SWOG S0806: A Phase I/II Trial of Vorinostat (SAHA) in Combination With Rituximab-CHOP in Patients With Newly Diagnosed Advanced Stage Diffuse Large B-Cell Lymphoma (DLBCL)

Fast Facts

Phase I completed
CTCAE v.4; AJCC staging book 7th ed.;
Vorinostat provided

ELIGIBILITY CRITERIA

1. Patients must have biopsy proven, newly diagnosed Diffuse Large B-Cell Lymphoma (DLBCL) with Stage II bulky, Stage III or Stage IV disease, with an IPI or R-IPI score greater than 0 (see Section 4.0). A report providing confirmation of CD20 expression must be submitted per Section 14.4
2. Pathology review: Adequate sections from the original diagnostic specimen must be available for submission for review by the SWOG Lymphoma Pathology Laboratory as outlined in Section 12.0. An adequate biopsy requires sufficient tissue to establish the architecture and WHO histologic subtype with certainty. Fine needle aspiration or cytology is not adequate.
3. Patients must be offered the opportunity to consent to the correlative science studies. Patients are encouraged to submit specimens for correlative studies as outlined in Section 15.0; however, specimen submission is not a requirement for participation in the study.
4. Patients must have measurable disease (see Section 10.0). Measurable disease must be determined by CT scan of chest, abdomen and pelvis performed within 28 days prior to registration. CT reports must be submitted per Section 14.4. PET/CT may be substituted for CT scan only if CT scan is of diagnostic quality and is contrast enhanced.
5. Patients must be ≥ 18 years of age.
6. Patients must have a unilateral bone marrow aspirate and biopsy for staging performed within 42 days prior to registration.
7. Patients must not have clinical evidence of central nervous system involvement by lymphoma. Any laboratory or radiographic tests performed within 42 days prior to registration to assess CNS involvement must be negative.
8. Patients must not have received prior chemotherapy, radiation, or antibody therapy for lymphoma. Steroid pre-medication for IV contrast allergy is allowed.
9. Patients must have Zubrod performance status of 0-2 (see Section 10.4).
10. Patients must have serum LDH measured within 28 days prior to registration.
11. Patients must have an ANC > 1,000/mcL and platelets > 100,000/mcL within 28 days prior to registration, unless due to bone marrow infiltration by lymphoma.
12. Patients must have a cardiac ejection fraction ≥ institutional lower limit of normal (ILLN) by MUGA scan or 2-D ECHO with no significant abnormalities within 42 days prior to registration.
13. Patients must not have received valproic acid (an HDAC inhibitor) within 28 days prior to registration.
14. Patients must have no known hypersensitivity to the components of treatment.
15. Patients must be willing to discontinue taking any medications that are generally accepted to have a risk of causing Torsades de Pointes while on study (http://torsades.org).
16. Patients known to be HIV positive are not eligible. Existing therapeutic options are effective and study design does not support assessing the efficacy of treatment on those with HIV.
17. No other prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, *in situ* cervical cancer, adequately treated Stage I or II cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease free for five years.
18. Patients must not be pregnant or nursing due to potential for congenital abnormalities, and of harm to nursing infants due to this treatment regimen. Women/men of reproductive potential must have agreed to use an effect contraception method. A women is considered to be of "reproductive potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate patient chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures.
19. All patients must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.

20. At the time of patient registration, the treating institution's name and ID number must be provided to the Data Operations Center in Seattle in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered into the data base.

Pre-study Parameters

1. History and physical including height, weight and baseline abnormalities assessment
2. Labs including CBC with differential and platelets, LDH. Recommended labs: Serum creatinine, Potassium, Calcium, Magnesium, total bilirubin, AST, ALT, uric acid, serum β-2 micorglobulin, PT/INR or PTT for patients on anticoagulants, HPV screening for patients at high risk for HPV infection
3. Bone marrow biopsy and aspirate
4. CT chest, abdomen, pelvis or PET/CT if CT if of diagnostic quality and with contrast
5. MUGA or Echo, EKG (may be completed after registration, but prior to treatment)

Treatment

Agent	Dose	Route	Day	Schedule
Vorinostat	400 mg	PO	Days 1-5	Every 21 days for 8 cycles
Rituximab	375 mg/m^2	IV infusion	Day 3	Every 21 days for 8 cycles
Cyclophosphamide	750 mg/m^2	IV infusion	Day 3	Every 21 days for 8 cycles
Doxorubicin	50 mg/m^2	IV push	Day 3	Every 21 days for 8 cycles
Vincristine	1.4 mg/m^2 (max 2 mg)	IV push	Day 3	Every 21 days for 8 cycles
Prednisone	100 mg	PO once daily	Days 3-7	Every 21 days for 8 cycles

See section 7.5 to 7.10 for complete treatment details.

Vorinostat provided.