ALADDIN

Evaluation de l'ajout du darolutamide à l'hormonothérapie et à la radiothérapie chez des patients atteints d'un cancer de prostate avec métastases ganglionnaires pelviennes

Phase : III

Type d'essai : Académique / Institutionnel

Etat de l'essai : Ouvert

Objectif principal

Survie sans progression.

Résumé / Schéma de l'étude

Experimental : Arm A : ADT + Intensity-Modulated Image-Guided Radiation Therapy + Darolutamide ADT will be associated with LHRH agonists or antagonists for 24 months. Darolutamide regimen will be of 2 tablets of 300 mg orally twice daily for 24 months.
Arm B : ADT + Intensity-Modulated Image-Guided Radiation Therapy + Placebo of Darolutamide ADT will be associated with LHRH agonists or antagonists for 24 months. Darolutamide regimen will be of 2 tablets of 300 mg orally twice daily for 24 months.

Critères d'inclusion

1 Newly diagnosed, histologically confirmed prostate adenocarcinoma.
2 ≥ 18 years old.

3 Initial staging with Pelvic MRI, CT-scan and or Choline or PSMA PET-CT.

4 Any T stage.

5 Pelvis lymph nodes metastases (upper limit defined as the L4/L5 interspace).

6 Intention to treat with long-term androgen deprivation therapy (24 months).

7 Hormonal therapy with LH-RH agonist or antagonist is allowed up to 2-months prior to randomization.

8 Able to receive either protocol therapy and life expectancy of at least 36 months, ECOG Performance Status (PS) 0-2.

9 Blood counts at screening : hemoglobin ≥ 9.0 g/dl, absolute neutrophil count ≥ 1500/µl ($1.5x10^9$/l), platelet count ≥ 100,000/µl ($100x10^9$/l) (patient must not have received any growth factor or blood transfusion within 7 days of the hematology laboratory obtained at screening).

10 Screening values of serum alanine aminotransferase (ALT) and/or aspartate transaminase (AST) < 2.5 x ULN, total bilirubin < 1.5 x ULN (except patients with a diagnosis of Gilbert's disease), creatinine < 2.0 x ULN.

11 Sexually active patients, unless surgically sterile, must agree to use condoms as an effective barrier method during the study treatment and for 3 months after the end of the study treatment.

12 Written informed consent.

13 Willing and expected to comply with follow-up schedule.

14 Affiliated to the social security system.

Critères de non-inclusion

1 Lymph nodes metastases outside of the pelvis.

2 Bone or visceral metastases.

3 Prior systemic therapy for locally-advanced prostate cancer.

4 Prior treatment with : Second generation AR inhibitors such as enzalutamide, ARN-509, ODM-201, other investigational AR inhibitors, CYP17 enzyme inhibitor such as abiraterone acetate, TAK-700 or Oral ketoconazole longer than for 28 days. Use of estrogens, 5-α reductase inhibitors (finasteride, dutasteride) or AR inhibitors (bicalutamide, flutamide, nilutamide, cyproterone acetate) within 28 days before randomization.

5 Prior chemotherapy or immunotherapy for prostate cancer, except adjuvant/neoadjuvant treatment, completed > 2 years before randomization.

6 Use of systemic corticosteroid with dose greater than the equivalent 10 mg of prednisone/day within 28 days before randomization.

7 Severe or uncontrolled concurrent disease, infection or co-morbidity that, in the opinion of the investigator, would make the patient inappropriate for enrolment.

8 Initiation of treatment with bisphosphonate or denosumab within 12 weeks before randomization.

9 Patients receiving bone loss prevention treatment on a stable dose of e.g. bisphosphonate or denosumab for at least 28 days before randomization can continue the treatment during the study.

10 Known hypersensitivity to the study treatment (RT, ADT, darolutamide/placebo) or any of its ingredients.

11 Major surgery within 28 days before randomization.

12 Any of the following within 6 months before randomization: stroke, myocardial infarction, severe/unstable angina pectoris, coronary/peripheral artery bypass graft; congestive heart failure New York Heart Association (NYHA) Class III or IV or arterial thromboembolic event.

13 Uncontrolled hypertension as indicated by a resting systolic BP > 160 mmHg or diastolic BP > 100 mmHg at screening. Patients may be re-screened after adjustments of anti- hypertensive medications.

14 Prior malignancy. Adequately treated basal cell or squamous cell carcinoma of skin or superficial bladder cancer that has not spread behind the connective tissue layer (i.e. pTis, pTa, and pT1) is allowed, as well as any other cancer for which chemotherapy has been completed > 5 years ago and from which the patient has been disease-free.

15 Gastrointestinal disorder or procedure which expects to interfere significantly with absorption of study treatment.

16 Active viral hepatitis, active human immunodeficiency virus (HIV) or chronic liver disease.

17 Participation in another interventional clinical trial and any concurrent treatment with any investigational drug within 28 days before randomization.

18 Any condition that in the opinion of the investigator would impair the patients' ability to comply with the study

procedures.

19 Unable to swallow study medications and comply with study requirements.

20 Galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

21 History of bilateral hip replacements making IMRT impossible.

22 Contra-indications for the administration of any of the study treatments (RT, ADT, Darolutamide/placebo) or any of its ingredients.

23 Patient under guardianship, administrative tutorship and incapable to give informed consent.

Calendrier prévisionnel

Lancement de l'étude : Août 2022
Fin estimée des inclusions : Février 2026
Nombre de patients à inclure : 152

Etablissement(s) participant(s)

> Sainte-Catherine Institut du Cancer Avignon - Provence (ICAP)

(84) VAUCLUSE

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Promoteur(s)

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