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

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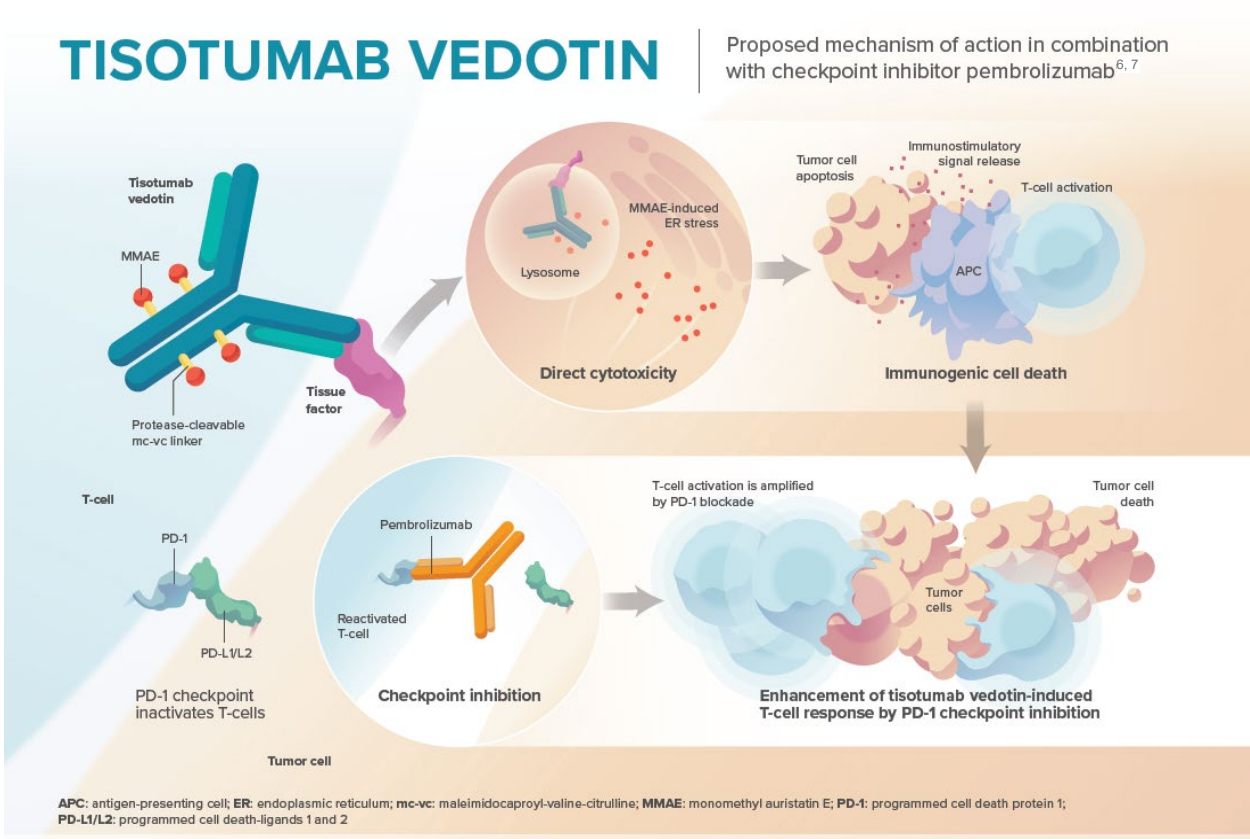
Financial Disclosures

- **Ignace Vergote** declares the following relationships:
  - Consulting or Advisory Role: Agenus, Akesobio, AstraZeneca, Bristol Myers Squibb, Deciphera Pharmaceuticals, Eisai, Elevar Therapeutics, F. Hoffmann-La Roche, Genmab, GSK, Immunogen, Jazz Pharmaceuticals, Karyopharm, Mersana, MSD, Novocure, Novartis, Oncoinvent, OncXerna, Sanofi, Seagen, Sotio, Verastem Oncology, Zentalis
  - Research Funding: Amgen, Roche
  - Travel Expenses: Karyopharm, Genmab
  - Other Relationship: Contracted (via KULeuven) Oncoinvent AS

Background

- Recurrent or metastatic cervical cancer (r/mCC) is a disease of high unmet medical need, affecting primarily younger women
- In 1L, OS benefit demonstrated by pembrolizumab + chemotherapy led to approval in the US and EU for PD-L1 positive r/mCC (KN-826; OS HR: 0.64, PFS HR: 0.62)[1-3]
- Tisotumab vedotin (TV) monotherapy received US accelerated approval based on clinically meaningful and durable response for 2L+ r/mCC (innovaTV 204; ORR: 24%, mDOR: 8.3 months)[4,5]
- Previous reports from dose-escalation and selected dose expansion cohorts of innovaTV 205 suggest potentially enhanced anti-tumor activity with tolerable safety profile of TV in combination with pembrolizumab (pembro), carboplatin (carbo), or bevacizumab (bev)



r/mCC, recurrent or metastatic cervical cancer; TV, tisotumab vedotin.

