Essai Clinique

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Titre	A Clinical and Molecular Risk-Directed Therapy for Newly Diagnosed Medulloblastoma
Protocole ID	SJMB12
ClinicalTrials.gov ID	NCT01878617
Type(s) de cancer	Pédiatrique divers
Phase	Phase II
Institution	CENTRE HOSPITALIER UNIVERSITAIRE SAINTE-JUSTINE
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Statut	Actif en recrutement
But étude	Historically, medulloblastoma treatment has been determined by the amount of leftover disease present after surgery, also known as clinical risk (standard vs. high risk). Recent studies have shown that medulloblastoma is made up of distinct molecular subgroups which respond differently to treatment. This suggests that clinical risk alone is not adequate to identify actual risk of recurrence. In order to address this, we will stratify medulloblastoma treatment in this phase II clinical trial based on both clinical risk (low, standard, intermediate, or high risk) and molecular subtype (WNT, SHH, or Non-WNT Non-SHH). This stratified clinical and molecular treatment approach will be used to evaluate the following: • To find out if participants with low-risk WNT tumors can be treated with a lower dose of radiation to the brain and spine, and a lower dose of the chemotherapy drug cyclophosphamide while still achieving the same survival rate as past St. Jude studies with fewer side effects. • To find out if adding targeted chemotherapy after standard chemotherapy will benefit participants with SHH positive tumors. • To find out if adding new chemotherapy agents to the standard chemotherapy will improve the outcome for intermediate and high risk Non-WNT Non-SHH tumors. • To define the cure rate for standard risk Non-WNT Non-SHH tumors treated with reduced dose cyclophosphamide and compare this to participants from the past St. Jude study. All participants on this study will have surgery to remove as much of the primary tumor as safely possible, radiation therapy, and chemotherapy. The amount of radiation therapy and type of chemotherapy received will be determined by the participant's treatment stratum. Treatment stratum assignment will be based on the tumor's molecular subgroup assignment and clinical risk. The participant will be assigned to one of three medulloblastoma subgroups determined by analysis of the tumor tissue for tumor biomarkers: • WNT (Strata W): positive for WNT biomarkers • SHH (Strata S): positive for SHH biomarkers • Non-WNT Non-SHH, Failed, or Indeterminate (Strata N): negative for WNT and SHH biomarkers or results are indeterminable Participants will then be assigned to a clinical risk group (low, standard, intermediate, or high) based on assessment of: • How much tumor is left after surgery • If the cancer has spread to other sites outside the brain [i.e., to the spinal cord or within the fluid surrounding the spinal cord, called cerebrospinal fluid (CSF)] • The appearance of the tumor cells under the microscope • Whether or not there are chromosomal abnormalities in the tumor, and if present, what type (also called cytogenetics analysis)

Critères d'éligibilité	• Medulloblastoma or medulloblastoma variants including posterior fossa PNET as documented by an institutional pathologist. • Age greater than or equal to 3 years and less than 22 years of age at the time of diagnosis. • No previous radiotherapy, chemotherapy or other brain tumor directed therapy other than corticosteroid therapy and surgery. • Patients must begin treatment as outlined in the protocol within 36 days of definitive surgery (day of surgery is day 0; definitive surgery includes second surgeries to resect residual tumor). • Adequate performance status: children < 10-Lansky Score ≥ 30; children ≥ 10-Karnofsky ≥ 30 (except for posterior fossa syndrome). • Females of child-bearing potential cannot be pregnant or breast-feeding. Female participants > 10 years of age or post-menarche must have a negative serum or urine pregnancy test prior to enrollment. • Biological parent(s) of participant (child) enrolling on this protocol. These parents will be assigned to cohort P. The exclusion criteria below do not apply to this cohort. Participants in the Stratum S maintenance chemotherapy portion of the study must meet the criteria below prior to start of vismodegib therapy: • Must be > 10 years at the time of start of maintenance • Must be skeletally mature defined as females with a bone age ≥ 15 years and males with a bone age ≥ 17 years • Must agree to effective contraception if participant has reproductive potential Participants in the exercise intervention portion of the study must meet all criteria below: • Must be > 5 years at the time of enrollment • Must have no congenital heart disease • Must be capable of performing the exercise intervention at the time of baseline assessment as determined by the treating physician. Participants in the cognitive remediation intervention portion of the study must meet all criteria below: • Completed protocol-directed radiation therapy • ≥5 years at the time of remediation intervention consent • English as primary language and training aide who speaks English available to participate in required sessions • No significant cognitive impairment operationalized as either an IQ < 70 for children with St. Jude SJMB12 study baseline testing or based on clinician judgment baseline IQ missing • No major sensory or motor impairment that would preclude valid cognitive testing (e.g., unresolved posterior fossa syndrome, blindness, poorly controlled seizures/photosensitive epilepsy, psychosis) or a major psychological condition that would preclude completion of the intervention (e.g., significant oppositionality, autism spectrum disorder, severe anxiety or depressive symptoms)
Critères d'exclusion	• CNS embryonal tumor other than medulloblastoma or PNET in the posterior fossa, for example, patients with diagnosis of Atypical Teratoid / Rhabdoid Tumor (ATRT), supratentorial PNET, pineoblastoma, ependymoblastoma, ETANTR are excluded. • Research participants with other clinically significant medical disorders that could compromise their ability to tolerate protocol therapy or would interfere with the study procedures or results history.