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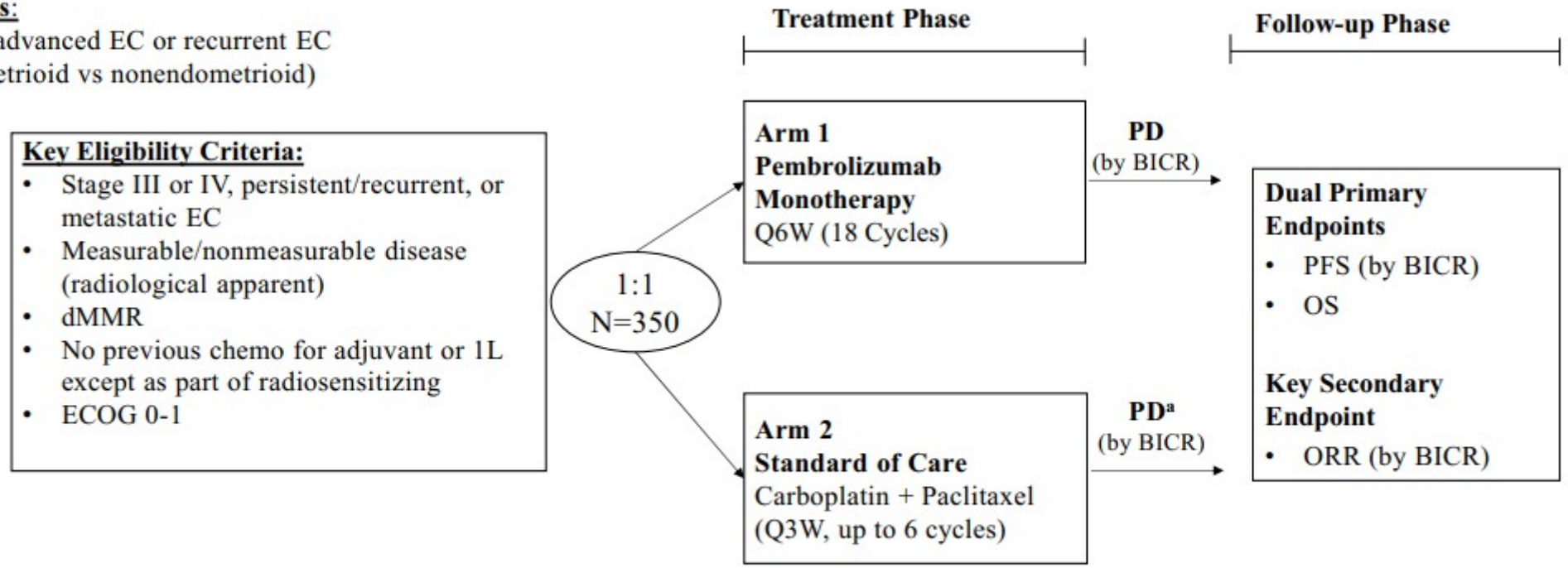
A Phase 3 Randomized, Open-label, Active-comparator Controlled Clinical Study of Pembrolizumab versus Platinum Doublet Chemotherapy in Participants With Mismatch Repair Deficient (dMMR) Advanced or Recurrent Endometrial Carcinoma in the First-line Setting

SCDU Oncologia
AO Ordine Mauriziano

Study design

Stratification Factors:
- Newly diagnosed advanced EC or recurrent EC
- Histology (endometrioid vs nonendometrioid)



1L=first line; BICR=blinded independent central review; dMMR=deficient mismatch repair; EC=endometrial carcinoma; ECOG=Eastern Conference Oncology Group; ORR=objective response rate; OS=overall survival; PD=progressive disease; PFS=progression-free survival; Q3W=every 3 weeks; Q6W=every 6 weeks.

[a]Participants who were randomized to Arm 2 (chemotherapy) and experience BICR-assessed disease progression per RECIST 1.1, will have an opportunity to participate in the Crossover Phase to receive up to 18 cycles of pembrolizumab 400 mg Q6W, upon Sponsor consultation.

Main Inclusion Criteria

- Histologically confirmed diagnosis of **Stage III or IV or recurrent EC or carcinosarcoma** (mixed Mullerian tumor) that is centrally confirmed as dMMR.
- **Radiographically evaluable disease**, either measurable or nonmeasurable per RECIST 1.1, as assessed by the investigator.
- Has received **no prior systemic therapy** for advanced EC.
  Note: May have received prior hormonal therapy for treatment of EC, provided that it was discontinued ≥1 week prior to randomization.
- **Female**, at least **18 years** of age at the time of signing the informed consent (either Authorization for Release of Tumor Tissue or main study consent).
- **ECOG** performance status of **0 or 1** within 7 days before randomization
- Provides an **archival tumor tissue sample or newly obtained** (core, incisional, or excisional) biopsy of a tumor lesion not previously irradiated for verification of dMMR status and histology.
- Participants HBsAg positive and/or with a history of HCV infection could be admitted.
- Adequate organ function.

Main Exclusion Criteria

- **Uterine mesenchymal tumor** such as an endometrial stromal sarcoma, leiomyosarcoma, or other types of pure sarcomas. Adenosarcomas are also not allowed. Neuroendocrine tumors are also not allowed.
- EC of any histology that is **pMMR**.
- Is a candidate for **curative-intent** surgery or curative-intent radiotherapy.
- Has received prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent or with an agent directed to another stimulatory or coinhibitory T-cell receptor (eg, CTLA-4, OX40, CD137).
- Has received prior systemic anticancer therapy.
- **Diagnosis of immunodeficiency** or is receiving chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior the first dose of study intervention.

Main Exclusion Criteria

- A major operation not recovered adequately from the procedure and/or any complications from the operation before starting study intervention.
- Has received a live or live-attenuated vaccine within 30 days before the first dose of study intervention. Administration of killed vaccines and COVID-19 vaccines are allowed.
- Known **additional malignancy** that is progressing or has required active treatment within the past 3 years.
- Known **active CNS metastases** and/or carcinomatous meningitis. Participants with previously treated brain metastases may participate provided they are radiologically stable, (ie, without evidence of progression) for at least 4 weeks by repeat imaging, clinically stable and without requirement of steroid treatment for at least 14 days before the first dose of study intervention.