1. US FDA, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&varApplNo=125514; 2. Colombo N, et al. *N Engl J Med*. 2021;385(20):1856-1867; 3. https://www.ema.europa.eu/en/medicines/human/EPAR/Keytruda; 4. Coleman RL, et al. *Lancet Oncol*. May 2021;22(5):609-619; 5. US FDA, https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761208Orig1s000lbledt.pdf; 6. Breij EC, et al. *Cancer Res*. 2014;74:1214-1226.; 7. Gray, et al. Society for Immunotherapy of Cancer. 2021

ENGOT-cx8/GOG-3024 /innovaTV 205: Dose Expansion Phase

Phase 1b: Dose Escalation[1]

- ✓ No DLTs
- ✓ MTD not reached
- ✓ RP2D identified
- ✓ Acceptable safety profile
- ✓ Encouraging anti-tumor activity

Phase 2: Dose Expansion[2]

Data cut for all dose expansion arms reported here: February 28, 2022

1L TV + Pembro[b]	No prior systemic therapy for r/mCC	N=33 **Median f/u: 18.8 mos**	TV 2.0 mg/kg IV (Q3W) + Pembro 200 mg IV (Q3W)	**Primary endpoint:** Objective response rate[a] per RECIST v1.1
2L/3L TV + Pembro[b]	r/mCC with disease progression on/after 1–2 prior systemic therapies	N=35 **Median f/u: 15.0 mos**	TV 2.0 mg/kg IV (Q3W) + Pembro 200 mg IV (Q3W)	**Secondary endpoints:** • AEs and laboratory parameters • Duration of response • Time to response • Progression free survival • Overall survival
1L TV + Carbo	No prior systemic therapy for r/mCC	N=33 **Median f/u: 14.6 mos**	TV 2.0 mg/kg IV (Q3W) + Carbo AUC 5 IV (Q3W)	

1L TV + Pembro in patients with r/mCC: First disclosure
2L/3L TV + Pembro & 1L TV + Carbo: Updated with longer follow-up

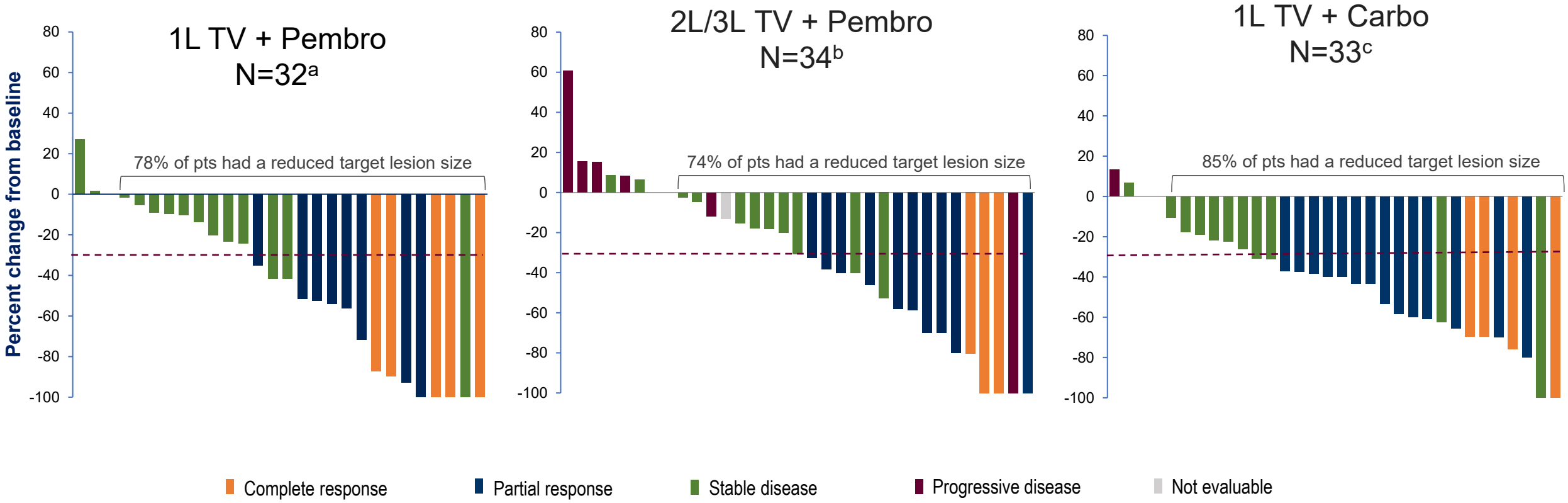
[a]Tumor response assessed every 6 weeks; [b]Pembro will be administered up to 35 cycles, approximately 2 years.
f/u, follow-up; r/mCC, recurrent or metastatic cervical cancer; TV, tisotumab vedotin.
1. Monk B, et al. International Gynecologic Cancer Society: 2021; 2. Vergote I, et al. European Society for Medical Oncology 2021 (initial disclosure of 1L TV + carbo and 2L/3L TV + pembro)

