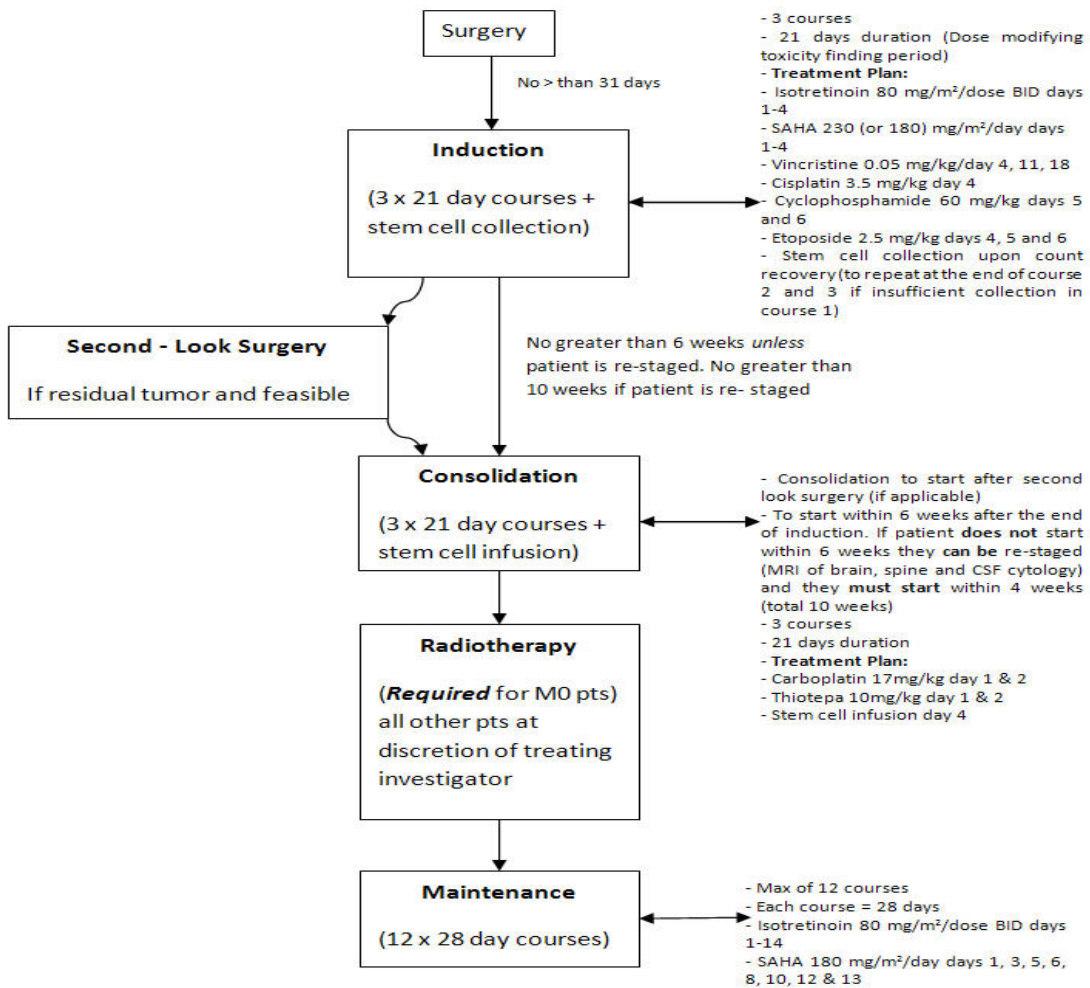


PBTC 026: Protocol Abstract and Schema

Description

This is a multicenter, feasibility trial of SAHA combined with isotretinoin and chemotherapy to examine the feasibility of the drug regimen and to describe the toxicity of this combination in children between 2 months and less than 4 years of age. Treatment will comprise Induction therapy for 3 courses, Consolidation therapy for 3 courses, Radiotherapy (**required** for M0 medulloblastoma patients, all other patients at the discretion of the investigator) and maintenance therapy for 12 courses.

