Abstract 5531

Tisotumab Vedotin in 2L/3L Recurrent or Metastatic Cervical Cancer: Subsequent Therapy Data From ENGOT-cx12/GOG-3057/innovaTV 301

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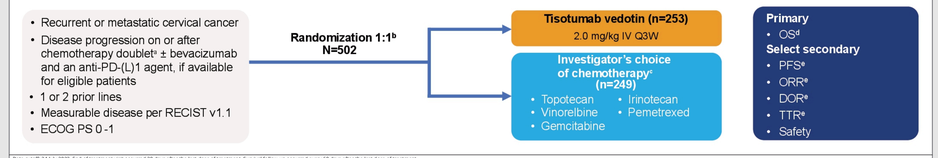
Background

- The recent evolution of the recurrent or metastatic cervical cancer (r/mCC) treatment landscape has led to new questions on treatment sequencing with respect to immunotherapy for novel treatments such as tisotumab vedotin[1,2]
- Tisotumab vedotin is an antibody-drug conjugate (ADC) directed to tissue factor and linked to the microtubule-disrupting agent monomethyl auristatin E (MMAE)[3]
- Tisotumab vedotin was granted full approval by the US Food and Drug Administration as a monotherapy for adult patients with r/mCC with disease progression on or after chemotherapy[4,5]
- Here, we report additional details on prior and subsequent therapies from the Phase 3 ENGOT-cx12/GOG-3057/innovaTV 301 study (NCT04697628) of tisotumab vedotin vs chemotherapy in patients with r/mCC in second-line (2L) or third-line (3L) setting

Methods

- innovaTV 301 is a global, randomized, open-label Phase 3 study of tisotumab vedotin vs investigator's choice of chemotherapy in patients with r/mCC who have received 1 or 2 prior lines of systemic therapy for their r/mCC[6] (**Figure 1**)
- Eligible patients had r/mCC with disease progression on or after chemotherapy doublet[a] ± bevacizumab and an anti–PD-(L)1 agent, if available for eligible patients
- The primary end point was overall survival (OS)
- Descriptive analyses on subsequent anticancer therapy are reported

Figure 1: Study design for innovaTV 301



Data cutoff: 24 July 2023. End of treatment visit occurred 30 days after the last dose of treatment. Survival follow-up occurred every 60 days after the last dose of treatment.
DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; IV, intravenous; ORR, objective response rate; PD-1, programmed death-1 protein; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PS, performance status; Q3W, once every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.
[a]Standard-of-care systemic chemotherapy doublet defined as paclitaxel + cisplatin, or paclitaxel + carboplatin, or paclitaxel + topotecan/irinotecan. [b]Patients were stratified by ECOG PS, prior bevacizumab therapy, prior anti-PD-(L)1 therapy, and geographic region. [c]Chemotherapy regimens were given at the following doses: topotecan, 1 or 1.25 mg/m² IV on days 1 to 5, every 21 days; vinorelbine, 30 mg/m² IV on days 1 and 8, every 21 days; gemcitabine, 1000 mg/m² IV on days 1 and 8, every 21 days; irinotecan, 100 or 125 mg/m² IV weekly for 28 days, every 42 days; pemetrexed, 500 mg/m² on day 1, every 21 days. [d]OS was defined as the time from the date of randomization to the date of death due to any cause. [e]Assessed by investigator.
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Results

Patients

- Of 502 patients randomized, 253 received tisotumab vedotin and 249 received chemotherapy of the investigator's choice (**Table 1**)
- In general, the baseline and treatment characteristics were similar between patients in the tisotumab vedotin arm and the chemotherapy arm
- All patients had received prior systemic therapy

Table 1: Baseline patient and treatment characteristics

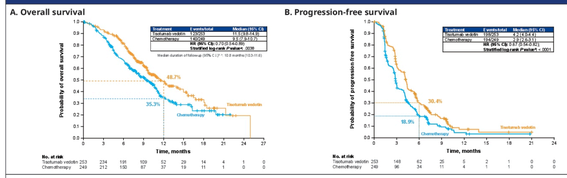
	Tisotumab vedotin (n=253)	Chemotherapy (n=249)
Median age (range), years	51 (26-80)	50 (27-78)
Region, n (%)		
US	16 (6.3)	14 (5.6)
Europe	106 (41.9)	104 (41.8)
Asia	85 (33.6)	88 (35.3)
Other	46 (18.2)	43 (17.3)
Baseline ECOG PS, n (%)		
0	137 (54.2)	136 (54.6)
1	116 (45.8)	113 (45.4)
Biopsy evaluable, n (%)	210 (83.0)	194 (77.9)
Positive membrane TF expression[a]	194 (92.4)	183 (94.3)
Prior systemic therapy or radiation for cervical cancer, n (%)	253 (100)	249 (100)
Prior bevacizumab	164 (64.8)	157 (63.1)
Prior anti–PD-(L)1 therapy	71 (28.1)	67 (26.9)
Prior radiation therapy for cervical cancer	205 (81.0)	203 (81.5)
Prior recurrent/metastatic systemic regimens, n (%)[b]		
1	159 (62.8)	149 (59.8)
2	93 (36.8)	100 (40.2)

