A Study to Evaluate the Efficacy, Safety, and Tolerability of IMU-838 (vidofludimus calcium) versus Placebo in Adults with Relapsing Multiple Sclerosis (RMS)

11/09/2025 04:13:16

Main Information

Primary registry identifying number
LBCTR2023115324

Protocol number
P3-IMU-838-RMS-01 (ENSURE-1)

MOH registration number
.

Study registered at the country of origin
No

Study registered at the country of origin: Specify
.

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency
31/08/2023

Primary sponsor
Immunic AG

Primary sponsor: Country of origin
Germany

Date of registration in primary registry
04/12/2023

Date of registration in national regulatory agency
31/08/2023

Public title
A Study to Evaluate the Efficacy, Safety, and Tolerability of IMU-838 (vidofludimus calcium) versus Placebo in Adults with Relapsing Multiple Sclerosis (RMS)

Acronym
ENSURE 1

Scientific title
A Multi-Center, Randomized, Double-Blinded Phase 3 Study to Evaluate the Efficacy, Safety, and Tolerability of IMU-838 versus Placebo in Adults with Relapsing Multiple Sclerosis (ENSURE-1)

Acronym
ENSURE 1

Brief summary of the study: English

ENSURE-1 is a multi-centre, randomized, Phase 3, placebo-controlled study, with the main 72-week double-blind period and the extension 8 years open-label period. The study will evaluate the efficacy, safety, and tolerability of IMU-838 in adults with RMS. Patients will be randomly assigned in a 1:1 ratio to receive either IMU-838 or placebo in a double-blind fashion. For the first week (Days 1 to 7), patients will take a 15 mg tablet of IMU 838 or placebo once daily in the morning. Starting at Week 2 (Day 8), the patients will take a 30 mg tablet of IMU-838 or placebo once daily in the morning. The patients will return to the site every 12 weeks for study assessments and receipt of the next 12-week supply of study medication. The double-blind treatment period will last for a maximum of 72 weeks for patients with no MS breakthrough event (MSBE; defined as confirmed relapse or confirmed disability progression during the double-blind treatment). Patients with a confirmed MSBE will be required to re-consent to one of the 3 study continuation options: to remain in the randomized double-blind treatment, to switch to rescue open-label treatment with IMU-838 or to switch to any rescue treatment outside this trial. If choosing any of these three options, patients will continue the regular visit schedule up to Week 72.
The patients completing the main study will have the option to start open label extension (OLE) treatment with IMU-838 for a duration of up to 8 years.
The primary objective of this study is to demonstrate the efficacy of IMU-838 vs. placebo in adult patients with active RMS in delaying the occurrences of relapses based on time to first relapse (T2FR), as determined by the Independent Neurology Evaluation Committee (INEC), within the main 72-week double-blind period of the study.

The Secondary Objectives are the followings:
•to evaluate the effect of IMU-838 versus placebo on volume of new T2 lesions
•to evaluate the effect of IMU-838 versus placebo on disability progression
•to evaluate the effect of IMU-838 versus placebo on cognitive performance
•to evaluate the effect of IMU-838 versus placebo on whole brain atrophy.

