KARTA BADANIA
NAZWA BADANIA: A Phase 1, Open-Label Study of the Safety, Pharmacokinetics, and Pharmacodynamics of JNJ-64264681 in Participants with Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia
NUMER PROTOKOŁU: **88998377LYM1001**
WSKAZANIE- C85.1 - Chłoniak z komórek B, nieokreślony

Inclusion Criteria

Each potential participant must satisfy all of the following criteria to be enrolled in the study:

1. Participants must be ≥18 years of age.
2. Participants must have Eastern Cooperative Oncology Group (ECOG) performance status grade of 0 or 1 (Section 10.7).
3. Criterion amended per Amendment 3.

3.1 Criterion amended per Amendment 4.

3.2 Participants must have histological documentation of disease: B-cell NHL or CLL/SLL requiring therapy (defined below for Part 1 and Part 2).

Part 1:

B-cell NHL: The following histologies of B-cell NHL that require systemic treatment will be enrolled, with the following disease-specific criteria:

Diffuse Large B-Cell Lymphoma and High-grade B-cell Lymphoma
Received first-line chemotherapy and at least 1 subsequent line of systemic therapy that may or may not include autologous stem cell transplantation.

[redacted]

Follicular Lymphoma (Including Transformed Follicular Lymphoma)
Previously treated with at least 2 prior lines of systemic therapy, including a standard anti-CD20 antibody.
Mantle Cell Lymphoma or Waldenström Macroglobulinemia
Relapsed or progressing/nonresponsive to at least 2 prior lines of systemic therapy (prior BTK inhibitor treatment acceptable, provided discontinuation not due to disease progression)
Marginal Zone Lymphoma (Including MALT Lymphoma)
Previously treated with at least 2 prior lines of therapy appropriate for the individual patient's disease (eg, *H. pylori*-positive gastric MALT lymphoma must have failed prior *H. pylori* eradication therapy as one of their prior lines).

CLL/SLL: CLL/SLL that meets criteria for systemic treatment per the iwCLL guidelines and is relapsed or progressing/nonresponsive after at least 2 prior systemic therapies. If the participant had prior treatments that included BTK inhibitors they must not have progressed on that line of treatment.

Part 2: All above requirements for Part 1 apply. In addition, participants must have

measurable disease as defined by the appropriate disease response criteria (see Table 8).
- B-cell NHL (including SLL that does not meet iwCLL criteria for CLL): In addition to the above requirements, participants must have measurable disease as defined by the appropriate disease response criteria (see Table 8). Specific cohorts will have malignancies with mutational status of interest, as determined by the sponsor, based on the results of the archived (or fresh) tumor biopsy obtained at screening and as reported by the study-site. DLBCL will likely be restricted to nongerminal center B-cell like (non-GCB) subtype unless data from Part 1 suggest that GCB DLBCL may benefit.
4. Participants must have hematology laboratory parameters within the following ranges. Values must be without transfusions or growth factors for at least 7 days prior to the first dose of study drug.
a. Hemoglobin ≥8 g/dL
b. Platelets ≥50 x 109
/L
c. Absolute neutrophil count ≥0.75 x 109
/L
5. Criterion amended per Amendment 3.
5.1 Participants must have chemistry laboratory parameters within the following range:
a. AST and ALT ≤3 x upper limit of normal (ULN)
b. Total bilirubin ≤1.5 x the ULN, except for patients with Gilbert's syndrome
c. Calculated or measured creatinine clearance ≥60 mL/min/(1.73 m2
)
6. Participants must have cardiac parameters within the following range: corrected QT interval (QTcF) ≤480 milliseconds based on the average of triplicate assessments performed as close as possible in succession (the full set of triplicates should be completed in less than 10 minutes).
7. Women of childbearing potential must have a negative highly sensitive serum pregnancy test (eg, □-human chorionic gonadotropin [□-hCG]) at screening, and a negative serum or urine pregnancy test prior to the first dose of study drug.
8. Women must be (as defined in Section 10.5, Appendix 5: Contraceptive and Barrier Guidance and Collection of Pregnancy Information).
a. Not of childbearing potential
b. Of childbearing potential and practicing a highly effective, preferably userindependent method of contraception (failure rate of <1% per year when used consistently and correctly) and agree to remain on a highly effective method while receiving study drug and until 30 days after last dose. Examples of highly effective methods of contraception are located in Section 10.5, Appendix 5: Contraceptive and Barrier Guidance and Collection of Pregnancy Information
9. Men must wear a condom during the study for 7 days after the last dose of study drug when engaging in any activity that allows for passage of ejaculate to another person. Men who engage in sexual activity with a woman of childbearing potential must continue to wear a condom for 90 days after the last dose of study drug. Male participants should also be advised of the benefit for a female partner to use a highly effective method of contraception as condoms may break or leak.
10. Women must agree not to donate eggs (ova, oocytes) for the purposes of assisted reproduction during the study and for a period of at least 30 days after the last study drug administration.
11. Participants must be willing and able to adhere to the lifestyle restrictions specified in this

