CERVICAL CARCINOMA

Giorgio Bogani, M.D., Ph.D.

Fondazione IRCCS Isitituto Nazionale dei Tumori di Milano

MaNGO
Mario Negri Gynecologic Oncology

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CERVICAL CARCINOMA FIRST LINE TREATMENT

- INTERLACE (ACCRUAL CLOSED)
- ENGOT-CX11 (ACCRUAL CLOSED)
- SENTICOL III (ONGOING)
- ENGOT-CX19_eVOLVE (NEW)

RECURRENT CERVICAL CARCINOMA TREATMENT

- ENGOT CX10-BEATCC (ACCRUAL CLOSED)

INTERLACE

INTERLACE – induction chemotherapy followed by standard chemoradiation vs standard chemoradiation alone in patients with locally advanced cervical cancer

Randomise

Carboplatin AUC2 & Paclitaxel 80mg/m²
Weeks 1-6

Weeks 7 – 13 Standard CRT

Standard CRT

Standard CRT : 40—50.4Gy in 20-28 fractions plus Intracavitary brachytherapy to give total EQD2 dose of 78-86Gy to point A/volume. Weekly cisplatin 40mg/m² x 5 weeks

Primary Endpoint
Overall Survival

ENGOT Model B
Lead Group: NCRI
Sponsor: University College of London

Target Recruitment: **500**

Accrual Closed on 17 Nov 2022

MaNGO (Italy): 1 site open – 8 patients recruited

Current status

- In Follow up – global end of trial expected to be Q1 2026
- Planning to present initial results at ESMO 2023

MK3475-A18 ENGOT-cx11 : A Randomized, Phase 3, Double-Blind Study of Chemoradiotherapy With or Without Pembrolizumab for the Treatment of High-risk, Locally Advanced Cervical Cancer (KEYNOTE-A18/ENGOT-cx11/GOG-3047)

ENGOT Model C
Lead Group: MITO
Sponsor: MSD

High Risk Locally Advanced Cervical Cancer:
-FIGO Stage IB2-IIB (node positive disease)
-FIGO Stage III-IVA (either node-postive or node-negative disease)

R: 1:1
N=980

Control Arm

Cisplatin (40mg/m^2 x 5 infusions [1 infusion per week]) and radiotherapy (EBRT followed by brachytherapy) in combination with
Placebo (Q3W, 5 infusions)

Placebo (Q6W, 15 infusions)

Dual Primary Endpoints:
- OS
- PFS

Experimental Arm

Cisplatin (40mg/m^2 x 5 infusions [1 infusion per week]) and radiotherapy (EBRT followed by brachytherapy) in combination with
Pembrolizumab 200 mg (Q3W, 5 infusions)

Pembrolizumab 400 mg (Q6W, 15 infusions)

Database Lock for final analysis expected for January 2025

SENTICOL III : International prospective validation trial of sentinel node biopsy in cervical cancer (GINECO-CE106 / ENGOT-Cx24)

Squamous or adenocarcinoma of the cervix,
Stage **Ia1** with lympho vascular emboli **, Ib1, Ib2, IIa1 (FIGO 2018)**
Maximum diameter **≤ 40mm**.

Frozen section (bilateral detection, safety algorithm)

Patients with bilateral detection without macroscopic suspicious node and negative frozen section on SLN **(pN0)**

Patients with nodal involvement **(pN1)**

Followed in a separate cohort to record treatment and outcomes

Randomisation
1 : 1

Arm A (experimental) :
SLN biopsy only
+ hysterectomy or trachelectomy

Arm B (reference) :
SLN biopsy
+ Pelvic Lymphadenectomy
+ hysterectomy or trachelectomy

DFS, RFS, QOL, OS

ENGOT Model B
Lead Group: GINECO
Sponsor: Centre Hospitalier Universitaire de Besançon

SENTICOL III : International prospective validation trial of sentinel node biopsy in cervical cancer (GINECO-CE106 / ENGOT-Cx24)

Study update

- Planned number of patients : **950**
- Current accrual :**762** randomized patients
- Patients in screening: **30** patients
- Patients registered in the pn1 cohort**:** **49** patients
- Patients screen-failed: **104** patients
- **MaNGO** included **37** patients, 2 sites active
  (IEO Milano e San Gerardo Monza)

Next important steps are

Descriptive analysis on patient randomized before 2022 for ESGO 2024.

Interim analysis that will be launched once we have 45 DFS, currently there are 32 DFS.

