COG-ANBL00B1: Neuroblastoma Biology Studies

FAST FACTS
Eligibility Reviewed and Verified By
_____ MD/DO Date_____
_____ RN Date_____
Consent Version Dated_____

PATIENT ELIGIBILITY:

Important note: The eligibility criteria listed below are interpreted literally and cannot be waived (per COG policy posted 5/11/01). All clinical and laboratory data required for determining eligibility of a patient enrolled on this trial must be available in the patient's medical/research record which will serve as the source document for verification at the time of audit.

___1. A **provisional (preliminary) determination** of the International Neuroblastoma Staging System (INSS) stage MUST be reported at the time of enrollment, and definitive INSS stage must be reported within 3 weeks following diagnosis. The date of diagnosis is defined as the date of the surgical biopsy or other definitive diagnostic procedure. **Every effort should be made to report definitive risk group factors (age, INSS stage, degree of resection, whether the patient is symptomatic) within 2 weeks of diagnosis, and these risk group factors MUST be reported within 3 weeks following diagnosis**.

___2. Patient enrollment must be completed within 21 days of the definitive diagnostic procedure.

___3. Patients must be enrolled on the ANBL00B1 protocol before entering a front-line COG therapeutic study. In case emergency therapy is required (further explained in section 4.2.2), enrollment onto ANBL00B1 should occur concurrently with enrollment onto the appropriate clinical trial.

___4. All newly diagnosed patients with suspected neuroblastoma, suspected ganglioneuroblastoma, or suspected ganglioneuroma/maturing subtype seen at COG institutions are eligible for this study.

___5. Patients may not have received chemotherapy prior to enrollment on ANBL00B1 and procurement of study-related tissues with the following exception:

- Patients that in the opinion of the treating physician are too ill to undergo pre-treatment tissue biopsy and require EMERGENT chemotherapy may be enrolled on ANBL00B1. Please see the appropriate open COG therapeutic trial for further study-specific eligibility regarding EMERGENT therapy. Documentation of the emergent nature of therapy initiation is required. See Section 4.2.4 for required specimens in such cases.

___6. Specimens required for eligibility:
It is required that a good faith effort (*documented by specimen tracking*) be made to submit a neuroblastoma sample (tumor, metastasis, and/or tumor-involved bone marrow) of sufficient quality for *MYCN* analysis in the Neuroblastoma Reference Laboratory in order for any newly diagnosed patient to be enrolled on ANBL00B1. This should be obtained prior to initiation of therapy.

___7. Exceptions

- In rare cases, patients may be deemed too ill to undergo pre-treatment tissue biopsy and require EMERGENT therapy. The following eligibility guidelines apply to these cases:
  For presumed INSS stage 4S patients: Efforts to submit tumor tissue (e.g., primary tumor, skin nodule, or metastatic site) within 96 hours of EMERGENT therapy initiation should be made. However, if the child is deemed too unstable for such a procedure they may still be enrolled as long as pre-treatment peripheral blood and serum have been submitted as described in Sections 5.1.3 and 5.1.4.
  For all other INSS stages: Tumor tissue should be obtained as soon as possible within 96 hours of EMERGENT therapy initiation. Patients without tumor tissues submitted within this time-frame are not eligible for enrollment.
  Note: It may not be possible to obtain all necessary tumor biomarkers for therapy stratification in such cases. If a patient enrolled on ANBL00B1 undergoes an *additional diagnostic procedure* within 96 hours of initiating therapy, additional tumor specimens may be submitted to obtain biomarkers used for risk classification. The decision to perform such procedures, and/or submit these specimens, is to be made by the managing clinicians and should reflect the clinical need to know the status of such biomarkers.
- Patients enrolled on ANBL1232 in Group A (either A1 or A2) will not have a tumor biopsy or resection upfront. Tumor tissue submission is therefore not required for these patients to enroll on ANBL00B1. A peripheral blood and serum sample is the only specimen required to be submitted for this group of patients. Should they undergo a biopsy or resection at a later date tumor can be submitted for biomarker testing at this time.

EXCLUSION CRITERIA:

___1. Patients with relapsed neuroblastoma who were not enrolled on ANBL00B1 at original diagnosis are **NOT eligible**. Samples should be submitted as part of the **ABTR04B1** protocol.

Summary of Tissue Submission Requirements and Requests.

SPECIMEN	SEND TO
Tumor ▪ Snap frozen tumor tissue (> 1 gm optimal, but send any available frozen samples, no upper limit). At least one specimen from the primary (if present) and metastatic areas (if present). ▪ If no snap-frozen tumor is available for *MYCN* analysis, see Section 5.1.2.2.	Neuroblastoma Reference Laboratory See Appendix I
Tumor Slides And Paraffin Blocks, submit within 2 weeks of initial surgical procedure ▪ Stained (2 H & E from each block) and unstained slides (10 slides from the most representative blocks) (not all blocks) for central pathology review must be submitted as outlined in Appendix I. ▪ We strongly encourage submission of paraffin blocks to BPC at the time of slide submission in case additional slides need to be cut and/or for banking. Label as described in Appendix I. ▪ Also see Section 5.1.2.2	See Appendix I
Blood ▪ Obtain 10 mL of peripheral blood for genetic studies and serum banking. Five mL is sufficient for infants and children < 10 kg. ▪ Divide sample equally (or draw directly into appropriate tubes) and place half in a lavender top tube (EDTA), and half in a serum separator tube (SST). See Appendix I for further labeling and shipping instructions. ▪ **These samples are required for enrollment of patients without submission of tumor samples as described in Section 4.2.4.** ▪ **NOTE:** If blood is not sent before therapy is initiated it is not suitable for serum banking. Please ensure the WBC count is at least 2,000/mm^3 to ensure sufficient DNA for banking.	See Appendix I
ADDITIONAL SPECIMENS FOR STAGE 4 AND SUSPECTED HIGH-RISK PATIENTS enrolling on ANBL0532 ▪ See Appendix II ▪ See 5.1.5, 5.1.6 and Appendix II	See Appendix II
Bone Marrow ▪ To submit tumor-involved bone marrow, collect a minimum of 2 ml of marrow in a syringe filled with preservative-free heparin (100 units/mL of bone marrow) and place in a green top (sodium heparin) tube, or lavender top (EDTA) tube.	See Appendix II