HM2021-31: A Phase 1b Open-Label Study to Evaluate the Safety and Anti-cancer Activity of Loncastuximab Tesirine in Combination with Other Anti-cancer Agents in Patients with Relapsed or Refractory B-cell Non-Hodgkin Lymphoma (LOTIS-7)

Status: Recruiting

Eligibility Criteria

Sex: All
Age Group: 18 years and over

Inclusion Criteria:

Male or female participant aged 18 years or older Pathologic diagnosis of relapsed (disease that has recurred following a response) or refractory (disease that failed to respond to prior therapy) B-NHL (2016 World Health Organization classification) who have failed, or been intolerant to any approved therapy and had received at least two systemic treatment regimens in dose-escalation part; and at least one systemic treatment regimen in dose-expansion part DLBCL (including transformed diseases, but for Arms E and F, including transformed FL only) HGBCL FL MZL MCL (for Arm C only) BL (for Arm C only) Life expectancy of at least 24 weeks according to Investigator's judgement Need of systemic treatment for any of the listed indications as assessed by the investigator, including indolent B-NHLs (e.g. FL and MZL) Measurable disease as defined by the 2014 Lugano Classification Availability of formalin-fixed paraffin-embedded tumor tissue block ECOG performance status 0 to 2 Adequate organ function Women of childbearing potential (WOCBP) must agree to use a highly effective method of contraception from the time of giving informed consent until at least 10 months after the last dose of loncastuximab tesirine. Men with female partners who are of childbearing potential must agree to use a condom when sexually active or practice total abstinence from the time of giving informed consent the first dose until at least 7 months after the last dose of loncastuximab tesirine. Men must refrain from donating sperm during this same period. For the arm that includes glofitamab, WOCBP must agree to use contraceptive methods that result in a failure of <1% per year or remain abstinent (refrain from heterosexual intercourse) during the treatment period and for at least 18 months after pretreatment with obinutuzumab. For the arm that includes mosunetuzumab, WOCBP must agree to use contraceptive methods that result in a failure of <1% per year or remain abstinent (refrain from heterosexual intercourse) during the treatment period and for at least 3 months after the final dose of mosunetuzumab and tocilizumab (if applicable).

Exclusion Criteria:

Known history of hypersensitivity resulting in treatment discontinuation to or positive serum human ADA to a CD19 antibody Previous therapy with loncastuximab tesirine Previous treatment with polatuzumab vedotin, glofitamab or mosunetuzumab (applied to relevant arm and/or cohort of the specific drug administered) Participants who received previous treatment of polatuzumab vedotin containing regimen will be excluded from Arm C Participants who received previous treatment of glofitamab containing regimen will be excluded from Arm E Participants who received previous treatment of mosunetuzumab containing regimen will be excluded from Arm F Allogenic or autologous stem cell transplant within 60 days prior to start of study drug (C1 D1) Human immunodeficiency virus (HIV) seropositive Serologic evidence of chronic hepatitis B virus (HBV) infection and unable or unwilling to receive standard prophylactic antiviral therapy or with detectable HBV viral load Serologic evidence of hepatitis C virus (HCV) infection without completion of curative treatment or with detectable HCV viral load History of confirmed progressive multifocal leukoencephalopathy History of Stevens-Johnson syndrome, toxic epidermal necrolysis, or macrophage activation syndrome (MAS)/hemophagocytic lymphohistiocytosis (HLH) Lymphoma with active central nervous system (CNS) involvement at the time of screening, including leptomeningeal disease Clinically significant third space fluid accumulation (i.e., ascites requiring drainage or pleural effusion that is either requiring drainage or associated with shortness of breath) Breastfeeding or pregnant Significant medical comorbidities Major surgery, radiotherapy, chemotherapy, or other anti-neoplastic therapy, within 14 days prior to start of study drugs (C1 D1), except shorter if approved by the Sponsor Live vaccine within 4 weeks prior to C1D1 Failure to recover to Grade ≤1 (Common Terminology Criteria for Adverse Events [CTCAE] version 5.0) from acute non-hematologic toxicity (Grade ≤2 alopecia) due to previous therapy prior to screening Active second primary malignancy other than non-melanoma skin cancers, non-metastatic prostate cancer, in situ cervical cancer, ductal or lobular carcinoma in situ of the breast, or other malignancy that the Sponsor's medical monitor and Investigator agree and document should not be exclusionary Extra Exclusion Criteria for Arms E (includes glofitamab) and F (includes mosunetuzumab) Note: as applicable, the arm-specific exclusion criteria may supersede the general ones, such as stem cell transplant. Prior allogeneic stem cell transplant and solid organ transplant Autologous stem cell transplant within 100 days prior to C1D1 History of CNS lymphoma or leptomeningeal infiltration Current or history of CNS disease, such as stroke, epilepsy, CNS vasculitis, or neurodegenerative disease Known active infection, reactivation of a latent infection, whether bacterial, viral, fungal, mycobacterial, or other pathogens (excluding fungal infections of nail beds), or any major episode of infection requiring hospitalization or treatment with intravenous (IV) antibiotics within four weeks prior to C1D1 Active or history of autoimmune disease or immune deficiency, including but not limited to, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, antiphospholipid antibody syndrome, Wegener granulomatosis, Sjögren syndrome, Guillain Barré syndrome, or multiple sclerosis, with certain exceptions Prior treatment with anti-cancer/lymphoma targeted therapies (e.g., tyrosine kinase inhibitors, systemic immunotherapeutic/immunostimulating agents, including, but not limited to, cluster of differentiation 137 agonists or immune checkpoint blockade therapies, including anti-cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), anti-programmed cell death protein 1 (PD1), and anti-programmed death ligand 1 (PDL1) therapeutic antibodies, radio-immunoconjugates, ADCs, immune/cytokines and monoclonal antibodies) or treatment with systemic immunosuppressive medication (including, but not limited to, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor agents) within 4 weeks or five half-lives of the drug, whichever is shorter, prior to C1D1, or anticipation of need for systemic immunosuppressive medication during study treatment, with certain exceptions Prior treatment with chimeric antigen receptor T-cell therapy within 30 days prior to C1D1 Toxicities from prior anti-cancer therapy including immunotherapy that did not resolve to ≤ Grade 1 with the exception of alopecia, endocrinopathy managed with replacement therapy and stable vitiligo Any history of immune-related Grade ≥3 AE with the exception of endocrinopathy managed with replacement therapy Ongoing corticosteroid use >25 mg/day of prednisone or equivalent within 4 weeks prior and during study treatment Administration of a live attenuated vaccine within 4 weeks prior to the first dose of study treatment or anticipation that such a live attenuated vaccine will be required during the study or within 5 months after last dose of study treatment Extra Exclusion Criteria for Arm E (includes glofitamab) only. • Known history of hypersensitivity to obinutuzumab

Conditions & Interventions

Interventions:
Drug: Glofitamab, Drug: Loncastuximab Tesirine, Drug: Mosunetuzumab, Drug: Obinutuzumab, Drug: Polatuzumab Vedotin
Keywords:
Clinics and Surgery Center (CSC)

More Information

Description: This protocol aims to characterize the safety and tolerability of loncastuximab tesirine in combination with gemcitabine, lenalidomide, polatuzumab vedotin, or umbralisib, and to identify the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) for any of the combinations in subjects with relapsed or refractory B-cell Non-Hodgkin Lymphoma. This project aims to address the resistance mechanisms to single agent therapies and enhance efficacy by engaging different targets, in synergistic or additive manner.
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Phase: Phase I
IRB Number: STUDY00015805
