Essai Clinique

Généré le 06 mai 2024 à partir de

Titre	Treatment of Newly Diagnosed Diffuse Anaplastic Wilms Tumors (DAWT) and Relapsed Favorable Histology Wilms Tumors (FHWT)
Protocole ID	AREN1921
ClinicalTrials.gov ID	NCT04322318
Type(s) de cancer	Pédiatrique divers
Phase	Phase II
Type étude	Clinique
Institution	CHU DE QUEBEC – UNIVERSITE LAVAL CHUL ET CENTRE MERE-ENFANT SOLEIL 2705 boulevard Laurier, Québec, QC, G1V 4G2
Ville	
Investigateur principal	Dr Bruno Michon
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Statut	Actif en recrutement
But étude	This phase II trial studies how well combination chemotherapy works in treating patients with newly diagnosed stage II-IV diffuse anaplastic Wilms tumors (DAWT) or favorable histology Wilms tumors (FHWT) that have come back (relapsed). Drugs used in chemotherapy regimens such as UH-3 (vincristine, doxorubicin, cyclophosphamide, carboplatin, etoposide, and irinotecan) and ICE/Cyclo/Topo (ifosfamide, carboplatin, etoposide, cyclophosphamide, and topotecan) work in different ways to stop the growth of tumor cells, either by killing the cells, by stopping them from dividing, or by stopping them from spreading. This trial may help doctors find out what effects, good and/or bad, regimen UH-3 has on patients with newly diagnosed DAWT and standard risk relapsed FHWT (those treated with only 2 drugs for the initial WT) and regimen ICE/Cyclo/Topo has on patients with high and very high risk relapsed FHWT (those treated with 3 or more drugs for the initial WT).

Critères d'éligibilité	• Patients with newly diagnosed stages 2 - 4 diffuse anaplastic Wilms tumor must be enrolled on AREN03B2 and have risk assignment or final pathology classification (if at delayed nephrectomy) results available prior to enrollment on AREN1921. Enrollment on AREN03B2 is not applicable for patients with relapsed favorable histology Wilms tumor
	• Patients with the following diagnoses are eligible for this study:
	  • Newly diagnosed stages 2 - 4 diffuse anaplastic Wilms tumor as confirmed by central review
	  • Favorable histology Wilms tumor at first relapse. Relapsed FHWT patients must have previously achieved remission for their initial FHWT diagnosis to be eligible for this study. The relapse risk groups are defined as follows, regardless of radiation therapy:
	  • Standard-Risk relapse: Patients who received two chemotherapy agents for frontline therapy; primarily actinomycin D and vincristine
	  • High-Risk relapse: Patients who received three chemotherapy agents for frontline therapy; primarily vincristine, actinomycin D and doxorubicin or vincristine, actinomycin D and irinotecan
	  • Very High-Risk relapse: Patients who received four or more chemotherapy agents as part of initial therapy; primarily Regimen M or its variations
	• Patients with newly diagnosed DAWT must have had histologic verification of the malignancy. For relapsed FHWT patients, biopsy to prove recurrence is encouraged, but not required
	  • Note: for relapsed FHWT patients, an institutional pathology report confirming favorable histology Wilms tumor (from relapse, if available, or from original diagnosis) must be available for upload prior to initiation of protocol therapy
	• Patients with newly diagnosed stages 2 - 4 diffuse anaplastic Wilms tumor must be enrolled on AREN1921 within 2 weeks of the first tumor-directed surgery or biopsy procedure

