

Key inclusion criteria:

- Age \geq 18 years old or legal adult age at the time of signing the ICF
- Participants with a history of NHL, including:
 - o R/R DLBCL (ie, DLBCL not otherwise specified (NOS) or high-grade B-cell lymphoma with MYC and BCL2 rearrangements) de novo or transformed or
 - o R/R FL
- At least 2 prior lines of therapy and the participant must have exhausted or must be not eligible for available therapy (including CAR-T cell therapy and bispecific monoclonal antibodies) or be unwilling to receive them and must fulfill the following criteria, prior to enrollment
- Measurable disease and tumor accessible for tumor biopsy
- Subjects must follow the Pregnancy Prevention Plan
- Absolute neutrophil count (ANC) \geq $1 \times 10^9/L$ (without growth factor support)
- Platelet count \geq $75 \times 10^9/L$
- Hemoglobin \geq 9 g/dL
- AST and ALT \leq 3.0 x ULN, or \leq 5.0 x ULN if liver involvement
- Total bilirubin \leq 1.5 x ULN
- K, Mg and Ca within normal range, or correctable with supplements
- Estimated serum creatinine clearance \geq 50 mL/min using Modification of Diet in Renal Disease (MDRD) method

Key exclusion criteria:

- ECOG performance status \geq 2
- Serious or uncontrolled medical disorders: uncontrolled HTN, cardiovascular, cerebrovascular disease, other malignancy, other significant acute or chronic medical illness, active or uncontrolled infection, or the presence of laboratory abnormalities, that places participants at unacceptable risk if participating in this study
- Non-hematological toxicity related to prior anti-cancer therapy and/or surgery, unless the toxicity is either resolved, returned to baseline or Grade \leq 2, or deemed irreversible (possibility for consultation with Medical Monitor)
- Known SARS-CoV-2 infection within 10 days for mild or asymptomatic infections or 20 days for severe/critical illness prior to C1D1
- Known or suspected central nervous system (CNS) involvement
- Prior systemic anti-cancer treatment (approved or investigational) \leq 5 half-lives or 4 weeks prior to starting BMS-986458, whichever is shorter
- Prior radiation therapy \leq 4 weeks prior to starting BMS-986458
- Prior CAR-T or other T-cell targeting treatment (approved or investigational) \leq 4 weeks prior to C1D1
- Prior therapy with CRBN-modulating drug (eg. lenalidomide, pomalidomide) \leq 4 weeks prior to C1D1
- Participant on chronic systemic immunosuppressive therapy or corticosteroids, or with clinically significant graft-versus-host disease (GVHD)
- Prior live virus vaccines \leq 4 weeks prior to the first dose of study intervention
- Previous COVID-19 vaccine within 7 days of C1D1
- Inability to comply with restrictions and prohibited treatments as listed in Protocol Sec.7.7 (Con. Meds)

- (precautionary language for substrates, inhibitors and inducers of CYP3A, P-gp inducers, transporters, and PPI and H2 blockers; also drugs known to prolong QT interval)
- Participants with known seropositive or active infection with HIV, or active infection with HBV or HCV
- Clinically significant cardiovascular disease, QTcF \geq 470 msec on screening ECG
- Evidence of organ dysfunction or any clinically significant deviation from normal in physical examination, vital signs, or clinical laboratory determinations.