INO-VATE (INotuzumab Ozogamicin trial to inVestigAte Tolerability and Efficacy) STUDY: A Phase 3 Study Of Inotuzumab Ozogamicin Plus Rituximab For Relapsed/Refractory Aggressive Non-Hodgkin Lymphoma Patients Who Are Not Candidates For Intensive High-Dose Chemotherapy

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

INTRODUCTION

- 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.
- CD22 is an important modulator of B-cell lymphocyte function and survival, and is expressed only on mature B-cells, which may allow for targeted delivery of the cytotoxic agent.
- 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.

RATIONALE

Based on the results of Study 101, a Phase 2 clinical trial in combination with rituximab in patients with relapsed or refractory aggressive NHL, Pfizer has designed the INO-VATE study to evaluate the efficacy of inotuzumab ozogamicin plus rituximab compared with an active comparator arm (investigator's choice of rituximab + bendamustine or rituximab + gemcitabine) in relapsed or refractory aggressive NHL patients who are not candidates for intensive high-dose chemotherapy.

- Currently approximately 50 percent of patients with aggressive NHL relapse following standard of care treatment.
  - For relapsed patients able to undergo high-dose chemotherapy, an autologous stem cell transplant may be considered.
  - For relapsed patients who are ineligible for autologous stem cell transplant, the current two year overall survival is less than 10 percent, with an average survival of six to nine months.

OBJECTIVES

- Primary: Overall survival
- Secondary: Safety and tolerability, Overall response rate, Progression-free survival, Duration of response, Patient-reported health-related quality of life

STUDY DESIGN

- Phase 3, randomized, open-label, two-arm study:
  - Arm A: Patients will receive rituximab 375 mg/m² by intravenous infusion on day 1 every 28 days consisting of 3 to 6 cycles followed by inotuzumab ozogamicin in combination with rituximab, in a dosing schedule of inotuzumab ozogamicin 1.8 mg/m² by intravenous infusion on day 2 every 28 days consisting of 3 to 6 cycles
  - Arm B: Patients will receive the investigator’s choice of either
rituximab plus gemcitabine or rituximab plus bendamustine.

- For patients receiving rituximab plus gemcitabine, dosing of rituximab 375 mg/m² by intravenous infusion will occur on days 1, 8, 15, and 22 of cycle 1, and day 1 of cycles 2 to 6 every 28 days and will consist of 3 to 6 cycles. Dosing of gemcitabine 1000 mg/m² will occur on days 1, 8, and 15 every 28 days and will consist of 3 to 6 cycles.
- For patients receiving rituximab plus bendamustine, dosing of rituximab 375 mg/m² by intravenous infusion will occur on day 1 every 28 days and will consist of 3 to 6 cycles, and bendamustine dosing of 120 mg/m² by intravenous infusion will occur on days 1 and 2 every 28 days and will consist of 3 to 6 cycles.
- A minimum of three cycles is planned. A maximum of three additional cycles (six in total) may be administered.¹⁰

### SELECTED ELIGIBILITY CRITERIA

- **Selected Inclusion Criteria:**¹⁰
  - Relapsed/refractory/persistent CD20+/CD22+ aggressive NHL (diffuse large B-cell lymphoma (DLBCL), transformed indolent lymphoma with DLBCL, primary mediastinal large B-cell lymphoma)
  - Up to 3 prior regimens containing cytotoxic chemotherapies
  - Not candidates for intensive high-dose chemotherapy, with or without an autologous stem cell transplant

- **Selected Exclusion Criteria:**¹⁰
  - Prior allogeneic hematopoietic stem cell transplant (HSCT); autologous transplant within prior four months
  - Anti-CD22 treatment or radioimmunotherapy within prior six months
  - Contraindication to both investigator choice regimens
  - Chronic liver disease, history of veno-occlusive disease

### NUMBER OF PATIENTS

- An anticipated 377 patients will be enrolled from research sites in the United States and ex-US.¹⁰


