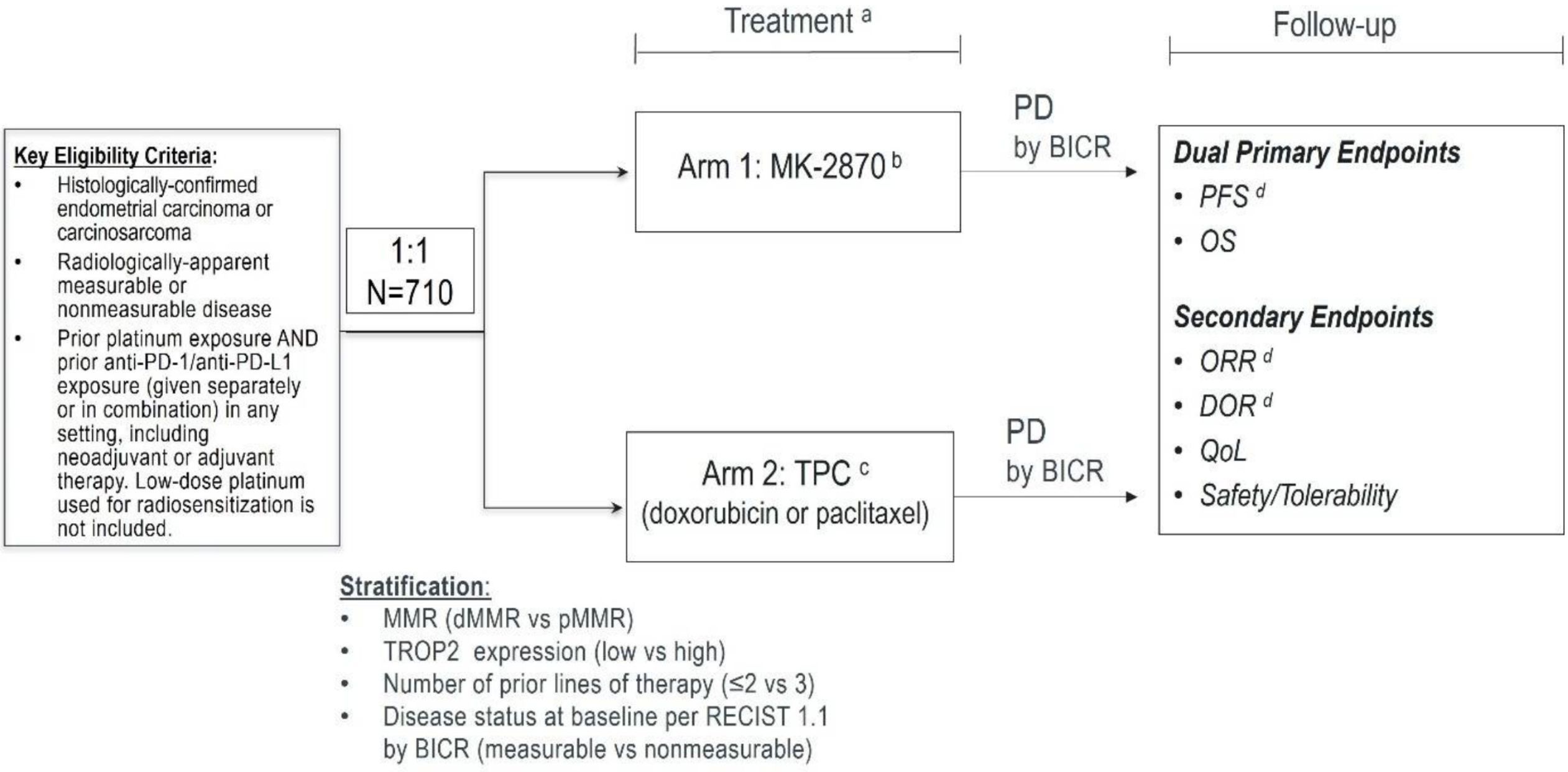
MK 2870-005

- **Study Title**: 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 in Participants With Endometrial Cancer Who Have Received Prior Platinum-based Chemotherapy and Immunotherapy

- **Study Population**:
  - Histologically-confirmed endometrial carcinoma or carcinosarcoma
  - Radiologically-apparent measurable or nonmeasurable disease
  - Prior platinum exposure AND prior anti-PD-1/anti-PD-L1 exposure (given separately or in combination) in any setting, including neoadjuvant or adjuvant therapy. Low-dose platinum used for radiosensitization is not included.


