GMI-1271 is a potent oral nucleotide carboxyalkyl diphosphate. E-selectin inhibition has been shown to decrease tumor burden, improve drug delivery to tumor cells and the bone marrow niche while supporting hematopoietic stem cell mobilization. GMI-1271 is currently being developed in the treatment of acute myeloid leukemia, multiple myeloma, and solid tumors.

Objectives

1. To assess the pharmacokinetics (PK) of single IV doses of GMI-1271 when administered to healthy volunteers
2. To evaluate the effects of GMI-1271 on the following biomarkers
   - sICAM-1
   - CD34+ cell count
   - sE-selectin
   - PT/PTT
   - sTF
   - IL-10
   - von Willebrand factor activity
   - Prothrombin fragment 1.2
   - Thrombin coagulation cascade
   - Other markers of cell activation and adhesion

Methods

Method 1: Single Dose Escalation, Double-Blind, Placebo-Controlled Trials in Healthy Volunteers

- **Participants**: 64 healthy volunteers (32 per study arm, aged 18-75 years, BMI 18-35 kg/m², American Society of Anesthesiologists (ASA) Class I or II, no malignancy or immunosuppression, no history of blood transfusions or medication use for 30 days prior to study entry).
- **Dose Levels**: 2 mg/kg, 3 mg/kg, 5 mg/kg.

Results

- **Pharmacokinetics**: The following occurred in <2 subjects:
  - **Nausea**: 1 (9)
  - **Asthma**: 1 (9)
  - **Cutaneous reaction**: 1 (9)
  - **Fatigue**: 2 (4)
  - **All above AEs reported as unrelated to GMI-1271/placebo.

- **Biomarkers**: Results showed a favorable safety, pharmacokinetic, and biomarker profile.

- **Conclusion**: GMI-1271 was well tolerated and demonstrated favorable safety and PK characteristics.

Conclusion

GMI-1271 offers a promising therapeutic option for the management of acute venous thromboembolism (VTE) by decreasing and delaying inflammatory cell recruitment into the post-thrombus vein wall. This phenomenon has been shown to decrease thrombus weight and has the potential to reduce complications of VTE. Cancer-associated E-selectin is shown to increase tumor sensitivity to chemotherapy by targeting the interactions between tumor cells and the immune system.

Funding: Study 1 was sponsored by GlycoMimetics, Inc. Study 2 is funded through the NHLBI VITA contract HHSN268201400012C.

References

1. **Background**: Show a Favorable Safety, Pharmacokinetic, and Biomarker Profile
2. **Methods**: First in Human Phase 1 Single Dose Escalation Studies of the E-Selectin Antagonist GMI-1271
3. **Results**: Pharmacokinetics
4. **Summary and Conclusions**: GMI-1271 is well tolerated with a favorable safety profile and no evidence of changes in bleeding time.

First in Human Phase 1 Single Dose Escalation Studies of the E-Selectin Antagonist GMI-1271

Show a Favorable Safety, Pharmacokinetic, and Biomarker Profile