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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Declaration of Interests

Ignace Vergote

- Consulting (2019-2021)
- Aksebio (2021), Amgen (Europe) GmbH (2019), AstraZeneca (2019-2022),-Clovis Oncology Inc. (2019-2019),Carrick Therapeutics (2019),Deciphera Pharmaceuticals (2020-2021),-Eisai (2021), Elevar Therapeutics (2020), F. Hoffmann-La Roche Ltd (2019-2021), Genmab (2019-2021), GSK (2019-2021), Immunogen Inc. (2019-2022), Jazzpharma (2021-2022), Karyopharm (2021), Mersana (2020), Millennium Pharmaceuticals (2019), MSD (2019-2022), Novocure (2020-2022), Novartis (2021), Octimet Oncology NV (2019), Oncoinvent AS (2019-2022), Sotio a.s. (2019-2022), Verastem Oncology (2020), Zentalis (2020)
- Contracted research (via KULeuven)
- Oncoinvent AS (2019-2020)
- Genmab (2019-2019)
- Grants/Corporate sponsored research
- Amgen (2019-2020)
- Roche (2019-2020)
- Accomodations, Travel expenses (2019-2020)
- Amgen, MSD, Tesaro, AstraZeneca, Roche

Unmet Need in Recurrent/Metastatic Cervical Cancer (r/mCC) and Study Rationale

- While **1L platinum-taxane doublets + bevacizumab** (if eligible) have improved survival outcomes in r/mCC, safer, more effective options are needed[1-4]
- **TV**, an investigational antibody-drug conjugate that targets tissue factor, is under development for the treatment of several solid tumors, including cervical cancer[5]
- A **pivotal phase 2 single-arm** 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 r/mCC[6]
- The **RP2D** for TV in combination with pembrolizumab, carboplatin, and bevacizumab in r/mCC was recently reported (Monk et al. IGCS 2021). Data from 2 expansion cohorts from that study (TV/carboplatin in 1L and TV/pembrolizumab in 2L+ r/mCC patients) are reported

[1]Minion LE, et al. *Gynecol Oncol*. 2018; 148(3): 609–621; [2]Tewari KS, et al. *N Engl J Med*. 2014;370(8):734-743; [3]Ebina Y, et al. *Int J Clin Oncol*. 2019;24(1):1-19; [4]Abu-Rustum NR et al. (https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf, accessed 01/07/2021); [5]Breij EC, et al. *Cancer Res*. 2014;74(4):1214-1226; [6]Coleman RL, et al. *Lancet Oncol*. 2021;22(5):609-619.

1L, first-line; 2L+, second-line and beyond; IV, intravenously; mDOR, median duration of response; ORR, objective response rate; Q3W, every 3 weeks; r/mCC, recurrent/metastatic cervical cancer; TV, tisotumab vedotin.

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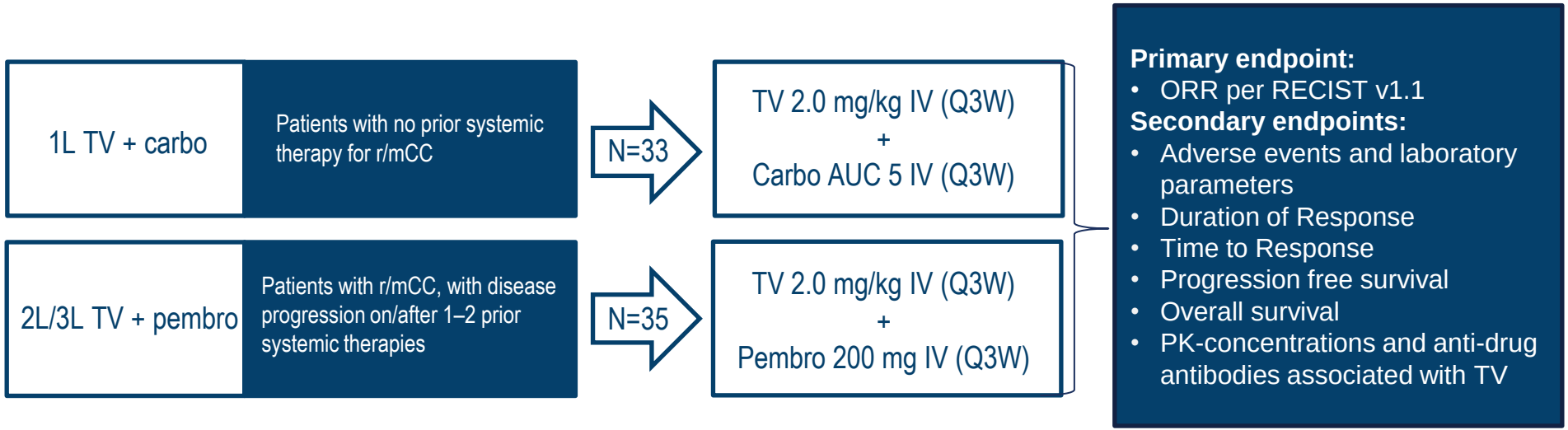
Dose-expansion phase: 1L TV + carbo and 2L/3L TV + pembrolizumab cohorts



