KARTA BADANIA
NAZWA BADANIA: A Phase 1/2a, First-in-human Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of HDP-101 in Patients With Plasma Cell Disorders Including Multiple Myeloma
NUMER PROTOKOŁU: **HDP-101-01**
WSKAZANIE- C90.0 - Szpiczak mnogi

Criteria

Inclusion Criteria

Patients are eligible to be included in the study only if all of the following criteria apply:

1. Patients who have signed an informed consent and are willing to comply with the requirements and restrictions listed in the study protocol.
2. Male or female aged ≥18 years at the time of informed consent.
3. Life expectancy >12 weeks, as determined by the Investigator.
4. Eastern Cooperative Oncology Group (ECOG, Appendix 9) Performance Status (PS) of 0 to 2 (tumor related performance).
5. A confirmed diagnosis of active MM according to the diagnostic criteria established by the International Myeloma Working Group (IMWG). 15
6. Must have undergone SCT or is considered transplant ineligible.
7. Must have undergone prior treatments with antimyeloma therapy which must have included an immunomodulatory drug, proteasome inhibitor, and antiCD38 treatment, alone or in combination. Patients who are intolerant to these therapies or have contraindications are eligible if other eligibility criteria are fulfilled. Patient must have failed last line of treatment (refractory to or relapsed after last line of treatment) or had to permanently discontinue the last line of therapy due to toxicity (toxicity and reason for permanent discontinuation has to be documented in the electronic case report form [eCRF]). In addition, the patient should either refractory or intolerant to any established standard of care therapy providing a meaningful clinical benefit for the patient assessed by the Investigator.
8. a) Phase 1 part only: patients with non-secretory or oligo-secretory myeloma (NSMM) not meeting the measurability criteria described in 8.b) are eligible (all other eligibility criteria must apply).
   b) Phase 2a part only - measurable disease defined as:
   • Serum M-protein ≥0.5 g/dL, or
   • Urine M-protein ≥200 mg/24 hours, or
   • Serum-free light chains (FLC) assay: involved FLC level ≥10 mg/dL (100 mg/L) provided serum FLC ratio is abnormal (<0.26 or >1.65).
9. Acute toxicities from any prior therapy, surgery, or radiotherapy must have resolved to

Grade 0 or 1 as per the NCI-CTCAE Version 5.0, except for alopecia and Grade 2 neuropathy.

1. Adequate organ system function as defined in Table 12:

Table 12 Adequate Organ System Functions

Organ System	Laboratory Values
Hematologic	
Absolute neutrophil count[a]	$\geq 1.0 \times 10^9$/L
Platelet count	$\geq 50 \times 10^9$/L and absent platelet transfusion for ≥7 days
Hemoglobin	>8.0 g/dL and absent RBC transfusion for ≥7 days
Activated partial thromboplastin time/partial thromboplastin time	≤1.5 × ULN
Renal	
Measured CrCl (using 24-h-urine), if a measured CrCl is not available, the calculated CrCl using the Cockcroft-Gault-Formula can be used	≥60 mL/min.
Albuminuria	≤500 mg/24 hours
Hepatic:	
Total serum bilirubin	≤1.5 × ULN (isolated bilirubin >1.5 and ≤3.0 × ULN is acceptable if bilirubin is fractionated and direct bilirubin <35%)
Aspartate and alanine transaminases	≤1.5 × ULN

CrCl = creatinine clearance, ULN = upper limit normal, RBC = red blood cell

[a] Without Growth factor support for the past 14 days.

11. A female patient is eligible to participate if she is of

• Nonchildbearing potential (ie, physiologically incapable of becoming pregnant) defined as premenopausal females with a documented tubal ligation or hysterectomy; or postmenopausal defined as 12 months of spontaneous amenorrhea (in questionable cases a blood sample with simultaneous follicle-stimulating hormone [FSH] >40 MIU/mL and estradiol <40 pg/mL [<147 pmol/L] is confirmatory). Women on hormone replacement therapy (HRT) and whose menopausal status is in doubt are treated like women of childbearing potential unless they discontinue their HRT to allow confirmation of postmenopausal status prior to study enrollment. For most forms of HRT, at least 2 to 4 weeks will elapse between the cessation of therapy and the blood draw; this interval depends on the type and dosage of HRT. Following confirmation of their postmenopausal status, they can resume use of HRT during the study without use of a contraceptive method.

• Women of childbearing potential must have a negative urine pregnancy test 7 days before the first administration of the study treatment and on Day 1 before first dose of study treatment and commit to either abstain continuously from heterosexual intercourse or to use 2 methods of reliable birth control simultaneously, during the study and for 4 months following the last dose of the study treatment. This includes 1 highly effective form of contraception (tubal ligation, intrauterine device, hormonal [birth control pills, injections, hormonal patches, vaginal rings, or implants] or partner's vasectomy) and 1 additional effective contraceptive method (male latex or synthetic condom, diaphragm, or cervical cap).