Baseline Demographics and Clinical Characteristics

Demographics and Characteristics	1L TV + Pembro (N = 33)	2L/3L TV + Pembro (N = 35)	1L TV + Carbo (N = 33)
Age, median (range), years	47 (29 - 76)	47 (31 - 73)	51 (25 - 78)
Race (White), n (%)	31 (93.9)	27 (77.1)	28 (84.8)
Ethnicity (Not Hispanic/Latino), n (%)	32 (97.0)	29 (82.9)	29 (87.9)
ECOG performance status, n (%)			
0	25 (75.8)	22 (62.9)	21 (63.6)
1	8 (24.2)	13 (37.1)	12 (36.4)
Cancer recurrence at the time of screening, n (%)	26 (78.8)	31 (88.6)	30 (90.9)
Histology, n (%)			
Squamous	22 (66.7)	19 (54.3)	24 (72.7)
Adenocarcinoma	11 (33.3)	15 (42.9)	8 (24.2)
Adenosquamous	0	0	1 (3.0)
Other	0	1 (2.9)	0
PD-L1 positive[a], n (%)	28 (96.6)[b]	22 (81.5)[b]	NA
Prior radiotherapy, n (%)	25 (75.8)	30 (85.7)	27 (81.8)
Prior chemoradiation, n (%)	24 (72.7)	19 (54.3)	23 (69.7)
Prior lines of systemic regimen[c], n (%)			
0	33 (100)	0	33 (100)
1	0	25 (71.4)	0
2	0	10 (28.6)[d,e]	0
Prior bevacizumab[f], n (%)	NA	19 (54.3)	NA

[a]Prevalence of CPS PD-L1 ≥ 1. [b]Based on evaluable biopsies, n=29 and 27 for 1L and 2L/3L TV + Pembro, respectively. [c]Systemic regimen administered in the metastatic or recurrent setting, excludes chemoradiation. [d]Includes 1 patient receiving prior 1L treatment with nivolumab + ipilimumab. [e]Includes 1 patient receiving prior 2L treatment with pembro. [f]Adjuvant and neoadjuvant settings are excluded. There were 2 Asian patients each in the 1L and 2L/3L TV + Pembro arms, and 1 in the 1L TV + Carbo arm. The number of Hispanic/Latino patients was 1, 0, and 0, respectively; ethnicity is missing for 0, 6, and 4 patients, respectively.
TV, tisotumab vedotin

