KARTA BADANIA
NAZWA BADANIA: An Open Label, Phase 2 Clinical Trial of MEN1703as Monotherapy and in Combination with Glofitamab in Patients with Relapsed or Refractory Aggressive B-cell Non-Hodgkin Lymphoma
NUMER PROTOKOŁU: **JASPIS-01**
WSKAZANIE- C85.7 - Inne określone postacie chłoniaka nieziarniczego

Inclusion Criteria

Each participant must meet the following inclusion criteria to be eligible for enrolment in the study:

1. Age ≥18 years old at time of written informed consent, provided prior to Screening.
2. Documented histological confirmation of aggressive B-cell non-Hodgkin lymphoma including DLBCL NOS and transformed indolent B-cell lymphoma, according to the 5th edition of the WHO classification of lymphoid neoplasms (Alaggio 2022).
3. R/R disease having received at least 2 prior lines of systemic treatment for aggressive B-cell non-Hodgkin lymphoma, and:
   • Additional for Group 1: anti-CD3xCD20 bispecific antibody treatment naïve
   • Additional for Group 2: exhausted all standard, available treatment options.
4. At least 1 measurable site of disease based on computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET)-CT scan with involvement of 2 or more clearly demarcated lesions and or nodes.
5. Availability of lymph node tissue at Screening suitable for diagnostic, disease assessment, and pharmacodynamic testing requirements per protocol (see Section 8.2.2). Archival sample is permitted if obtained ≤8 weeks after relapse or confirmation of refractory disease following most recent treatment.

Note: An exception to this window for an archival sample may be approved by the Medical Monitor where there is reasonable justification that is it representative of the clinical status at Screening.

6. Life expectancy of ≥12 weeks.
7. Eastern Cooperative Oncology Group (ECOG) Performance Status 0, 1 or 2.
8. Adequate organ function at Screening, including: a) Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≤2.5X the upper limit of normal (ULN);
   b) Total bilirubin ≤1.5X ULN; Patients with documented history of Gilbert's Syndrome and in whom total bilirubin elevations are accompanied by elevated indirect bilirubin are eligible;
   c) Adequate renal function: serum creatinine ≤1.5X ULN or a creatinine clearance (CrCl) calculated by Cockroft-Gault formula of ≥50 mL/min for patients in whom, in the investigator's judgment, serum creatinine levels do not adequately reflect renal function (see Section 15);
   d) Left ventricular ejection fraction (LVEF) ≥40% as per local assessment practice.

9. Adequate hematologic function defined as the following: a) Lymphocyte count <5.0 ×109/L
   b) Platelet count ≥75 ×109/L (or, in the presence of bone marrow involvement or splenomegaly, ≥50 ×109/L), and platelet transfusion free within 14 days prior to first dose of study drug
   c) Hemoglobin ≥10.0 g/dL (6.2 mmol/L) and transfusion free within 21 days prior to first dose of study drug
   d) Absolute neutrophil count (ANC) ≥1.5 ×109/L.

10. Coagulation parameters as follows: prothrombin time (PT)/international normalized ratio (INR) and partial thromboplastin time (PTT) <1.5X ULN.
11. Negative serum pregnancy test at Screening and within 3 days of first dose of drug (applies to women of child-bearing potential [WOCBP] only; menopausal status is defined as serum follicle stimulating hormone level ≥30 IU/L in the absence of hormone replacement therapy, or complete

absence of menses for at least 12 consecutive months which is not due to medication; or successful surgical sterilization).
12. Agree to use highly effective contraceptive methods (Section 13.1) during treatment and for 1 month after stopping study drug (applies to women and men of childbearing potential only). Sexually active male participants are asked to advise their female partners of childbearing potential to also use highly effective contraception for the same time period.
13. Agree not to donate blood, eggs (ova) or sperm, during study participation and for 1 month after the last dose of study drug (Section 13.1).

