BGB-16673-304

Inclusion Criteria

- Signed ICF, being capable of giving written IC
- ≥ 18 years old or legal age for consent (whichever is older) at the time of IC.
- CLL/SLL requiring treatment diagnosis, based on 2018 iwCLL criteria.
- Previous treatment for CLL/SLL with a cBTKi, with documented disease relapsed after or refractory to at least 1 line of therapy including a cBTKi (if cBTKi is discontinued due solely to toxicity, patient is not eligible).
- For SLL, must have measurable disease by CT Scan or MRI, defined as ≥ 1 lymph node > 1.5 cm in longest diameter and measurable in 2 perpendicular diameters.
- ECOG PS of 0 to 2
- Adequate organ function during screening, after checking:
- Adequate bone marrow function as defined by:
- ANC ≥ 1000/mm3 (or ≥ 750/mm3 for patients with bone marrow involvement) without growth factor support within 7 days.
- Platelets ≥ 75,000/mm3 (or ≥ 50,000/mm3 for patients with bone marrow involvement), without growth factor support or transfusion within 7 days.
- Hemoglobin ≥ 7.5 g/dL (may be post-transfusion); patients may have hemoglobin < 7.5 g/dL if the reduced hemoglobin is secondary to bone marrow infiltration by CLL.
- Estimated glomerular filtration rate ≥ 30 mL/min as determined by the Chronic Kidney Disease Epidemiology Collaboration equation 2021
- Serum total bilirubin ≤ 1.5 x ULN (total bilirubin must be < 3 x ULN with conjugated bilirubin ≤ 1.5 x ULN for patients with Gilbert syndrome)
- Adequate liver function as indicated by AST and ALT ≤ 3.0 x ULN.
- Adequate blood clotting function as defined by international normalized ratio≤ 1.5 x ULN and aPTT ≤ 1.5 x ULN.
- Amylase ≤ 1.5 x ULN, and lipase ≤ 1.5 x ULN
- Female patients of childbearing potential willing to use a highly effective method of birth control and refrain from egg donation for the duration of the study and ≥ 30 days after the last dose of BGB-16673 or 5 weeks after last dose of pirtobrutinib. In both Arm A and Arm B, all women of childbearing potential must undergo a highly sensitive serum pregnancy test ≤ 14 days before the first dose of study drug, which should be repeated ≤ 24 hours prior to administration of the first dose of study drug.
- Nonsterile male patients willing to use a highly effective method of birth control and refrain from sperm donation for the duration of the study and for ≥ 30 days after the last dose of BGB-16673 or 3 months after the last dose of pirtobrutinib.

Exclusion Criteria

- Known prolymphocytic leukemia or history of, or currently suspected, Richter's transformation.
- Following treatment / procedure prior to subject enrollment:
- Autologous stem cell transplant or chimeric antigen receptor-T cell therapy in the last 3 months.
- Allogenic stem cell transplant ≤ 6 months before the first dose of the study drug
- History of severe allergic reactions or hypersensitivity to the active ingredient and excipients of study drug
- Unable to comply with protocol requirements
- Current or history of central nervous system involvement (as documented by imaging, cytology, or biopsy) by CLL/SLL.
- Malignancy ≤ 3 years before randomization except for CLL/SLL and any locally recurring cancer that has been treated curatively**
- History of ischemic stroke or intracranial hemorrhage within 6 months before first dose
- Active fungal, bacterial and/or viral infection requiring parenteral systemic therapy
- Positive HIV serology (HIV antibody) status.
- Positive serologic status reflecting active hepatitis B or C infection**
- Prior exposure to any BTK protein degraders or ncBTKi
- Patients with any major surgical procedure ≤ 28 days before first dose of study drug.
- Patients with clinically significant cardiovascular disease**
- Biologic and/or immunologic-based anticancer therapy(ies) including experimental therapy(ies) ≤ 28 days or ≤ 5 half-lives (whichever is shorter) before the first dose of study drug, or, who have received systemic chemotherapy or radiation therapy ≤ 14 days or ≤ 5 half-lives (whichever is shorter) before the first dose of study drug.
- Corticosteroid given with antineoplastic intent ≤ 7 days before the first dose of study drug.
- Treatment with warfarin or other vitamin K antagonists.
- History of known bleeding disorder**
- Experience of potential life-threatening bleeding related to a BTKi with signs or symptoms of hemodynamic compromise, or bleeding in a critical area or organ, or bleeding associated with a decrease in the hemoglobin level of at least 2 g/dL.
- BTKi, tyrosine kinase inhibitor, or other targeted small molecules admin with antineoplastic intent ≤ 7 days or ≤ 5 half-lives (whichever is shorter) before the first dose of study drug
- Toxicities to anticancer therapy not recovered to baseline or stabilized**
- Admin of live vaccine ≤ 28 days before the first dose of study drug**
- Chinese patent medicine with anticancer activity approved by the China National Medical Products Administration (regardless of the type of cancer) used ≤ 14 days before the first dose of study drug.

- underlying medical conditions (including laboratory abnormalities) or alcohol or drug abuse or dependence that will interfere with the administration of study drug, safety evaluation or potential impaired compliance with study conduct.
- Pregnant or breastfeeding female patients.
- Patients with concurrent participation in another therapeutic clinical study.
- Patients who are unable to swallow tablets or with disease/procedure significantly affecting gastrointestinal function
- Receiving treatment with a strong CYP3A inhibitor or strong CYP3A inducer ≤ 14 days or 5 half-lives, whichever is longer, before the first dose of study drug OR requiring long term use of strong CYP3A inhibitors or inducers.