Essai Clinique

Généré le 19 mai 2024 à partir de

Titre	TALAPRO-3 : étude de phase III à répartition aléatoire et à double insu portant sur l'administration du talazoparib associé à l'enzalutamide par rapport à un placebo associé à l'enzalutamide chez des hommes atteints d'un cancer de la prostate métastatique sensible à la castration avec mutation du gène DDR
Protocole ID	TALAPRO-3
ClinicalTrials.gov ID	NCT04821622
Type(s) de cancer	Prostate
Phase	Phase III
Stade	Résistant à la castration - métastatique
Type étude	Clinique
Médicament	Talazoparib avec enzalutamide versus placebo avec enzalutamide
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	
Investigateur principal	Dr à venir
Coordonnateur	Rodrigo Skowronski 514-934-1934 poste 36275
Statut	Actif en recrutement
But étude	The purpose of the study is to evaluate the safety and efficacy of talazoparib in combination with enzalutamide compared with placebo in combination with enzalutamide in participants with DDR-deficient mCSPC.
Critères d'éligibilité	• Male participants at least 18 years of age at screening • Histologically or cytologically confirmed adenocarcinoma of the prostate without neuroendocrine differentiation, small cell or signet cell features. If the participant does not have a prior histological diagnosis, a baseline de novo biopsy must be used to confirm the diagnosis and may also be used to support biomarker analysis. • Confirmation of DDR gene mutation status by prospective or historical analysis (with sponsor pre-approval) of blood (liquid biopsy) and/or de novo or archival tumor tissue using FoundationOne Liquid CDx or FoundationOne CDx. • Willing to provide tumor tissue when available (de novo or archived) for retrospective molecular profiling analysis, if not already provided as part of inclusion criterion 3. • Unless prohibited by local regulations or ethics committee decision, consent to a saliva sample collection for retrospective sequencing of the same DDR genes tested on tumor tissue and blood (liquid biopsy), or a subset thereof, and to serve as a germline control in identifying tumor mutations. • Ongoing ADT with a GnRH agonist or antagonist for participants who have not undergone bilateral orchiectomy must be initiated before randomization and must continue throughout the study. • Metastatic prostate cancer documented by positive bone scan (for bone disease) or metastatic lesions on CT or MRI scan (for soft tissue). Participants whose disease spread is limited to regional pelvic lymph nodes are not eligible. Note: a finding of superscan at baseline is exclusionary. • Prior treatment of mCSPC with docetaxel is not permitted. • Treatment with estrogens, cyproterone acetate, or first-generation anti-androgens is allowed

	until randomization.
	• Other prior therapy allowed for mCSPC; ≤3 months of ADT (chemical or surgical) with or without approved NHT in mCSPC (ie, abiraterone + prednisone, apalutamide, or enzalutamide), if required prior to randomization, with no radiographic evidence of disease progression or rising PSA levels prior to Day 1.
	• Participant may have received palliative radiation or surgery for symptomatic control secondary to prostate cancer, which should have been completed at least 2 weeks prior to randomization. NOTE: Radical prostatectomy or definitive radiotherapy to the primary tumor for metastatic castration-sensitive prostate cancer with curative intent is not permitted.
	• ECOG performance status 0 or 1.
	• Adequate organ function within 28 days before the first study treatment on Day 1, defined by the following:
	  • ANC ≥1500/µL, platelets ≥100,000/µL, or hemoglobin ≥9 g/dL (may not have received growth factors or blood transfusions within 14 days before obtaining the hematology laboratory tests at screening).
	  • Total serum bilirubin <1.5 × ULN (<3 × ULN for participants with documented Gilbert syndrome or for whom indirect bilirubin concentrations suggest an extrahepatic source of elevation).
	  • AST or ALT <2.5 × ULN (<5 × ULN if liver function abnormalities are due to hepatic metastasis).
	  • Albumin >2.8 g/dL.
	  • eGFR ≥30 mL/min/1.73 m2 by the MDRD equation.
	• Sexually active participants that in the opinion of the investigator are capable of ejaculating, must agree to use a condom when having sex with a partner (female or male) from the time of the first dose of study treatment through 4 months after last dose of study treatment (or, if talazoparib/placebo has been stopped more than a month earlier than enzalutamide, through 3 months after last dose of enzalutamide). Must also agree for female partner of childbearing potential to use an additional highly effective form of contraception from the time of the first dose of study treatment through 4 months after last dose of study treatment (or, if talazoparib / placebo has been stopped more than a month earlier than enzalutamide, through 3 months after last dose of enzalutamide) when having sex.
	• Must agree not to donate sperm from the first dose of study treatment to 4 months after the last dose of study treatment (or, if talazoparib/placebo has been stopped more than a month earlier than enzalutamide, through 3 months after last dose of enzalutamide).
	• Participants who are willing and able to comply with all scheduled visits, treatment plan, laboratory tests, lifestyle considerations, and other study procedures, including being able to manage electronic diaries. The PRO assessments are not required to be completed if a patient does not understand the language(s) available for a specific questionnaire and/or cannot complete the specific questionnaire independently.
	• Capable of giving signed informed consent.