protocol12. Criterion amended per Amendment 4.
12.1 Criterion modified per Amendment 3.
12.2 Participants with B-cell NHL must have tumor tissue available at baseline. This is not required for participants with CLL or leukemic non-nodal MCL.
A fresh tumor biopsy is preferred. If a fresh biopsy is not obtained, archived tissue must be available.
13. Participants must sign an ICF indicating their understanding of the purpose and the procedures required for the study, and their willingness to participate in the study. Consent is to be obtained prior to the initiation of any study-related tests or procedures that are not part of standard of care for the participant's disease.
5.2. Exclusion Criteria
Any potential participant who meets any of the following criteria will be excluded from participating in the study.
1. Criterion amended per Amendment 3.
1.1. Participant has known active CNS involvement.
2. Participant has received prior solid organ transplantation.
3. Participant has received prior stem cell transplant, defined as:
 Received an autologous stem cell transplant ≤3 months before the first dose of study drug.
 Prior treatment with allogenic stem cell transplant ≤6 months before the first dose of study drug, has evidence of graft versus host disease, or requires immunosuppressant therapy.
4. Participants with active (expected to require systemic treatment) second malignancies are excluded. Participants with nonmelanoma skin cancers, or unrelated malignancies with minimal risk of requiring systemic treatment or otherwise interfering with study endpoints, may be included at the discretion of the investigator with agreement from the sponsor's medical monitor.
5. Criterion amended per Amendment 4.
5.1 Criterion amended per Amendment 3.
5.2. Participant has history of progression of disease while treated with a BTK inhibitor. Participants who have discontinued prior BTK inhibitors due to participant or doctor choice without evidence of progression or intolerable class-related toxicity will be eligible6. Participant has known allergies, hypersensitivity, or intolerance to JNJ-64264681 or its excipients (refer to the IB).
25
7. Criterion amended per Amendment 4.
7.1 Criterion amended per Amendment 3.
7.2 Participant has been treated with an investigational drug (including investigational vaccines) within five half-lives or 2 weeks before the planned first dose of study drug.
8. Participant is taking long-term corticosteroids (>10 mg daily prednisone equivalents). A short course (eg, >10 mg daily prednisone equivalents for less than 7 days) of corticosteroids is permitted. Inhaled or topical steroids, and adrenal replacement doses ≤10 mg daily prednisone equivalents, are permitted in the absence of active autoimmune disease.
If corticosteroids were used to treat immune-related adverse events associated with prior therapy, ≥7 days must have elapsed since the last dose of corticosteroid.
9. Participant is experiencing toxicities from previous anticancer therapies that have not resolved to baseline levels, or to Grade 1 or less (except for alopecia and peripheral neuropathy).
10. Participant has a history of clinically significant cardiovascular disease within the

