Best Available Therapy Versus Autologous Hematopoietic Stem Cell Transplant for Multiple Sclerosis (BEAT-MS)

Status: RECRUITING

Eligibility Criteria

Age: 18 years to 55 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

1. Age 18 to 55 years, inclusive, at the time of the screening Visit -2. 2. Diagnosis of MS according to the 2017 McDonald Criteria139. 3. EDSS ≤ 6.0 at the time of randomization (Day 0). 4. T2 abnormalities on brain MRI that fulfill the 2017 McDonald MRI criteria for dissemination in space139. A detailed MRI report or MRI images must be available for review by the site neurology investigator. 5. Highly active treatment-resistant relapsing MS, defined as ≥ 2 episodes of disease activity in the 36 months prior to the screening visit (Visit -2). The two disease activity episodes will be a clinical MS relapse or MRI evidence of MS disease activity and must meet all the criteria described below: 1. At least one episode of disease activity must occur following ≥ 1 month of treatment with one of the following: (i) an oral DMT approved by the FDA for the treatment of relapsing MS, or (ii) a monoclonal antibody approved by the FDA for the treatment of relapsing MS, or (iii) rituximab. Qualifying DMTs include: dimethyl fumarate, diroximel fumarate, monomethyl fumarate, teriflunomide, cladribine, daclizumab, ponesimod, siponimod, ozanimod, fingolimod, rituximab, ocrelizumab, natalizumab, alemtuzumab, ublituximab, and ofatumumab, and 2. At least one episode of disease activity must have occurred within the 12 months prior to the screening visit (Visit -2), and 3. At least one episode of disease activity must be a clinical MS relapse (see item c.i. below). The other episode(s) must occur at least one month before or after the onset of the clinical MS relapse, and must be either another clinical MS relapse or MRI evidence of disease activity (see item c.ii. below): i. Clinical MS relapse must be confirmed by a neurologist's assessment and documented contemporaneously in the medical record. If the clinical MS relapse is not documented in the medical record, it must be approved by the study adjudication committee (see Section 3.5), and ii. MRI evidence of disease activity must include ≥ 1 unique active lesion on one or more brain or spinal cord MRIs. Detailed MRI reports or MRI images must be available for review by the site neurology investigator. A unique active lesion is defined as either of the following: 1\. A gadolinium-enhancing lesion, or 2. A new non-enhancing T2 lesion compared to a reference scan obtained not more than 36 months prior to the screening visit (Visit -2). 6\. Candidacy for treatment with at least one of the following high efficacy BAT DMTs: cladribine, natalizumab, alemtuzumab, ocrelizumab, ofatumumab, ublituximab and rituximab. Candidacy for treatment for each BAT DMT is defined as meeting all of the following: 1. No prior disease activity episode, as defined in Inclusion Criterion #5, with the candidate BAT DMT, and 2. No contraindication to the candidate BAT DMT, and 3. No treatment with the candidate BAT DMT in the 12 months prior to screening. 7\. Completion of COVID-19 vaccination series, according to the current Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) recommendations, ≥ 14 days prior to randomization (Day 0). 8\. Positive for VZV antibodies, or completion of at least one dose of the varicella zoster glycoprotein E (gE) Shingrix vaccine at least 4 weeks prior to randomization (Day 0). 9\. Insurance approval for MS treatment with at least one candidate BAT DMT (see Inclusion Criterion #6). 10\. Ability to comply with study procedures and provide informed consent, in the opinion of the investigator. 11\. Females of childbearing potential (defined in Section 5.4.3.1) and males with female partners of childbearing potential are required to adhere to the contraception provisions of Section 5.4.3.1. 12\. For participants who use medicinal or recreational marijuana, willingness to substitute MARINOL® if randomized to AHSCT (Section 5.4.2.6).

Exclusion Criteria:

1. Diagnosis of primary progressive MS according to the 2017 McDonald criteria. 2. History of neuromyelitis optica spectrum disorder or MOG antibody disease. 3. Prior treatment with an investigational agent within 3 months or 5 half-lives, whichever is longer. Agents authorized by the FDA for prevention or treatment of COVID-19 are not considered investigational. 4. Either of the following within one month prior to randomization (Day 0): 1. Onset of acute MS relapse, or 2. Treatment with intravenous methylprednisolone 1000 mg/day for 3 days or equivalent. 5. Initiation of any BAT DMT (see Section 5.2.1) between Visit -2 and randomization (Day 0). 6. Brain MRI or cerebrospinal fluid (CSF) examination indicating a diagnosis of progressive multifocal leukoencephalopathy (PML). 7. History of cytopenia consistent with the diagnosis of myelodysplastic syndrome (MDS). 8. Presence of unexplained cytopenia, polycythemia, thrombocythemia or leukocytosis. 9. History of sickle cell anemia or other hemoglobinopathy. 10. Evidence of past or current hepatitis B or hepatitis C infection, including treated hepatitis B or hepatitis C. Hepatitis B surface antibody following hepatitis B immunization is not considered to be evidence of past infection. 11. Presence or history of mild to severe cirrhosis. 12. Hepatic disease with the presence of either of the following: 1. Total bilirubin ≥ 1.5 times the upper limit of normal (ULN) or total bilirubin ≥ 3.0 times the ULN in the presence of Gilbert's syndrome, or 2. Alanine Aminotransferase (ALT) or Aspartate Aminotransferase (AST) ≥ 2.0 times the ULN. 13. Positive COVID-19 PCR test, or alternative nucleic acid amplification test (NAAT) per institutional standards, within 14 days prior to randomization (Day 0). 14. Evidence of HIV infection. 15. Positive QuantiFERON

