National Cancer Institute

TEDDI-R Trial Summary Sheet

Trial Title

Phase 1 Study of Ibrutinib and Immuno-Chemotherapy Using Dose-Adjusted Temozolomide, Etoposide, Doxil, Dexamethasone, Ibrutinib, Rituximab (DA-TEDDI-R) in Primary CNS Lymphoma

Research Objective

Identify the maximum tolerated dose (MTD) of ibrutinib or the dose that achieves adequate cerebrospinal fluid (CSF) concentrations, whichever comes first, when ibrutinib is given with dose-adjusted temozolomide, etoposide, Doxil, dexamethasone, ibrutinib, rituximab (DA-TEDDI-R).

Why This Study Is Important

Primary central nervous system lymphoma (PCNSL) is a rare subtype of diffuse large B-cell lymphoma (DLBCL). The outcome for patients with this diagnosis is inferior compared with systemic DLBCL and therefore is a need to develop more effective therapies. Most PCNSLs appear to be of activated B-cell (ABC) origin, and ibrutinib has been effective in treating systemic DLBCL of ABC origin; therefore, we are conducting this study, in which ibrutinib is incorporated in a novel chemotherapy platform.

Design

This is a phase 1 study of 40 patients with newly diagnosed or relapsed PCNSL. This study will have two components:

- **Phase 1:** Identify the MTD of ibrutinib, or the dose at which ibrutinib achieves a concentration of no more than 100 nM in the CSF, when given in combination with DA-TEDDI-R immunochemotherapy.
- **Expansion cohort**: Safety and tolerability of the regimen in relapsed, refractory, or previously untreated PCNSL (DLBCL type) will be assessed at the final ibrutinib dose with DA-TEDDI-R. Secondary objectives will be to evaluate progression-free survival and overall survival.

Considerations for Participation

Eligible patients must have histologically or cytologically confirmed primary central nervous system DLBCL. Both newly diagnosed patients and patients with relapsed or refractory disease are eligible. At least two weeks must have passed since prior chemotherapy, biological therapy, radiation therapy, major surgery, or other investigational or anticancer therapy that is considered disease-directed. Patients age 18 and over are eligible, and must have adequate organ function. For more details about eligibility criteria, please see the full study record.

This trial is being conducted at the National Institutes of Health (NIH) Clinical Center in Bethesda, Maryland.

For more information, please contact Peggy Shovlin, RN, at mshovlin@nih.gov or Kieron Dunleavy, M.D., at kieron.dunleavy@nih.gov.

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