Essai Clinique

Généré le 16 mai 2025 à partir de

Titre	Randomized, Multicenter, Open-label, Phase 3 Study of Mirvetuximab Soravtansine in Combination With Bevacizumab Versus Bevacizumab Alone as Maintenance Therapy for Patients With FR?-high Recurrent Platinum-sensitive Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancers Who Have Not Progressed After Second Line Platinum-based Chemotherapy Plus Bevacizumab
Protocole ID	GLORIOSA
ClinicalTrials.gov ID	NCT05445778
Type(s) de cancer	Ovaire
Phase	Phase III
Type étude	Clinique
Médicament	Mirvetuximab Soravtansine avec bevacizumab versus bevacizumab seul en thérapie d'entretien
Institution	CIUSSS DE L'EST-DE-L'ILE-DE-MONTREAL PAV. MAISONNEUVE/PAV. MARCEL-LAMOUREUX 5415 boul. de l'Assomption, Montréal, QC, H1T2M4
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Statut	Actif en recrutement
But étude	GLORIOSA is a Phase 3 multicenter, open label study designed to evaluate the safety and efficacy of mirvetuximab Soravtansine as maintenance therapy in participants with platinum-sensitive ovarian, primary peritoneal or fallopian tube cancers with high folate receptor-alpha (FRα) expression.
Critères d'éligibilité	• Patients must be ≥ 18 years of age • Patients must have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. • Patients must have a confirmed diagnosis of high-grade serous epithelial ovarian, primary peritoneal, or fallopian tube cancer. • Patients must be willing to provide an archival tumor tissue block or slides, or must undergo a procedure to obtain a new biopsy using a low-risk, medically routine procedure for IHC confirmation of high FRα expression (reported as "positive") as defined by the Ventana FOLR1 Assay. Patients must be confirmed FRα-high as defined by FRα positivity of ≥ 75% of tumor membrane staining at ≥ 2+ intensity (PS2+) for entry into the study. • Prior BRCA testing on the tumor or prior germline testing is required for eligibility. If not done prior, tumor or germline testing will need to be done before study entry. Somatic and germline BRCA-positive patients must have received prior treatment with a PARPi in maintenance following first-line treatment. Note: Local tumor or germline BRCA testing will be acceptable for stratification. If the patient has not been tested, recommend archival tumor samples to be assessed for tissue BRCA. All patients who have received prior first line PARPi maintenance and/or bevacizumab are eligible. • Patients' disease must have relapsed after 1 line (first line) of platinum-based chemotherapy and must be platinum-sensitive defined as progression greater than 6 months from last dose of primary platinum therapy. • Patients must be appropriate for, currently be on, or have completed platinum-based triplet therapy in the second line (recurrent PSOC). • After completion of triplet therapy and before randomization, patients must have received no less than 4 and no greater than 8 cycles of platinum-based triplet therapy in the second line, to include no less than 3 cycles of bevacizumab in combination with platinum-based chemotherapy. If the number of cycles received is less than 6 due to toxicity, this must be

	documented and toxicity assessed as unlikely related to bevacizumab. Note: A minimum of 4 cycles of combination chemotherapy is required. If carboplatin, paclitaxel, gemcitabine, or pegylated liposomal doxorubicin (PLD) is stopped due to toxicity, up to 4 additional cycles of single agent in combination with bevacizumab is acceptable if appropriately documented.
	• After completion of triplet therapy and before randomization: In the case of interval secondary cytoreductive surgery, patients are permitted to have received only 2 cycles of bevacizumab if given in combination with the last 3 cycles of platinum-based triplet therapy in the second line. In the case of primary cytoreductive surgery before secondline platinum-based triplet therapy, patients must have received no fewer than 3 cycles of bevacizumab in combination with platinum-based chemotherapy after their surgery and before randomization.
	• Patients either will receive (per investigator's choice), must be receiving, or have received paclitaxel, gemcitabine, or pegylated liposomal doxorubicin as the partner drug to platinum-based triplet therapy in the second line.
	• After completion of triplet therapy and before randomization, patients must have achieved a CR, PR, or SD, per the investigator, in the second line to be eligible for randomization into the study population. All patients will have CT or MRI scans and CA-125 measurements at least 3 weeks but no more than 8 weeks after their last planned dose of triplet therapy and before randomization.
	• Patients must be randomized no later than 8 weeks from the last dose of platinum-based triplet therapy in the second line.
	• After completion of triplet therapy and before randomization, patients must meet one of the following criteria:
	  • Have at least 1 lesion that meets the definition of measurable disease by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 (radiologically measured by the investigator), and determined by the investigator to either have SD or a PR to their treatment; or
	  • Have persistently elevated CA-125 without measurable disease and determined by the investigator to have either SD or a PR to their treatment; or
	  • Have clinically no evidence of disease by both radiographic interpretation by the investigator and normalization of their CA-125, determined to be a CR.
	• Patients must have stabilized or recovered (to Grade 1 or baseline) from all prior therapy-related toxicities (except alopecia).
	• Patients must have completed any major surgery at least 4 weeks before the first dose of study treatment (either Run-In or maintenance therapy) and have recovered or stabilized from the side effects of prior surgery before the first dose of treatment on study.
	• Patients must have adequate hematologic, liver, and kidney functions defined as follows:
	  • Absolute neutrophil count (ANC) ≥ 1.5 × 109/L (1500/µL) without granulocyte colony-stimulating factor in the prior 10 days or long-acting white blood cell (WBC) growth factors in the prior 10 days of C1D1 of maintenance treatment.
	  • Platelet count ≥ 100 × 109/L (100,000/µL) without platelet transfusion in the prior 10 days of C1D1 of maintenance treatment
	  • Hemoglobin ≥ 9.0 g/dL without packed red blood cell (PRBC) transfusion in the prior 10 days of C1D1 of maintenance treatment
	  • Serum creatinine ≤ 1.5 × upper limit of normal (ULN)
	  • Aspartate aminotransferase and alanine aminotransferase ≤ 3.0 × ULN
	  • Serum bilirubin ≤ 1.5 × ULN (patients with documented diagnosis of Gilbert syndrome are eligible if total bilirubin < 3.0 × ULN)
	  • Serum albumin ≥ 2 g/dL
	• Patients must be willing and able to sign the informed consent form (ICF) and to adhere to the protocol requirements.
	• Females of childbearing potential (FCBP) must agree to use highly effective contraceptive method(s) (as defined in Section 5.10.7) while on study medication and for at least 3 months after the last dose.
	• FCBP must have a negative pregnancy test within 4 days before the first dose of therapy.

