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Titolo:	Studio di fase 3, randomizzato, in aperto, multicentrico su Sacituzumab Tirumotecan (sac-TMT, MK-2870) in trattamento di mantenimento con o senza bevacizumab rispetto alla terapia standard in pazienti con carcinoma ovarico avanzato HRD-negativo di nuova diagnosi dopo chemioterapia di prima linea a base di platino (MK2870-021/TroFuse-021/ENGOT-ov85/GOG-3102)
Patologia:	Carcinoma ovarico
Tipo di studio:	Interventistico con farmaco
Tipologia:	Profit
Fase:	III
Principali criteri di inclusione:	1. Has histologically confirmed FIGO Stage III or Stage IV, EOC (high-grade predominantly serous, endometrioid [any grade], carcinosarcoma, mixed Müllerian with high-grade serous component, clear cell, or low-grade serous OC), primary peritoneal cancer, or fallopian tube cancer. Note: Enrollment of participants with low-grade serous OC will be capped at 4% of the total population. 2. Has undergone PDS or IDS. Note: Participant who has not undergone debulking may be eligible after discussion with Sponsor and require a Sponsor communication form. 3. Must have completed at least 4 cycles but no more than 6 cycles of 1L platinum-based chemotherapy. Note: If a participant undergoes IDS, at least 2 but preferably 3 cycles of 1L platinum- based chemotherapy should be administered after surgery. • 1L platinum-based chemotherapy must have included 1 of the following combinations: - Carboplatin: AUC 5 or 6 mg/mL•min q3w + Paclitaxel: 80 mg/m2 qw. - Carboplatin: AUC 5 mg/mL•min q3w + Paclitaxel: 175 mg/m2 q3w. - Carboplatin: AUC 2 mg/mL•min qw + Paclitaxel: 60 mg/m2 qw. • The interval between the last dose of 1L platinum-based chemotherapy and randomization must be no longer than 12 weeks. 4. Has a response of CR, PR, SD, or NED by the investigator to 1L platinum-based chemotherapy at the time of screening. The evaluation of response to 1L platinum-based chemotherapy on both RECIST 1.1 and CA-125 levels and be performed between 3 and 6 weeks after the last dose of platinum-based chemotherapy. • CR is defined as disappearance of all measurable/assessable disease and normalization of CA-125 levels.

	• PR is per RECIST 1.1 with or without normalization of CA-125 levels, or the absence of measurable/assessable disease without normalization of CA-125 levels. • NED is defined as no measurable/assessable disease after debulking surgery plus no radiologic evidence of disease and a normal CA-125 level after chemotherapy. • SD is per RECIST 1.1 with or without normalization of CA-125 levels. Note: Participants who received bevacizumab in combination with 1L platinum-based chemotherapy and have a response of SD at the time screening must continue with bevacizumab as 1L maintenance treatment (see Inclusion Criterion number 5). 5. Participants intended to receive bevacizumab as 1L maintenance treatment during the study must be a candidate for bevacizumab treatment, have a measured or calculated creatinine clearance value of ≥45 mL/min, and must have received at least 2 courses of bevacizumab 15 mg/kg q3w or equivalent dose (with no dose reductions) in combination with the 1L platinum-based chemotherapy. 6. Participants are not eligible to receive PARPi as 1L maintenance treatment according to the investigator. Demographics 7. Is assigned female sex at birth, who is at least 18 years of age at the time of providing the informed consent. Follow local regulatory requirements if the legal age of consent for participation is >18 years of age. 8. Has provided tumor tissue that is not previously irradiated for central determination of TROP2 and HRD status. 9,. 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 are eligible. 10. Adequate organ function as defined in the following table (Table 5). Specimens must be collected within 7 days before the start of randomization. 11. An ECOG performance status of 0 to 1 assessed 7 days before randomization.
Principali criteri di esclusione:	1. Has nonepithelial cancers (germ cell tumors and sex cord-stromal tumors), borderline tumors (low malignant potential) mucinous, seromucinous that is predominately mucinous, malignant Brenner’s tumor, and undifferentiated carcinoma. 2. Has known active CNS metastases and/or carcinomatous meningitis. Participants with brain metastases may participate provided they were previously treated (except with chemotherapy) and are radiologically stable for

