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| **Study Title** | **MITO27: Randomized Phase II study on MK-3475 plus chemotherapy versus chemotherapy alone in recurrent, platinum-resistant ovarian cancer** |
| **Primary Objective** | • To assess overall survival (OS) of the combination of chemotherapy plus Pembrolizumab with respect to chemotherapy alone |
| **Secondary Objectives** | • To assess progression free survival (PFS) of patients receiving chemotherapy plus pembrolizumab with respect to patients receiving chemotherapy alone.<br><br>• To assess the response rate (RECIST 1.1 criteria) of patients receiving chemotherapy plus pembrolizumab with respect to patients receiving chemotherapy alone.<br><br>• To assess the safety and tolerability of patients receiving chemotherapy plus pembrolizumab with respect to patients receiving chemotherapy alone.<br><br>• To assess patient-reported outcome (PRO) of patients receiving chemotherapy plus pembrolizumab with respect to patients receiving chemotherapy alone utilizing the disease-related symptoms – physical (DRS–P) subscale of the National Comprehensive Cancer Network-Functional Assessment of Cancer Therapy (NCCN-FACT) FACT-Ovarian Symptom Index 18 (FOSI-18) Changes and using Euro-Quality of Life 5D (eEQ-5D) tool. |
| **Inclusion Criteria** | 1. Platinum resistant (platinum free interval 1-6 months from last platinum dose) ovarian, Fallopian tube or primary peritoneal cancer;<br>2. Be willing and able to provide written informed consent/assent for the trial;<br>3. Be ≥ 18 years of age on day of signing informed consent;<br>4. Have measurable disease or evaluable based on RECIST 1.1 (patients with only CA 125 increase without evidence of disease are not included);<br>5. Be willing to provide tissue from a newly obtained core or excisional biopsy of a tumor lesion. Newly-obtained is defined as a specimen obtained up to 6 weeks (42 days) prior to initiation of treatment on Day 1. Subjects for whom newly-obtained samples cannot be provided (e.g. inaccessible or subject safety concern) may submit an archived specimen;<br>6. Have a performance status of 0 or 1 on the ECOG Performance Scale;<br>7. Demonstrate adequate organ function as defined in **Errore. L'origine riferimento non è stata trovata.**, all screening labs should be performed within 10 days of treatment initiation;<br>8. Female subject of childbearing potential should have a negative urine or serum pregnancy within 72 hours prior to receiving the first dose of study medication. If the urine test is positive or cannot |

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| | be confirmed as negative, a serum pregnancy test will be required;<br><br>9. Female subjects of childbearing potential should be willing to use 2 methods of birth control or be surgically sterile, or abstain from heterosexual activity for the course of the study through 120 days after the last dose of study medication (Reference Section 6.5.2). Subjects of childbearing potential are those who have not been surgically sterilized or have not been free from menses for > 1 year. |
| **Exclusion Criteria** | 1. Is currently participating and receiving study therapy or has participated in a study of an investigational agent and received study therapy or used an investigational device within 4 weeks of the first dose of treatment;<br><br>2. Has received >2 previous CHT lines;<br><br>3. Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of trial treatment;<br><br>4. Has a known history of active TB (Bacillus Tuberculosis);<br><br>5. Hypersensitivity to pembrolizumab or any of its excipients;<br><br>6. Has had a prior anti-cancer monoclonal antibody (mAb) within 4 weeks prior to study Day 1 or who has not recovered (i.e., ≤ Grade 1 or at baseline) from adverse events due to agents administered more than 4 weeks earlier;<br><br>7. Has had prior chemotherapy, targeted small molecule therapy, or radiation therapy within 2 weeks prior to study Day 1 or who has not recovered (i.e., ≤ Grade 1 or at baseline) from adverse events due to a previously administered agent:<br><br>- Note: Subjects with ≤ Grade 2 neuropathy are an exception to this criterion and may qualify for the study;<br><br>- Note: If subject received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting therapy;<br><br>8. Has a known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin or squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cervical cancer and other solid tumors within the last 2 years;<br><br>9. Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis. Subjects with previously treated brain metastases may participate provided they are stable (without |

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| | evidence of progression by imaging for at least four weeks prior to the first dose of trial treatment and any neurologic symptoms have returned to baseline), have no evidence of new or enlarging brain metastases, and are not using steroids for at least 7 days prior to trial treatment. This exception does not include carcinomatous meningitis which is excluded regardless of clinical stability;<br><br>10. Has active autoimmune disease that has required systemic treatment in the past 2 years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (eg., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment;<br><br>11. Has an history of, or any actual evidence of active, non-infectious pneumonitis that required steroids treatment;<br><br>12. Has an active infection requiring systemic therapy;<br><br>13. Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the subject's participation for the full duration of the trial, or is not in the best interest of the subject to participate, in the opinion of the treating investigator;<br><br>14. Has known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial;<br><br>15. Is pregnant or breastfeeding, or expecting to conceive children within the projected duration of the trial, starting with the pre-screening or screening visit through 120 days after the last dose of trial treatment;<br><br>16. Has received prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent;<br><br>17. Has a known history of Human Immunodeficiency Virus (HIV) (HIV 1/2 antibodies);<br><br>18. Has known active Hepatitis B (e.g., HBsAg reactive) or Hepatitis C (e.g., HCV RNA [qualitative] is detected);<br><br>19. Has received a live vaccine within 30 days of planned start of study therapy.<br><br>*Note: Seasonal influenza vaccines for injection are generally inactivated flu vaccines and are allowed; however intranasal influenza vaccines (e.g., Flu-Mist®) are live attenuated vaccines, and are not allowed.* |
| **Number of Patients to enroll** | 138 |

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