

ACNS 1422

Satellite Educational Training Module

JANUARY 2023

Presented to: Satellite Clinic Healthcare Providers
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ACNS 1422

- A Phase 2 Study of Reduced Therapy for Newly Diagnosed Average-Risk WNT-Driven Medulloblastoma Patients

Background

- Medulloblastoma is the most common malignant brain tumor in children and accounts for approximately 20 % of all brain tumors in children and adolescents under the age of 18 years
- Current therapy includes maximal surgical resection, craniospinal radiation with a boost to the tumor bed, and adjuvant chemotherapy
- Using these modalities, the survival is approximately 80 % for patients with standard-risk disease (defined as residual tumor less than 1.5 cm² and no evidence of disease in the head, spine or cerebrospinal fluid) and 65 % for those with high-risk disease
- More recently it is now established that medulloblastoma comprises at least four molecularly distinct disease subgroups:
 - WNT/Wingless (WNT)
 - Sonic Hedgehog (SHH) with wildtype p53 or with p53 mutation,
 - Group 3
 - Group 4

Background (cont.)

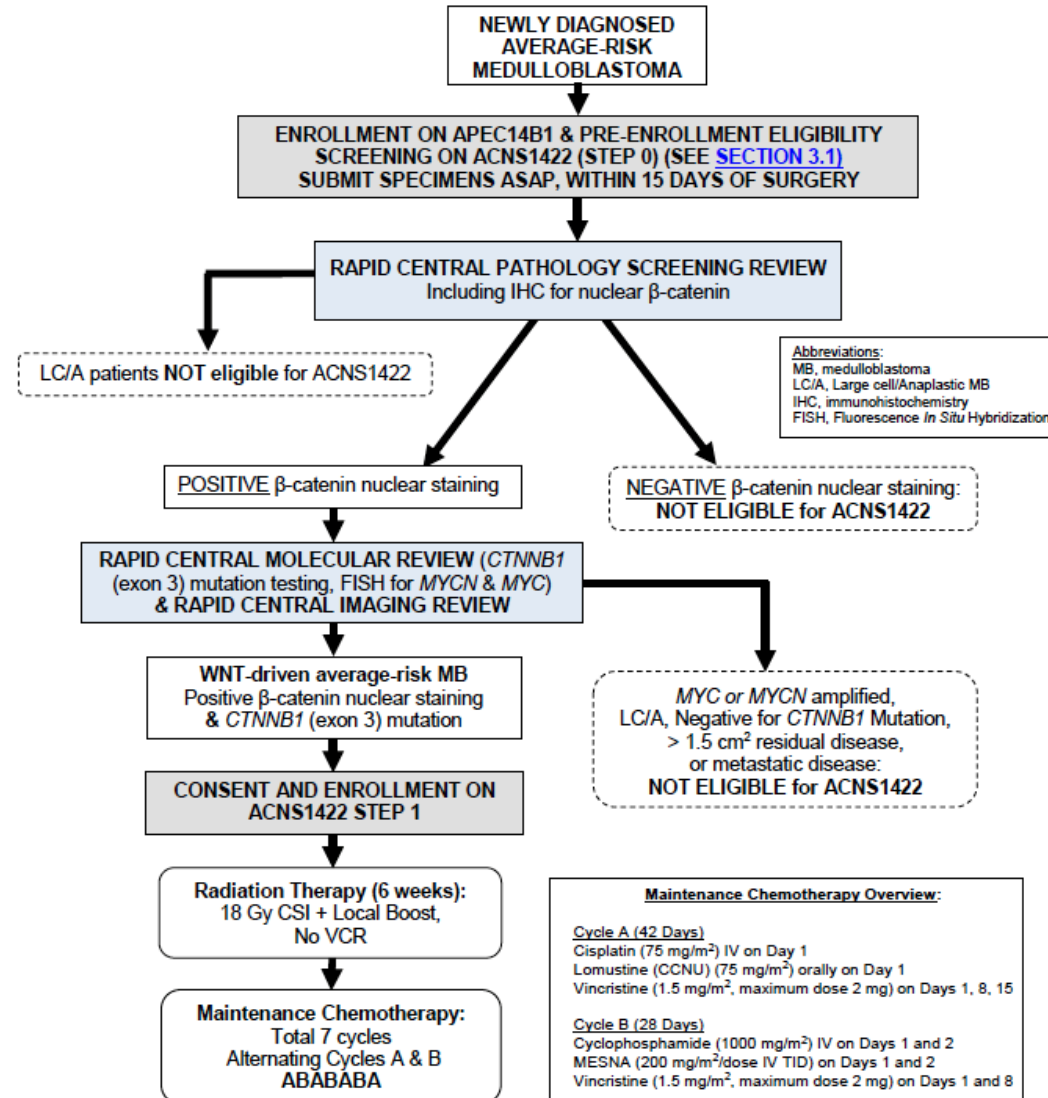
- WNT-subgroup medulloblastoma accounts for approximately 10% of medulloblastoma patients, generally occurs in older patients (median age 10 years), is rarely metastatic
- These tumors have been demonstrated to have excellent survival using contemporary therapy, with a 5-year event-free survival (EFS) of over 90%
- There is a suggestion therefore that this molecular subtype of medulloblastoma may benefit from receiving less craniospinal radiation without compromising outcome.