6 months prior to the first dose of study drug including, but not limited to:
a. Myocardial infarction
b. Severe or unstable angina
c. Clinically significant cardiac arrhythmias
d. Uncontrolled hypertension
e. Stroke or transient ischemic attack
f. Venous thromboembolic events (ie, pulmonary embolism) within 1 month prior to the first dose of study drug; uncomplicated (Grade ≤2) deep vein thrombosis is not considered exclusionary.
g. Congestive heart failure (New York Heart Association class III-IV) (see Section 10.8, Appendix 8: New York Heart Association Classification of Functional Capacity)
h. Pericarditis or clinically significant pericardial effusion
i. Myocarditis
j. Endocarditisk. Long QT syndrome
11. Criterion amended per Amendment 3.
11.1. Participant has clinically significant pulmonary compromise that requires supplemental oxygen use to maintain adequate oxygenation.
12. Participant has prolonged coagulation values (prothrombin time, international normalized ratio, activated partial thromboplastin time) in the absence of direct oral anticoagulants treatment, at screening that are clinically significant, or has a history of subdural hematoma, abnormal bleeding tendency, congenital bleeding diathesis.
13. Participant has active liver cirrhosis of Child Pugh Class B.
14. Participant is unable to swallow capsules or tablets or has malabsorption syndrome, disease that significantly affects gastrointestinal function, resection of the stomach or small bowel, symptomatic inflammatory bowel disease or ulcerative colitis, or partial or complete bowel obstruction. If any of these conditions exist, the site should discuss with the sponsor to determine participant eligibility.
15. Participant has evidence of active viral, bacterial, or fungal infection requiring systemic anti-infective treatment within 7 days before the first dose of study drug.
16. Participant has a known positive test result for human immunodeficiency virus or acquired immune deficiency syndrome , unless viral load is undetectable and CD4 count is above 200 on stable highly active antiretroviral therapy (note: see prohibited therapies in Section 6.5.2).
17. Criterion amended per Amendment 4.
17.1. Participant has active or chronic hepatitis B or hepatitis C infection (see Appendix 2: Clinical Laboratory Tests and Appendix 12: Hepatitis B Virus Screening).
Hepatitis B infection is defined by (a) a positive test for hepatitis B surface antigen (HBsAg), or (b) a test panel that is positive for anti-hepatitis B core antigen (HBc) and negative for HBsAg and hepatitis B surface antibody (anti-HBsAb). Appendix 12 describes the test panels that will not be excluded. Specifically, a test panel that is positive for anti-HBc, positive for anti-HBsAb, and negative for anti-HBsAg will be eligible; and for participants enrolled with this panel of results the treating physician should use their discretion and institutional guideline to decide whether (a) PCR based test of HBV is warranted at screening and repeated during treatment, and (b) prophylactic treatment for HBV reactivation is necessary.
Hepatitis C infection is defined by a positive hepatitis C virus (HCV) antibody test, with subsequent confirmation with positive HCV RNA test. 18. Participant experienced trauma or had major surgery (eg, entailing entry into a major
body cavity, or significant blood loss or fluid shifts) within 28 days prior to the first

dose of study drug. Note: Participants with planned minor surgical procedures to be conducted under local anesthesia may participate).
19. Participant has any serious underlying medical or psychiatric condition (eg, alcohol or drug abuse, dementia or altered mental status); or any issue that would impair the ability of the participant to receive or tolerate the planned treatment at the investigational site, to understand informed consent, or due to which, in the opinion of the investigator, participation would not be in the best interest of the participant (eg, could compromise the participant's well-being) or that could prevent, limit, or confound the protocolspecified assessments.
20. Participant is pregnant, or breastfeeding, or planning to become pregnant while enrolled in this study or within 30 days after the last dose of study drug.
21. Participant plans to father a child or donate sperm for the purpose of reproduction while enrolled in this study or within 90 days after the last dose of study drug.
22. Participant requires a prohibited medication that cannot be discontinued or substituted, or temporally interrupted during the study; see Section 6.5.2 for prohibited therapies.
23. Participant has received a live attenuated vaccine within 1 month before the planned first dose of study drug.