Clinical Trial Summary For out of hours Service

Trial name & Study design

Phase 1B
COUPLET STUDY – Open label non Randomized study.

A PHASE IB COMBINATION STUDY OF RUCAPARIB (CO-338) AND ATEZOLIZUMAB (MPDL3280A) IN PATIENTS WITH ADVANCED **GYNECOLOGIC CANCERS** AND **TRIPLE-NEGATIVE BREAST CANCER**

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Indication for use.

This is a Phase Ib, open-label, non-randomized study in patients with previously treated advanced ovarian or endometrial cancer and platinum-sensitive ovarian cancer or TNBC to investigate the dose, safety, pharmacokinetics, and preliminary efficacy of rucaparib in combination with atezolizumab.

Trial regimen

Combination of Rucaparib oral medication + Atezolizumab Intravenous Infusion.

- 21-day Run-in period of Oral Rucaparib 400mg BD.

- Followed by 21-day cycles of Oral Rucaparib 400mg + Atezolizumab 1200mg IV combined.

SIDE EFFECTS OF THE DRUGS USED IN WO39409 STUDY

ATEZOLIZUMAB

SIDE EFFECTS KNOWN TO BE ASSOCIATED WITH ATEZOLIZUMAB

Common (occur in more than 10% of patients)	• Fatigue • Arthralgia • Asthenia • Decreased appetite • Diarrhoea • Abdominal pain • Dyspnoea	• Headache • Pruritus • Nausea • Fever • Rash • Vomiting • Myalgia, musculoskeletal pain and bone pain
Less common (occur in 1%–10% of patients)	• Chills • Dysphagia • Elevated liver enzymes • Hyperglycaemia • Hypersensitivity • Hypokalaemia • Hyponatremia • Hypotension • Hypothyroidism	• Colitis • Hypoxia • Flu-like symptoms • Infusion-related reaction • Muscular weakness • Musculoskeletal pain • Peripheral neuropathy • Pneumonitis • Thrombocytopenia
Rare but potentially serious (occur in less than 1% of patients)	• Adrenal insufficiency • Diabetes • Hyperthyroidism • Hepatitis • Guillain-Barré syndrome • Meningoencephalitis	• Myasthenic syndrome/myasthenia gravis • Pancreatitis • Increase in amylase and lipase • Diabetic ketoacidosis • Hypophysitis • Myocarditis • Nephritis

SIDE EFFECTS POTENTIALLY ASSOCIATED WITH ATEZOLIZUMAB

- Immunogenicity
- Teratogenicity
- Uveitis
- Myositis and myopathies including rhabdomyolysis
- Vasculitis
- Autoimmune haemolytic anaemia
- Severe cutaneous adverse reactions

Systemic Immune Activation may occur when atezolizumab is combined with other immune-modulating drugs.

RUCAPARIB

SIDE EFFECTS ASSOCIATED WITH RUCAPARIB

Common (occur in >10% of patients)	• ALT/AST increased • Blood creatinine increased • Dysgeusia • Decreased appetite • Constipation • Diarrhoea • Epigastric pain • Dyspepsia • Nausea • Insomnia	• Rash • Fatigue • Anaemia • Thrombocytopenia • Neutropenia • Pyrexia • Vomiting • Dizziness • Dyspnoea • Photosensitivity
Less common (occur in 1%–10% of patients)	• Hypercholesterolaemia • Leukopenia • Lymphopenia • Palmar-plantar erythrodysesthesia	• Transaminases increased • Hypophosphatemia • Pruritus • Upper respiratory tract infection
Rare but potentially serious (occur in <1% of patients)	• Myelodysplastic syndrome • Febrile neutropenia	• Acute myeloid leukaemia

Myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML) have been reported in a very small number of patients treated with rucaparib.

Events of MDS and AML have also been reported with PARP inhibitors similar to rucaparib. At this time, it is not known whether rucaparib or other PARP inhibitors cause MDS or AML, or if these developed as a result of previous chemotherapy these patients received.

SIDE EFFECTS POTENTIALLY ASSOCIATED WITH THE ATEZOLIZUMAB AND RUCAPARIB COMBINATION

Side effects common to both experimental drugs may include liver damage, with symptoms such as abdominal pain, unexplained nausea, and vomiting.

Dose Modification Criteria
No changes to be made without consultation with PI and Trials office

Important: For management of toxicities, consult network Immune Related Toxicity Management Guidelines in emergency situation.

For any consultations out of hours please communicate this on Varian

The research nurses will check this every morning and liaise with the Oncology Principal Investigator