E.7 : Essai POLO

Promoteur Hospices Civils de Lyon	**RCP** : Neuro-oncologie **Organe et situation** : Oligodendroliome/Adjuvant	**Identité patient**
Investigateur principal Elodie Vauléon (30.04) **IARC** Ina Dembélé (44.11)	**POLO-Oligodendrogliome**/Phase III	*Coller ici l'étiquette du patient*
	A randomized trial of delayed radiotherapy in patients with 1p/19q codeleted low-grade oligodendrogliomas requiring active treatment other than surgery	
	Critère principal : Survie globale sans détérioration cognitive	

CRITÈRES D'INCLUSION

- Tumor is co-deleted for 1p and 19q based and IDH-mutant (IDH1 or IDH2) according to local diagnosis
- Histological confirmation of low-grade oligodendroglioma by central pathological review according to WHO 2016 classification
- Age ≥ 18 years
- Patients with one or several prior surgical procedure for a low-grade oligodendroglioma and who undergo a resurgery are eligible if they have not received prior radiotheray or chemotherapy and if the last histological diagnosis is a low-grade oligodendroglioma
- Patients who undergo an initial follow-up after surgery or re-surgery are eligible if there is no evidence of anaplastic transformation on MRI (no new contrast enhancement, no obvious modification of the growth rate)
- Patients requiring an oncological treatment other than surgery because of one or more of the following characteristics:

*Progressive disease defined as documented growth prior to inclusion
*Symptomatic disease defined as the presence of neurological or cognitive symptoms or refractory seizures defined as having both persistent seizures interfering with everyday life activities other than driving a car and three lines of anti-epileptic drug regimen had not worked, including at least one combination regimen.
*Age ≥ 40 and any surgical therapy
*Age < 40 with prior and subtotal resection or biopsy (i.e., anything less than gross total resection)

- Willing and able to complete neurocognitive examination and the QOL
- Karnofsky performance status ≥ 60
- The following laboratory values obtained ≤ 21 days prior to registration:
    - Absolute neutrophil count (ANC) ≥1500 /mm3
    - Platelet count ≥100,000 / mm3
    - Hemoglobin > 9.0 g/dL
    - Total bilirubin ≤ 1.5 x upper limit of normal (ULN)
    - SGOT (AST) ≤ 3 x ULN
- Negative serum or urine pregnancy test done ≤ 7 days prior to registration, for women of childbearing potential only.
- Provide informed written consent

CRITÈRES D'EXCLUSION

- Pregnant and nursing women
- Men or women of childbearing potential who are unwilling to employ adequate contraception for up to 6 months following the completion of PCV.
- Received any prior radiation therapy or chemotherapy for any CNS neoplasm.
- Co-morbid systemic illnesses or other severe concurrent disease which would make the patient inappropriate for entry into this study or interfere significantly with the proper assessment of safety and toxicity of the prescribed regimens.
- Concomitant serious immunocompromised status (other than that related to concomitant steroids).
- Uncontrolled intercurrent illness or psychiatric illness/social situations that would limit compliance with study requirements.
- Receiving any other investigational agent which would be considered as a treatment for the primary neoplasm.
- Other active malignancy within 5 years of registration. Exceptions: Non-melanotic skin cancer or carcinoma-in-situ of the cervix.
- Contra-indication to CCNU: hypersensitivity to CCNU, wheat allergy, association to yellow fever vaccin
- Contra-indication to Procarbazine: severe renal failure, severe hepatic failure, hypersensitivity to procarbazine, association to yellow fever vaccin
- Contra-indication to Vincristine: hypersensitivity to vincristine, neuromuscular disorder (for example demyelinating Charcot-Mary Tooth neuropathy), severe renal failure, severe hepatic failure.
- Not depending from the french system of health assurance
- Any vulnerable person: minor, person under guardianship or curatorship, person in emergency situation and unable to give their consent

BILAN D'INCLUSION

Dans les 28 jours avant le début du traitement :

1. Consentement éclairé (≥ 48 heures entre présentation et signature)
2. Examen clinique + KPS
3. IRM cérébrale
4. Biologie : NFS-plaquettes, urée, créatinine, biologie hépatique
5. Examen neuropsychologique (durée : 1h30)
6. Bloc tumoral (confirmation du diagnostic d'oligodendrogliome de bas grade, résultat centralisé pour inclusion sous 14 jours ouvrés)
7. Prélèvement sanguin (consentement spécifique)

Prescriptions médicales à fournir

☐ Bons d'imagerie

TRAITEMENT

Bras A : RT + 6 cycles de PCV

- Radiothérapie 50,4 Gy en 28 fractions de 1,8 Gy par IMRT ou protonthérapie
- PCV (1 cycle = 6 semaines)
  - CCNU 90 mg/m² (1er cycle) puis 110 mg/m² (Cycles 2 à 6 sauf toxicité) PO J1
  - Vincristine 1,4 mg/m² (Maximum 2 mg) IV J8 et J9
  - Procarbazine 60 mg/m² PO J8 à J21

Bras B : 6 cycles de PCV (1 cycle = 6 semaines) :

- CCNU 90 mg/m² (1er cycle) puis 110 mg/m² (Cycles 2 à 6 sauf toxicité) PO J1
- Vincristine 1,4 mg/m² (Maximum 2 mg) IV J8 et J9
- Procarbazine 60 mg/m² PO J8 à J21

Traitement à débuter : Dans les 6 semaines après la date de randomisation

Validation des critères d'éligibilité par l'investigateur

A tracer sur le formulaire de Recherche Clinique présent dans HM