Critères d'exclusion	• Patients with endometrioid, clear cell, mucinous, or sarcomatous histology; mixed tumors containing any of the above histologies; or low-grade/borderline ovarian tumor
	• More than one line of prior chemotherapy before current/planned triplet therapy. Lines of prior anticancer therapy are counted with the following considerations:
	  • Neoadjuvant ± adjuvant therapies are considered 1 line of therapy if the neoadjuvant and adjuvant correspond to 1 fully predefined regimen; otherwise, they are counted as 2 prior regimens.
	  • Maintenance therapy (eg, bevacizumab, PARPi) will be considered part of the preceding line of therapy (ie, not counted independently).
	  • Change due to toxicity will be considered part of the proceeding line of therapy.
	• Patients with PD while on or following platinum-based triplet therapy
	• After completion of triplet therapy and prior to randomization: Patients who receive an intervening dose of bevacizumab after the last dose of triplet therapy before randomization
	• Patients with prior wide-field radiotherapy affecting at least 20% of the bone marrow
	• Patients with > Grade 1 peripheral neuropathy per Common Terminology Criteria for Adverse Events (CTCAE)
	• 7. Patients with active or chronic corneal disorders, history of corneal transplantation, or active ocular conditions requiring ongoing treatment/monitoring, such as uncontrolled glaucoma, wet age-related macular degeneration requiring intravitreal injections, active diabetic retinopathy with macular edema, macular degeneration, presence of papilledema, and/or monocular vision
	• Patients with serious concurrent illness or clinically relevant active infection, including but not

limited to the following:
    - Active hepatitis B or C infection (whether or not on active antiviral therapy)
    - HIV infection
    - Active cytomegalovirus infection
    - Any other concurrent infectious disease requiring intravenous (IV) antibiotics within 2 weeks before the first dose of maintenance therapy Note: Testing at screening is not required for the above infections unless clinically indicated.
- Patients with a history of multiple sclerosis or other demyelinating diseases and/or Lambert-Eaton syndrome (paraneoplastic syndrome)
- Patients with clinically significant cardiac disease including, but not limited to, any of the following:
    - Myocardial infarction ≤ 6 months prior to C1D1 of maintenance treatment
    - Unstable angina pectoris
    - Uncontrolled congestive heart failure (New York Heart Association > class II)
    - Uncontrolled ≥ Grade 3 hypertension (per CTCAE)
    - Uncontrolled cardiac arrhythmias
- Patients with a history of hemorrhagic or ischemic stroke within 6 months before enrollment
- Patients with a history of cirrhotic liver disease (Child-Pugh Class B or C)
- Patients with a previous clinical diagnosis of noninfectious interstitial lung disease, including noninfectious pneumonitis (exception: Grade 1 noninfectious pneumonitis diagnosed on or within 6 weeks after treatment with an immunotherapeutic agent used in the treatment of their malignancy that has resolved per investigator or resolution of the radiologic findings)
- History of bowel obstruction (including sub-occlusive disease) related to underlying disease within 6 months before the start of maintenance study treatment (triplet therapy for Run-In patients).
- History of abdominal fistula or gastrointestinal perforation
- Intra-abdominal abscess, evidence of rectosigmoid involvement by pelvic examination, bowel involvement on CT scan, or clinical symptoms of bowel obstruction within 4 weeks prior to randomization (or within 4 weeks prior to starting triplet therapy for Run- In patients)
- Clinically significant proteinuria: urine-protein to creatinine (UPC) ratio ≥ 1.0 or urine dipstick result ≥ 2+; patients with UPC ratio ≥ 1.0 or ≥ 2+ proteinuria should undergo 24-hour urine collection and must show result ≤ 1 g of protein in a 24-hour period.
- History of Grade 4 thromboembolic events
- Patients not appropriate for bevacizumab 15 mg/kg dosing at the start of maintenance therapy as per the treating physician
- Patients requiring use of folate-containing supplements (eg, folate deficiency)
- Patients with prior hypersensitivity to monoclonal antibodies (mAbs)
- Women who are pregnant or breastfeeding
- Patients who received prior treatment with MIRV or other FRα-targeting agents
- Patients with untreated or symptomatic central nervous system metastases
- Patients with a history of other malignancy within 3 years prior to signing study consent Note: Patients with tumors with a negligible risk for metastasis or death (eg, controlled basal cell carcinoma or squamous cell carcinoma of the skin, or carcinoma in situ of the cervix or breast) are eligible.
- Prior known hypersensitivity reactions to study drugs or any of their excipients