Brief summary of the study: Arabic

ENSURE-1 هي دراسة من المرحلة 3، متعددة المراكز، عشوائية التوزيع، مزدوجة التعمية و مؤلفة من 72 أسبوعا" من الفترة التعمية المزدوجة و فترة تمديد 8 سنوات. ستقوم الدراسة بتقييم فعالية وسلامة وتحمل IMU-838 في البالغين الذين يعانون من RMS. سيتم تعيين المرضى بشكل عشوائي بنسبة 1: 1 لتلقي إما IMU-838 أو الدواء الوهمي بطريقة مزدوجة التعمية. في الأسبوع الأول (الأيام من 1 إلى 7) ، أو دواء وهمي مرة واحدة يوميًا في الصباح. بدءًا من الأسبوع الثاني (اليوم الثامن) IMU 838 مجم من 15 سيأخذ المرضى قرصًا عيار 30 مجم من IMU-838 سيأخذ المرضى قرصًا بحجم 12 أو دواء وهمي مرة واحدة يوميًا في الصباح. سيعود المرضى إلى الموقع كل 12 أسبوعًا. ستستمر فترة العلاج المزدوج التعمية لمدة أقصاها 72 أسبوعًا لإجراء تقييمات الدراسة واستلام الكمية التالية من أدوية الدراسة لمدة 12 أسبوعًا ؛ يُعرف بأنه انتكاس مؤكد أو تطور إعاقة مؤكد أثناء MSBE) للمرضى الذين لم يتعرضوا لحدث اختراق مرض التصلب العصبي المتعدد العلاج مزدوج التعمية).
مؤكد إعادة الموافقة على أحد خيارات مواصلة الدراسة الثلاثة: البقاء في العلاج العشوائي مزدوج MSBE سيُطلب من المرضى الذين لديهم أو التبديل إلى أي علاج إنقاذ خارج هذه الدراسة. في حالة اختيار أي من هذه IMU-838 التعمية ، أو التبديل إلى العلاج المفتوح باستخدام الخيارات الثلاثة ، سيستمر المرضى في جدول الزيارة المنتظم حتى الأسبوع 72.
سيكون لدى المرضى الذين أكملوا الدراسة الرئيسية خيار بدء العلاج بملصق مفتوح IMU-838 باستخدام (OLE) لمدة تصل إلى 8 سنوات .

الهدف الأساسي من هذه الدراسة هو إثبات فعالية IMU-838 مقابل الدواء الوهمي في المرضى البالغين الذين لديهم RMS نشط في تأخير حدوث الانتكاسات بناءً على الوقت حتى الانتكاس الأول (T2FR) ، كما تحدده لجنة تقييم طب الأعصاب المستقلة ، (INEC). على النحو الذي تحدده لجنة تقييم طب الأعصاب المستقلة ، (T2FR) حدوث الانتكاسات بناءً على الوقت حتى الانتكاس الأول خلال فترة التعمية المزدوجة البالغة 72 أسبوعًا من الدراسة .

الأهداف الثانوية هي ما يلي:
• مقابل الدواء الوهمي على حجم آفات IMU-838 الجديدة T2 لتقييم تأثير
• مقابل الدواء الوهمي على تطور الإعاقة IMU-838 لتقييم تأثير
• مقابل الدواء الوهمي على الأداء المعرفي IMU-838 لتقييم تأثير
• مقابل الدواء الوهمي على ضمور الدماغ بالكامل IMU-838 لتقييم تأثير.

Health conditions/problem studied: Specify

Relapsing Multiple Sclerosis

Interventions: Specify

Patients will be randomly assigned in a 1:1 ratio to receive either IMU-838 or placebo in a double-blind fashion. For the first week (Days 1 to 7), patients will take a 15 mg tablet of IMU 838 or placebo once daily in the morning. Starting at Week 2 (Day 8), the patients will take a 30 mg

tablet of IMU-838 or placebo once daily in the morning. The patients will return to the site every 12 weeks for study assessments and receipt of the next 12-week supply of study medication. The double-blind treatment period will last for a maximum of 72 weeks for patients with no MS breakthrough event (MSBE; defined as confirmed relapse or confirmed disability progression during the double-blind treatment). Patients with a confirmed MSBE will be required to re-consent to one of the 3 study continuation options: to remain in the randomized double-blind treatment, to switch to rescue open-label treatment with IMU-838 or to switch to any rescue treatment outside this trial. If choosing any of these three options, patients will continue the regular visit schedule up to Week 72.
The patients completing the main study will have the option to start open label extension (OLE) treatment with IMU-838 for a duration of up to 8 years.

