

COG- AHOD0831
A Non-Randomized Phase III Study of Response Adapted Therapy for the Treatment
of Children with Newly Diagnosed High Risk Hodgkin Lymphoma

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. Study enrollment must take place within five (5) calendar days of beginning protocol therapy. If enrollment takes place before starting therapy, the date protocol therapy is projected to start must be no later than *five (5)* calendar days after enrollment. Study enrollment must occur within 28 days of staging. If more than 28 days elapse before study enrollment, restaging of disease is required prior to study enrollment to confirm eligibility. Therefore, any imaging study that is > 28 days old must be repeated. All clinical and laboratory studies to determine eligibility must be performed within 7 days prior to enrollment unless otherwise indicated.
- ___2. Ages 0-21 years inclusive.
- ___3. Patients with newly diagnosed, pathologically confirmed classical Hodgkin lymphoma or nodular lymphocyte-predominant Hodgkin lymphoma meeting one of the following clinical stages are eligible:
 - All Stage III with B symptoms
 - All Stage IV with B symptoms

Only in the rare situation of equivocal imaging results below the diaphragm, surgical staging is to be used instead of clinical staging. See Appendix II for definitions of clinical staging, B symptoms and bulk disease.
- ___4. Patients may not have received any previous chemotherapy, biological modifiers such as monoclonal antibody therapy or radiation therapy. Patients may not have received corticosteroids within 28 days of enrollment on this protocol, except as specified in Section 4.2 for emergent treatment for respiratory distress or spinal cord compression, or for treatment of contrast agent allergy required for CT scan.
- ___5. Organ Function Requirements:
 - Adequate renal function defined as:
 - Creatinine clearance or radioisotope GFR ≥ 70 mL/min/1.73 m² or
 - A serum creatinine based on age/gender as follows:

Age	Maximum Serum Creatinine (mg/dL)	
	Male	Female
1 month to < 6 months	0.4	0.4
6 months to < 1 year	0.5	0.5
1 to < 2 years	0.6	0.6
2 to < 6 years	0.8	0.8
6 to < 10 years	1	1
10 to < 13 years	1.2	1.2
13 to < 16 years	1.5	1.4
≥ 16 years	1.7	1.4

The threshold creatinine values in this Table were derived from the Schwartz formula for estimating GFR (Schwartz et al. J. Peds, 106:522, 1985) utilizing child length and stature data published by the CDC.

- Adequate liver function defined as:
 - Total bilirubin ≤ 1.5 x upper limit of normal (ULN) for age, and

- SGOT (AST) or SGPT (ALT) < 2.5 x upper limit of normal (ULN) for age.
- Adequate cardiac function defined as:
 - Shortening fraction of $\geq 27\%$ by echocardiogram, or
 - Ejection fraction of $\geq 50\%$ by radionuclide angiogram (MUGA), unless due to large mediastinal mass from HL.
 - No pathologic prolongation of QTc interval on 12-lead ECG.
- Adequate pulmonary function defined as:
 - FEV1/FVC > 60% by pulmonary function test (PFT), unless due to large mediastinal mass from HL.
 - For children who are unable to cooperate for PFTs, the criteria are: no evidence of dyspnea at rest, no exercise intolerance, and a pulse oximetry > 92% on room air.

___6. **Optional Studies** - There are no optional biology studies included in this trial. However, enrollment on the companion biology study AHOD04B1 (or successor biology study), is encouraged. Please note that AHOD04B1 includes pre-therapy specimens.

EXCLUSION CRITERIA:

- ___1. Pregnancy and breast feeding Females who are pregnant or breast feeding are not eligible for this study since fetal toxicities and teratogenic effects have been noted for several of the study drugs.
- ___2. Female patients of childbearing potential are not eligible unless a negative pregnancy test result has been obtained.
- ___3. Males and females of reproductive potential are not eligible unless they have agreed to use an effective contraceptive method. This must be documented in the medical record.

REQUIRED OBSERVATIONS:

Required Clinical, Laboratory and Disease Evaluations

Obtain prior to start of phase unless otherwise indicated.

STUDIES TO BE OBTAINED

- History & Physical with documentation of sizes of all lymph nodes
- CBC/Differential, ESR, Electrolytes, BUN, Creatinine, AST or ALT, Bili
- Biopsy
- Bilateral bone marrow biopsy
- ECG
- ECHO or MUGA
- PFTs, DLCO if > 5 yrs
- CXR (PA, lateral)**
- CT: neck, chest, abdomen, pelvis**
- 18Fluorodeoxyglucose (FDG) Imaging** (FDG-PET)
- Pregnancy test †

Recommended:

- LH/FSH, estradiol or testosterone
 - Sperm analysis/banking
- † A negative pregnancy test is required prior to enrollment for females of childbearing potential only.
- ** See Section 15.3 for imaging central review requirements and Section 16.10 for quality assurance documentation that must be submitted prior to the start of RT. **NOTE: Imaging studies must also be submitted at relapse** (see Section 15.3).

TOXICITIES AND DOSAGE MODIFICATIONS:

See Section 5.0.

CENTRAL REVIEW OF IMAGING STUDIES:

Central review of images will be performed by QARC to confirm institutional reporting.