1L/2L,first-/ second-line; Carbo, carboplatin; IV, intravenously; ORR, objective response rate; Pembro, pembrolizumab; Q3W, every 3 weeks; 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	51.0 (25 – 78)	47.0 (31 – 73)
ECOG performance status, n (%)		
0	21 (63.6)	22 (62.9%)
1	12 (36.4)	13 (37.1%)
Histology, n (%)		
Squamous	24 (72.7)	19 (54.3)
Adenocarcinoma	8 (24.2)	15 (42.9)
Other	1 (3.0)	1 (2.9)
PD-L1 positive,[a] n (%)	N/A	22 (81.5)[b]
Prior chemoradiation, n (%)	21 (63.6)	18 (51.4)
Prior lines of systemic regimen,[c] n (%)		
0	33 (100)	0
1	0	26 (74.3)[d]
2	0	9 (25.7)[e]
Prior bevacizumab,[f] n (%)	N/A	18 (51.4)

[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 prior treatment with nivolumab + ipilimumab in the 1L setting.
[e]Includes one prior treatment with pembrolizumab in the 2L setting.
[f]Adjuvant and neoadjuvant settings are excluded.

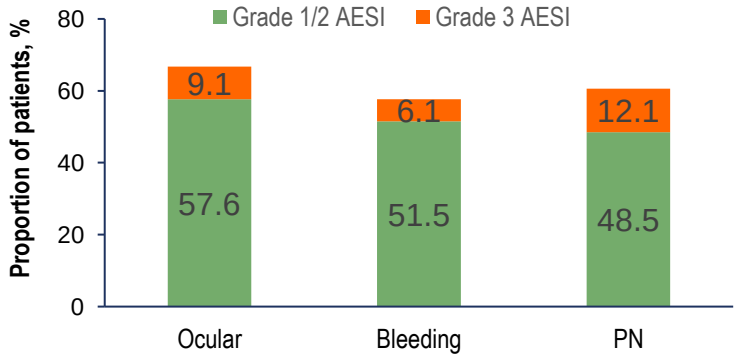
CPS, combined positive cells; ECOG, Eastern Cooperative Oncology Group; N/A, not applicable; TV, tisotumab vedotin.

Summary of Efficacy & Safety for 1L TV + Carbo

Parameters	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+)

Treatment ongoing in 9 patients. +, censored.

	TV + Carbo (N=33)
Patients with ≥1 TEAE, n (%) AE related to TV	33 (100.0) 32 (97.0)
Grade ≥3 AE, n (%) Grade ≥3 AE related to TV	26 (78.8) 19 (57.6)
SAE, n (%) SAE related to TV	14 (42.4) 5 (15.2)
Fatal AE, n (%) Fatal AE related to TV	0 0



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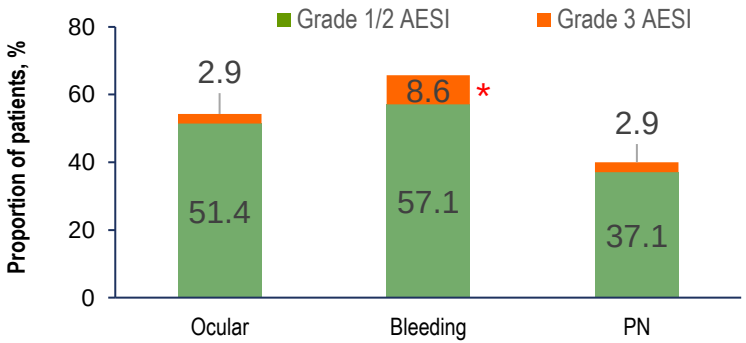
1L, first-line; AE, adverse event; AESI, adverse event of special interest; carbo, carboplatin; FU, follow-up; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PN; peripheral neuropathy; r/mCC, recurrent/metastatic cervical cancer; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TV, tisotumab vedotin.

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

Parameters	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]	13 (38) [22 – 56]
Complete response, n (%)	2 (6)
Partial response, n (%)	11 (32)
Stable Disease, n (%)	12 (35)
Progressive disease, n (%)	7 (21)
Not evaluable, n (%)	2 (6)
Median DOR, 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+)

[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.

	TV + Pembro (N = 35)
Patients with ≥1 TEAE, n (%)	35 (100.0)
AE related to TV	34 (97.1)
Grade ≥3 AE, n (%)	26 (74.3)
Grade ≥3 AE related to TV	16 (45.7)
SAE, n (%)	18 (51.4)
SAE related to TV	5 (14.3)
Fatal AE, n (%)	1 (2.9)
Fatal AE related to TV	0



*One patient had a grade 4 bleeding event.

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+, censored; 1L, first-line; AE, adverse event; AESI, adverse event of special interest; DOR, duration of response; FU, follow-up; NR, not reached; ORR, objective response rate; OS, overall survival; pembro, pembrolizumab; PFS, progression-free survival; PN; peripheral neuropathy; r/mCC, recurrent/metastatic cervical cancer; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TV, tisotumab vedotin.

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** as interventions in r/mCC
- Dose expansion cohort of **TV + pembrolizumab in 1L r/mCC** in this study is being evaluated and will reported at a future meeting

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