Key inclusion and exclusion criteria: Inclusion criteria

1. Male or female patient (age ≥18 to ≤55 years).
2. Patients with an established diagnosis of MS according to 2017 McDonald Criteria .
3. Patients with RMS comprising of relapsing remitting MS (RRMS) and active secondary progressive MS, both defined according to Lublin criteria 1996 and 2014.a

a Patients are eligible for this trial if their disease modifying treatment has failed due to efficacy, safety, or tolerability issues, if they have contraindications or no access to treatment, or if they refuse the offered MS treatment.

4. Active disease as defined by Lublin 2014 evidenced prior to Screening by:
a. At least 2 relapsesa in the last 24 months before randomization, or
b. At least 1 relapsea in the last 12 months before randomization , or
c. A positive Gd+ MRI scan (brain and/or spine) in the last 12 months prior to randomization.

aRelapses must have been assessed and documented by a physician in the patient files.

5. EDSS score between 0 and 5.5 (inclusive) at SV1.
6. Female patients:
a. must be of non-childbearing potential, ie, surgically sterilized (hysterectomy, bilateral salpingectomy, bilateral oophorectomy at least 6 weeks before SV1) or postmenopausal (where postmenopausal is defined as no menses for 12 months without an alternative medical cause), or
b. if of childbearing potential, must have a negative pregnancy test at SV1 (blood test) and before the first IMP intake (Day 1 blood or urine test). They must agree not to attempt to become pregnant, must not donate ova, and must use a highly effective contraceptive method (see below) together with a barrier method between study consent and 30 days after the last intake of the IMP.
c. highly effective forms of birth control are those with a failure rate less than 1% per year and include:
i. oral, intravaginal, or transdermal combined (estrogen and progestogen containing) hormonal contraceptives associated with inhibition of ovulation.
ii. oral, injectable, or implantable progestogen-only hormonal contraceptives associated with inhibition of ovulation.
iii. intrauterine device or intrauterine hormone-releasing system.
iv. bilateral tubal occlusion.
v. vasectomized partner (ie, the patient's male partner underwent effective surgical sterilization before the female patient entered the clinical study and is the sole sexual partner of the female patient during the clinical study).
vi. sexual abstinence (acceptable only if it is the patient's usual form of birth control/lifestyle choice; periodic abstinence [eg, calendar, ovulation, symptothermal, postovulation methods] and withdrawal are not acceptable methods of contraception).
d. Barrier methods of contraception include:
i. condom.
ii. occlusive cap (diaphragm or cervical/vault caps) with spermicidal gel/film/cream/suppository.
7. Male patients must agree not to father a child or to donate sperm starting at SV1, throughout the clinical study, and for 30 days after the last intake of the IMP. Male patients must also:
a. abstain from sexual intercourse with a female partner (acceptable only if it is the patient's usual form of birth control/lifestyle choice), or
b. use adequate barrier contraception during treatment with the IMP and until at least 30 days after the last intake of the IMP, and
c. if they have a female partner of childbearing potential, the partner should use a highly effective contraceptive method as outlined in inclusion criterion 5.
d. if they have a pregnant partner, they must use condoms while taking the IMP to avoid exposure of the fetus to the IMP.
8. Willingness and ability to comply with the protocol.
9. Patients are able to read and understand the given information about the study (including their language capabilities) and provide written informed consent prior to any study-related procedure.

