Tumor Shrinkage:
Maximum Change in Target Lesion Size From Baseline



Time to Response and Duration of Response per RECIST 1.1

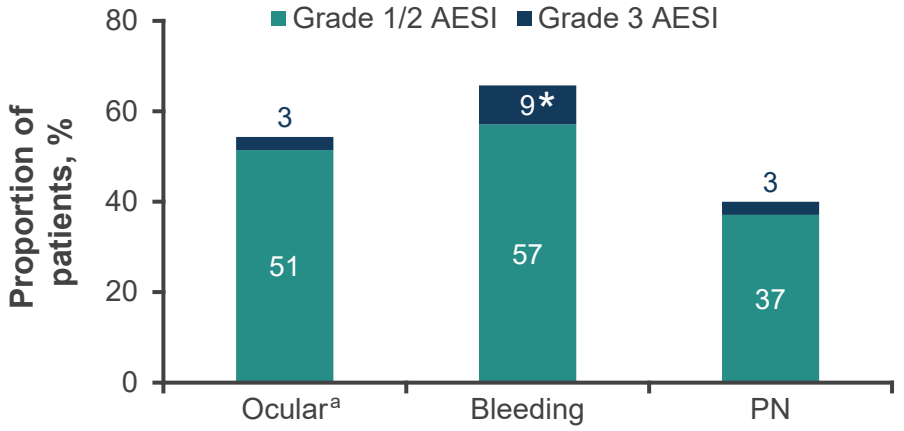


Data cut-off: July 1, 2021.
*Patients with an initial PR that later improved to confirmed CR.
2L/3L, second-/third-line; CR, complete response; PR, partial response; pembro, pembrolizumab; RECIST, Response Evaluation Criteria in Solid Tumors; TV, tisotumab vedotin.

Summary of Safety for 2L/3L TV + Pembro

Common AEs (>20% of patients)	TV + Pembro (N=35)	
Preferred terms	**Grade 1/2, n (%)**	**Grade 3+, n (%)**
Anemia	9 (26)	10 (29)[a]
Diarrhea	17 (49)	2 (6)
Nausea	16 (46)	0
Fatigue	12 (34)	3 (9)
Epistaxis	13 (37)	0
Hypomagnesia	10 (29)	2 (6)[a]
Constipation	11 (31)	1 (3)
Alopecia	11 (31)	0
Decreased appetite	11 (31)	0
Vomiting	11 (31)	0
Asthenia	6 (17)	3 (9)
Hypokalemia	7 (20)	2 (6)
Urinary tract infection	6 (17)	3 (9)
Conjunctivitis	9 (26)	0
Dry eye	9 (26)	0
Peripheral sensory neuropathy	9 (26)	0
Arthralgia	8 (23)	0
Blood creatine phosphokinase	7 (20)	1 (3)

	TV + Pembro (N=35)
Patients with ≥1 TEAE, n (%)	35 (100)
AE related to TV	34 (97)
AEs leading to discontinuation of TV, n (%)	12 (34)
Grade ≥3 AE, n (%)	26 (74)
Grade ≥3 AE related to TV	16 (46)
SAE, n (%)	18 (51)
SAE related to TV	5 (14)
Fatal AE, n (%)	1 (3)
Fatal AE related to TV	0



Data cut-off: July 1, 2021.
Each AESI category consists of multiple AE preferred terms.
* One patient had a grade 4 event.
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[a] Includes one grade 4 event.
2L/3L, second-/third-line; AE, adverse event; AESI, adverse event of special interest; pembro, pembrolizumab; PN, peripheral neuropathy SAE, serious adverse event; TEAE, treatment-emergent adverse event; TV, tisotumab vedotin.

Author's Conclusions

- Acknowledging the limited sample size, both 1L TV + carbo and 2L/3L TV + pembrolizumab showed **encouraging and durable antitumor activity** in patients with r/mCC
- These regimens had a manageable and **acceptable safety** profile
- These data support further research to evaluate additional **TV combinations** (TV [2.0 mg/kg] + carboplatin [AUC 5 mg/mL] + pembrolizumab [200 mg] +/- bevacizumab [15 mg/kg]) as interventions in 1L+ r/mCC (NCT03786081)
- Dose expansion cohort of **TV + pembrolizumab in 1L r/mCC** in this study is being evaluated and will be reported at a future meeting

1L, first-line; 2L/3L, second-/third-line; AUC, area under the curve; carbo, carboplatin; r/mCC, recurrent/metastatic cervical cancer; TV, tisotumab vedotin.

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