

FAST FACTS

MATCH Treatment Subprotocol Z1M: Phase 2 Study of Nivolumab and BMS-986016 (Relatlimab) in Patients with LAG-3+ Tumors with Mismatch Repair Deficiency (MMR-d) after Progression on Anti-PD-1/PD-L1 Therapy

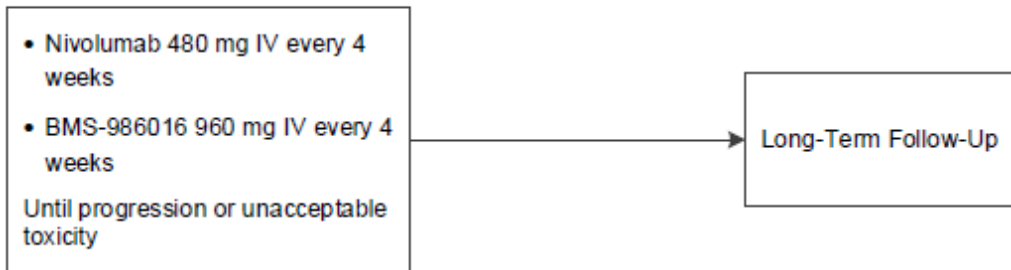
Registration to Treatment

1. Patients must fulfill all eligibility criteria outlined in Section 3.1 of MATCH Master Protocol (excluding Section 3.1.6) at the time of registration to treatment step (Step 1, 3, 5, 7).
2. Patients must have mismatch repair deficiency based on one of the following:
 - a. Mismatch repair testing done in any laboratory under CLIA conditions with IHC for MLH1/MSH2 +/-MSH6 +/-PMS2
 - b. PCR-based microsatellite testing using a validated assay done in any laboratory under CLIA conditions
 - c. A MATCH designated laboratory determination of MMR status by DNA sequencing.
NOTE: See Appendix I for a list of the actionable markers of interest indicating mismatch repair deficiency and corresponding Levels of Evidence.
3. Patients must have LAG-3 expression at $\geq 1\%$ as determined via the MATCH Master Protocol.
NOTE: For patients entering the study, all patients must have LAG-3 testing performed as described in the MATCH Master Protocol. This includes patients entering the study via the outside assay process (Appendix XIV of the MATCH Master Protocol).
4. Patients with active melanoma are ineligible
5. Patients must have an electrocardiogram (ECG) within 8 weeks prior to treatment assignment and must have no clinically important abnormalities in rhythm, conduction or morphology of resting ECG (e.g. complete left bundle branch block, third degree heart block).
Date of ECG: _____
6. Patients must have Troponin T (TnT) or I (TnI) $< 2 \times$ ULN. Patients with TnT or TnI levels between >1 to $2 \times$ ULN will be allowed to register if repeat levels within 24 hours are $\leq 1 \times$ ULN. If TnT or TnI levels are >1 to $2 \times$ ULN within 24 hours, the patients may undergo a cardiac evaluation and be considered for treatment. When repeat levels within 24 hours are not available, a repeat test should be conducted as soon as possible. If TnT or TnI repeat levels beyond 24 hours are $< 2 \times$ ULN, the patient may undergo cardiac evaluation and be considered for treatment.
7. Patients must not have known hypersensitivity to nivolumab and BMS-986016 or compounds of similar chemical or biologic composition.
8. Patients must not have a history of severe hypersensitivity reaction to any monoclonal antibody.
9. Patients must have had prior therapy on PD-1/PD-L1 therapy with progression on therapy or within 6 months of completion of PD-1/PD-L1 inhibitor therapy
10. Patients must not have a history of toxic epidermal necrolysis (Stevens-Johnson syndrome).
11. Patients must not have received growth factors, including but not limited to granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (GM-CSF), erythropoietin, etc. within 2 weeks of study drug administration. Use of such agents while on study is also prohibited. Prior use of growth factors should be documented in the patient's medical history.

12. Patients must not have a history of any autoimmune disease: inflammatory bowel disease, (including ulcerative colitis and Crohn's Disease), rheumatoid arthritis, systemic progressive sclerosis (scleroderma), systemic lupus erythematosus (SLE) autoimmune vasculitis (e.g., Wegener's Granulomatosis), CNS or motor neuropathy considered to be of autoimmune origin (e.g., Guillian-Barre Syndrome, Myasthenia Gravis, Multiple Sclerosis). Patients are permitted to enroll if they have vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune condition only requiring hormone replacement, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger (precipitating event). Entry of patients with autoimmune diagnoses not listed here must be approved by the protocol chair.
13. Patients must not be on supplemental home oxygen.
14. Patients must not have prior treatment with anti-LAG3 inhibitors.
15. Patients must not have evidence of interstitial lung disease.
16. Patients with a requirement for steroid treatment or other immunosuppressive treatment: Patients will be excluded if they have a condition requiring systemic treatment with either corticosteroids (>10 mg daily prednisone equivalents) within 14 days of study drug administration. Inhaled or topical steroids and adrenal replacement doses >10 mg daily prednisone equivalents are permitted in the absence of active autoimmune disease.
17. Patients of childbearing potential and patients who are sexually active with a patient of childbearing potential must use accepted and effective methods of contraception or abstain from sexual intercourse for at least one week prior to the start of treatment and for the duration of study participation. Patients of childbearing potential must continue to use accepted and effective methods of contraception for 5 months after the last dose of protocol treatment. In addition, patients of childbearing potential must have a negative serum pregnancy test within 2 weeks prior to registration with a minimum sensitivity of at least 50 IU/L and it must be repeated within 24 hours prior to the first dose of nivolumab and BMS-986016. Patients must also not donate sperm while on study treatment. These supersede the requirements in the EAY131 MASTER protocol eligibility section regarding pregnancy testing and contraception requirements.
18. Patients with Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) infection may be eligible provided they have the following:
 - There must be no evidence of clinically significant hepatic injury from hepatitis virus infection.
 - For HBV, patients must be on suppressive therapy and have undetectable HBV viral load.
 - For HCV, patients must either be on suppressive therapy for HCV or have already completed therapy thought to have eradicated HCV.
19. Patients must meet one of the following criteria:
 - a. Patients must have tumor amenable to image guided or direct vision biopsy and be willing and able to undergo a tumor biopsy to obtain tissue for research. Biopsy must not be considered to be more than minimal risk to the patient.
 - b. Patient will be undergoing a procedure due to medical necessity prior to start of treatment during which the tissue may be collected.
 - c. Formalin-fixed paraffin-embedded tumor tissue block(s) or unstained sectioned slides are available for submission following pre-registration. Criteria for the submission of FFPE tissue are:
 - i. Tissue must have been collected within 6 months prior to pre-registration to step 0.
 - ii. Collection of the tissue was after the completion of PD-1/PD-L1 therapy.

- iii. Formalin-fixed paraffin-embedded tumor tissue block(s) must meet the minimum requirements outlined in Section 9.3.2 of the Master Protocol.
NOTE: If tissue submitted for central LAG-3 testing meets this criteria, additional tissue is not necessary.

Schema



Cycle = 28 days
Accrual Goal: 35