Inclusion Criteria for the Extension Period of the Study, Open-Label-Treatment
1. Completed full visit schedule of the MP up to 72 weeks (with the V8/EOMP completed and no more than 1 regular study visit omitted), independent of the patient's treatment:
a. Double-blind treatment, or
b. Open-label rescue IMU-838 treatment, or
c. Rescue treatment outside this trial (observational phase) but with double-blind treatment of at least 24 weeks in this trial and approved by the sponsor.
2. Performed a full and complete Week 72 visit (Visit 8; which also serves as an EOMP visit and includes the Visit 8 MRI examination)

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

Key inclusion and exclusion criteria: Age maximum

18 55

Key inclusion and exclusion criteria: Exclusion criteria

Exclusion Criteria for the Main Period of the Study
Multiple sclerosis-related exclusion criteria:
1. Patients with non-active secondary progressive MS and primary progressive MS.
2. Any disease other than MS that may better explain the signs and symptoms, including history of complete transverse myelitis.
3. Clinical signs or presence of laboratory findings suggestive for neuromyelitis optica (NMO) spectrum disorders or myelin oligodendrocyte glycoprotein (MOG)-IgG-associated encephalomyelitis.
4. Any MRI finding, which puts in question the MS diagnosis, including but not limited to a longitudinally extensive spinal cord lesion.
5. History of malignancy of any organ system (other than localized basal cell carcinoma of the skin or adequately treated cervical cancer), treated or untreated, within the past 5 years, regardless of whether there is evidence full remission at the current time.
6. Any active and uncontrolled coexisting autoimmune disease, other than MS (except for type 1 diabetes mellitus and inflammatory bowel disease).
7. An MS relapse ending within 30 days before SV1 and/or during the Screening Period (until Day 1).
8. Any corticosteroid treatment for relapse given within 30 days before SV2.
Therapy exclusion criteria:
9. Use of experimental/investigational drug (with the exception of COVID-19 vaccines
approved by emergency use authorization) within 8 weeks or 5 times the respective half-life before the date of informed consent, whichever is longer, and throughout the duration of the study; and/or participation in drug clinical studies within 6 months prior to Screening (For selected approved marketed products, if used as an investigational drug, exclusion criterion 11 applies).
10. Any previous treatment with:
a. total lymphoid irradiation
b. bone marrow transplantation
c. stem cell transplantation
d. cladribine, alemtuzumab, or belimumab, including their biosimilars

Lifelong:• cyclophosphamide
• mitoxantrone, if cumulative life-time dose >60 mg/m² or if
evidence of cardiotoxicity following mitoxantrone treatment
Within 12 months:• any use of DHODH inhibitors, including teriflunomide or leflunomide
• anti-CD 19/20 (ocrelizumab, rituximab, ofatumumab, including their biosimilars and investigational products)
• mitoxantrone
• daclizumab
Within 6 months:• natalizumab
• calcineurin inhibitors (eg, tacrolimus, cyclosporine, or pimecrolimus)
• immunoglobulins
• azathioprine
Within 3 months: • plasmapheresis
• any cytokine (other than interferon) or anti-cytokine therapy
• methotrexate
• Sphingosine-1-receptor (S1P) modulators (including, but not limited, fingolimod, siponimod, and ozanimod)
•Tofactinib
•mycophenolate mofetil or mycophenolate sodium

• recurrent pulsed intravenous or intrathecal corticosteroid treatments.
Within 30 days• dimethyl fumarate, monomethyl fumarate, and diroximel fumarate
• slow-release (pegylated) forms of interferons or depot formulations of glatiramer acetate
Within 7 days• interferon-β
• glatiramer acetate

12. Any use of adrenocorticotrophic hormone (ACTH) or occasional use of systemic corticosteroids (oral or intravenous) 30 days before SV2.
13. Any use of the following concomitant medications is prohibited during Screening and
throughout the duration of the study:
a. any medication known to significantly increase urinary elimination of uric acid, in particular lesinurad, as well as uricosuric drugs such as probenecid
b. treatments for any malignancy, in particular irinotecan, paclitaxel, tretinoin,
bosutinib, sorafinib, enasidenib, erlotinib, regorafenib, pazopanib, and nilotinib
c. any drug significantly restricting water diuresis, in particular vasopressin and
vasopressin analogs

