

LBA32

Tisotumab vedotin in previously treated recurrent or metastatic cervical cancer: Results from the phase II innovaTV 204/GOG-3023/ENGOT-cx6 study

R.L. Coleman¹, D. Lorusso², C. Gennigens³, A. González-Martín⁴, L. Randall⁵, D. Cibula⁶, B. Lund⁷, L. Woelber⁸, S. Pignata⁹, F. Forget¹⁰, A. Redondo¹¹, R. Rangwala¹², S.D. Vindeløv¹³, M. Chen¹², J.R. Harris¹², L. Nicacio¹⁴, M.S.L. Teng¹⁴, M. Smith¹², B.J. Monk¹⁵, I.B. Vergote¹⁶

¹ Medical Oncology, US Oncology, The Woodlands, Houston, TX, USA, ² Gynecologic Oncology, Multicentre Italian Trials in Ovarian Cancer and Gynaecological Malignancies Group (MITO) and Scientific Directorate and Department of Women and Child Health, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, ³ Medical Oncology, Department of Medical Oncology, Centre Hospitalier Universitaire de Liège, Liège, Belgium, ⁴ Medical Oncology, Grupo Español de Investigación en Cáncer de Ovario (GEICO) and Department of Medical Oncology, Clínica Universidad de Navarra, Madrid, Spain, ⁵ Medical Oncology, Massey Cancer Center, Virginia Commonwealth University, Richmond, CA, USA, ⁶ Gynecologic Oncology, Central and Eastern European Gynecologic Oncology Group (CEGOG) and Department of Obstetrics and Gynecology, First Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic, ⁷ Medical Oncology, Aalborg University Hospital, Aalborg, Denmark, ⁸ Gynecologic Oncology, Arbeitsgemeinschaft Gynäkologische Onkologie (AGO) Study Group and University Medical Center Hamburg-Eppendorf, Hamburg, Germany, ⁹ Medical Oncology, MITO and Istituto Nazionale per lo Studio e la Cura dei Tumori, "Fondazione G. Pascale" IRCCS, Milan, Italy, ¹⁰ Medical Oncology, Centre Hospitalier de l'Ardenne, Libramont, Belgium, ¹¹ Medical Oncology, Grupo Español de Investigación en Cáncer de Ovario (GEICO) and Hospital Universitario La Paz-IdiPAZ, Madrid, Spain, ¹² Medical Oncology, Genmab US, Inc., Princeton, NJ, USA, ¹³ Medical Department, Genmab A/S, Copenhagen, Denmark, ¹⁴ Medical Affairs, Seattle Genetics, Inc., Bothell, WA, USA, ¹⁵ Gynecologic Oncology, Arizona Oncology (US Oncology Network), University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA ¹⁶ Gynecologic Oncology, Belgium and Luxembourg Gynaecological Oncology Group, University of Leuven, Leuven Cancer Institute, Leuven, Belgium

Background

Recurrent or metastatic cervical cancer (r/mCC) is a global medical problem with few effective treatments, especially in the second- or third-line settings where available therapies have very limited activity. The phase 2 study innovaTV 204 was conducted to assess the potential of tisotumab vedotin, a tissue factor-directed antibody-drug conjugate, to address this high unmet need in patients with r/mCC.

Methods

Patients with r/mCC with disease progression on or after doublet chemotherapy with bevacizumab (if eligible by local standards) and ≤ 2 prior systemic regimens received tisotumab vedotin 2.0 mg/kg IV once every 3 weeks until disease progression or unacceptable toxicity. The primary endpoint was confirmed objective response rate (cORR) as assessed by independent review committee (IRC). Secondary endpoints included duration of response (DOR), time to response (TTR), and progression-free survival (PFS) by IRC, overall survival (OS), and safety.

Results

Of 101 patients treated (median 6 doses), median age was 50 years, 68% had squamous histology, and 63% received bevacizumab plus doublet chemotherapy as first-line treatment. cORR (IRC) was 24%, including 7% with complete response (CR) (Table). Disease control rate (DCR) was 72%. At a median follow-up of 10 months the median DOR was 8.3 months, median PFS was 4.2 months, and median OS was 12.1 months. Response rates were generally consistent across subgroups explored. The most common treatment-related adverse events (TRAEs) were alopecia (38%), epistaxis (30%), and nausea (27%). Grade 3 ocular, bleeding, and peripheral neuropathy TRAEs (prespecified adverse events of interest) occurred in 2%, 2%, and 7% of patients, respectively. Table: LBA32

