KARTA BADANIA
NAZWA BADANIA: An Open-Label Clinical Trial of RVU120 as Monotherapy and in Combination with Ruxolitinib in Patients with Intermediate or High-Risk, Primary or Secondary Myelofibrosis
NUMER PROTOKOŁU: **POTAMI-61**
WSKAZANIE- D75.8 - Inne określone choroby krwi i narządów krwiotwórczych

Inclusion Criteria
Each participant must meet all of the following inclusion criteria at Screening to be eligible for enrolment in the study:
1. Age ≥18 years at time of provision of informed consent.
2. Diagnosis of primary or secondary MF according to the revised World Health Organization (WHO) criteria (Arber 2022).
3. Intermediate or high-risk disease according to the DIPSS for MF.
4. Participants in Cohort 1: Resistant or refractory to prior JAK inhibitor treatment or ineligible for JAK inhibitor treatment in the opinion of the investigator.
Participants in Cohort 2: Suboptimal response to JAK inhibitor treatment.
Note: a suboptimal response to JAK inhibitor treatment is defined as spleen size increase by palpation >25% after the first 3 months of treatment with a JAK inhibitor or persistent splenomegaly (spleen volume of >450 cm3
) after at least 6 months of JAK inhibitor
treatment and presence of 1 symptom score ≥5 or 2 symptom scores ≥3, new or persistent red blood cell (RBC) transfusion dependence.
Participants in Cohort 3 (optional cohort): naïve to previous treatment with JAK inhibitor.
5. Measurable splenomegaly as demonstrated by:
 palpable spleen measuring ≥5 cm below the left costal margin. The edge of the spleen should be measured from the mid-clavicular line on the left side of the abdomen to the point of greatest splenic protrusion
or
 spleen volume of ≥450 cm3 measured by MRI or CT.
6. Active symptoms of MF as demonstrated by a symptom score of at least 5 points (on a 0 to 10 scale) on at least one of the symptoms or a score of 3 or greater on at least 2 of the following symptoms: night sweats, itchiness, abdominal discomfort, pain under ribs on left side, early satiety, bone or muscle pain, and inactivity.
7. Eastern Cooperative Oncology Group (ECOG) performance score of 0-2.
8. Adequate hematologic function defined as the following:
a. absolute neutrophil count (ANC) ≥1.0 × 109
/L (without growth factor support)
b. PLT count ≥50 × 109
/L (Cohort 2 and Cohort 3 only).
9. Adequate renal function defined as calculated or measured creatinine clearance (CrCl) of ≥30 mL/minute using the formula of Cockcroft and Gault (see Section 15)
10. Adequate liver function defined as the following:
a. aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤3 × upper limit of normal (ULN)
b. alkaline phosphatase (ALP) ≤2 × ULN (ALP ≤5 × ULN for participants with isozymes specific to bone)
c. bilirubin <2 × ULN or bilirubin ≤3 × ULN if due to Gilbert's disease.
11. For WOCBP, a negative pregnancy test must be confirmed during Screening and ≤3 days prior to Cycle 1 Day 1. WOCBP must commit to using a highly effective method of

contraception during study participation and until 28 weeks (approximately 6.5 months) after the last dose of study drug (Section 13.1)
or
For males, an effective barrier method of contraception must be used during study participation and until 28 weeks (approximately 6.5 months) after the last dose of RVU120, if the participant is sexually active with a WOCBP (Section 13.1). 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.
12. Agree not to donate blood, eggs (ova) or sperm, during study participation and until 28 weeks (approximately 6.5 months) after the last dose of study drug (Section 13.1).
13. Investigator considers the participant to be suitable for participation in the clinical study by assessing that they: understand the requirements of the clinical study and can give informed consent; can comply with study medication dosing requirements and all studyrelated procedures and evaluations and are not considered to be potentially unreliable and/or not cooperative.

5.3 Exclusion Criteria

Each participant must not meet any of the following exclusion criteria to be eligible for enrolment in the study:
1. Peripheral blood blast count of ≥10% or bone marrow blast count of ≥10%.
2. Prior history of hematopoietic stem cell transplant.
3. Participation in any other study in which receipt of an investigational new drug occurred within 4 weeks prior to Cycle 1 Day 1.
4. Active known second malignancy with the exception of any of the following:
a. Adequately treated basal cell carcinoma, squamous cell carcinoma of the skin, or in situ cervical cancer
b. Adequately treated Stage I cancer from which the participant is currently in remission and has been in remission for ≥2 years
c. Low-risk prostate cancer with 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 ≥3 years5. Known or suspected allergy to RVU120 or RUX.
6. Impairment of gastrointestinal function or gastrointestinal disease that may significantly alter the absorption of RVU120 (e.g., active inflammatory bowel disease, ulcerative disease, malabsorption syndrome, short bowel syndrome, uncontrolled nausea, vomiting or diarrhea).
7. Major surgical procedure or significant traumatic injury within 28 days before Cycle 1 Day 1, or anticipation of need for major surgical procedure during the course of the study. Placement of a vascular access device or minor surgery is permitted within 14 days before Cycle 1 Day 1 (provided that the wound has healed).
8. Ongoing systemic infection requiring antibiotic, antiviral, or antifungal treatment. Note: prophylactic treatment is allowed.
9. Significant cardiac dysfunction defined as myocardial infarction within 12 months of Cycle 1 Day 1, New York Heart Association (NYHA) Class III or IV heart failure, uncontrolled dysrhythmias, poorly controlled angina (Section 17), or left ventricular ejection fraction (LVEF) <40% as per echocardiography or multiple gated acquisition (MUGA) scan.
10. Taking any medications, herbal supplements, or other substances (including smoking) that are known to be strong inhibitors or moderate/strong inducers or sensitive substrates of CYP1A2, within less than 5 half-lives prior to Cycle 1 Day 1 (Section 16). Note: Any exception should be discussed with the Medical Monitor.

11. History of ventricular arrhythmia, or QTc ≥470 ms (Bazett's formula; Section 18).
12. Known active human immunodeficiency virus (HIV) infection defined 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 a viral load of more than 400 copies/mL prior to Screening
d. on ART or prophylactic antimicrobials that are expected to cause significant drugdrug interactions or overlapping toxicities with study treatment (HIV testing is not required unless mandated locally).
13. Current active liver disease from any cause including hepatitis A (hepatitis A virus IgM positive), hepatitis B (hepatitis B virus [HBV] surface antigen positive), or hepatitis C (hepatitis C virus [HCV] antibody positive, confirmed by HCV RNA). Participants with HCV with undetectable virus after treatment are eligible. A prior history of HBV is acceptable if quantitative PCR for HBV DNA is negative.
14. Pregnant or lactating females.
15. Any other prior or current medical or psychiatric condition, intercurrent illness, surgical history, physical or electrocardiogram (ECG) findings, laboratory abnormalities, or extenuating circumstance (e.g., alcohol or drug addiction) that, in the Investigator's opinion, could jeopardize participant safety or interfere with the objectives of the study.