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Titolo:	Studio di fase 3, multicentrico, randomizzato e in aperto, volto a valutare trastuzumab deruxtecan rispetto alla chemioterapia standard di cura, con o senza radioterapia, come trattamento adiuvante in pazienti con carcinoma endometriale con espressione di HER2 (IHC 3+/2+). (DESTINY-Endometrial02/DS8201-854/GOG-3122/ENGOT-en30/GINECO)
Patologia:	Carcinoma endometriale
Tipo di studio:	Interventistico farmacologico
Tipologia:	Profit
Fase:	III
Principali criteri di inclusione:	1. Sign and date the Tissue SCR ICF, prior to HER2 central testing. Sign and date the main SCR ICFs, prior to the start of any trial-specific qualification procedures not included in the Tissue SCR ICF. 2. Adults ≥18 years at the time the ICF is signed 3. Has histologically confirmed diagnosis of epithelial endometrial carcinoma. All histology's are allowed except for sarcomas (carcinosarcomas are allowed). 4. Is newly diagnosed FIGO 2023 Stage IIC (including Stage IICmp53abn) or Stage III.□ Note: FIGO 2023 Stage IIC includes disease with aggressive histological types (aggressive histological types are composed of high-grade EECs (grade 3), serous, clear cell, undifferentiated, mixed, mesonephric-like, gastrointestinal mucinous type carcinomas, and carcinosarcomas) with any myometrial involvement. FIGO 2023 Stage III includes disease with local and/or regional spread of the tumor of any histological subtype. 5. Has HER2-expression (IHC 3+/2+) per 2016 ASCO-CAP gastric cancer IHC scoring guidelines as confirmed by central laboratory testing. 6. Has adequate archived tumor tissue sample (sample from surgery is strongly recommended) available for assessment of HER2 status by central laboratory. 7. Has an MMR IHC local test result from an approved and/or validated test, according to the local regulations. Note: The MMR status does not define whether a participant will be enrolled in the trial or not (ie, participant can be enrolled regardless of the MMR status). 8. Is eligible for combination treatment with carboplatin and paclitaxel as adjuvant therapy per SoC and Investigator discretion

	Note: For participants with dMMR Stage III disease, a discussion regarding the appropriateness of ICIs must take place with the participant before considering their participation in the trial. Reasons for not selecting ICIs for participants with dMMR Stage III disease will be collected in the eCRF. 9. Has undergone curative intent surgery that included hysterectomy and bilateral salpingo-oophorectomy. Pelvic lymph node sampling, para-aortic lymph node sampling, including sentinel lymph node, and lymph node dissection are optional but strongly encouraged. Note: If prior oophorectomy for reasons other than endometrial cancer, participants may still be eligible for trial. 10. Is disease-free with no evidence of loco-regional disease or distant metastasis post-operatively on imaging assessed by investigator and confirmed by BICR. Note: Histopathology assessment should be conducted for any suspected recurrence not observed on imaging before randomization. 11. Trial intervention to start within 8 weeks of endometrial cancer surgery date 12. Has not received any radiotherapy or systemic therapy, including immunotherapy, hormonal therapy, radiosensitizer chemotherapy or HIPEC, in any setting including the neoadjuvant setting for endometrial cancer. 13. Has LVEF ≥ 50% within 28 days before randomization. 14. ECOG performance status of 0 or 1 assessed no more than 14 days prior to randomization.
Principali criteri di esclusione:	1. Has uterine mesenchymal tumor such as an endometrial stromal sarcoma, leiomyosarcoma, or other types of pure sarcomas. Adenosarcomas are also not allowed. 2. Has recurrent or FIGO 2023 Stage IV (see Table 13.1) 3. Has measurable residual tumor after surgery as determined by BICR assessment. 4. Is known to have a POLE mutation from an approved and/or validated local test, according to local regulations, if available 5. Has a medical history of MI within 6 months before randomization/enrollment,symptomatic CHF (NYHA Class II to IV). articipants with Troponin levels above ULN at SCR (as defined by the manufacturer), and without any MI related symptoms should have a cardiologic consultation during SCR Period to rule out MI. 6. Has a QTcF prolongation to > 480 msec based on average of the SCR

	triplicate12-lead ECG. 7. Any of the following within the past 6 months prior to enrollment: cerebrovascular accident, transient ischemic attack, or other arterial thromboembolic event. 8. Has a history of (noninfectious) ILD/pneumonitis that required corticosteroids, has current ILD/pneumonitis, or where suspected ILD/pneumonitis cannot be ruled out by imaging at SCR. 9. Clinically severe pulmonary compromise resulting from intercurrent pulmonary illnesses including, but not limited to, any underlying pulmonary disorder (ie, pulmonary emboli within 3 months of the trial enrollment, severe asthma, severe COPD, restrictive lung disease, pleural effusion, etc.) and any autoimmune, connective tissue, or inflammatory disorder with potential pulmonary involvement (eg, rheumatoid arthritis, Sjogren's syndrome, sarcoidosis, etc.), or prior pneumonectomy. 10. History of other active malignancy within 3 years prior to enrollment, with the exception of those with a negligible risk of metastasis or death (eg, 5-year OS rate >90%) and treated with expected curative outcome (such as adequately treated carcinoma in situ of the cervix, nonmelanoma skin carcinoma, ductal carcinoma in situ). 11. History of hypersensitivity to the trial intervention or their excipients or any known contraindication (included in the approved local labels) to treatment with, including hypersensitivity to, the trial intervention. 12. History of severe hypersensitivity reactions to other monoclonal antibodies. 13. Has any evidence of severe or uncontrolled systemic diseases (including active bleeding diatheses or active infection, substance abuse) or other factors that, in the Investigator's opinion, make it undesirable for the participant to participate in the trial or which would jeopardize compliance with the protocol. SCR for chronic conditions is not required. 14. Has an uncontrolled infection requiring systemic antibiotics, antivirals or antifungals. Participants with localized fungal infections of skin or nails are eligible.
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