Immune response exclusion criteria

14. Conditions (including previous organ transplant) requiring treatments negatively affecting the immune system.
15. Clinically significantly low lymphocyte and/or neutrophil count (Common Terminology Criteria for AEs Grade of 2 or higher), ie, lymphocyte count <800/mm³ (0.8 x 109/L) and/or neutrophil count <1500/mm³ (1.5 x 109/L).
16. History of chronic systemic infections within 6 months before the date of informed consent, including but not limited to tuberculosis and human immunodeficiency virus (HIV). HIV infection that is undetectable within the prior 6 months is not an exclusion criterion.
17. Positive test for SARS-CoV-2 within 14 days prior to randomization. These patients can be randomized earlier if they have 2 consecutive tests confirming negative virus status.
18. Positive Mycobacterium tuberculosis IFNγ release assay (Tbc-IGRA) at SV1.
19. HIV-antigen-antibody (HIV-Ag/Ab) test at SV1.a
20. Any live vaccinations within 30 days before the date of informed consent or during the study except for any virus-based SARS-CoV-2 or

influenza vaccine. Please note that mRNA-based vaccinations are allowed at any time.

Other medical history and concomitant disease exclusion criteria:
21. Presence of the following laboratory values at SV1
a. platelet count <100,000/mm³ (<100 x 109/L)
b. serum creatinine >1.5 x ULN
c. total bilirubin, ALT, or GGT >1.5 x ULN
d. serum uric acid levels at SV1 >1.2 x ULN
e. indirect (unconjugated) bilirubin >1.2 x ULN
22. Renal impairment defined as estimated glomerular filtration rate (eGFR)≤60 mL/min/1.73m.b
23. Known or suspected Gilbert syndrome.
24. Diagnosis or suspected liver function impairment, which may cause fluctuating liver function tests during this study, as assessed by the investigator.
25. Known history of nephrolithiasis or underlying condition with a strong association of nephrolithiasis, including hereditary hyperoxaluria or hereditary hyperuricemia. As an exception, included can be only patients with history of a singular period of nephrolithiasis currently recovered (symptom free within at least 3 years prior to screening visit), while stones were not composed of uric acid or oxalate.
26. History or clinical diagnosis of gout.
27. History or presence of serious or acute heart disease such as uncontrolled cardiac dysrhythmia or arrhythmia, uncontrolled angina pectoris, cardiomyopathy, or uncontrolled congestive heart failure (New York Heart Association [NYHA] class 3 or 4. Note: NYHA class 3: Cardiac disease resulting in marked limitation of physical activity. Patients are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain. NYHA class 4: Cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.
28. Clinically relevant, severe pulmonary diseases, uncontrolled hypertension, or poorly controlled diabetes (HbA1c >9.0).
29. History or presence of any major medical or psychiatric illness (eg, severe depression, schizophrenia, psychotic disorder), history of suicide attempt, or current suicidal ideation, if any of those conditions in the opinion of the investigator could create undue risk to the patient or could affect adherence with the study protocol.
30. Epilepsy or seizures not adequately controlled by treatment.
31. Any other substantial medical condition that in the opinion of the investigator could create undue risk to the patient or could affect adherence with the study protocol.
32. Current or past (within 12 months of informed consent) drug abuse (does not include therapeutic use of tetrahydrocannabinol [THC]).
33. Any condition that would prevent the patient from undergoing an MRI scan, including:
a. claustrophobic conditions
b. unable to receive Gd-based MRI-contrast agents due to history of hypersensitivity to Gd-based contrast agents, or severe renal insufficiency
c. presence of metallic implants incompatible with brain MRI
General exclusion criteria:
34. Legal incapacity, limited legal capacity, or any other condition that makes the patient unable to provide consent for the study.
35. An employee of an investigator or sponsor or an immediate relative of an investigator or sponsor.
36. Patients institutionalized due to judicial or administrative order.
37. Pregnant or breastfeeding women or with intention to become pregnant during the study.
a.If the test for HIV-Ag/Ab at Screening show reactive or borderline results, a confirmatory Nucleic Acid Amplification Test (NAAT) will automatically be performed for detection of viral RNA in blood. If no viral RNA is detected and the clinical history and current clinical status of the patient, and other laboratory examinations also do not indicate a current infection, the patient will not be excluded from the study.
b.Calculated according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