Critères d'exclusion	• Other acute or chronic medical (concurrent disease, infection, including chronic stable HIV, HBV, or HCV infection, or co-morbidity) or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that interferes with a participant's ability to participate in the study, may increase the risk of associated with study participation or study treatment administration, or may interfere with the interpretation of study results, and, in the investigator's judgment, make the participant inappropriate for entry into the study. HIV/HBV/HCV testing is not required unless mandated by local health authority.
	• History of seizure or any condition (as assessed by investigator) that may predispose to seizure (eg, prior cortical stroke, significant brain trauma), including any history of loss of consciousness or transient ischemic attack within 12 months of randomization.
	• Major surgery (as defined by the investigator) within 4 weeks before randomization.
	• Known or suspected brain metastasis or active leptomeningeal disease.
	• Symptomatic or impending spinal cord compression or cauda equina syndrome.
	• Any history of MDS, AML, or prior malignancy except for the following:
	  • Carcinoma in situ or non-melanoma skin cancer.
	  • A cancer diagnosed and treated ≥3 years before randomization with no subsequent evidence of recurrence.
	  • American Joint Committee on Cancer Stage 0 or Stage 1 cancer <3 years before randomization that has a remote probability of recurrence in the opinion of the investigator and the sponsor.
	• In the opinion of the investigator, any clinically significant gastrointestinal disorder affecting absorption.
	• Clinically significant cardiovascular disease, including any of the following:
	  • Myocardial infarction or symptomatic cardiac ischemia within 6 months before randomization.
	  • Congestive heart failure New York Heart Association class III or IV.
	  • History of clinically significant ventricular arrhythmias (eg, sustained ventricular tachycardia, ventricular fibrillation, torsade de pointes) within 1 year before screening.
	  • History of Mobitz II second degree or third-degree heart block unless a permanent pacemaker is in place.
	  • Hypotension as indicated by systolic blood pressure <86 mm Hg at screening.
	  • Bradycardia as indicated by a heart rate of <45 beats per minute on the screening electrocardiogram.
	  • Uncontrolled hypertension as indicated by systolic blood pressure >170 mm Hg or

diastolic blood pressure >105 mm Hg at screening. However, participants can be rescreened after adequate control of blood pressure is achieved.

- Active COVID-19 infection detected by viral test or based on clinical diagnosis (as assessed by investigator). Asymptomatic participants with no active COVID-19 infection detected but positive antibody tests, indicating past infection are allowed.
- Prior ADT in the adjuvant/neoadjuvant setting, where the completion of ADT was less than 12 months prior to randomization and the total duration of ADT exceeded 36 months.
- Participant received treatment with systemic glucocorticoids greater than the equivalent of 10 mg per day of prednisone within 4 weeks prior to randomization, intended for the treatment of prostate cancer.
- Any previous treatment with DNA-damaging cytotoxic chemotherapy (ie, platinum based therapy) within 5 years prior to randomization, except for indications other than prostate cancer.
- Prior treatment with a PARPi, or known or possible hypersensitivity to enzalutamide, any of enzalutamide capsule excipients or to any talazoparib/placebo capsule excipients.
- Prior treatment in any setting with NHT, except as described in Inclusion Criterion #10.
- Current use of potent P-gp inhibitors within 7 days prior to randomization.
- Treatment with any investigational study intervention within 4 weeks before randomization. Exception: COVID-19 vaccines authorized under an emergency use authorization (or equivalent) can be administered without a washout period.
- Baseline 12-lead ECG that demonstrates clinically relevant abnormalities that may affect participant safety or interpretation of study results (eg, QTcF interval >470 msec, complete LBBB, signs of an acute or indeterminate age myocardial infarction, ST-T interval changes suggestive of myocardial ischemia, second or third degree AV block, or serious bradyarrhythmias or tachyarrhythmias). If the baseline uncorrected QT interval is >470 msec, this interval should be rate-corrected using the Fridericia method and the resulting QTcF should be used for decision making and reporting. If QTc exceeds 470 msec, or QRS exceeds 120 msec, the ECG should be repeated 2 more times and the average of the 3 QTc or QRS values should be used to determine the participant's eligibility. Computer-interpreted ECGs should be overread by a physician experienced in reading ECGs before excluding participants.
- Investigator site staff or Sponsor employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members.