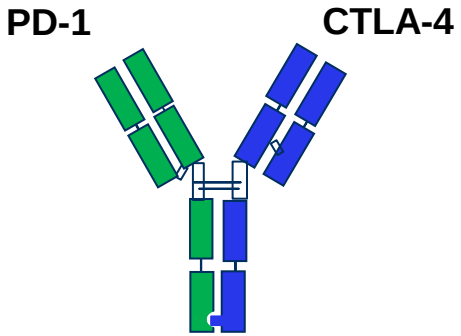
Kindly reminder to request your team to well complete the eCRF concerning DFS, that means

- 1st progression
- Diagnosis of 2nd cancer
- Death

eVOLVE Background – MEDI5752 (Volrustomig)

- PD-1 + CTLA-4 inhibition is effective in many tumor types; delivery of high doses of anti-CTLA-4 co-administered with anti-PD-1 has been limited by toxicity.
  - In first-line RCC, Nivo 3 mg/kg + Ipi 1 mg/kg achieves ORR ~40%, CR ~10%.[1]
  - Higher doses of Nivo + Ipi not clinically tolerable (Nivo 3 mg/kg + Ipi 3 mg/kg → G3/4 AE 83.3%).[2]
- **Volrustomig is a monovalent bispecific mAb, engineered to fully bind PD-1 while preferentially binding CTLA-4 on PD-1+ activated T cells, to deliver distinct biologic effects compared to co-administration.[3]**

Volrustomig: A monovalent bispecific antibody



- Affinity to human CTLA-4: 0.42 nM
- Affinity to human PD-1: 0.81 nM
- Fc isotype: human IgG1-TM (reduced antibody-dependent cellular cytotoxicity)
- CTLA-4 arm = Tremelimumab arm

1. Albiges L et al, ESMO Open 2020;5(6):e001079; 2. Hammers HJ et al, JCO 2017; 3. Dovedi SJ, et al. Cancer Discov. 2021;11:1100–17.
AE, adverse event; CR, complete response; CTLA-4, cytotoxic T lymphocyte-associated antigen-4; Ipi, ipilimumab; mAb, monoclonal antibody; Nivo, nivolumab; ORR, objective response rate; PD-1, programmed cell death-1; RCC, renal cell carcinoma; TM, triple mutation

Study design – eVOLVE-Cervical/ENGOT-cx19

Screening period FIGO 2018 IIIC-IVA cervical cancer (LN involvement)	Randomization	Treatment period	Endpoints

Part I: Diagnosis (Day-154) to Day-1

Patient consenting process step 1:

- Tumor sample submission and analysis
  - PD-L1 expression by VENTANA PD-L1 (SP263) Assay
- **Initial staging procedures** completed prior to any component of definitive treatment

Part II: Day -56 to -1

Patient consenting process step 2:

- After completion of SOC CCRT (≥4 cycles)
- No progression after SOC CCRT
- Grade > 1 toxicities resolved prior to randomization
- ECOG 0 or 1

Max **56** days after the end of CCRT

N=1000

R 1:1

Arm A

Volrustomig 750mg IV Q3W for 24 months

Arm B

Placebo IV Q3W for 24 months

Stratification factors

- PD-L1 expression (PD-L1 high expression vs. low/negative)
- FIGO stage (IIIC1 vs. IIIC2 vs. IVA)
- Region (Asia vs. non-Asia)

ENGOT Model C
Lead Group: GEICO
Sponsor: Astrazeneca
GOG involved

Primary Endpoint: PFS in PD-L1 high population (Inv)

Secondary Endpoint:

Key: PFS in ITT (Inv), OS in PD-L1 high population/ITT

Others: PFS (BICR), 12mons-PFS, 24mons-PFS, 36mons-OS, ORR, DOR, PFS2, TFST, incidence of local progression and distant disease progression, PK, ADAs, safety and tolerability, ePROs

Exploratory Endpoint: ctDNA, T cell proliferation/clonal expansion, baseline tumor immune and genomic profile, ePROs