	at least 4 weeks as confirmed by repeat imaging performed during study screening, are clinically stable, and no steroids were used for the management of symptoms related to brain metastases within 14 days prior to randomization. Stable brain metastases should be established prior to the first dose of study intervention. Note: Participants with known untreated, asymptomatic brain metastases (ie, no neurological symptoms, no requirement for corticosteroids, or no minimal surrounding edema, and no lesion >1.5 cm) may participate but will require regular imaging of the brain as a site of disease. 3. Has history of documented severe dry eye syndrome, severe Meibomian gland disease and/or blepharitis, or severe corneal disease that prevents/delays corneal healing. 4. Has active inflammatory bowel disease requiring immunosuppressive medication or previous history of inflammatory bowel disease (eg, Crohn's disease, ulcerative colitis, or chronic diarrhea). 5. Has uncontrolled, significant cardiovascular disease or cerebrovascular disease, including New York Heart Association Class III or IV congestive heart failure, unstable angina, myocardial infarction, uncontrolled symptomatic arrhythmia, prolongation of QtcF interval to >480 ms, and/or other serious cardiovascular and cerebrovascular diseases within the 6 months preceding randomization. 6. Has uncontrolled hypertension. Note: This applies only to participants who have received bevacizumab during 1L platinum-based chemotherapy. Use of antihypertensive medications to control blood pressure is allowed in all participants. 7. Has current, clinically relevant bowel obstruction (including sub-occlusive disease), abdominal fistula or gastrointestinal perforation, related to underlying OC. Note: This applies only to participants who will receive bevacizumab. 8. Has history of hemorrhage, hemoptysis or active gastrointestinal bleeding within 6 months prior to randomization. Note: This applies only to participants who will receive bevacizumab. 9. Participants who discontinued bevacizumab during 1L platinum-based chemotherapy due to any AE related to bevacizumab are not eligible to receive bevacizumab. 10. Has a history of (noninfectious) pneumonitis/ILD that required steroids or has current pneumonitis/ILD. Prior/Concomitant Therapy 11. Received prior treatment with a TROP2-targeted ADC.

	12. Received prior treatment with a topoisomerase I-containing ADC. 13. Is currently receiving a strong inducer/inhibitor of CYP3A4 that cannot be discontinued for the duration of the study. The required washout period before starting maintenance study intervention is 2 weeks. 14. Received prior systemic anticancer therapy including investigational agents within 4 weeks or 5 half-lives (whichever is shorter) before randomization. Note: If the participant received bevacizumab in combination with 1L platinum-based chemotherapy and is planned to continue bevacizumab in the study, bevacizumab may be continued during the screening period. 15. Received prior radiotherapy within 2 weeks of start of study intervention, or radiation-related toxicities, requiring corticosteroids. Note: Two weeks or fewer of palliative radiotherapy for non-CNS disease is permitted. The last palliative radiotherapy treatment must have been performed at least 7 days before randomization. 16. Received a live or live-attenuated vaccine within 30 days before randomization. Administration of killed vaccines is allowed. 17. Has intraperitoneal chemotherapy planned or has been administered as 1L therapy. 18. Has severe hypersensitivity (≥Grade 3) to sac-TMT, bevacizumab, and/or any of their excipients, and other biologic therapy. Note: participants with known sensitivity to CHO cell products or other recombinant human or humanized antibodies are prohibited from receiving bevacizumab during the study. Prior/Concurrent Clinical Study Experience 19. Has received an investigational agent or has used an investigational device within 4 weeks prior to randomization. Note: Participants who have entered the follow-up phase of an investigational study may participate as long as it has been 4 weeks (28 days) after the last dose of the previous investigational agent. 20. Participants who received 1L platinum-based chemotherapy without bevacizumab and have a response of SD at the time of screening are not eligible. Diagnostic Assessments 21. Has an HRD-positive, unknown, or inconclusive status as determined by the central laboratory. 22. Has either an unknown or unevaluable TROP2 test result from the central

	laboratory 23. Known additional malignancy that is progressing or has required active treatment within the past 3 years. Note: Participants with basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or carcinoma in situ, excluding carcinoma in situ of the bladder, that have undergone potentially curative therapy are not excluded. Note: Participants with synchronous primary endometrial cancer or a past history of primary endometrial cancer that met the following conditions are not excluded: Stage not greater than I-A; no more than superficial myometrial invasion, without vascular or lymphatic invasion; no poorly differentiated subtypes, including papillary serous, clear cell or other FIGO Grade 3 lesions.
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