1. Any ongoing, clinically significant (as assessed by the investigator) TEAE (started after intake of IMP) or laboratory abnormality (including blood chemistry and urinalysis) that, upon discretion of the investigator, should prohibit further treatment with study medication in this trial.a
2. Significant treatment non-compliance (defined as having taken <70% of study medication) or study non-compliance during the MP (as assessed by the investigator, in consultation with the medical monitor), and/or inability or unwillingness to follow instructions by study personnel.
3. Multiple significant protocol deviations during the MP that are assessed by the investigator, in consultation with the medical monitor, to negatively affect further patient cooperation in this study.
4. Use of experimental/investigational drug (with the exception of COVID-19 vaccines approved by emergency use authorization) and/or participation in another clinical trial of an investigational drug throughout the duration of the EP open-label treatment period.
aIf a TEAE(s) is the reason for exclusion from the EP open-label treatment period, the eligibility can be re-assessed up to 12 weeks following the last treatment in the MP

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Therapy

Trial scope: Specify scope

N/A

Study design: Allocation

Randomized controlled trial

Study design: Masking

Blinded (masking used)

Study design: Control

Placebo

Study phase

3

Study design: Purpose

Treatment

Study design: Specify purpose

N/A

Study design: Assignment

Parallel

Study design: Specify assignment

N/A

IMP has market authorization

No

IMP has market authorization: Specify

Name of IMP

vidofludimus calcium (IMU-838).

Year of authorization

Month of authorization

Type of IMP

Immunological

Pharmaceutical class

Vidofludimus calcium is a novel compound that selectively inhibits human dihydroorotate dehydrogenase (DHODH) which plays a major role in the de novo pyrimidine synthesis. The metabolic stress secondary to DHODH inhibition leads to a reduction of pro-inflammatory cytokine release including interleukin (IL)-17 (IL-17A and IL-17F) and interferon gamma (IFNγ), and to an increased apoptosis in activated lymphocytes.

Therapeutic indication

Vidofludimus calcium, the active substance of IMU-838, is a novel compound that selectively inhibits human DHODH which plays a major role in the de novo pyrimidine synthesis. As de novo pyrimidine synthesis is extensively used in rapidly proliferating human or virus-infected cells, DHODH inhibitors constitute an attractive therapeutic approach to a variety of diseases including inflammatory diseases, virus infections,
and oncology.
IMU-838 is currently under development for the treatment of IBD, MS (RRMS, RMS,PMS), and PSC
IBD comprises primarily two disorders: UC and CD. The hallmark of both diseases is chronic, uncontrolled mucosal inflammation. Currently, there are a variety of treatments available but a significant proportion of patients with IBD does not respond or develop side effects to currently available treatments. MS is also an inflammatory disease where inflammation occurs mainly in the CNS (brain and spinal cord). Oral disease-modifying drugs are the treatment of choice. The DHODH inhibitor teriflunomide is an oral disease-modifying drug currently approved in the USA and EU but is associated with a high rate of clinically relevant AEs. Inflammation is also a major player in PSC that is characterized by chronic inflammation and
fibrosis of the intrahepatic and extrahepatic bile ducts. For PSC there is currently no authorized drug available. Thus, for all indications described above new treatments are needed.
Vidofludimus calcium was also explored in the treatment of COVID-19 and showed indication of clinical activity. Viral infections such as SARS-CoV-2, are an increasing and probably long-lasting health problem. Antivirals are urgently needed for the effective control of these viral infectious diseases. However, besides intensive efforts to find therapeutic antiviral agents, reports on specific and effective drugs with low
toxicity are rare.