12. Male patients must have had a prior vasectomy or commit to use an effective contraception

(complete abstinence from sexual intercourse, latex or synthetic condom and during sexual intercourse with a female a double-barrier method including a condom and occlusive cap [diaphragm or cervical/vault caps] plus spermicidal agent [foam/gel/film/cream/suppository]) from the time of first study treatment infusion until 3 months following the last study treatment infusion to allow for clearance of any altered sperm.

5.2 Exclusion Criteria

Patients are excluded from the study if any of the following criteria apply:

1. For patient entering the Phase 2a part only: Prior treatment with any approved or experimental BCMA-targeting modalities are not allowed including but not limited to chimeric antigen receptor-T or natural killer (NK) cell treatment, mono or bispecific antibodies and other BCMA-ADCs. (Note that patients in the Phase 1 part could have had any type of prior BCMA directed treatment providing they fulfilled all other inclusion and exclusion criteria).
2. History of allergic reactions to any component of the study treatment.
3. Known central nervous system involvement.
4. Plasma cell leukemia (total plasma cell count of at least 2 × 109 /L) at Screening.
5. History of congestive heart failure classified as Class ≥ III based on the New York Heart Association Classification or Grade 3/4 unstable angina pectoris within 6 months ofenrollment, presence of unstable atrial fibrillation, ECG with QTc ≥480 ms, cardiac arrhythmia, or uncontrolled hypertension.
6. Treatment with systemic anticancer therapy within 4 weeks or 5 t½s of the agent if t½ is known (whichever is shorter) before first dose of the study treatment. Anticancer therapies include cytotoxic chemotherapy, targeted inhibitors, and immunotherapies, but do not include radiotherapy or corticosteroids.
7. Higher dose of systemic corticosteroids, defined as oral dexamethasone >40 mg/day (for patients aged >75 years reduced to >20 mg/day) or equivalent, within 3 days prior to the first study treatment infusion.
8. Currently participating in a study and receiving study therapy or participated in a study of an investigational agent and received study therapy or used an investigational device within 2 weeks of the first dose of study treatment.
9. Autologous or allogenic SCT within 12 weeks before the first infusion or is planning for autologous SCT.
10. Symptomatic graft versus host disease post allogenic hemopoietic cell transplant within 12 months prior to the first study treatment infusion.
11. Significant surgical intervention within 21 days prior to the first study treatment infusion or ongoing post-operative complications.
12. Patients who have a history of being nonresponsive to platelet and/or RBC transfusions and expected lack of adequate support with blood products on demand.
13. Radiotherapy within 21 days prior to the first study treatment infusion, or localized palliative radiotherapy within 7 days prior to the first study treatment infusion, therapy with radio-immuno-conjugates performed less than 3 months prior to the first dose of study treatment.
14. Herbal remedies interfering or stimulating the metabolic pathways (eg, mistletoe extract) or known to potentially interfere with major organ function (eg, hypericin) within 21 days prior to the first study treatment infusion.
15. History of any other malignancy known to be active, with the exception of completely removed in situ cervical intraepithelial neoplasia, nonmelanoma skin cancer, ductal carcinoma in situ, early-stage prostate cancer that has been adequately treated. Malignancies which are adequately treated and requiring hormonal therapies only to prevent the recurrence

of the malignancy other than multiple myeloma may be permitted after discussion with and agreement of the Sponsor's Medical Monitor (eg, breast cancer treated with hormonal therapies).
16. Known human immunodeficiency virus infection.
17. Patients with active infection requiring systemic anti-infective (eg, antibiotic or antiviral) therapy. Patients who are successfully treated with systemic anti-infective treatment and have no clinical signs of infection for at least 2 days may be enrolled as per the discretion of the Investigator.
18. Patients with positive test results for hepatitis B surface antigen or Hepatitis B core antigen, 19. Patients with positive test results for hepatitis C virus (HCV) infection are excluded regardless of viral load. If the hepatitis C antibody test is positive, a confirmatory polymerase chain reaction or recombinant immunoblot assay (RIBA) test should be performed. If the RIBA test is negative, patient is eligible for study.
20. Current active liver or biliary disease (with the exception of Gilbert's syndrome or asymptomatic gallstones), liver metastases, or other stable chronic liver disease per the Investigator's assessment.
21. Pregnancy or breast feeding.
22. Refusal to use effective methods of contraception.
23. Legal incapacity/limited legal capacity for providing informed consent.
24. Any serious and/or unstable preexisting medical, psychiatric disorder, or other conditions (including lab abnormalities) that could interfere with patient's safety, obtaining informed consent, or compliance to the study procedures.
25. Pneumonia or symptomatic pneumonitis (symptoms include but not limited to shortness of breath, wheezing, dyspnea, decrease oxygen saturation).