Anti-Tumor Activity: Best Reduction in Target Lesion Size



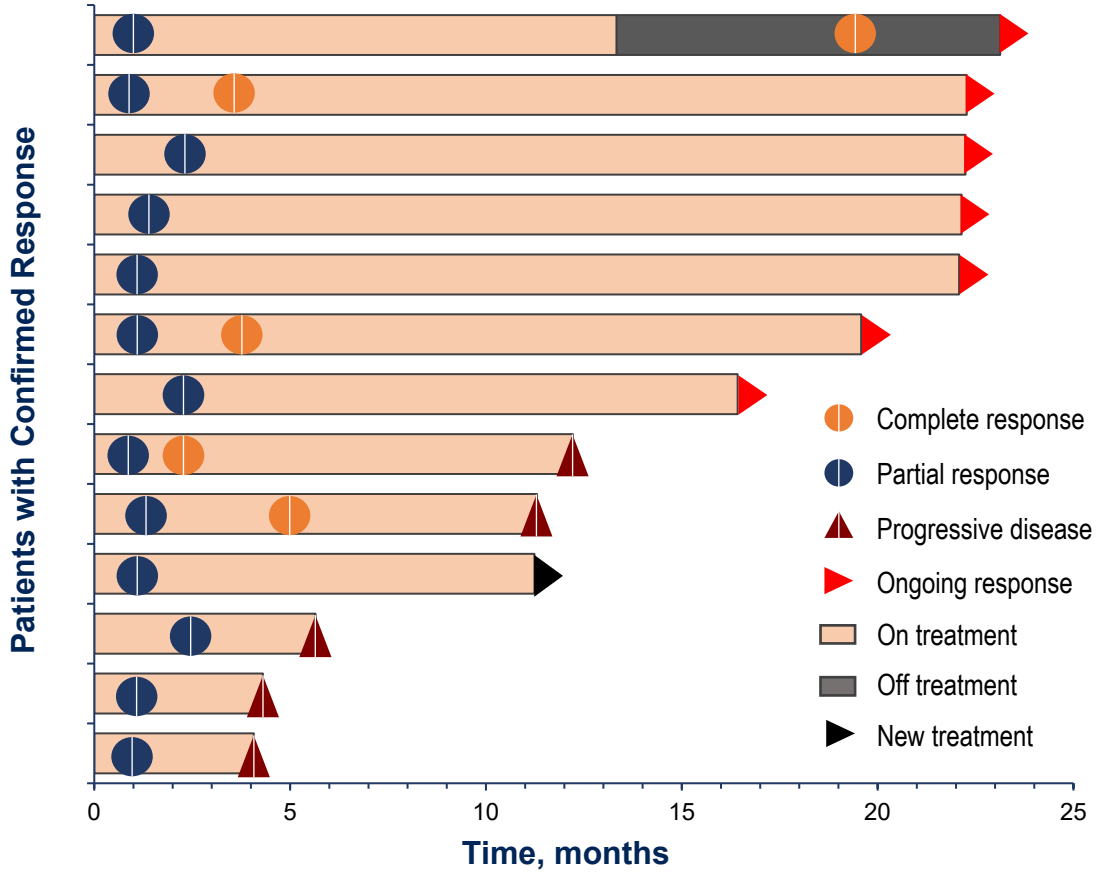
Consistent and compelling reduction in target lesions across treatment arms

[a]Data representative of 28 patients (4/32 patients in the full-analysis set did not have post-baseline scans); [b]Data representative of 33 patients (1/34 patients in the full-analysis set did not have post-baseline scans); [c]Data representative of 32 patients (1/33 patients in the full-analysis set did not have post-baseline scans).
TV, tisotumab vedotin

Anti-Tumor Activity – 1L TV + Pembro

Efficacy Parameter	1L TV + Pembro (N = 32*) Median f/u: 18.8 months
Confirmed ORR, % [95% CI]	40.6 [23.7 – 59.4]
Complete response	5 (15.6)
Partial response	8 (25.0)
Stable disease	14 (43.8)
Progressive disease	1 (3.1)
Not evaluable	4 (12.5)
DCR[a], % [95% CI]	84.4 [67.2 – 94.7]
Median DOR[b], months (range)	NR (2.8 – 21.9+)
Median time to response, months (range)	1.4 (1.2 – 2.8)
Median PFS[c], months [95% CI]	5.3 [4.0 – 12.2]
Median OS[d], months (range)	NR (0.5 – 24.9+)

+, censored; NR, not reached.
*1 patient was excluded from the full-analysis set due to receiving incorrect study drug.
[a]Defined as SD (at least 5 weeks after the first dose of study treatment) or confirmed CR or PR.
[b]8 patients are censored; [c]12 patients are censored; [d]19 patients are censored.



