



Alliance A041501: A Phase III Trial to Evaluate the Efficacy of the Addition of Inotuzumab Ozogamicin (A Conjugated Anti-CD22 Monoclonal Antibody) to Frontline Therapy in Young Adults (Ages 18-39 Years) with Newly Diagnosed Precursor B-Cell ALL

Daniel J. DeAngelo, MD, PhD

Dana-Farber Cancer Institute

TAP TO
RETURN TO
KIOSK MENU

Rationale

Inotuzumab ozogamicin is an antibody targeting CD22 conjugated with a cytotoxic antitumor antibiotic (calicheamicin). This agent is in development for the treatment of acute lymphoblastic leukemia (ALL). CD22 is expressed on the malignant cells of the majority of B-lymphocyte malignancies, including on the surface of lymphoblasts in the vast majority of patients with ALL (approximately 95%). Weekly dosing on days 1, 8, and 15 every 4 weeks is chosen for use in this trial as it has been shown to be generally safe and well tolerated in the previously Pfizer Pharmaceuticals Study B1931010.



Rationale

Objectives

Study Schema

Treatment Plan

Eligibility Criteria

Follow Up

Please use the headings above to navigate through the different sections of the poster



Alliance A041501: A Phase III Trial to Evaluate the Efficacy of the Addition of Inotuzumab Ozogamicin (A Conjugated Anti-CD22 Monoclonal Antibody) to Frontline Therapy in Young Adults (Ages 18-39 Years) with Newly Diagnosed Precursor B-Cell ALL

Daniel J. DeAngelo, MD, PhD

Dana-Farber Cancer Institute

TAP TO
RETURN TO
KIOSK MENU



Rationale

Objectives

Study Schema

Treatment Plan

Eligibility Criteria

Follow Up

Please use the headings above to navigate through the different sections of the poster

Objectives

Primary

- To confirm tolerability of the combination regimen with the addition of inotuzumab ozogamicin to the pediatric-inspired regimen of CALGB 10403.
- To determine whether the addition of inotuzumab ozogamicin significantly improves the event-free survival (EFS) in patients who achieve an induction response achieved with the pediatric-inspired regimen of CALGB 10403, without censoring for transplant.

Secondary

- To determine the impact of inotuzumab ozogamicin on disease-free (DFS) and overall survival (OS) in patients who achieve an induction response.
- To determine whether the addition of inotuzumab ozogamicin significantly improves the event-free survival (EFS) in patients who achieve an induction response achieved with the pediatric-inspired regimen of CALGB 10403, with censoring for transplant.
- To determine the impact of inotuzumab ozogamicin on minimal residual disease (MRD) and correlate this with the EFS, DFS and OS.
- To determine the prognosis based on patients' LDA gene signature in terms of EFS, DFS, and OS after treatment with or without inotuzumab ozogamicin when added to the C10403 backbone regimen.
- To evaluate the toxicity and tolerability of the addition of inotuzumab ozogamicin to the pediatric-inspired regimen of CALGB 10403.



Alliance A041501: A Phase III Trial to Evaluate the Efficacy of the Addition of Inotuzumab Ozogamicin (A Conjugated Anti-CD22 Monoclonal Antibody) to Frontline Therapy in Young Adults (Ages 18-39 Years) with Newly Diagnosed Precursor B-Cell ALL

Daniel J. DeAngelo, MD, PhD

Dana-Farber Cancer Institute

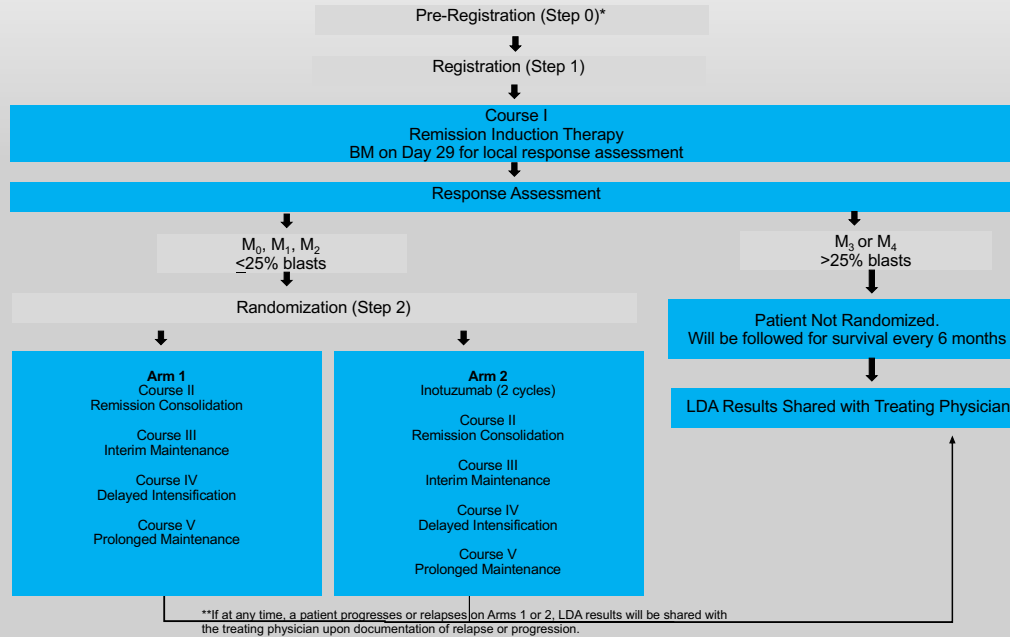
**TAP TO
RETURN TO
KIOSK MENU**



- Rationale
- Objectives
- Study Schema**
- Treatment Plan
- Eligibility Criteria
- Follow Up

Please use the headings above to navigate through the different sections of the poster

Study Schema



Limited Access Participating Alliance Institutions (Confirmation of Tolerability portion): MA036/Dana-Farber Cancer Institute, IL057/University of Chicago Comprehensive Cancer Center, NC007/University of North Carolina at Chapel Hill, OH007/Ohio State University Medical Center.

Participating NCTN Groups (Phase III only): ALLIANCE/Alliance for Clinical Trials in Oncology, ECOG-ACRIN/ECOG-ACRIN Cancer Research Group, NRG/NRG Oncology, SWOG/SWOG



Alliance A041501: A Phase III Trial to Evaluate the Efficacy of the Addition of Inotuzumab Ozogamicin (A Conjugated Anti-CD22 Monoclonal Antibody) to Frontline Therapy in Young Adults (Ages 18-39 Years) with Newly Diagnosed Precursor B-Cell ALL

Daniel J. DeAngelo, MD, PhD

Dana-Farber Cancer Institute

TAP TO
RETURN TO
KIOSK MENU

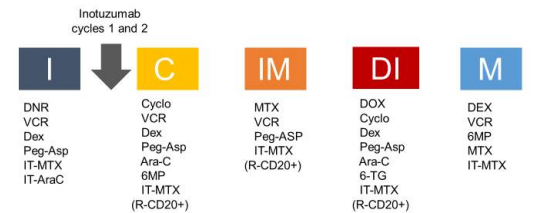
Treatment Plan



- Rationale
- Objectives
- Study Schema
- Treatment Plan**
- Eligibility Criteria
- Follow Up

- Prior to initiation of therapy, patients need to be evaluated for CNS and testicular disease at diagnosis.
- Course I is to begin \leq 5 days of registration (Step 1).
- Patients must meet eligibility in the protocol in order to be randomized.
- Randomization must occur within 21 days after completion of remission induction therapy.
- Patients will be assigned to treatment Arms 1 or 2 according to the results of Day 1-29 bone marrow. Patients who achieve M2 or better (M0, M1, M2) will be randomized to Arm 1 (C10403 backbone) or Arm 2 (C10403 backbone with two 28-day cycles of inotuzumab (1.5 mg/m² per cycle unless found to not be sufficiently tolerable)).
- Patients who fail remission induction (M3 or M4) not be eligible for randomization, and the treating physician will be provided with LDA results.

Alliance 041501 US Intergroup Study for AYA: Randomized Phase 3 trial (CD22+; Ph-)¹



***CD20+ Patients will Receive Rituximab with I, C, IM, DI**
Maintenance therapy continues for 2 (F) to 3 (M) years CD22 positive B-cell ALL²

1. <https://clinicaltrials.gov/ct2/show/NCT01350693>. Accessed November 21, 2017.
2. Stock W et al. 56th Annual Meeting of the American Society of Hematology (ASH 2014). Abstract 796.

Please use the headings above to navigate through the different sections of the poster

- For patients who relapse at any time on Arms 1 or 2, LDA results will be provided to the treating physician. Patients randomized to Arm 1 will go straight to Consolidation Course II (refer to schema).
- Patients on Arm 1 should not receive inotuzumab.
- Patients randomized to Arm 2 will receive two 28-day cycles of inotuzumab.



Alliance A041501: A Phase III Trial to Evaluate the Efficacy of the Addition of Inotuzumab Ozogamicin (A Conjugated Anti-CD22 Monoclonal Antibody) to Frontline Therapy in Young Adults (Ages 18-39 Years) with Newly Diagnosed Precursor B-Cell ALL

Daniel J. DeAngelo, MD, PhD

Dana-Farber Cancer Institute

TAP TO
RETURN TO
KIOSK MENU



a National Cancer Institute program

- Rationale
- Objectives
- Study Schema
- Treatment Plan
- Eligibility Criteria**
- Follow Up

Eligibility Criteria

Key Registration Eligibility Criteria

- Newly diagnosed patients with CD-22 positive B-cell acute lymphoblastic leukemia (WHO criteria). Burkitt type ALL is not eligible.
- Patients who have BCR-ABL fusion transcript determined by FISH or RT-PCR or t(9;22) (q34;q11) by cytogenetics are not eligible for this trial and should be considered for enrollment on studies that incorporate imatinib or other tyrosine kinase inhibitors during induction.
- Prior Treatment
 - No prior therapy for acute leukemia except emergency therapy (corticosteroids or hydroxyurea for ≤ 7 days) for blast cell crisis, or renal failure due to leukemia infiltration of the kidneys
 - Single-dose intrathecal cytarabine is allowed prior to registration (see also Section 7.1.1.2).
 - Prior steroid therapy is allowed.
- Not pregnant and not nursing.
- Age ≥ 18 years and < 40 years.
- ECOG Performance Status 0-2
- Patients with Down Syndrome are excluded from this study due to the likelihood of excessive toxicity. These patients should be treated in consultation with a pediatric oncologist

Confirmation of Tolerability

- To ensure safety and tolerability, researchers will treat the first 6 patients who respond to induction therapy with the Arm 2 regimen (i.e., the inotuzumab combination regimen) and will evaluate and confirm the tolerability of this regimen when inotuzumab is given at Dose Level 0 (0.5 mg/m²/day on Day 1, 8, and 15 of a 28-day cycle [total dose per cycle is 1.5 mg/m²/cycle]).

Phase III

- No prior therapy with the only exceptions being prior treatment with corticosteroids or hydroxyurea and a single dose of intrathecal cytarabine. Systemic chemotherapy must begin within 72 hours of this intrathecal therapy.

Please use the headings above to navigate through the different sections of the poster



- Rationale
- Objectives
- Study Schema
- Treatment Plan
- Eligibility Criteria

Follow Up

Please use the headings above to navigate through the different sections of the poster

Alliance A041501: A Phase III Trial to Evaluate the Efficacy of the Addition of Inotuzumab Ozogamicin (A Conjugated Anti-CD22 Monoclonal Antibody) to Frontline Therapy in Young Adults (Ages 18-39 Years) with Newly Diagnosed Precursor B-Cell ALL

Daniel J. DeAngelo, MD, PhD

Dana-Farber Cancer Institute

TAP TO RETURN TO KIOSK MENU



Related Publication

A pediatric regimen for older adolescents and young adults with acute lymphoblastic leukemia: results of CALGB 10403

Blood 2019 133:1548-1559

Stock W, Luger SM, Advani AS, et al.

Funding Support

Alliance A041501 is funded by the National Institutes of Health through National Cancer Institute grant awards, and in part by Baxalta/Servier Group and Pfizer, Inc.

Contact Us

Study Chair: Daniel J. DeAngelo, MD, PhD
E-mail: daniel_deangelo@dfci.harvard.edu
Phone: 617-632-2645

Protocol Coordinator: Destin Carlisle
E-mail: dcarlisle@uchicago.edu