Therapeutic benefit

Vidofludimus inhibited the release of key inflammatory cytokines such as IL-17A, IL-17F and IFN□ from stimulated immune cells in vitro, pharmacological effects which match well the underlying pathophysiology of IBD.
In a Phase 2 trial both, 30 mg/day and 45 mg/day vidofludimus calcium as IMU-838 statistically significantly reduced CUA MRI lesions up to Week 24 compared to placebo in patients with RRMS. Further endpoints, based on other MRI parameters and clinical endpoints such as relapse events, also indicated towards beneficial effects of IMU-838 treatment (30 mg/day and 45 mg/day) as compared to placebo. A small cohort sub-trial showed either no or only small effects of a lower (10 mg) IMU-838 dose on MRI and other parameters indicating that the 30 mg IMU-838 once daily dose is the lowest dose with clinically relevant effects in RRMS patients.
This Cohort 2 sub-trial was performed during the COVID-19 pandemic and 7 patients in the Cohort 2 had a corona virus infection. The incidence of such an infection was higher in the placebo group (3/12 patients, 25%) than IMU-838 group (4/47 patients, 9%) suggesting that IMU-838 may reduce the risk of COVID-19 infections because of its antiviral properties. Posthoc analyses on confirmed disease worsening (CDW) indicated that IMU-838 prevented 12-week and 24-week CDW when compared to placebo rates.
A first interim analysis of the ET of this study in which patients are treated with 30 mg and 45 mg IMU-838 showed that only few patients on continuous IMU-838 treatment develop 12- or 24-week CDW events over 2 years. The CDW rates observed were on the lower end of those observed with currently approved MS medications in historical trials. These results indicate that the beneficial effects of IMU-838 on CDW during the main treatment period were maintained in the ET period.

Study model

N/A

Study model: Explain model

N/A

Study model: Specify model

N/A

Time perspective

N/A

Time perspective: Explain time perspective

N/A

Time perspective: Specify perspective

N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention

Samples without DNA

Biospecimen description

Hematology: erythrocytes, leukocytes, differential leukocyte count (neutrophils, eosinophils, basophils, lymphocytes, and monocytes), hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, and platelets
Serology: hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBcAb), hepatitis C virus antibody (HCV-Ab), and HIV-Ag/Ab combined test, and a Tbc-IGRA
Blood chemistry: AST, ALT, AP, GGT, total bilirubin, unconjugated (indirect) and conjugated (direct) bilirubin, creatinine, uric acid, BUN, eGFR CKD-EPI equation.
Sodium, potassium, magnesium, chloride, inorganic phosphate, calcium, creatine phosphokinase, lactate dehydrogenase, amylase, lipase, C-reactive protein, total protein, albumin, glucose, hemoglobin A1c, triglycerides, and cholesterol
Coagulation: Prothrombin time, activated partial thromboplastin time, and international normalized ratio (INR)

Blood samples (about 1 – 3 Tablespoons at each visit |), during screening and approximately every 12 weeks

Other tissues:
-Biomarkers: neurofilament light chains, John Cunningham virus (JCV), Epstein-Barr virus
-(EBV) antibody in serum, EBV-DNA in saliva
- Neurofilament light chain
- Glial Fibrillary Acidic Protein (GFAP) biomarker)

Target sample size

1050

Actual enrollment target size

Date of first enrollment: Type

Anticipated

Date of first enrollment: Date

01/06/2023

Date of study closure: Type

Anticipated

Date of study closure: Date

28/02/2034

Recruitment status

Pending

Recruitment status: Specify

Date of completion

IPD sharing statement plan

No

IPD sharing statement description

No IPD sharing statement plan

Additional data URL

https://classic.clinicaltrials.gov/ct2/show/NCT05134441

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
nap	nap

Sources of Monetary or Material Support

Name
Immunic AG

Secondary Sponsors

Name
nap

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Aziz Zoghbi	MCT-CRO, Berytech Technology and Health, 5th Floor Damascus Road, Beirut, Lebanon	Lebanon	00961 71008269	aziz.zoghbi@mct-cro.com	Director of Country Oversight and Management MENA, Gulf and Africa
Scientific	Halim Abboud	Hotel Dieu de France	Lebanon	00961 03535711	halim.abboud@usj.edu.lb	PI
Scientific	Samia Khoury	Amercican University of Beirut Medical Center	Lebanon	00961 3 818218	sk88@aub.edu.lb	PI