Schema



OBJECTIVES

Primary Objectives

1. To investigate the feasibility of administering SAHA and Isotretinoin for three days prior and concomitant with cisplatin based chemotherapy over three courses of induction chemotherapy.
2. To describe the toxicity of administering SAHA and Isotretinoin for three days prior and concomitant with cisplatin based chemotherapy over three courses of induction chemotherapy.

Secondary Objectives

1. To estimate the preliminary response rate of this approach in patients with measurable residual disease (primary site and/or metastatic sites).
2. To estimate disease specific progression-free and overall survival, in the context of a feasibility study.
3. To investigate prognostic values of histopathological classification and biological markers in the context of a feasibility study.

PATIENT SELECTION

Eligibility assessment timelines

- Imaging studies related to tumor assessment must be performed within 31 days prior to treatment initiation.
- All laboratory evaluations necessary to establish eligibility for study entry must be done within two (2) weeks prior to registration.

All patients must meet the following inclusion and exclusion criteria. **NO EXCEPTIONS WILL BE GIVEN.**

Inclusion Criteria

Age

Patients must be at least 2 months of age and less than 48 months (< 4 yrs) on the date of consent.

Tumor

Patients must have a histologically confirmed newly-diagnosed medulloblastoma excepting localized (M0) desmoplastic medulloblastoma; or supratentorial PNET including pineoblastomas.

Available Pre-Trial Tumor Material

Patient must have adequate pre-trial tumor material available for use in the biology studies (see section 7.1.1).

Performance status

Lansky Performance Score (LPS for ≤ 16 years of age) ≥ 30 assessed within two weeks prior to registration

Prior/Concurrent Therapy

Prior Radiation Therapy: No prior radiation therapy.

Organ Function: Documented within 14 days of registration and within 7 days of the start of treatment.

Bone Marrow:

- Absolute neutrophil count(ANC) $\geq 1000/\mu\text{l}$ (unsupported)
- Platelets $\geq 100,000/\mu\text{l}$ (unsupported)
- Hemoglobin $\geq 8 \text{ g/dL}$ (may be supported)

Renal: Serum creatinine ≤ 1.5 times upper limit of institutional normal for age or GFR $\geq 70 \text{ ml/min/1.73m}^2$.

Hepatic:

- Bilirubin < 1.5 times upper limit of normal for age
- SGPT (ALT) ≤ 1.5 times institutional upper limit of normal for age

Informed Consent

Signed informed consent according to institutional guidelines must be obtained.

Exclusion Criteria

Tumor

Patients with diagnosis of Atypical Teratoid / Rhabdoid Tumor (ATRT) and Desmoplastic M0 Medulloblastoma will be excluded from the study.

Concurrent Illness

Patients with any clinically significant unrelated systemic illness (serious infections or significant cardiac, pulmonary, hepatic or other organ dysfunction), that would compromise the patient's ability to tolerate protocol therapy or would likely interfere with the study procedures or results are excluded.

Prior/ Concurrent Therapy

- Patients receiving any other anticancer or investigational drug therapy are excluded.
- Patients having taken valproic acid within 2 weeks prior to initiation of treatment are excluded.

Inability to Participate

Patients with inability to return for follow-up visits or obtain follow-up studies required to assess toxicity to therapy.

Other

- Patients unable to begin chemotherapy within 31 days of definitive surgery are excluded.
- Patients with a parabens allergy.

Criteria to Start Therapy

Imaging Studies

Cranial MRI (with and without gadolinium) must be done pre-operatively. Post-operatively, Cranial MRI (with and without gadolinium) must be done, preferably within 48 hours of surgery. Entire spinal MRI must be obtained either pre-operatively (with gadolinium) or post-operatively (at least 2 weeks following surgery) prior to initiation of treatment (with and without gadolinium).

Laboratory Evaluations

Laboratory values (see section 4.1.6) must be no older than seven (7) days at the start of therapy. Laboratory tests need not be repeated if therapy starts within seven (7) days of obtaining labs to assess eligibility. In the event that a patient's clinical condition worsens, laboratory evaluations should be repeated within 48 hours prior to initiation of treatment. If a post-registration lab value is outside the limits, it must be rechecked prior to the start of therapy. If recheck is outside the limits of eligibility, the patient may not receive protocol therapy and will be considered off study.

Starting Treatment

Chemotherapy must begin within 31 days of definitive surgery.