CALGB-50303

Phase III Randomized Study of R-CHOP V. Dose-Adjusted EPOCH-R With Molecular Profiling in Untreated De Novo Diffuse Large B-Cell Lymphomas

ClinicalTrial.gov Identifier: NCT00118209

Study Background

Trial Description

This randomized phase III trial studies rituximab when given together with two different combination chemotherapy regimens to compare how well they work in treating patients with diffuse large B-cell non-Hodgkin's lymphoma. Monoclonal antibodies, such as rituximab, may block cancer growth in different ways by targeting certain cells. Drugs used in chemotherapy work in different ways to stop the growth of cancer cells, either by killing the cells, by stopping them from dividing, or by stopping them from spreading. Giving rituximab together with combination chemotherapy may kill more cancer cells. It is not yet known which combination chemotherapy regimen is more effective when given with rituximab in treating diffuse large B-cell non-Hodgkin's lymphoma. PURPOSE: This randomized phase III trial is studying rituximab when given together with two different combination chemotherapy regimens to compare how well they work in treating patients with diffuse large B-cell lymphoma.

Arms:

Arm A - R-CHOP: (Active Comparator): Patients receive the following treatment:

- Rituximab 375 mg/m^2 IV infusion on Day 1 prior to CHOP chemotherapy
- Cyclophosphamide 750 mg/m^2 IV on Day 1
- Doxorubicin 50 mg/m^2 IV on Day 1
- Vincristine 1.4 mg/m^2 IV (2 mg cap) on Day 1
- Prednisone 40 mg/m^2/day PO on Days 1-5
- Filgrastim or pegfilgrastim as defined in the protocol. Required ancillary medications are administered during all cycles as defined in the protocol. Cycles will be repeated every 21 days for 6 treatment cycles. Restaging will occur after Cycles 4 and 6.

Arm B - DA-EPOCH-R: (Experimental): Patients receive the following treatment: Cycle 1 Doses:

- Rituximab 375 mg/m^2 IV infusion on Day 1 prior to EPOCH chemotherapy
- Doxorubicin 10 mg/m^2/day CIVI on Days 1-4
- Etoposide 50 mg/m^2/day CIVI on Days 1-4
- Vincristine 0.4 mg/m^2/day (no cap) CIVI on Days 1-4 (total 1.6 mg/m2 over 96 hours)
- Cyclophosphamide 750 mg/m^2 IV on Day 5 (following completion of 96 hour infusions)
- Prednisone 60 mg/m^2 PO BID on Days 1-5
- Administer filgrastim 480 mcg subcutaneous daily from Day 6 until ANC > 5000 after the nadir (nadir usually between Days 10-12) or for 10 days (Days 6-15) if the ANC is not being monitored, during every cycle.

Doses for subsequent cycles will be determined by the absolute neutrophil (ANC) or platelet nadir from the previous cycle. Required ancillary medications are administered during all cycles as defined in the protocol. Cycles will be repeated every 21 days for a maximum of 6 cycles. Restaging will occur after Cycles 4 and 6.

Objectives:

PRIMARY OBJECTIVES:

I. To compare the event-free survival of rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, prednisone (R-CHOP) versus dose-adjusted (DA-) etoposide, prednisone, vincristine sulfate, doxorubicin hydrochloride, cyclophosphamide, and rituximab (EPOCH-R) chemotherapy in untreated cluster of differentiation (CD)20 positive (+) diffuse large B-cell lymphomas.

II. To develop a molecular predictor of outcome of R-CHOP and DA-EPOCH-R chemotherapy using molecular profiling.

SECONDARY OBJECTIVES:

I. To compare the response rates, overall survival and toxicity of R-CHOP versus DA-EPOCH-R.

II. To define the pharmacogenomics of untreated diffuse large B-cell lymphoma (DLBCL) and correlate clinical parameters (toxicity, response, survival outcomes and laboratory results) with molecular profiling.

III. To assess the use of molecular profiling for pathological diagnosis.

IV. To identify new therapeutic targets using molecular profiling.

V. To perform a comprehensive analysis of somatic alterations to the tumor genome and to understand which genomic alterations are somatically acquired by the tumor and which are encoded in the germ line of the patient.

VI. To identify biomarkers of response to chemotherapy by fludeoxyglucose F 18 (FDG)-positron emission tomography (PET)/computed tomography (CT) imaging that are predictive of histopathologic remissions and survival in patients with stage I (mediastinal), II, III, or IV untreated DLBCL.

VII. To evaluate the use of semiquantitative measurements of FDG uptake in defining FDG-PET/CT based biomarkers of response to chemotherapy in patients with DLBCL.

VIII. To determine whether FDG-PET/CT measurements of tumor response after the second cycle of chemotherapy can predict clinical response.

IX. To establish a standardized protocol for FDG-PET/CT image acquisition.

X. To determine additional FDG-PET/CT parameters (e.g., the ratio of tumor maximum standard uptake value [SUV max] to liver SUV mean; SUVs corrected for body surface area and lean body mass; nuclear medicine physician's assessment) and evaluate their utility in refining FDG-PET/CT based biomarkers of response to therapy.

XI. To evaluate inter-institutional reproducibility of FDG-PET/CT measurements for this indication.

OUTLINE: Patients are randomized to 1 of 2 treatment arms.

Study Milestones:

Start date: May 2005

Primary Completion Date: October 2017

Publication Information:

Analysis Type: Primary

Pubmed ID: 30939090

Citation: Bartlett NL, Wilson WH, Jung S, Hsi ED, Maurer MJ, Pederson LD, Polley MC, Pitcher BN, Cheson BD, Kahl BS, Friedberg JW, Staudt LM, Wagner-Johnston ND, Blum KA, Abramson JS, Reddy NM, Winter JN, Chang JE, Gopal AK, Chadburn A, Mathew S, Fisher RI, Richards KL, Schoder H, Zelenetz AD, Leonard JP. Dose-Adjusted EPOCH-R Compared With R-CHOP as Frontline Therapy for Diffuse Large B-Cell Lymphoma: Clinical Outcomes of the Phase III Intergroup Trial Alliance/CALGB 50303. Journal of Clinical Oncology. 2019.

Associated Datasets:

NCT00118209-D1-Dataset.csv (master),

NCT00118209-D2-Dataset.csv (adverse_events),

Dataset Information:

Dataset Name: NCT00118209-D2-Dataset.csv (adverse_events)

Description: Dataset NCT00118209-D2-Dataset.csv (adverse_events) is one of 2 datasets associated with PubMed ID 30939090. This dataset contains information that will allow you to reproduce the safety analysis and toxicity tables.

Data can be used to approximate published study findings, but exact reproduction of previous manuscripts may not be possible in some cases (e.g., when data must be modified for de-identification purposes or have undergone further data cleaning).

Primary cause of death was captured and analyzed independently from adverse events and is reported within the D1 dataset. Any discrepancies with Grade 5 data in D2 are due to data entry.

NCT00118209-D2-Dataset.csv (adverse_events) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Patient ID	patid		Contains patient ID.
Treatment Received	rx	DA-EPOCH-R, R-CHOP	
Body System	BODYSYS		Contains body system of the adverse event.
Grade	GRADE	1, 2, 3, 4, 0, 5	CTCAE Grade of adverse event.
Relationship to study meds	REL_SMED	PROBABLE, DEFINITE, POSSIBLE, UNLIKELY, NOT RELATED	Adverse event relationship to study medication. Missing indicates data was not collected.
Toxicity Code	TOXCODE		Contains the MedDRA toxicity code.
Toxicity	TOXICITY		Contains the CTCAE adverse event description.