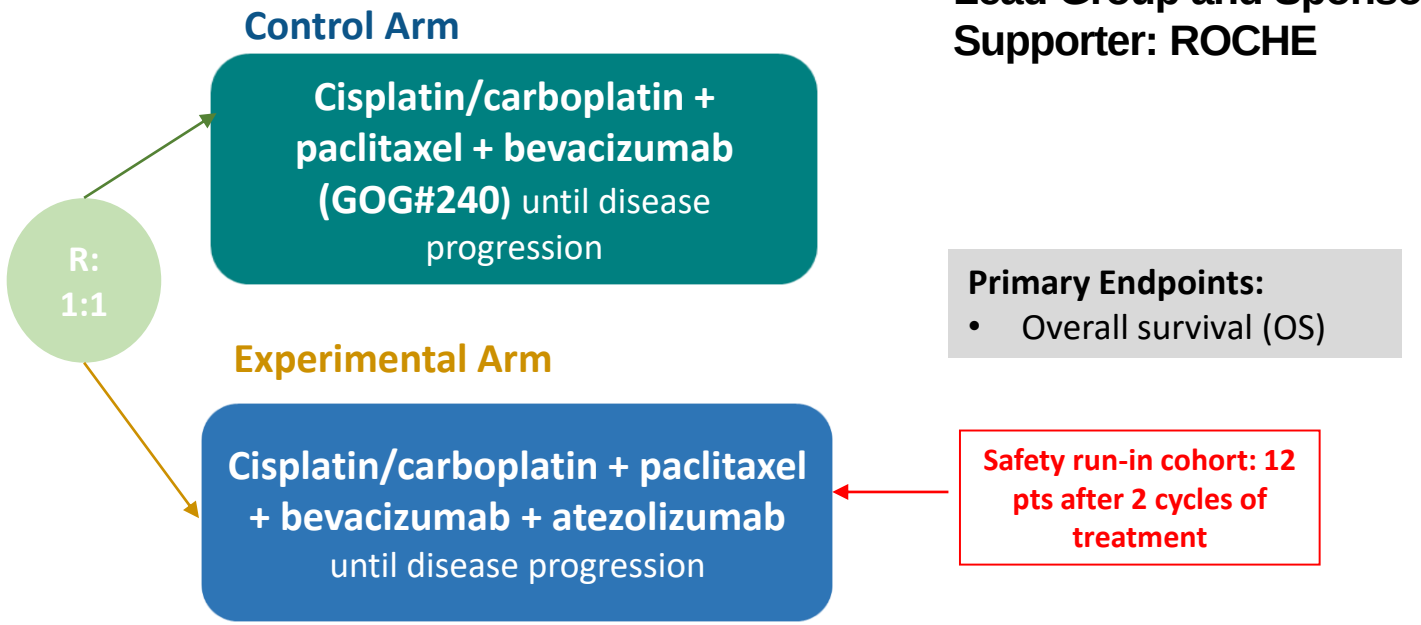
Note: changes marked in magenta

eVOLVE-Cervical/ENGOT-cx19 – MaNGO Interested sites

City	Hospital	First Name	Last Name
Lecco	Ospedale Manzoni	Antonio	Ardizzoia
Milano	Ist. Europeo di Oncologia	Nicoletta	Colombo
Milano	Istituto Naz. dei Tumori	Francesco	Raspagliesi
Reggio E	Arcispedale S. Maria N.	Alessandra	Bologna
Roma	Ospedale Umberto I	Federica	Tomao

BEAT cc
ENGOT-Cx10/GEICO 68-C / JGOG1084 / GOG-3030

- Primary Stage IVB, persistent or recurrent carcinoma of the cervix
- Measurable disease by RECIST v1.1
- ECOG-PS: 0-1
- No previous systemic chemotherapy for advanced or recurrent disease
- Available archival tumour for PD-L1 expression



ENGOT Model B

Lead Group and Sponsor: GEICO

Supporter: ROCHE

Primary Endpoints:
- Overall survival (OS)

N=404 Pts

Primary endpoint Final Analysis (OS): Q2-2024

Database lock for final PFS analysis is scheduled on **14th July 2023.** Plan to submit to **ESMO 2023 (20 – 24 October)**

BEAT cc
ENGOT-Cx10/GEICO 68-C / JGOG1084 / GOG-3030

Site	Principal Investigator	Total Screened	Screening Failure	Enrolled
IEO Milano	Nicoletta Colombo	9	2	7
Sant'Anna Torino	Dionyssios Katsaros	6	0	6
AOU Pisana	Angiolo Gadducci	3	0	3
IOV Padova	Giulia Tasca	2	1	1
TOTAL		**20**	**3**	**17**

Recruitment closed on August 4th 2021, 17 patients included from 4 MaNGO sites


THANK YOU