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| Titolo:                           | Studio di fase III aperto, in cieco per lo sponsor, randomizzato, controllato, multicentrico, su trastuzumab deruxtecan (T-DXd) più Rivlegostomig o pembrolizumab vs chemioterapia più pembrolizumab come terapia di prima linea per il carcinoma endometriale primario avanzato o ricorrente esprimente HER2 (IHC 3+/2+), con capacità di riparazione degli errori (pMMR). (DESTINY Endometrial01)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Patologia:                        | Tumore endometrio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Tipo di Studio:                   | interventistico con farmaco                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Tipologia                         | profit                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Fase:                             | 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Principali criteri di inclusione: | <p>Histologically confirmed diagnosis of epithelial endometrial carcinoma. All histologies are allowed except for sarcomas (carcinosarcomas are allowed).</p> <p>6. Following surgery or diagnostic biopsy, participant must have primary advanced disease (Stage III/IV) or first recurrent EC, and meet at least one of the following criteria:</p> <p>a) Primary Stage III (per FIGO 2023) disease with measurable disease at baseline per RECIST 1.1 based on the investigator's assessment. Primary Stage IV (per FIGO 2023) disease regardless of presence of measurable disease at baseline.</p> <p>c) First recurrent disease regardless of presence of measurable disease at baseline.</p> <p>NOTE: In the US, patients with Stage III EC will only be enrolled after Investigational Device Exemption (IDE) for the investigational in vitro diagnostic device (IVD) HER2 IHC assay is approved by the Center for Devices and Radiological Health.</p> <p>7. Endometrial cancer with HER2 IHC expression of 3+ or 2+ by prospective central testing.</p> <p>8. Endometrial cancer that is determined pMMR by prospective central IHC testing.</p> <p>9. Provision of adequate formalin fixed and paraffin embedded (FFPE) tumor tissue sample of a tumor lesion that was not previously irradiated for central HER2, MMR, and PD-L1 IHC testing and valid central test results for randomization/stratification.</p> <p>10. Prior therapy:</p> <p>a) Naïve to first-line systemic anticancer therapy. Participants may have received one prior line of adjuvant/neoadjuvant chemotherapy with curative intent (chemotherapy or chemoradiation) if disease recurrence or progression occurred <math>\geq 6</math> months after last dose of chemotherapy. Prior trastuzumab in the adjuvant/neoadjuvant setting is allowed.</p> <p>b) No prior exposure to ADCs or ICIs including (but not limited to) anti-PD-1/PD-L1/PD-L2 and anti-CTLA-4 antibodies and therapeutic anticancer vaccines.</p> <p>c) Participants may have received prior radiation therapy for the treatment of EC. Prior radiation therapy may have included pelvic radiation therapy, extended field pelvic/para-aortic radiation therapy, and/or intravaginal brachytherapy. Adequate treatment washout period is required.</p> |
| Principali criteri di esclusione: | <p>History of organ transplant.</p> <p>3. Uncontrolled intercurrent illness including, but not limited to ongoing or active known infection, serious chronic gastrointestinal conditions associated with diarrhea (e.g., active inflammatory bowel disease) and active non-infectious skin disease (including any grade rash, urticarial, dermatitis, ulceration, or psoriasis) requiring systemic treatment.</p> <p>4. Has spinal cord compression or clinically active central nervous system metastases, defined as untreated and symptomatic, or requiring therapy with corticosteroids or anticonvulsants to control associated symptoms.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Struttura                         | SCDU Oncologia medica                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Contatto                          | Prof. Giorgio Valabrega<br>giorgio.valabrega@unito.it                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |