Inotuzumab ozogamicin (CMC-544)  

Inotuzumab ozogamicin is an investigational agent and has not been approved by regulatory agencies.

| ABOUT INOTUZUMAB OZOGAMICIN | • Inotuzumab ozogamicin is an investigational antibody-drug conjugate (ADC) comprised of a monoclonal antibody (mAb) targeting CD22, a cell surface antigen expressed on approximately 90 percent of B-cell malignancies, linked to a cytotoxic agent.  
  • When inotuzumab ozogamicin binds to the CD22 antigen on malignant B-cells, it is absorbed into the cell, at which point the cytotoxic agent calicheamicin is released to destroy the cell.  
    o Calicheamicin is a natural product of bacteria that was first discovered in caliche clay and was found to be toxic to normal and cancerous cells.  

| WHAT IS THE SIGNIFICANCE OF AN ANTIBODY-DRUG CONJUGATE (ADC)? | • Chemotherapy is designed to eliminate fast-growing cancer cells, but it can also harm healthy proliferating cells, which causes side effects.  
  • Linking an ADC with a cytotoxic agent may allow chemotherapy to directly target the cancer cell.  
    o Focused delivery of the cytotoxic agent to tumor cells may maximize its antitumor effect while minimizing its normal tissue exposure, potentially resulting in an improved therapeutic index.  
    o Targeted delivery is expected to result in fewer toxicities than nontargeted systemic delivery of currently used cytotoxic combination chemotherapy.  

| THE ROLE OF CD22 | • CD22 is an important modulator of B-cell lymphocyte function and survival.  
  • CD22 is expressed only on mature B-cells, which allows for targeted delivery of the cytotoxic agent.  
    o Therefore, CD22 targeted chemotherapy is not expected to affect other tissue and should not impact the ability to generate new B-cells.  
  • Studies have shown that adding an ADC targeting CD22, such as inotuzumab ozogamicin, to existing treatments for B-cell non-Hodgkin lymphoma (NHL) may provide additional anti-tumor activity.  
    o Currently, approximately 50 percent of patients with aggressive NHL relapse following treatment with standard of care treatment.  
  • Additionally, there is preclinical evidence that an ADC targeting CD22, such as inotuzumab ozogamicin, may provide antitumor activity against CD22 positive acute lymphoblastic leukemia (ALL).  
    o CD22 has been shown to be expressed on the surface of more than 90 percent of leukemic blasts in a vast majority of B-Cell ALL patients.  

| CLINICAL STUDIES | Pfizer is continuing to explore a clinical development program to determine which patients may benefit from inotuzumab ozogamicin in different B-cell malignancies:  

| Phase 3 | INO-VATE NHL (INotuzumab Ozogamicin trial to inVestigAte Tolerability and Efficacy) Study 1008 – A multicenter, open-label, randomized, Phase 3 study of inotuzumab ozogamicin administered in combination with rituximab compared to defined investigator’s choice therapy in subjects with relapsed or refractory CD22-positive aggressive NHL who are not candidates for intensive high-dose...
chemotherapy.¹¹

- INO-VATE ALL Study 1022 – An open-label, randomized, Phase 3 study of inotuzumab ozogamicin compared to a defined investigator’s choice of chemotherapy in adult patients with relapsed or refractory CD22+ acute lymphoblastic leukemia (ALL).¹²

**Phase 2**

- Study 2005 – An open-label, single-arm Phase 2 study of inotuzumab ozogamicin plus rituximab in subjects with relapsed/refractory CD22-positive diffuse large B-cell lymphoma, eligible for autologous stem cell transplantation.¹³
- Study 2001 – A Phase 2 study of inotuzumab ozogamicin in subjects with indolent NHL that is refractory to or has relapsed after rituximab and chemotherapy or radioimmunotherapy.¹⁴

**Phase 1**

- Study 1010 – An open-label, Phase 1 study of inotuzumab ozogamicin in subjects with relapsed or refractory CD22-positive ALL.¹⁵

For more information, please visit www.pfizercancertrials.com or www.clinicaltrials.gov or call toll-free 1-877-369-9753 (in the United States and Canada) or +1-646-277-4066 (outside of the United States and Canada).
1 Boni J et al. Modeling the Pharmacokinetic/Pharmacodynamic Platelet Response of Inotuzumab Ozogamicin, a Novel Antibody Drug Conjugate, Administered Alone or in Combination with Rituximab in Patients with Non-Hodgkin’s Lymphoma. Accepted Poster Presentation at the European Society of Medical Oncology 2010 Annual Meeting, October 8-12, 2010. Milan, Italy.