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu de France	Halim Abboud	Neurologist	Approved
Amercican University of Beirut Medical Center	Samia Khoury	Neurologist	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
American University of Beirut Medical Center	19/10/2023	Karine Ismail	irb@aub.edu.lb	00961 1 35 00 00 – Ext 5445
Hotel Dieu de France	06/07/2023	Nancy Alam	nancy.alam@usj.edu.lb	009611421229

Countries of Recruitment

Name
Lebanon
Albania
Bulgaria
Georgia
India
Lithuania
Mexico
Republic of Moldova
The Former Yugoslav Rep of Macedonia
Ukraine
United States of America
Jordan
Belarus
Bosnia and Herzegovina
Colombia
Estonia
Georgia
Greece
Latvia
Lithuania

The Former Yugoslav Rep of Macedonia
Mexico
Republic of Moldova
Peru
Poland
Romania
Russian Federation
Republic of Serbia
South Africa
Turkey
United Kingdom

Health Conditions or Problems Studied

Condition	Code	Keyword
active Relapsing Multiple Sclerosis (RMS)	Multiple sclerosis (G35)	active Relapsing Multiple Sclerosis (RMS)

Interventions

Intervention	Description	Keyword
IMU-838 (vidofludimus calcium)	Eligible patients will be randomized (1:1) in a blinded fashion to either placebo or IMU-838.	Treatment

Primary Outcomes

Name	Time Points	Measure
The primary objective is to demonstrate the efficacy of IMU-838 versus placebo in adult patients with active RMS in delaying the occurrences of relapses based on time to first relapse (T2FR)	Time to first confirmed relapse, as determined by the Independent Neurology Evaluation Committee (INEC), relapse occurred after the start of treatment administration and before the end of the main period (EOMP), censored at a maximum of 72 weeks, Visit 8 (V8)/EOMP	Hazard ratio (HR) for relapsefree survival between patients randomized to IMU-838 and placebo

Key Secondary Outcomes

Name	Time Points	Measure
The secondary efficacy objective is to evaluate the effect of IMU-838 versus placebo on volume of new T2-lesions	Changes in total volume of new T2-lesions from baseline (BL, SV2) magnetic resonance imaging (MRI) until Week 24 MRI	Mean difference in the volume of new T2 lesions between IMU- 838- and placebo-treated patients, on a logarithmic scale
The secondary efficacy objective is to evaluate the effect of IMU-838 versus placebo on disability progression	Time to 12-week confirmed disability worsening (12wCDW) as assessed on Expanded Disability Status Scale (EDSS); as defined in this protocol during the MP (censored until at Week 72/EOMP visit but with confirmation potentially done within EP, if applicable)	HR for no worsening survival between IMU-838- and placebotreated patients
The secondary efficacy objective is to evaluate the effect of IMU-838 versus placebo on cognitive performance	Time to confirmed clinically relevant changes in Symbol Digit Modalities Test (SDMT) in the MP (censored Week 72/EOMP)	HR for no changes survival between IMU-838- and placebotreated patients
The secondary efficacy objective is to the effect of IMU-838 versus placebo on whole brain atrophy	Annualized rate of percentage changes in whole brain volume from BL MRI to until V8/EOMP MRI	Difference in mean rate of the percentage change in whole brain volume between IMU-838- and placebo-treated patients

Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files