(surgery/biopsy is day 0), except for patients who received prior therapy for presumed favorable histology Wilms tumor, later confirmed to have diffuse anaplastic Wilms tumor at subsequent review
- Patients with newly diagnosed DAWT who undergo upfront nephrectomy must have at least 1 lymph node sampled prior to study enrollment
- Patients must have a performance status corresponding to Eastern Cooperative Oncology Group (ECOG) scores of 0, 1 or 2. Use Karnofsky for patients > 16 years of age and Lansky for patients =< 16 years of age
- Patients must have a life expectancy of >= 8 weeks
- Diffuse Anaplastic Wilms Tumor: Patients with diffuse anaplastic histology must have had no prior systemic therapy, except in the following situations:
    - Patients with diffuse anaplastic Wilms tumor who received no more than 12 weeks of pre nephrectomy chemotherapy for what was originally presumed to be favorable histology Wilms tumor, subsequently confirmed to be diffuse anaplastic Wilms tumor at delayed nephrectomy.
    - Patients with diffuse anaplastic Wilms tumor who received no more than 6 weeks of chemotherapy following upfront nephrectomy or biopsy for presumed favorable histology Wilms tumor based on institutional review, but subsequently corrected to diffuse anaplastic Wilms tumor based on the AREN03B2 initial risk assignment results.
    - Treatment consisting of vincristine/doxorubicin/ cyclophosphamide initiated on an emergent basis and within allowed timing as described
    - Patients who received prior therapy for presumed favorable histology Wilms tumor, later identified to have diffuse anaplastic Wilms tumor as per above, must begin study treatment starting at cycle 3 (week 7) of regimen UH 3. For treatment details specific to this group of patients. Patients who received emergency radiation to preserve organ function are eligible as noted
- Relapsed Favorable Histology Wilms Tumor: Patients must not have received prior chemotherapy for their relapsed favorable histology Wilms tumor diagnosis. In addition, patients must have fully recovered from the acute toxic effects of all prior chemotherapy, immunotherapy, or radiotherapy prior to entering this study
    - Myelosuppressive chemotherapy: Must not have received within 2 weeks of entry onto this study
    - Radiation therapy (RT): >= 2 weeks (wks) must have elapsed for local palliative RT (small port); >= 6 months must have elapsed if prior craniospinal RT or if >= 50% radiation of pelvis; >= 6 wks must have elapsed if other substantial BM radiation. Patients with relapsed favorable histology Wilms tumor who received emergency radiation to preserve organ function are eligible and do not need to washout with the above criteria
- Patients may not be receiving any other investigational agents (within 4 weeks prior to study enrollment)
- Peripheral absolute neutrophil count (ANC) >= 750/uL (performed within 7 days prior to enrollment)
- Platelet count >= 75,000/uL (transfusion independent) (performed within 7 days prior to enrollment)
- Hemoglobin >= 8.0 g/dL (may receive red blood cell [RBC] transfusions) (performed within 7 days prior to enrollment)
- Patients with high-risk or very high-risk relapsed FHWT who will be treated with Regimen ICE/Cyclo/Topo, must have renal function assessed by creatinine clearance or radioisotope glomerular filtration rate (GFR) and meet the following requirement:
    - Creatinine clearance or radioisotope GFR >= 60 mL/min/1.73 m^2 (performed within 7 days prior to enrollment)
- Patients diagnosed with stage 2-4 DAWT or standard risk relapsed FHWT, who will be treated with Regimen UH 3, may either obtain a creatinine clearance, radioisotope GFR (meeting the above criteria of GFR >= 60 mL/min/1.73 m^2), or an adequate serum creatinine as per the following table:
    - Age: Maximum Serum Creatinine (mg/dL)
    - 1 month to < 6 months: 0.4 (male and female)
    - 6 months to < 1 year: 0.5 (male and female)
    - 1 to < 2 years: 0.6 (male and female)
    - 2 to < 6 years: 0.8 (male and female)
    - 6 to < 10 years: 1 (male and female)
    - 10 to < 13 years: 1.2 (male and female)
    - 13 to < 16 years: 1.5 (male), 1.4 (female)
    - >= 16 years: 1.7 (male), 1.4 (female)
- Total bilirubin =< 1.5 x upper limit of normal (ULN) for age or direct bilirubin =< ULN for patients whose total bilirubin > 1.5 x ULN (performed within 7 days prior to enrollment)
- Serum glutamic-oxaloacetic transaminase (SGOT) (aspartate aminotransferase [AST]) or serum glutamate pyruvate transaminase (SGPT) (alanine aminotransferase [ALT]) < 2.5 x upper limit of normal (ULN) for age or =< 5 x ULN for patients with liver metastases (performed within 7 days prior to enrollment)
- Shortening fraction of >= 27% by echocardiogram, or ejection fraction of >= 50% by radionuclide angiogram (performed within 7 days prior to enrollment)

Critères d'exclusion	• Patients with a history of bilateral Wilms tumor (synchronous or metachronous)
	• Patients with any uncontrolled, intercurrent illness including, but not limited to, ongoing or active infection, or symptomatic congestive heart failure (defined as grade 2 or higher heart failure per Common Terminology Criteria for Adverse Events [CTCAE] version 5.0)
	• Relapsed FHWT patients who did not receive frontline chemotherapy (e.g., very low risk FHWT initially observed without chemotherapy) or received only one chemotherapy agent for frontline therapy
	• For patients with high-risk or very high-risk relapsed FHWT:
	  • Patients with renal tubular acidosis (RTA) as evidenced by serum bicarbonate < 16 mmol/L and serum phosphate =< 2 mg/dL (or < 0.8 mmol/L) without supplementation
	• For stages 2-4 DAWT and standard-risk relapsed FHWT patients:
	  • Chronic inflammatory bowel disease and/or bowel obstruction
	  • Concomitant use of St. John's wort, which cannot be stopped prior to the start of trial treatment
	• Female patients who are pregnant since fetal toxicities and teratogenic effects have been noted for several of the study drugs. A pregnancy test is required for female patients of childbearing potential
	• Lactating females who plan to breastfeed their infants
	• Sexually active patients of reproductive potential who have not agreed to use an effective contraceptive method for the duration of their study participation