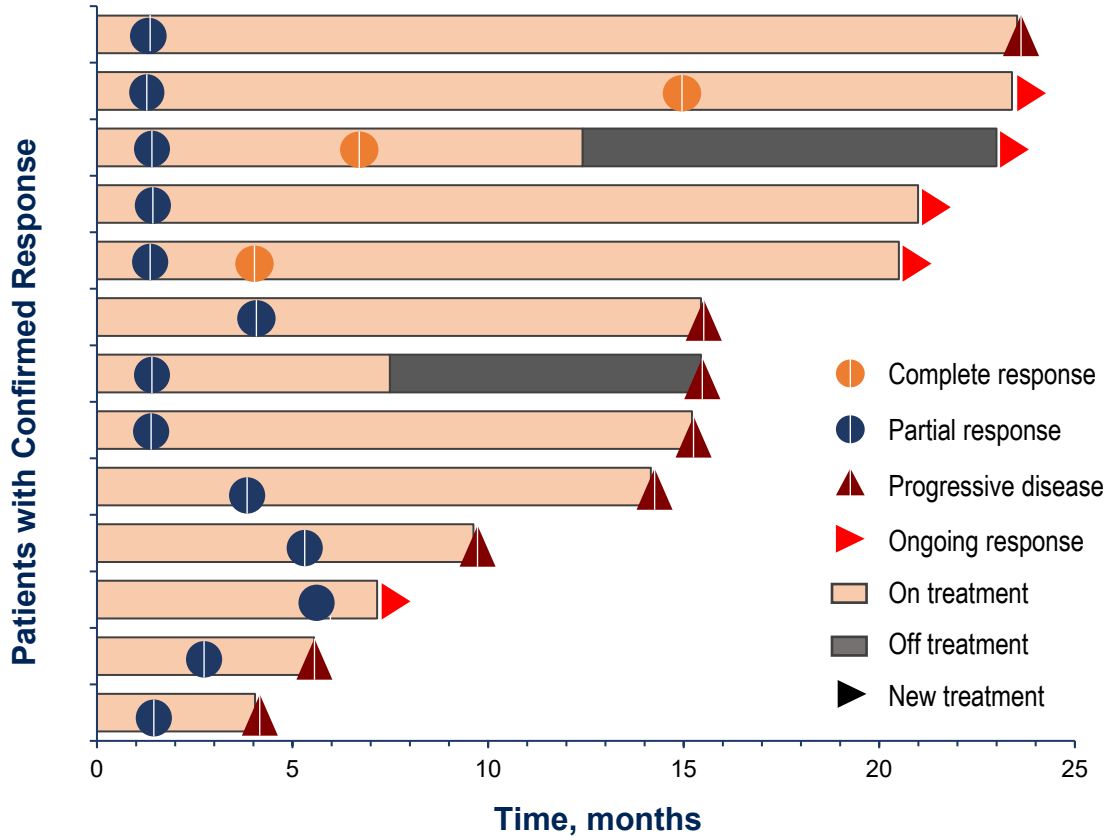
With 18.8 months median follow-up, compelling, durable preliminary efficacy was observed in 1L with >50% of responders with ongoing response

DCR, disease control rate; f/u, follow-up; TV, tisotumab vedotin

Anti-Tumor Activity – 2L/3L TV + Pembro

Efficacy Parameter	2L/3L TV + Pembro (N = 34*) Median f/u: 15.0 months
Confirmed ORR, % [95% CI]	38.2 [22.2 – 56.4]
Complete response	3 (8.8)
Partial response	10 (29.4)
Stable disease	12 (35.3)
Progressive disease	7 (20.6)
Not evaluable	2 (5.9)
DCR[a], % [95% CI]	73.5 [55.6 – 87.1]
Median DOR[b], months [95% CI]	14.0 [2.8 – NR]
Median time to response, months (range)	1.4 (1.3 – 5.8)
Median PFS[c], months [95% CI]	5.6 [2.7 – 14.2]
Median OS[d], months [95% CI]	15.3 [9.9 – NR]

+, censored; NR, not reached
*1 patient was excluded from the full analysis set as they had no target lesions at baseline.
[a]Defined as SD (at least 5 weeks after the first dose of study treatment) or confirmed CR or PR.
[b]5 patients are censored; [c]10 patients are censored; [d]14 patients are censored



