

## E.6 : Essai LUMEN 1-MENINGIOME

<b>Promoteur</b> EORTC Brain Tumor Group	<b>RCP ; ONU</b> <b>Organe et situation : Méningiome/Grade 1 à 3</b> <b>LUMENI-MENINGIOME/Phase II</b>	<b>Identité patient</b>
<b>Investigateur principal</b> Elodie VAULEON (30.04)	[ <sup>177</sup> Lu]Lu-DOTATATE for recurrent meningioma (LUMEN-1) : a randomized phase II study	<i>Coller ici l'étiquette du patient</i>
<b>ARCI</b> Angéline DUCHESNE (30.06)		
<b>Critère principal : Survie sans progression (critères RANO)</b>		

### CRITÈRES D'INCLUSION

- Adult patient  $\geq 18$  years of age
- Histologically confirmed diagnosis of meningioma (all grades, 1-3 per WHO CNS5, are eligible)
- WHO performance status 0-2
- Measurable disease (at least 10 x 10 mm contrast enhancing lesion) on cranial MRI no more than two weeks prior to enrolment.
- Radiologically documented progression of any existing tumour (growth  $> 25\%$  in the last two years) or appearance of new lesions (including intra- and extracranial manifestations)
- Somatostatin receptor (SSTR)-positive confirmed by PET imaging with scan performed within four weeks before randomization (baseline SSTR-PET is considered as positive when meningioma uptake intensity exceeds a SUVmax of 2.3).
- At least one prior surgery and one line of external beam radiotherapy for meningioma, if technically feasible
- Adequate liver, renal and haematological function within four weeks prior to enrolment
  - Neutrophils  $\geq 1.5 \times 10^9/L$ , haemoglobin  $\geq 9$  g/dL or haemoglobin  $\geq 5.6$  mmol/L, platelets  $\geq 100 \times 10^9/L$
  - Total bilirubin  $\leq 1.5 \times ULN$ , except for patients with Gilbert's syndrome who are excluded if total bilirubin  $> 3.0 \times ULN$  or direct bilirubin  $\geq 1.5 \times ULN$
  - SGPT/ALT and SGOT/AST  $\leq 2.5 \times ULN$
  - Albumin  $\geq 30$  g/L
  - Creatinine clearance  $> 40$  ml/min as calculated by CKD-EPI 2021
- Participants must have the following electrolyte values within normal limits or corrected to be within normal limits with supplements prior to first dose of study medication:
  - Potassium (potassium level of up to 6.0 mmol/L is acceptable at study entry if associated with creatinine clearance  $\geq 60$  mL/min calculated using CKD-EPI formula). Mild decrease below lower limit of normal (LLN) is acceptable at study entry if considered not clinically significant by investigator.
  - Total magnesium, with the exception of magnesium level  $> ULN - 3.0$  mg/dL (1.23 mmol/L) associated with creatinine clearance  $\geq 60$  mL/min calculated using CKD-EPI formula. Mild decrease below LLN is acceptable at study entry if considered not clinically significant by Investigator.
  - Total calcium (corrected for serum albumin) level of up to 12.5 mg/dL (3.1 mmol/L) is acceptable at study entry if associated with creatinine clearance  $\geq 60$  mL/min calculated using CKD-EPI formula. Mild decrease below LLN is acceptable at study entry if considered not clinically significant by Investigator.
  - Patients who are receiving corticosteroid treatment with dexamethasone, must be treated with a dose of  $\leq 4$  mg/day (or other corticosteroids equivalent dose) for a minimum of 7 days prior to the initiation of study treatment.

- Women of childbearing potential (WOCBP) must have a negative serum (or urine) pregnancy test within 72 hours prior to enrolment. A positive urine pregnancy test result must immediately be confirmed using a serum test. A pregnancy test will have to be reported within 7 days prior to the first dose of the study treatment.

**Note:** women of childbearing potential are defined as premenopausal females capable of becoming pregnant (i.e., females who have had any evidence of menses in the past 12 months, with the exception of those who had prior hysterectomy). However, women who have been amenorrhoeic for 12 or more months are still considered to be of childbearing potential if the amenorrhea is possibly due to prior chemotherapy, antioestrogens, low body weight, ovarian suppression, or other reasons.

- Patients of childbearing / reproductive potential should use adequate birth control measures during the study treatment period and for at least 7 months after the last dose of treatment. A highly effective method of birth control is defined as a method which results in a low failure rate (i.e., less than 1% per year) when used consistently and correctly. Such methods include:
  - Combined (oestrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal)
  - Progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable)
  - Intrauterine device (IUD)
  - Intrauterine hormone-releasing system (IUS)
  - Bilateral tubal occlusion
  - Vasectomized partner
  - Sexual abstinence (the reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the patient)
- Female subjects who are breast feeding should discontinue nursing prior to the first dose of study treatment and until 7 months after the last study treatment.
- Before patient's enrolment, written informed consent must be given according to ICH/GCP, and national/local regulations.