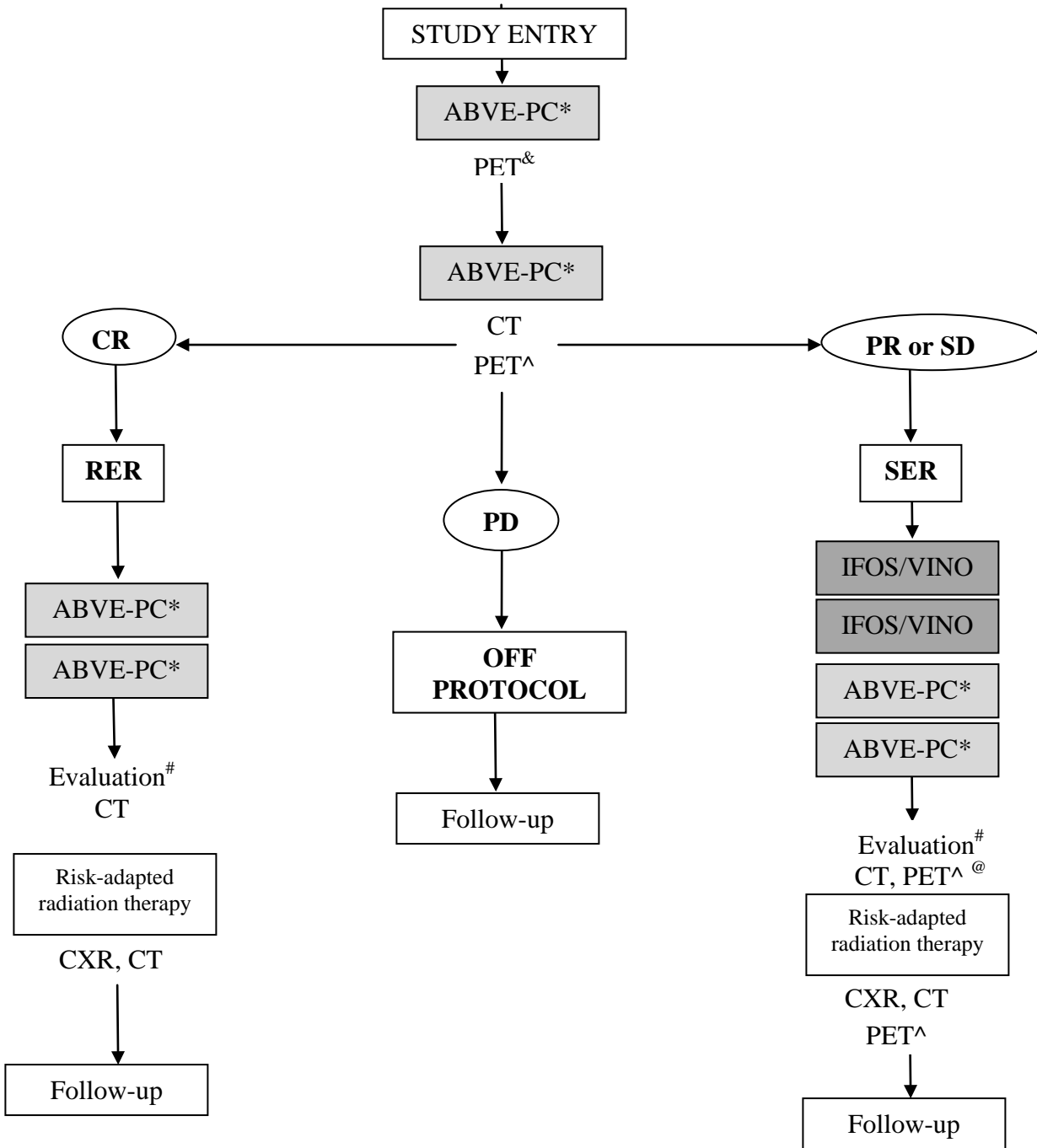
Studies to be submitted:

- Pre-Study (Baseline): chest radiograph; CT; FDG-PET imaging
- After Cycle 1 of ABVE-PC*: FDG-PET only if positive at baseline
- After Cycle 2 of ABVE-PC*: CT; FDG-PET only if positive after Cycle 1
- Prior to RT: CT; FDG-PET only if positive after Cycle 2
- At relapse: all imaging studies performed

TREATMENT PLAN:

INSERT schema from page 9 of protocol here

AHOD0831 EXPERIMENTAL DESIGN SCHEMA



ABVE-PC* = Doxorubicin/Bleomycin/Vincristine/Etoposide/Prednisone/Cyclophosphamide

IFOS/VINO = Ifosfamide/Vinorelbine

CR = complete response

PR = partial response

SD = stable disease

PD = progressive disease

RER = rapid early responder

SER = slow early responder

& Perform only if positive PET prior to initiating protocol therapy.

^ Perform only if previous PET was positive.

@ If PET is positive and biopsy confirms HL then patient will go off protocol therapy.

Stage IV patients only: if a positive bilateral bone marrow biopsy is obtained then patient will go off protocol therapy.