Treatment a
Follow-up
Key Eligibility Criteria:
• Histologically-confirmed endometrial carcinoma or carcinosarcoma
• Radiologically-apparent measurable or nonmeasurable disease
• Prior platinum exposure AND prior anti-PD-1/anti-PD-L1 exposure (given separately or in combination) in any setting, including neoadjuvant or adjuvant therapy. Low-dose platinum used for radiosensitization is not included.
1:1
N=710
Arm 1: MK-2870 b
Arm 2: TPC c
(doxorubicin or paclitaxel)
PD
by BICR
PD
by BICR
Dual Primary Endpoints
• PFS d
• OS
Secondary Endpoints
• ORR d
• DOR d
• QoL
• Safety/Tolerability
Stratification:
• MMR (dMMR vs pMMR)
• TROP2 expression (low vs high)
• Number of prior lines of therapy (≤2 vs 3)
• Disease status at baseline per RECIST 1.1 by BICR (measurable vs nonmeasurable)

ELIGIBILITY – INCLUSION CRITERIA 1/3

- Has a histologically-confirmed diagnosis of endometrial carcinoma or carcinosarcoma.
- Has radiographically evaluable disease, either measurable or nonmeasurable per RECIST 1.1, as assessed by BICR.
  Note: Participants with fluid-only disease (eg, pleural effusion or ascites, and no other radiographically apparent lesions) must have cytologic confirmation of malignancy.
- Has provided tumor tissue (most recent sample is preferred) that is not previously irradiated, for determination of MMR and TROP2 status and assessment of histology (by the central laboratory). Details pertaining to tumor tissue submission are provided in the Central Laboratory Manual.
- Is assigned female sex at birth, not pregnant or breastfeeding, at least 18 years of age at the time of providing the informed consent.
- Has ECOG performance status of 0 or 1 within 7 days before randomization.

ELIGIBILITY – INCLUSION CRITERIA 2/3

- Has received up to 3 prior lines of therapy for endometrial carcinoma, including systemic, platinum-based chemotherapy and anti-PD-1/anti-PD-L1 therapy, either separately or in combination.
  - Adjuvant +/- neoadjuvant therapy is considered 1 line of therapy.
  - The same regimen (eg, carboplatin and paclitaxel) if given in the adjuvant setting and then again in the recurrent or metastatic setting is considered 2 lines of therapy.
  - Chemotherapy given for radiosensitization will not be counted as a line of therapy (eg, cisplatin with EBRT); however, systemic chemotherapy given before or after as part of a multimodal approach would be considered 1 line of therapy.
  - Any change in chemotherapy regimen (substitution or change in entire regimen) due to toxicity in the absence of disease progression will be considered part of the same line of therapy.
  - Participants may have received other mAbs or targeted therapies, including but not limited to trastuzumab, bevacizumab, PARPi. The mAb (or targeted therapy) will count as a line of therapy if given as a single agent with the intention of inducing a systemic effect or significantly reducing overall tumor burden, but will not count as a line of therapy if given in combination with other systemic anticancer therapy and continued after as monotherapy (ie, maintenance).
  - Prior hormonal therapy, either alone or in combination with mTOR (everolimus), NTRK, or other combination partner is allowed and does not count as a line of therapy.
  - Maintenance therapy (eg, selinexor) will not be considered as a separate line of therapy.
    Note: There is no exclusion to the combination partner(s) for the prior anti-PD-1/ anti-PD-L1 therapy (ie, may have been received in combination with chemotherapy, tyrosine kinase inhibitor, or other therapies, including as part of a clinical study).