#### CRITERES D'EXCLUSION

- Local therapy (surgery and / or radiotherapy) indicated per local investigator. **Note:** in case of patients with multiple meningioma lesions, in whom resection and / or radiotherapy of individual lesions is indicated, patients may be included after local therapy (with a 4-week gap between surgery / end of radiotherapy and start of treatment), if at least one remaining lesion fulfils the inclusion criteria.
- Any prior systemic treatment regardless of the timing.
- Life expectancy is less than nine weeks.
- Prior or concurrent malignancy whose natural history or treatment has the potential to interfere with the safety or efficacy assessment of the study treatment.
- Contraindication to MRI, CT or PET
- Unstable cardiac conditions (congestive heart failure, angina pectoris, myocardial infarction within one year before enrolment, uncontrolled hypertension, clinically significant arrhythmias)
- Psychological, familial, sociological, or geographical conditions could potentially hamper compliance with the study protocol and follow-up schedule.
- Known hypersensitivity to the active substance or to any excipients.

## BILAN D'INCLUSION

### Dans les 4 semaines avant l'inclusion/randomisation :

- Antécédents médicaux et conditions médicales actuelles
- Informations sur la maladie primitive (date du diagnostic initial, histologie, aspects moléculaires et traitements antérieurs)
- Données démographiques (âge, sexe)
- Outil de dépistage de l'évaluation gériatrique G8 ( $\geq 70$  ans)
- Examen clinique, PS-ECOG
- Signes vitaux : pression artérielle, pouls, poids, taille et température corporelle
- Enregistrement de la dose de corticostéroïdes
- Médicaments concomitants
- ECG à 12 dérivations
- FEVG (*échographique ou scintigraphique*)
- Biologie locale : hématologie, biochimie, INR
- Questionnaires de qualité de vie : QLQ-C30 (v3), BN-20, IL46
- Echelle NANO
- SSTR-PET (*obligatoire*)
- Bloc archivé FFPE (*optionnel*)

### Dans les 2 semaines avant l'inclusion/randomisation :

- IRM cérébrale
- Scanner thoraco-abdominopelvien (*si cliniquement indiqué*)

### Dans les 3 jours avant l'inclusion/randomisation :

- Test de grossesse sérique ou urinaire (*si applicable*)

### Prescriptions médicales à fournir

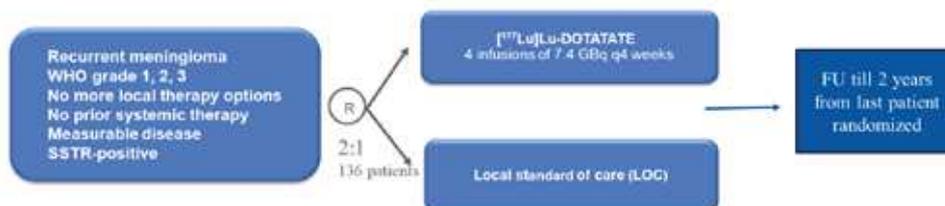
- FEVG (*échographique ou scintigraphique*)
- IRM cérébrale
- SSTR-PET
- Scanner thoraco-abdominopelvien (*si cliniquement indiqué*)

## TRAITEMENT

**Bras A (experimental) :** [<sup>177</sup>Lu]Lu-DOTATATE en perfusion IV de 7.4 GBq toutes les 4 semaines +/- 1 semaine (4 cycles)

**Bras B (standard) :** au de l'choix investigateur

- Hydroxycarbamide : 15 à 30 mg/kg x 1/jour PO
- Bevacizumab : 7,5 ou 15 mg/kg/3 semaines IV
- Sunitinib : 50 mg x 1/jour 4 semaines/6 PO
- Octreotide 20 mg (3 cycles) puis 30 mg/4 semaines IM
- Everolimus : 10 mg x 1/jour PO
- Soins Oncologiques de Support



**Randomisation :** 2:1

**Traitement à débiter :** dans les 3 semaines après la randomisation.

**Tracabilité du recueil du consentement**

*A renseigner dans CR médical d'annonce si le patient signe le jour même  
OU  
Dans l'onglet « Infos complément » du formulaire de Recherche Clinique sur HM le jour du screening.*

**Données nécessaires à l'inclusion**

*A renseigner dans la partie « Données nécessaires à l'inclusion » du formulaire de Recherche Clinique sur HM*

Classification histologique (WHO CNS5)       Grade 1       Grade 2-3

Age       ≤ 60 ans       > 60 ans

Taille de la tumeur       ≤ 43 mm       > 43 mm

Choix de traitement si bras B :

- Hydroxycarbamide
- Bevacizumab
- Sunitimib
- Octreotide
- Everolimus
- Soins Oncologiques de Support

Statut ménopausique : \_\_\_\_\_

Dose de corticoïdes : \_\_\_\_\_

**Validation des critères d'éligibilité par l'investigateur**

*A renseigner dans la partie « validation des critères d'inclusion » du formulaire de Recherche Clinique sur HM*