Exclusion Criteria

Each participant must not meet any of the following exclusion criteria to be eligible for enrolment in the study:
1. Primary central nervous system (CNS) lymphoma or CNS involvement by lymphoma at screening.
2. Received anti-cancer treatments, including cytotoxic chemotherapy, radiotherapy, hormonal therapy, biologic, immunotherapy, or investigational drugs within 14 days or 5 half-lives (whichever is shorter) before the first dose of study drug. Prior treatment with CAR-T cell or an anti-CD3xCD20 bispecific antibody therapy (permitted for Group 2 only), requires a wash out period of ≥4 weeks.
3. Concurrent participation in another therapeutic clinical study.
4. Ongoing clinically significant toxicity (for example, alopecia is not clinically significant) from any prior anti-cancer therapy that has not resolved to Grade 1 or less prior to the first dose of study drug.
5. Prior treatment with a PIM inhibitor.
6. Any prior therapy with a bispecific antibody targeting CD3 and CD20 (Group 1 only). Ryvu Therapeutics S.A.25 March2024Clinical Trial ProtocolMEN1703JASPIS-01
7.Known risk ofallergy toMEN1703 (both groups), glofitamabor anti-CD20 agent(s)(Group 1 only), or their excipients.
8.Contraindication to all uric acid lowering agents.
9.Majorsurgerywithin1 month priortofirstdoseofstudy drug.
10.Hematopoietic stemcell transplant within4 monthsprior to first dose of study drug.
11.Requires systemic immune-modulating therapy (regardless of dose) or hasconfirmed history or current autoimmune disease or other diseases resulting in permanent immunosuppression.
12.Exposed to live or liveattenuated vaccine(s)within 4 weeks prior to signing theinformed consent form (ICF).
13.Evidenceofongoing anduncontrolled systemicbacterial,fungal, orviralinfection, except fordocumented GradeCommon Terminology Criteria for Adverse Events (CTCAE)≤2 infections with evidenceof improvement or without evidence ofworsening infection.
14.Known human immunodeficiency virus (HIV)infectiondefined as any of the following:
a)CD4+ T-cell count of less than 350 cells/µL at Screening
b)AIDS-defining opportunistic infection within the past 12 months
c)On established antiretroviral therapy (ART) for less than 4 weeks or presenting with aviral load of more than 400 copies/mL prior to Screening
d)On ART or prophylactic antimicrobials that are expected to cause significant drug-drug interactions or overlapping toxicities with study treatment.

Note: HIV testing is not required unless mandated locally.
15.Current active liver disease from any cause including hepatitis A (hepatitis A virus IgMpositive), hepatitisB (hepatitis B virus [HBV] surface antigen positive), or hepatitis C(hepatitisC virus [HCV] antibody positive, confirmed by HCV RNA). Subjects with HCVwith undetectable virus after treatment areeligible. Subjects with a prior history of HBV areeligible if quantitative PCR for HBV DNA is negative.
16.Ongoing drug-induced pneumonitis.
17.Ongoing inflammatoryboweldisease.

18.Active known second malignancy, except for any of the following:
a)Adequately treated basal cell carcinoma, squamous cell carcinoma of the skin, or in situcervical cancer
b)Adequately treated Stage 1 cancerfrom which the participant is currently in remission

and has been in remission for ≥2 years
c)Low-risk prostate cancerwith a Gleason score <7 and a prostate-specific antigen (PSA)level <10 ng/mL
d)Any other cancer from which the participant has been disease-free for≥3years.
19.Received an agent known to be a sensitive CYP2D6 substrate ora CYP2D6 substrate with a narrow therapeutic range, a strong or moderateCYP2D6 inhibitor, or aBCRP inhibitor

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within 14 days or 5 half-lives (whichever is shorter), prior to the first dose of study drug.
20. Cardiac dysfunction is defined as myocardial infarction within 6 months of study entry, New York Heart Association (NYHA) Class III or IV heart failure, uncontrolled dysrhythmias, or poorly controlled angina.
21. Are receiving any active treatment for thrombosis.
22. History of serious ventricular arrhythmia (e.g., VT or VF, ≥3 beats in a row), or QT interval corrected for heart rate (QTc) ≥480 ms.
Note: QTc values up to 500 ms will be acceptable where patient's medical history e.g., bundle branch block, is known to cause mild QTc prolongation and the condition is well controlled.
23. Any disease, syndrome or condition which may significantly affect drug intake via oral route.
24. Planning to become pregnant or breastfeed during treatment and for 1 month after the last dose of study drug.
25. Any other prior or current medical condition, intercurrent illness, surgical history, physical or 12-lead electrocardiogram (ECG) findings, laboratory abnormalities, or extenuating circumstance (e.g., alcohol or drug addiction) that, in the investigator's opinion, could jeopardize patient safety or interfere with the objectives of the study.