CALGB-10201

A Phase III Study of Daunorubicin and Cytarabine +/- G3139 (Genasense, Oblimersen Sodium, NSC #683428, IND #58842), a BCL2 Antisense Oligodeoxynucleotide, in Previously Untreated Patients With Acute Myeloid Leukemia (AML) ≥ 60 Years

ClinicalTrials.gov Identifier: NCT00085124

Study Background

Trial Description

This randomized phase III trial is studying daunorubicin, cytarabine, and oblimersen to see how well they work compared to daunorubicin and cytarabine in treating older patients with previously untreated acute myeloid leukemia. Drugs used in chemotherapy, such as daunorubicin and cytarabine, work in different ways to stop cancer cells from dividing so they stop growing or die. Oblimersen may increase the effectiveness of daunorubicin and cytarabine by making cancer cells more sensitive to the drugs. It is not yet known whether daunorubicin and cytarabine are more effective with or without oblimersen in treating acute myeloid leukemia.

Arms:

Arm I: (Experimental): Remission induction therapy: Patients receive oblimersen IV continuously on days 1-10, cytarabine IV continuously on days 4-10, and daunorubicin IV on days 4-6. Patients who achieve CR proceed to consolidation therapy. Patients who do not achieve CR receive a second course of induction therapy. Second remission induction therapy: Patients receive oblimersen IV continuously on days 1-8, cytarabine IV continuously on days 4-8, and daunorubicin IV on days 4-5. Patients who achieve CR proceed to consolidation therapy.
Consolidation therapy: Patients receive oblimersen IV continuously on days 1-8 and high-dose cytarabine IV over 3 hours on days 4-8. Patients with a continuing CR receive a second course of consolidation therapy.

Arm II: (Experimental): Remission induction therapy: Patients receive cytarabine IV continuously on days 1-7 and daunorubicin IV on days 1-3. Patients who achieve CR proceed to consolidation therapy. Patients who do not achieve CR receive a second course of induction therapy. Second remission induction therapy: Patients receive cytarabine IV continuously on days 1-5 and daunorubicin IV on days 1 and 2. Patients who achieve CR proceed to consolidation therapy. Consolidation therapy:

Patients receive high-dose cytarabine IV over 3 hours on days 1-5. Patients with a continuing CR receive a second course of consolidation therapy.

Objectives:

- OBJECTIVES:
  - Primary
    - Compare outcome, in terms of overall survival, disease-free survival, event-free survival, and complete response rate, in older patients with previously untreated acute myeloid leukemia treated with daunorubicin and cytarabine with or without oblimersen.
  - Secondary
    - Determine the significance of expression of select Bcl-2 family member proteins known to be modulated by oblimersen (e.g., Bcl-2) or which potentially mediate resistance to oblimersen (e.g., Bcl-XL or Mcl-1) in predicting clinical outcomes in patients treated with these regimens.
    - Correlate clinical outcomes with serial changes in levels of mRNA and protein expression of Bcl-2, its pro-apoptotic binding partner Bax, and other anti-apoptotic Bax-binding proteins (e.g., Bcl-XL or Mcl-1) in patients treated with these regimens.
    - Determine the effect of pre-treatment characteristics (e.g., morphology, cytogenetics, molecular features, expression of multidrug resistance molecules, functional assays of drug efflux, prior myelodysplastic syndromes, age, and white blood cells) on toxicity of these regimens and outcomes in these patients.
- OUTLINE: This is a randomized, multicenter study. Patients are randomized to 1 of 2 treatment arms.
  - Arm I: Remission induction therapy: Patients receive oblimersen IV continuously on days 1-10, cytarabine IV continuously on days 4-10, and daunorubicin IV on days 4-6. Patients who achieve complete remission (CR) proceed to consolidation therapy. Patients who do not achieve CR receive a second course of induction therapy. Second remission induction therapy: Patients receive oblimersen IV continuously on days 1-8, cytarabine IV continuously on days 4-8, and daunorubicin IV on days 4-5. Patients who achieve CR proceed to consolidation therapy. Consolidation therapy: Patients receive oblimersen IV continuously on days 1-8 and high-dose cytarabine IV over 3 hours on days 4-8. Patients with a continuing CR receive a second course of consolidation therapy.
  - Arm II: Remission induction therapy: Patients receive cytarabine IV continuously on days 1-7 and daunorubicin IV on days 1-3. Patients who achieve CR proceed to consolidation therapy. Patients who do not achieve CR receive a second course of induction therapy. Second remission induction therapy: Patients receive cytarabine IV continuously on days 1-5 and

daunorubicin IV on days 1 and 2. Patients who achieve CR proceed to consolidation therapy. Consolidation therapy: Patients receive high-dose cytarabine IV over 3 hours on days 1-5. Patients with a continuing CR receive a second course of consolidation therapy. In both arms, treatment continues in the absence of disease progression, unacceptable toxicity, failure to achieve CR after 2 courses of remission induction therapy, the presence of leukemic cells in the cerebrospinal fluid, leukemic regrowth, or relapse during consolidation therapy. Patients are followed every 2 months for 2 years, every 3 months for 2 years, and then annually for 10 years.

- PROJECTED ACCRUAL: A total of 500 patients (250 per treatment arm) will be accrued for this study within 4.2 years.

Study Milestones:

Start date: December 2003

Primary Completion Date: June 2007

Publication Information:

Analysis Type: Primary

PubMed ID: 34251414

Citation: Walker AR, Marcucci G, Yin J, Blum W, Stock W, Kohlschmidt J, Mrozek K, Carroll AJ, Eisfeld AK, Wang ES, Jacobson S, Kolitz JE, Thakuri M, Sutamtewagul G, Vij R, Stuart RK, Byrd JC, Bloomfield CD, Stone RM, Larson RA. Phase 3 randomized trial of chemotherapy with or without oblimersen in older AML patients: CALGB 10201 (Alliance). Blood Adv. 2021 Jul 13;5(13):2775-2787. doi: 10.1182/bloodadvances.2021004233. PMID: 34251414; PMCID: PMC8288671.

Associated Datasets: NCT00085124-D1-Dataset.csv (pts), NCT00085124-D2-Dataset.csv (aes)

Dataset Information:

Dataset Name: NCT00085124-D2-Dataset.csv (aes)

Description: Dataset NCT00085124-D2-Dataset.csv (aes) is one of 2 datasets associated with PubMed ID 34251414. This dataset contains adverse event data.

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).

Blank values indicate data not applicable or missing, except where otherwise noted.

NCT00085124-D2-Dataset.csv (aes) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Adverse event	adverse_event		
Patient ID	patid		
Grade	GRADE_ID	0, 1, 2, 3, 4, 5	
Treatment related	newrelation	No, Yes	
Treatment phase	outer	CONSOLIDATION, INDUCTION, POST-TREATMENT	