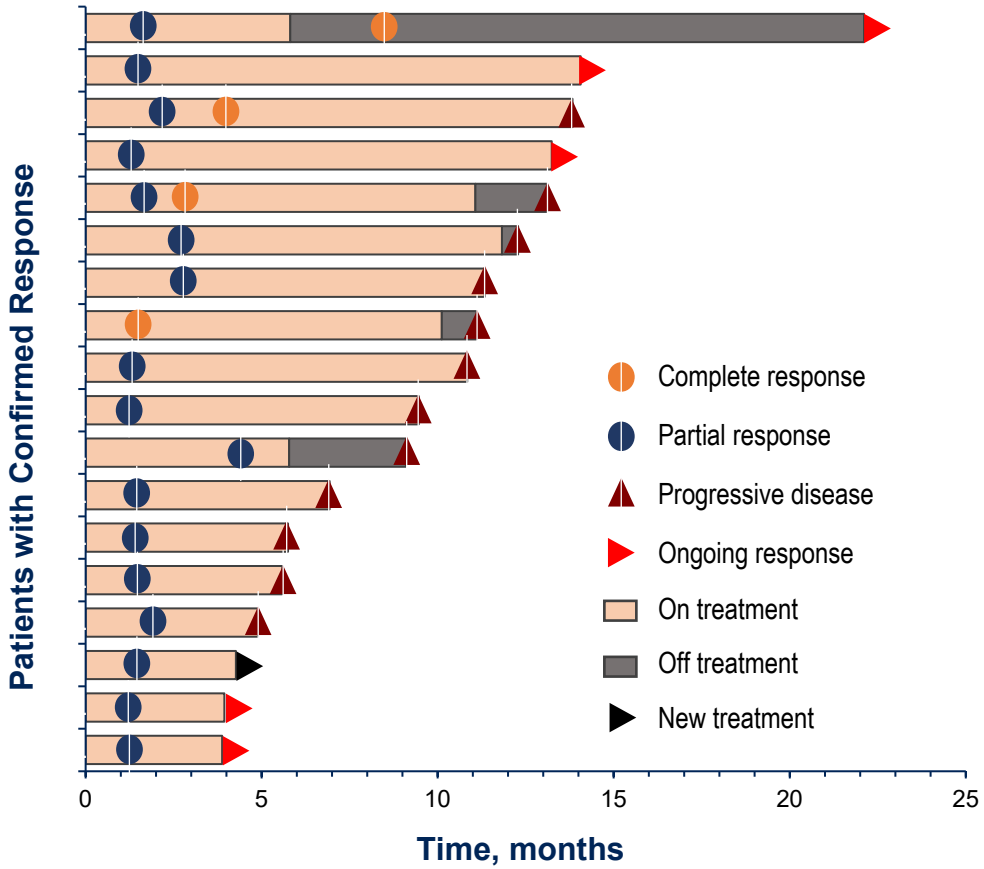
With 15 months median follow-up, compelling, durable preliminary efficacy was observed in 2L/3L with ~40% of responders ongoing in response

DCR, disease control rate; f/u, follow-up; TV, tisotumab vedotin

Anti-Tumor Activity – 1L TV + Carbo

Efficacy Parameter	1L TV + Carbo (N = 33) Median f/u: 14.6 months
Confirmed ORR, % [95% CI]	54.5 [36.4 – 71.9]
Complete response	4 (12.1)
Partial response	14 (42.4)
Stable disease	12 (36.4)
Progressive disease	2 (6.1)
Not evaluable	1 (3.0)
DCR[a], % [95% CI]	90.9 [75.7 – 98.1]
Median DOR[b], months [95% CI]	8.6 [4.2; 11.5]
Median time to response, months (range)	1.4 (1.1 – 4.4)
Median PFS[c], months [95% CI]	6.9 [4.0 – 11.1]
Median OS[d], months (range)	NR (0.8+ – 22.1+)

+, censored; NR, not reached.
[a]Defined as SD (at least 5 weeks after the first dose of study treatment) or confirmed CR or PR.
[b]4 patients are censored; [c]9 patients are censored; [d]22 patients are censored.

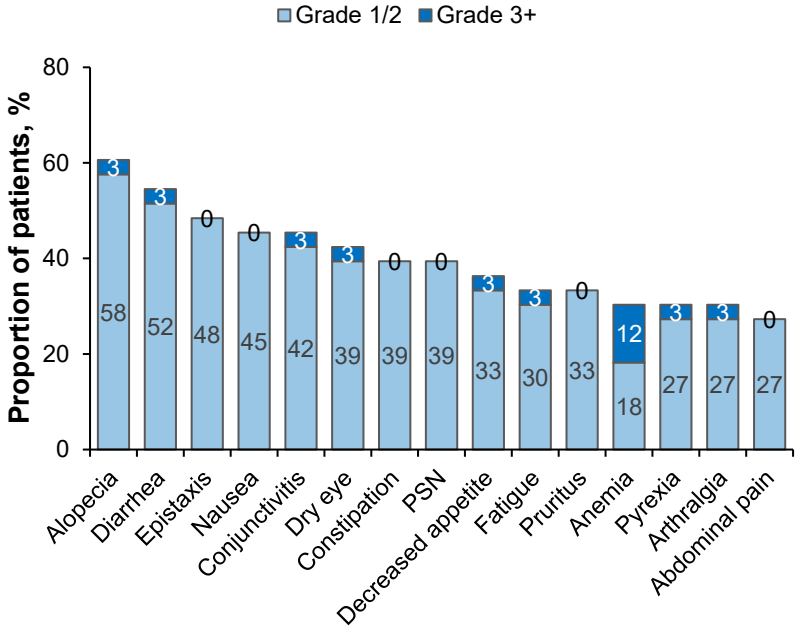


Compelling antitumor activity was observed in 1L patients with >50% experiencing a response and >90% with disease control