Data cutoff: 24 July 2023.
TF, tissue factor
[a]TF expression is defined as TF membrane expression ≥1% with immunohistochemistry; percentages are calculated based on number of evaluable biopsies. [b] One patient in the tisotumab vedotin arm had an unknown prior systemic regimen.
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Efficacy

- OS and PFS benefits with tisotumab vedotin compared with chemotherapy were observed (**Figure 2**)

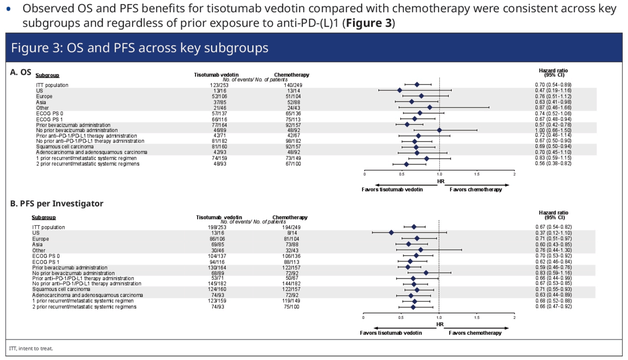
Figure 2: Overall survival and progression-free survival



HR, hazard ratio.
[a] The α-threshold for statistical significance is 0.0226 (2-sided), based on the actual number of OS events at interim analysis. [b] Median is estimated using Kaplan-Meier method, and 95% CI is calculated using the complimentary log-log transformation method. [c] Based on reverse Kaplan-Meier estimates. [d]The threshold for statistical significance is 0.0453 (2-sided), based on the actual number of PFS events at interim analysis.
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- Observed OS and PFS benefits for tisotumab vedotin compared with chemotherapy were consistent across key subgroups and regardless of prior exposure to anti-PD-(L)1 (**Figure 3**)

Figure 3: OS and PFS across key subgroups



ITT, intent to treat.

- ORR, disease control rate (DCR), and TTR in the ITT population are shown in **Table 2**

Table 2: Antitumor activity

	Tisotumab vedotin (n=253)	Chemotherapy (n=249)
ORR (95% CI), %	17.8 (13.3-23.1)	5.2 (2.8-8.8)
Odds ratio (95% CI)	4.0 (2.1-7.6)	
Best overall response, n (%)		
CR	6 (2.4)	0
PR	39 (15.4)	13 (5.2)
SD	147 (58.1)	132 (53.0)
PD	46 (18.2)	74 (29.7)
Not evaluable/Not available	15 (5.9)	30 (12.0)
DCR (95% CI), %[a]	75.9 (70.1-81.0)	58.2 (51.8-64.4)
Median TTR (range), months	1.6 (1.2-4.5)	1.7 (1.2-3.9)
Median DOR (95% CI), months	5.3 (4.2-8.3)	5.7 (2.8-NR)

CR, complete response; PR, partial response; PD, progressive disease; SD, stable disease.
[a] DCR defined as CR + PR + SD; CR and PR were confirmed responses. The minimum criteria for SD duration was ≥ 5 weeks after the date of randomization.
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Subsequent therapy

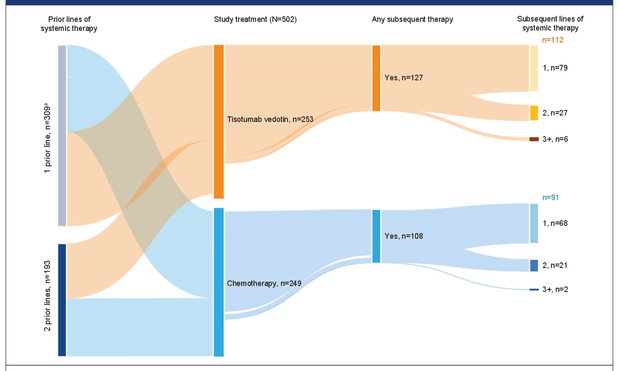
- Following study treatment discontinuation, 127 patients (50.2%) from the tisotumab vedotin arm and 108 (43.4%) from the chemotherapy arm received subsequent anticancer therapy, most commonly systemic therapy (**Table 3** and **Figure 4**)
  - More patients from the tisotumab vedotin arm were able to receive multiple lines of subsequent systemic therapy
  - Cytotoxic chemotherapy and immunotherapy were the most common types of subsequent anticancer therapies among patients in both treatment arms
    - Gemcitabine was the most common subsequent chemotherapy

