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-D1-Dataset.csv (pts)

Description: Dataset NCT00085124-D1-Dataset.csv (pts) is one of 2 datasets associated with PubMed ID 34251414. This dataset contains data presented in the publication except adverse event information.

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-D1-Dataset.csv (pts) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
2017 ELN genetic risk group	eln_2017_gen_risk_group	Adverse, Favorable, Intermediate, Unclassifiable	
Cytogenetic group	cytogenetic_group	CBF AML, Complex karyotype, No sample received or rejected cytogenetics, Normal karyotype, Other balanced rearrangements, Unbalanced abnormalities in non-complex karyotype	
Patient ID	patid		
Performance status	ps	0, 1, 2, 3	
Age (years)	age		
Complete remission (CR)	crever	No, Yes	
Arm	arm	A: G3139, B: Control	
Overall survival time (months)	surv_mos		
Overall survival status	surv_stat	Alive, Dead	
DFS time (months)	dfs_mos		
DFS status	dfs_stat	Event, No Event	
Received treatment	rectx	No, Yes	

LABEL	NAME	ELEMENTS	COMMENTS
Off treatment reason	endatrsn	Alternative therapy; Death after beginning protocol therapy; Death prior to beginning protocol therapy; Disease progression, relapse during active treatment; Other; Other complicating disease; Pt w/d after starting therapy; Pt w/d before starting therapy; Toxicity/side effects/complications; Treatment completed per protocol	
Disease type	dis_type	Post MDS, Primary (de novo) AML, Therapy-related AML	
EFS time (months)	efs2_mos		
EFS status	efs2_stat	Event, No Event	
Early death during the first 30 days of induction therapy	early_death	No, Yes	
Ethnicity	ethnicity	Hispanic or Latino, Non-Hispanic, Unknown	
Race	race	American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Pacific Islander, Not Reported, Unknown, White	
Sex	sex	Female, Male	
Transplant type	transplant_type	AlloHCT, AutoHCT	
DFS time (months) censoring at the time of allogeneic hematopoietic cell transplantation	dfs_mos_allo		

LABEL	NAME	ELEMENTS	COMMENTS
DFS status censoring at the time of allogeneic hematopoietic cell transplantation	dfs_stat_allo	Event, No Event	
EFS time (months) censoring at the time of allogeneic hematopoietic cell transplantation	efs2_mos_allo		
EFS status censoring at the time of allogeneic hematopoietic cell transplantation	efs2_stat_allo	Event, No Event	
OS time (months) censoring at the time of allogeneic hematopoietic cell transplantation	surv_mos_allo		
OS status censoring at the time of allogeneic hematopoietic cell transplantation	surv_stat_allo	Alive, Dead	
Specific transplant type for patients who received hematopoietic cell transplantation	trans_type	Autologous bone marrow, Autologous PBSC, Bone marrow from matched sibling, Bone marrow from matched unrelated, Other, PBSC from matched sibling, PBSC from matched unrelated donor	
ASXL1	asxl1	Mutated, WT	

LABEL	NAME	ELEMENTS	COMMENTS
RUNX1	runx1	Mutated, WT	
NPM1	npm1	Mutated, WT	
TP53	tp53	Mutated, WT	
FLT3 ITD	flt3_itd	Absent, Present	
CEBPA double mutation	cebpa_doub	Mutated, WT	
Entered induction phase	indcy1	No, Yes	
Received a second cycle of induction therapy	indcy2	No, Yes	
Received consolidation cycle 1	conscy1	No, Yes	As described by the data, seven patients received consolidation therapy without achieving CR in induction.
Received consolidation cycle 2	conscy2	No, Yes	
Received G3139 during consolidation	g3139_cons_rec	No, Yes	