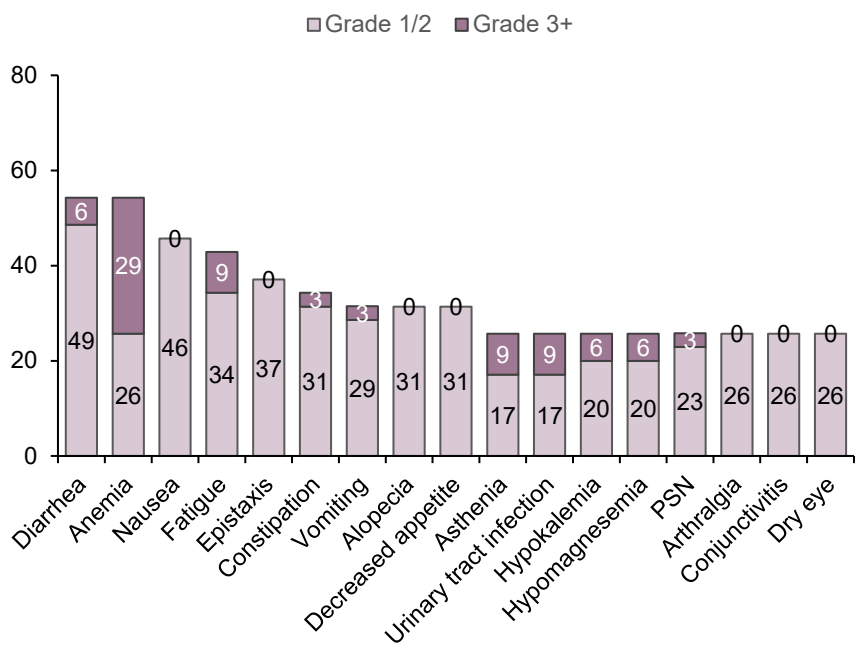
DCR, disease control rate; f/u, follow-up; TV, tisotumab vedotin

Safety Summary of Common AEs Reported >25% of Patients

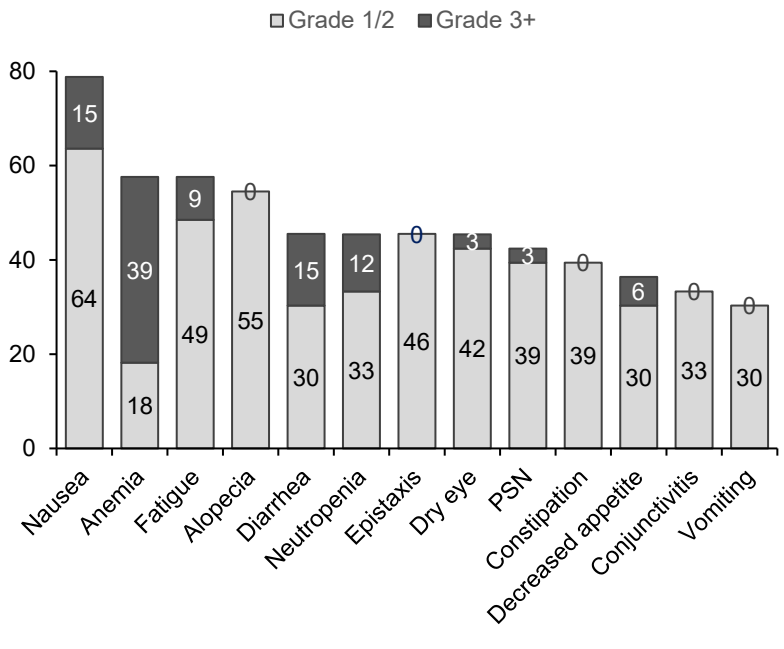
1L TV + Pembro[a]



2L/3L TV + Pembro[b]