Study Goal

- This phase 2 study will investigate the feasibility of reducing craniospinal radiation (18 Gy) with a limited target volume boost to the tumor bed (to a total of 54 Gy), in combination with a reduced chemotherapy approach, to assess whether the excellent survival outcome for patients with WNT-driven medulloblastoma can be maintained while simultaneously attempting to reduce treatment-related neurocognitive, social, and behavioral sequelae.

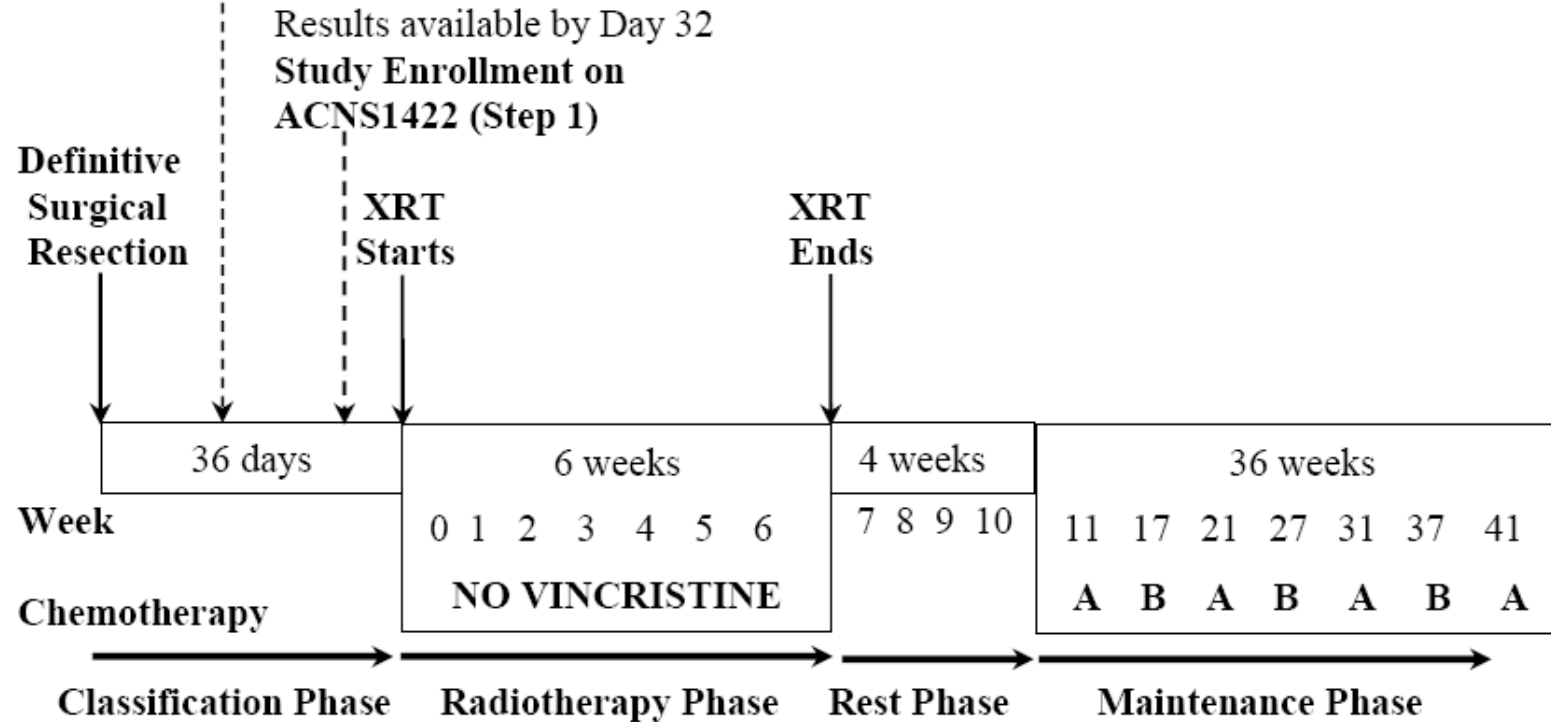
Study Design

EXPERIMENTAL DESIGN SCHEMA



Treatment Plan Overview

Specimens submitted for Central Review by **Day 15** on APEC14B1 and ACNS1422 Pre-Enrollment Eligibility Screening (Step 0). See [Section 3.1](#).
 Submit Imaging on APEC14B1 if tumor is positive for β -Catenin by IHC. See [Section 3.1.4](#).



Radiotherapy Phase

- This 6 week phase will take place in the treating radiation oncology centre
- Satellite centres may see patients in between radiation appointments for supportive care (management of nausea and vomiting, hydration, nutrition) or potentially blood product support (confirm hemoglobin and platelet targets with referring centre)
- Similarly, in the Rest Phase, patients may be seen in satellite for supportive care prior to initiating the Maintenance Phase

Maintenance Phase