•TB Gold,TB Gold Plus, or T-SPOT®.TB test results. PPD tuberculin test may be substituted for QuantiFERON

•TB Gold, TB Gold Plus, or T-SPOT®.TB test. 16. Active viral, bacterial, endoparasitic, or opportunistic infections. 17. Active invasive fungal infection. 18. Hospitalization for treatment of infections or parenteral (IV or IM) antibacterials, antivirals, antifungals, or antiparasitic agents within the 30 days prior to randomization (Day 0) unless clearance is obtained from an Infectious Disease specialist. 19. Receipt of live or live-attenuated vaccines within 6 weeks of randomization (Day 0). 20. Presence or history of clinically significant cardiac disease including: a. Arrhythmia requiring treatment with any antiarrhythmia therapy, with the exception of low dose beta blocker for intermittent premature ventricular contractions. b. Coronary artery disease with a documented diagnosis of either: i. Chronic exertional angina, or ii. Signs or symptoms of congestive heart failure. c. Evidence of heart valve disease, including any of the following: i. Moderate to severe valve stenosis or insufficiency, or ii. Symptomatic mitral valve prolapse, or iii. Presence of prosthetic mitral or aortic valve. 21. Left ventricular ejection fraction (LVEF) \< 50%. 22. Impaired renal function defined as eGFR \< 60 mL/min/1.73 m2, according to the CKD-EPI formula144. 23. Forced expiratory volume in one second (FEV1) \< 70% predicted (no bronchodilator). 24. Diffusing capacity of the lungs for carbon monoxide (DLCO) (corrected for Hgb) \< 70% predicted. 25. Poorly controlled diabetes mellitus, defined as HbA1c \> 8%. 26. History of malignancy, except adequately treated localized basal cell or squamous skin cancer, or carcinoma in situ of the cervix. Malignancies for which the participant is judged to be cured will be considered on an individual basis by the study adjudication committee (see Section 3.5). 27. Presence or history of any moderate to severe rheumatologic autoimmune disease requiring treatment, including but not limited to the following: systemic lupus erythematous, systemic sclerosis, rheumatoid arthritis, Sjogren's syndrome, polymyositis, dermatomyositis, mixed connective tissue disease, polymyalgia rheumatica, polychondritis, sarcoidosis, vasculitis syndromes, or unspecified collagen vascular disease. 28. Presence of active peptic ulcer disease, defined as endoscopic or radiologic diagnosis of gastric or duodenal ulcer. 29. Prior history of AHSCT. 30. Prior history of solid organ transplantation. 31. Positive pregnancy test or breastfeeding. 32. Failure to willingly accept or comprehend irreversible sterility as a side effect of therapy. 33. Psychiatric illness, mental deficiency, or cognitive dysfunction severe enough to interfere with compliance or informed consent. 34. History of hypersensitivity to rabbit or Escherichia coli-derived proteins. 35. Any metallic material or electronic device in the body, or other condition that precludes the participant from undergoing MRI with gadolinium administration, as determined by the site radiologist. 36. Presence or history of ischemic cerebrovascular disorders, including but not limited to transient ischemic attack, subarachnoid hemorrhage, cerebral thrombosis, cerebral embolism, or cerebral hemorrhage. 37. Presence or history of other neurological disorders, including but not limited to CNS or spinal cord tumor; metabolic or infectious cause of myelopathy; genetically-inherited progressive CNS disorder; CNS sarcoidosis; or systemic autoimmune disorders potentially causing progressive neurologic disease or affecting ability to perform the study assessments. 38. Presence of any medical comorbidity that the investigator determines will significantly increase the risk of treatment mortality. 39. Presence of

study assessments. 3. Presence of any medical comorbidity that the investigator determines will significantly increase the risk of treatment mortality. 3. Presence of any other concomitant medical condition that the investigator deems incompatible with trial participation.

Conditions & Interventions

Interventions:
PROCEDURE: Autologous Hematopoietic Stem Cell Transplantation, BIOLOGICAL: Best Available Therapy (BAT)
Conditions:
Relapsing Multiple Sclerosis, Relapsing Remitting Multiple Sclerosis, Secondary Progressive Multiple Sclerosis
Keywords:
Treatment-Resistant Relapsing Multiple Sclerosis (MS), Autologous Hematopoietic Stem Cell Transplantation (AHSCT), Autologous Peripheral Blood Stem Cells (PBMCs) Graft, Best Available Therapy (BAT), Disease-Modifying Therapy (DMT), BAT DMT

More Information

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