Antitumor activity of tisotumab vedotin in patients with r/mCC

	N=101
cORR,* n (%; 95% CI)	24 (24; 15.9-33.3)
CR, n (%)	7 (7)
PR, n (%)	17 (17)
SD, n (%)	49 (49)

	N=101
PD, n (%)	24 (24)
NE, n (%)	4 (4)
DOR,† n (%; 95% CI)	73 (72; 62.5-80.7)
Median DOR (95% CI), months	8.3 (4.3–not reached)
Median TTR (range), months	1.4 (1.1-5.1)
Median PFS (95% CI), months	4.2 (3.2-4.6)
Median OS (95% CI), months	12.1 (9.6-13.9)

* Assessed using RECIST v1.1. † Patients with a confirmed response (CR or PR confirmed at ≥ 4 wk later) or SD (measured ≥ 5 wk after first tisotumab vedotin dose). PR, partial response; SD, stable disease; PD, progressive disease; NE, not evaluable.

Conclusions

Tisotumab vedotin demonstrated durable, clinically meaningful activity in a broad patient population, with a manageable and tolerable safety profile. Tisotumab vedotin has the potential to be a new therapy for patients with r/mCC.

Clinical trial identification

NCT03438396.

Editorial acknowledgement

Medical writing and/or editorial assistance was provided by Nicholas Gast, PharmD, of ApotheCom (Boston, MA, USA). This assistance was funded by Genmab A/S.

Legal entity responsible for the study

Genmab A/S.

Funding

Genmab A/S.

Disclosure

R.L. Coleman: Honoraria (self): AbbVie; Honoraria (self): Aravive; Honoraria (self): Curio Science; Honoraria (self): Geistlich; Honoraria (self): Genmab; Honoraria (self): MoreHealth; Honoraria (self), Research grant/Funding (self): AstraZeneca; Honoraria (self): Genentech; Honoraria (self): GSK; Honoraria (self), Research grant/Funding (self): Janssen; Honoraria (self), Research grant/Funding (self): Merck; Honoraria (self): Myriad; Honoraria (self): Novocure; Honoraria (self): Roche; Honoraria (self): Tarveda Therapeutics; Honoraria (self): Tempus Labs; Honoraria (self): Tesaro; Research grant/Funding (self): Clovis Oncology; Research grant/Funding (self): Genentech-Roche; Research grant/Funding (self): OncoMed Pharmaceuticals; Research grant/Funding (self): USA National Cancer Institute. D. Lorusso: Honoraria (self), Travel/Accommodation/Expenses: Amgen; Honoraria (self), Travel/Accommodation/Expenses: AstraZeneca; Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: PharmaMar; Honoraria (self), Research grant/Funding (institution), Travel/Accommodation/Expenses, Non-remunerated activity/ies: GSK; Honoraria (self), Travel/Accommodation/Expenses: Roche; Honoraria (self), Research grant/Funding (institution): Merck; Honoraria (self): Immunogen; Honoraria (self), Speaker Bureau/Expert testimony: Clovis; Honoraria (self): Genmab; Non-remunerated activity/ies: Abbott. C. Gennigens: Advisory/Consultancy, Research grant/Funding (institution): AstraZeneca; Advisory/Consultancy: BMS; Advisory/Consultancy: GSK; Advisory/Consultancy, Travel/Accommodation/Expenses: Ipsen; Advisory/Consultancy: Lilly; Advisory/Consultancy: MSD; Advisory/Consultancy, Travel/Accommodation/Expenses: Pfizer; Advisory/Consultancy, Travel/Accommodation/Expenses: PharmaMar; Advisory/Consultancy, Travel/Accommodation/Expenses: Roche. A. González-Martín: Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution): Roche; Honoraria (self), Advisory/Consultancy: AstraZeneca; Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution), Non-remunerated activity/ies: Tesaro; Honoraria (self), Advisory/Consultancy: Clovis; Honoraria (self), Advisory/Consultancy: Pfizer/Merck; Honoraria (self), Advisory/Consultancy: Immunogen; Leadership role: GEICO (Grupo Español Investigación Cáncer de Ovario); Leadership role: ENGOT (European Network for Gynecological Oncologic Trials); Honoraria (self), Advisory/Consultancy: PharmaMar; Honoraria (self), Advisory/Consultancy: MSD; Honoraria (self), Advisory/Consultancy: Genmab; Honoraria (self), Advisory/Consultancy: Oncoinvent. L. Randall: Advisory/Consultancy, Travel/Accommodation/Expenses: Agenus; Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: AstraZeneca; Advisory/Consultancy, Travel/Accommodation/Expenses: Clovis; Advisory/Consultancy, Travel/Accommodation/Expenses: Genentech; Advisory/Consultancy, Travel/Accommodation/Expenses: GSK; Advisory/Consultancy, Travel/Accommodation/Expenses: Intuitive; Advisory/Consultancy, Travel/Accommodation/Expenses: Mersana; Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: Merck; Speaker Bureau/Expert testimony: GSK/Tesaro; Non-remunerated activity/ies: GOG Foundation. L. Woelber: Honoraria (self): Tesaro, Medac Oncology, Roche, MSD, AstraZeneca, GSK, Jenapharm, Teva, OmniaMed; Research grant/Funding (institution): Medac Oncology, Tesaro, Roche, MSD, Genmab;