- MUCH different intensity than Maintenance Therapy in Acute Lymphoblastic Leukemia and Lymphoblastic Lymphoma
- Two Main Alternating Cycles
- Maintenance Chemotherapy Overview:
 - Cycle A (42 Days)
 - Cisplatin (75 mg/m²) IV on Day 1
 - Lomustine (CCNU) (75 mg/m²) orally on Day 1
 - Vincristine (1.5 mg/m², maximum dose 2 mg) on Days 1, 8*, 15*
 - Cycle B (28 Days)
 - Cyclophosphamide (1000 mg/m²) IV on Days 1 and 2
 - MESNA (200 mg/m²/dose IV TID) on Days 1 and 2
 - Vincristine (1.5 mg/m², maximum dose 2 mg) on Days 1 and 8*
- * Therapy that could POTENTIALLY be delivered in Satellite

What do I need to know at the satellite?

- On study patients require a variety of imaging investigation and hearing testing that will be the responsibility of the referring centre
- While the majority of required blood work is collected on 'Day 1' of cycles, there are study required CBCs on Days 8 and 15
- The use of myeloid growth factors (filgrastim, pegfilgrastim) is allowed by note REQUIRED: confirm use with referring centre
- Reasons for satellite visits will include:
 - Chemotherapy (primarily vincristine)
 - Blood Work
 - Transfusion Support
 - Electrolyte monitoring (particularly post cisplatin)
 - Fever assessment and other supportive care

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