TroFuse
ONCOLOGY CLINICAL TRIALS

A Phase 3 Randomized, Active-controlled, Open-label, Multicenter Study to Compare the Efficacy and Safety of MK-2870 Monotherapy Versus Treatment of Physician's Choice as Second-line Treatment for Participants with Recurrent or Metastatic Cervical Cancer

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GOG FOUNDATION transforming the standard of care
NSGO-CTU Nordic Society of Gynaecological Oncology - Clinical Trial Unit
ENGOT European Network of Gynaecological Oncological Trial groups
MSD

Study Design

MK-2870 = sacituzumab tirumotecan (sac-TMT)

Key Eligibility Criteria:

Recurrent or metastatic cervical cancer that:

- ✓ Has progressed on or after 1 prior line of systemic platinum doublet treatment (with or without bevacizumab)
  AND
- ✓ Has received anti-PD-1/ anti-PD-L1 therapy as part of prior cervical cancer regimens

MK-2870 Run-in (N =20)

Single arm: **MK-2870** *4 mg/kg IV Q2W*

PD by BICR

Run-In portion:

Primary Endpoint

- ORR
- Safety/Tolerability

Phase 3 MK-2870

RAND 1:1 N=666

Arm 1: MK-2870 *4 mg/kg IV Q2W*

PD by BICR

Arm 2: Treatment of Physician's Choice (TPC) *(pemetrexed, topotecan, vinorelbine, gemcitabine, irinotecan OR TV)*

PD by BICR

Phase 3 portion:

Primary Endpoint

- OS

Secondary Endpoints

- PFS (BICR)
- ORR (BICR)
- DOR (BICR)
- QoL
- Safety/Tolerability

Stratification: 3 Factors

- ❖ Prior use of bevacizumab (yes vs. no)
- ❖ TROP2 expression (low + medium vs. high)
- ❖ Selection of TPC (TV vs other TPC)

Key **Inclusion** Criteria

Cervical Cancer	Has a histologically-confirmed diagnosis of **squamous cell carcinoma**, **adenosquamous carcinoma**, or **adenocarcinoma** of the cervix
Prior Treatments for Cervical Cancer	Has **recurrent** or **metastatic** cervical cancer - That has progressed on or after treatment with 1 prior line of systemic platinum doublet chemotherapy (with or without Bevacizumab) **AND** - Participants must have received anti-PD-1/anti-PD-L-1 therapy as part of prior cervical cancer regimens ➢ Note: Participants may have also received prior chemoradiotherapy in the LACC setting; this is not considered a line of treatment
Evaluable Disease	Has **measurable disease** per RECIST 1.1 **as assessed by the investigator.** - Lesions situated in a previously irradiated area are considered measurable if progression has been shown in such lesions
Tumor Tissue	Has provided tumor tissue (most recent sample is preferred) from a core or excisional biopsy of a tumor lesion not previously irradiated
Demographics	Is assigned female sex at birth, at least 18 years of age at the time of providing the informed consent
ECOG	Has ECOG performance status of 0 or 1 within 7 days before allocation/randomization

Informed Consent	Participant (or legally acceptable representative) has provided documented informed consent
Additional Categories	Participants who have AEs due to previous anticancer therapies must have recovered to ≤Grade 1 or baseline (except alopecia or vitiligo). - Participants with endocrine-related AEs who are adequately treated with hormone replacement therapy are eligible
Other Medical Conditions	- Participants with **HIV** that is well controlled on antiretroviral therapy (ART) are eligible - Participants who are **HBsAg** (Hepatitis B surface antigen) positive are eligible if they have received HBV antiviral therapy for at least 4 weeks, have an undetectable viral load prior to allocation/randomization, and remain on therapy - Participants with a history of **HCV** are eligible if the viral load is undetectable at screening and they have completed curative antiviral therapy at least 4 weeks prior to allocation/randomization - Adequate organ function laboratory values as per Table 6
Pemetrexed only	Participants for whom the plan is to treat with pemetrexed as the TPC must have a measured or calculated creatinine clearance value of ≥45 mL/min

*Additional inclusion criteria apply (Note: This statement must remain in the deck)

Key **Exclusion** Criteria

Histology	Has a histologically-confirmed diagnosis of • Glassy cell carcinoma variant, adenoid cystic carcinoma, adenoid basal carcinoma, neuroendocrine tumors, carcinoid, atypical carcinoid, small-cell carcinoma, large-cell neuroendocrine carcinoma, undifferentiated carcinoma
Prior Treatments for Cervical Cancer	• Received systemic therapy, including single-agent IO, in the second-line (or subsequent) setting • Received prior treatment with a TROP2-targeted ADC • Received prior treatment with a topoisomerase I inhibitor-containing ADC • Received prior systemic anticancer therapy including investigational agents within 4 weeks or 5 half-lives (whichever is shorter) before study intervention administration • Received prior radiotherapy within 2 weeks of start of study intervention, or has radiation-related toxicities, requiring corticosteroids • Note: Two weeks or fewer of palliative radiotherapy for non-CNS disease is permitted. The last radiotherapy treatment must have been performed at least 7 days before the first dose of study intervention
Medical Conditions	• Grade ≥2 peripheral neuropathy • H/o dry eye syndrome, severe Meibomian gland disease and/or blepharitis, or corneal disease • active inflammatory bowel disease requiring immunosuppressive medication or previous h/o inflammatory bowel disease • uncontrolled, significant cardiovascular disease or cerebrovascular disease
CNS Metastasis	• Active CNS metastases and/or carcinomatous meningitis. Participants with previously treated brain metastases may participate if they are radiologically stable, (i.e., without evidence of progression) for at least 4 weeks as confirmed by repeat imaging performed during study screening, are clinically stable and have not required steroid treatment for at least 14 days before the first dose of study intervention
TROP 2 status	• TROP2 test result from the Central Laboratory is reported as unknown or unevaluable (for the Phase 3 portion only) • Note: TROP2 status is required for stratification for the Phase 3 portion and must be determined before randomization
Concomitant Medications	• Requires treatment with strong inhibitors or inducers of **CYP3A4** within 14 days prior to the first dose of study medication and **throughout** the study; • Active infection requiring **systemic** therapy • Received a **live** or live-attenuated **vaccine** within 30 days before the first dose of study intervention
Other Conditions	• Has received an **investigational agent** or device within 4 weeks prior to study intervention administration; • Known **additional malignancy** that is progressing or has required active treatment within the past 3 years (some exceptions); • HIV-infected participants with a history of Kaposi's sarcoma and/or Multicentric Castleman's Disease
Severe Hypersensitivity	• Severe hypersensitivity (≥Grade 3) to sac-TMT or TPC and/or any of their excipients, or other biologic therapy. • Note: Intolerance to a TPC does not exclude a participant from the study if another TPC that the participant can tolerate is chosen prior to randomization (Phase 3 portion) per local standard of care

*Additional inclusion criteria apply (Note: This statement must remain in the deck)

Safety profile for sac-TMT is generally tolerable

- Overall safety profile is consistent with payload (irinotecan derivative) MOA
- Toxicity is generally manageable with dose interruption, reduction, or supportive care for AEs
- The most common AEs include anemia, cytopenia, neutropenia, stomatitis, rash, nausea, thrombocytopenia, alopecia, vomiting and transaminitis
- Premedication is required for all patients before MK-2870 infusion as severe or life-threatening infusion-related reactions may occur