ELIGIBILITY – INCLUSION CRITERIA 3/3

- 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.
- Adequate organ function as defined in Table (next page). Specimens must be collected within 7 days before the start of study intervention.
- HIV-infected participants must have well controlled HIV on ART
- Participants who are HBsAg positive are eligible if they have received HBV antiviral therapy for at least 4 weeks, and have undetectable HBV viral load prior to randomization.
  Note: Participants should remain on antiviral therapy throughout study intervention and follow local guidelines for HBV antiviral therapy post completion of study intervention.
- Participants with history of HCV infection are eligible if HCV viral load is undetectable at screening.
  Note: Participants must have completed curative antiviral therapy at least 4 weeks prior to randomization.

ELIGIBILITY – EXCLUSION CRITERIA 1/5

- Has neuroendocrine tumors or endometrial sarcoma, including stromal sarcoma, leiomyosarcoma, adenosarcoma, or other types of pure sarcomas.
- Is a candidate for curative-intent surgery or curative-intent radiotherapy at the time of enrollment.
- Has Grade ≥2 peripheral neuropathy.
- Has history of documented severe dry eye syndrome, severe Meibomian gland disease and/or blepharitis, or corneal disease that prevents/delays corneal healing.
- Has active inflammatory bowel disease requiring immunosuppressive medication or previous history of inflammatory bowel disease (eg, Crohn's disease, ulcerative colitis, or chronic diarrhea).
- 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 6 months prior to study intervention.

ELIGIBILITY – EXCLUSION CRITERIA 2/5

- Has recurrence of endometrial carcinoma or carcinosarcoma more than 6 months after completing platinum-based therapy administered in the curative-intent or adjuvant setting without any additional platinum-based therapy received in the metastatic or recurrent setting.
- Received more than 3 prior lines of therapy for endometrial carcinoma, including adjuvant therapy.
- Received prior treatment with single-agent nonplatinum based chemotherapy in the third-line setting.
  Note: Single-agent nonplatinum based chemotherapy in the first-line setting or second-line setting is allowed.
- Received prior treatment with a TROP2-targeted ADC.
- Received prior treatment with a topoisomerase I-containing ADC.
- Received prior systemic anticancer therapy including investigational agents within 4 weeks or 5 half-lives (whichever is shorter) before study intervention administration.

ELIGIBILITY – EXCLUSION CRITERIA 3/5

- 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 palliative radiotherapy treatment must have been performed at least 7 days before the first dose of study intervention.
- Received a live or live-attenuated vaccine within 30 days before the first dose of study intervention. Administration of killed vaccines is allowed.
  Refer to Section 6.5 for information on COVID-19 vaccines.
- Requires treatment with a strong inhibitor or inducer of CYP3A4 within 14 days before the first dose of study intervention and throughout the study.
- Has received an investigational agent or has used an investigational device within 4 weeks prior to study intervention administration.
  Note: Participants who have entered the follow-up phase of an investigational study may participate as long as it has been 4 weeks after the last dose of the previous investigational agent.
- Active infection requiring systemic therapy.

ELIGIBILITY – EXCLUSION CRITERIA 4/5

- 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.
- 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 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.
- HIV-infected participants with a history of Kaposi's sarcoma and/or Multicentric Castleman's Disease.
- Concurrent active Hepatitis B (defined as HBsAg positive and/or detectable HBV DNA) and Hepatitis C virus (defined as anti-HCV Ab positive and detectable HCV RNA) infection.
- Known hypersensitivity to MK-2870 or other biologic therapy.

ELIGIBILITY – EXCLUSION CRITERIA 5/5

- History or current evidence of any condition, therapy, laboratory abnormality, or other circumstance that might confound the results of the study or interfere with the participant's participation for the full duration of the study, such that it is not in the best interest of the participant to participate, in the opinion of the treating investigator.
- Known psychiatric or substance abuse disorder that would interfere with the participant's ability to cooperate with the requirements of the study.
- Known intolerance to MK-2870 or TPC and/or any of their excipients; for TPC, severe hypersensitivity (Grade ≥3) to both TPC is exclusionary.
- Note: Intolerance to one TPC (ie, either doxorubicin or paclitaxel) does not exclude a participant from the study if the other TPC that the participant can tolerate is chosen prior to randomization.
- Participants who have not adequately recovered from major surgery or have ongoing surgical complications.