Travel/Accommodation/Expenses: Medac Oncology, Tesaro. S. Pignata: Honoraria (self), Research grant/Funding (institution): AstraZeneca; Honoraria (self), Research grant/Funding (institution): MSD; Honoraria (self), Research grant/Funding (institution): Pfizer; Honoraria (self): GSK; Honoraria (self): Clovis; Honoraria (self): PharmaMar; Honoraria (self): Incyte; Honoraria (self), Research grant/Funding (institution): Roche. A. Redondo: Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: Roche; Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: PharmaMar; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: AstraZeneca; Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: GSK; Honoraria (self): Novartis; Honoraria (self), Advisory/Consultancy: Amgen; Honoraria (self), Advisory/Consultancy: Clovis; Research grant/Funding (institution): Eisai. R. Rangwala: Full/Part-time employment: Genmab. S.D. Vindeløv: Full/Part-time employment: Genmab A/S. M. Chen: Shareholder/Stockholder/Stock options, Full/Part-time employment: Genmab. J.R. Harris: Full/Part-time employment: Genmab. L. Nicacio: Full/Part-time employment: Seattle Genetics. M.S.L. Teng: Shareholder/Stockholder/Stock options, Full/Part-time employment: Seattle Genetics. M. Smith: Full/Part-time employment: Genmab. B.J. Monk: Honoraria (self), Advisory/Consultancy: AbbVie, Advaxis, Agenus, Amgen, Akeso Bio, Aravive; Honoraria (self), Advisory/Consultancy: AstraZeneca, Asymmetric Therapeutics, Boston Biomedical, ChemoCare, ChemoID, Circulogene, Clovis; Honoraria (self), Advisory/Consultancy: Conjupro, Dicepheria, Eisai, Geistlich, Genmab/Seattle Genetics, GOG Foundation; Honoraria (self), Advisory/Consultancy: Immunogen, Immunomedics, Incyte, Lovance, Janssen/J&J, Laekna Health Care; Honoraria (self), Advisory/Consultancy: Mateon, Merck, Mersana, Myriad, Nucana, Oncomed, Oncoquest, Perthera; Honoraria (self), Advisory/Consultancy: Pfizer, Precision Oncology, Puma, Regeneron, Roche/Genentech; Honoraria (self), Advisory/Consultancy: Samumed, Takeda, Tarveda, Tesaro/GSK, Vavotar Life Sciences, VBL, Vigeo; Full/Part-time employment: Arizona Oncology (US Oncology Network). I.B. Vergote: Advisory/Consultancy, Research grant/Funding (self), Travel/Accommodation/Expenses: Amgen (Europe) GmbH; Advisory/Consultancy, Travel/Accommodation/Expenses: AstraZeneca; Advisory/Consultancy: Clovis; Advisory/Consultancy: Carrick Therapeutics; Advisory/Consultancy: Debiopharm International; Advisory/Consultancy: F. Hoffman La Roche Ltd; Advisory/Consultancy, Research grant/Funding (self): Genmab; Advisory/Consultancy: GSK; Advisory/Consultancy: Immunogen; Advisory/Consultancy: Medical University of Vienna; Advisory/Consultancy: Millennium Pharmaceuticals; Advisory/Consultancy: MSD; Advisory/Consultancy: Octimet Oncology; Advisory/Consultancy, Research grant/Funding (self): Oncoinvent; Advisory/Consultancy: PharmaMar; Advisory/Consultancy, Research grant/Funding (self), Travel/Accommodation/Expenses: Roche; Advisory/Consultancy: Sotio; Advisory/Consultancy, Travel/Accommodation/Expenses: Tesaro; Advisory/Consultancy: Deciphera; Advisory/Consultancy: Verastem; Travel/Accommodation/Expenses: MSD/Merck Zurich + USA. All other authors have declared no conflicts of interest.