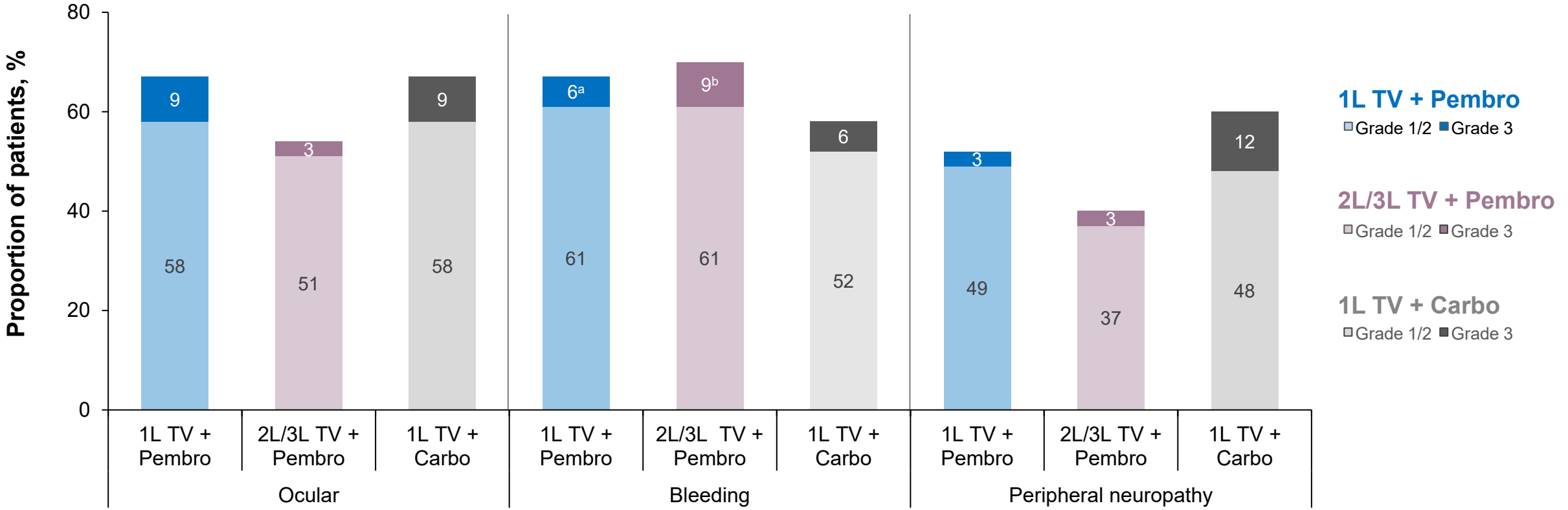
1L TV + Carbo



- Most TEAEs were grade 1 or 2
- Observed safety profile was generally consistent with those known for each individual agent
- There was a single grade 5 event with 1L TV + Pembro considered by the investigator to be related to trial treatment (due to disseminated intravascular coagulation)
- Immune-mediated AEs observed with TV + Pembro were consistent with known safety profile of checkpoint inhibitors

[a]8 (24.2%) patients discontinued TV due to AEs; [b]12 (34.3%) patients discontinued TV due to AEs; [c]7 (21.2%) patients discontinued TV due to AEs; AEs leading to discontinuation of TV were mostly related to ocular or neuropathic events.
PSN, peripheral sensory neuropathy; TV, tisotumab vedotin

Adverse Events of Special Interest with TV



[a]Includes one patient with grade 5 disseminated intravascular coagulation; [b]Includes one patient with grade 4 hematuria

AEs of special interest with TV were generally consistent across cohorts and were mostly grade 1-2

TV, tisotumab vedotin

Authors' Conclusions

- Dose expansion cohorts of TV in combination with pembro or carbo in r/mCC demonstrated encouraging and durable anti-tumor activity with tolerable safety profiles
  - 1L TV + pembro resulted in 41% confirmed ORR (16% CR) and median DOR was not reached at median follow-up of ~19 months
  - Updated data from 2L/3L TV + pembro (confirmed ORR: 38%), and 1L TV + carbo (confirmed ORR: 55%) continues to show promising efficacy with no new safety signals outside of known AEs of individual agents[1]
- These findings suggest a potential for TV to be incorporated into a combination regimen to further improve clinical outcomes in 1L r/mCC
- Further research to evaluate TV combinations (TV + carbo + pembro ± bev) in 1L+ r/mCC are ongoing [NCT03786081]
  - Disclosure of new cohort (Arm H) evaluating this combination is presented as a TiP at ASCO 2022 (TPS#5603)

r/mCC, recurrent or metastatic cervical cancer; TV, tisotumab vedotin

1. Vergote I, et al. *Ann Oncol*. 2021; 32 (5): S725-S772.

Acknowledgements

- We thank the patients, their families, and their caregivers for participating in this study
- This study was funded by Genmab A/S and Seagen Inc.
- This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA
- This study was sponsored by Genmab A/S, Seagen Inc., and supported by the and the European Network for Gynaecological Oncological Trials group (ENGOT), the Belgium and Luxembourg Gynaecological Oncology Group, and Gynecologic Oncology Group (GOG-partners)