Table 3: Subsequent anticancer therapies

	Tisotumab vedotin (n=253)	Chemotherapy (n=249)
Median time from last dose of study treatment to first subsequent therapy (range), weeks	6.7 (1-35)	5.4 (1-51)
Patients who received any subsequent anticancer therapy, n (%)	127 (50.2)	108 (43.4)
Systemic therapy for progressive disease	112 (44.3)	91 (36.5)
Palliative radiotherapy	23 (9.1)	21 (8.4)
Other	5 (2.0)	7 (2.8)
Subsequent systemic regimens, n (%)		
1	79 (31.2)	68 (27.3)
2	27 (10.7)	21 (8.4)
≥3	6 (2.4)	2 (0.8)
Patients with any subsequent systemic regimens, *n/N* (%)		
Tisotumab vedotin	1/112 (0.9)[a]	6/91 (6.6)
Cytotoxic chemotherapy	82/112 (73.2)	57/91 (62.6)
Immunotherapy	35/112 (31.3)	29/91 (31.9)
Chemo-immunotherapy	7/112 (6.3)	4/91 (4.4)
Investigational agent	6/112 (5.4)	7/91 (7.7)
Anti-angiogenic agent	1/112 (0.9)	1/91 (1.1)
Other/unknown	2/112 (1.8)	0/91

[a] Patient received subsequent therapy from commercial supply of tisotumab vedotin.

Figure 4: Prior and subsequent therapy

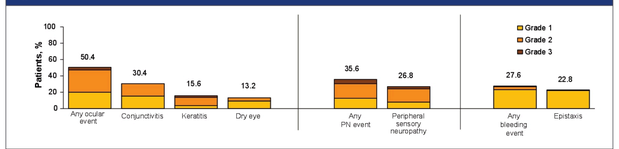


[a] One patient in the tisotumab vedotin arm had an unknown prior systemic regimen.

Safety

- The incidence of any-grade treatment-related adverse events (TRAEs) was similar across both arms (87.6% and 85.4% in the tisotumab vedotin and chemotherapy arms, respectively); Grade ≥3 events occurred in 29.2% and 45.2%
- Treatment-emergent treatment-related adverse events of special interest (AESIs) with tisotumab vedotin (**Figure 5**) were consistent with the known safety profile, including ocular, peripheral neuropathy (PN), and bleeding events
- No Grade 4 or 5 AESIs were observed

Figure 5: Treatment-related AESIs in ≥5% of patients in the tisotumab vedotin arm



Slomovitz BM. SGO 2024.

- Median time to resolution of AESIs (regardless of attribution) in the tisotumab vedotin arm is presented in **Table 4**

Table 4: Resolution or improvement of AESIs in the tisotumab vedotin arm

Ocular events	
Patients with any event, n/N (%)	132/250 (52.8)
Patients with all events resolved[a] or improved,[b] n/N (%)	92/132 (69.7)
Patients with some events resolved[a] or improved,[b] n/N (%)	32/132 (24.2)
Events resolved[a]/total ocular events	262/347
Time to onset of first event, median (range), months	1.22 (0-4.9)
Time to resolution[c], median (range), months	0.59 (0.1-12.6)
Peripheral neuropathy events	
Patients with any event, n/N (%)	96/250 (38.4)
Patients with all events resolved[a] or improved,[b] n/N (%)	35/96 (36.5)
Patients with some events resolved[a] or improved,[b] n/N (%)	7/96 (7.3)
Events resolved[a]/total peripheral neuropathy events	31/123
Time to onset of first event, median (range), months	2.38 (0-9.3)
Time to resolution[c], median (range), months	1.12 (0-12.1)
Bleeding events	
Patients with any event, n/N (%)	105/250 (42.0)
Patients with all events resolved[a] or improved,[b] n/N (%)	77/105 (73.3)
Patients with some events resolved[a] or improved,[b] n/N (%)	11/105 (10.5)
Events resolved[a]/total bleeding events	135/168
Time to onset of first event, median (range), months	0.43 (0-10.4)
Time to resolution[c], median (range), months	0.26 (0-7.2)

[a] Resolution is defined as events status outcome of "Recovered/Resolved" or "Recovered/Resolved with Sequelae." [b] For events that are not resolved, improvement is defined as ≥1 grade decrease from the highest grade as of the last assessment.
[c] Time to resolution is defined as time from the start date of the event to the end date of the same event.

Conclusions

- The ENGOT-cx12/GOG-3057/innovaTV 301 study showed a significant improvement in OS with tisotumab vedotin compared with chemotherapy
- Among patients who received subsequent systemic anticancer therapies, cytotoxic chemotherapy and immunotherapy were the most common therapies in both treatment arms
- The safety profile of tisotumab vedotin was manageable and consistent with the known safety profile
- Tisotumab vedotin provides meaningful clinical benefit and does not prevent the initiation of subsequent therapies, including immunotherapy

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