
BLU-263 is an investigational, novel, orally administered tyrosine kinase inhibitor (TKI) with high potency and selectivity towards the KIT D816V mutation and high in vitro potency in both the biochemical (dissociation constant, Kd=0.24 nm) and cellular (half-maximal inhibitory concentration, IC50=3.8 nm) settings. BLU-263 has a high degree of selectivity for KIT D816V with minimal CNS penetration, as demonstrated in preclinical studies and two phase 1 studies in healthy volunteers.外文

Overall, the results from the preclinical as well as clinical studies in volunteers indicate a beneficial profile that fulfills the clinical evaluation of BLU-263 alone and in combination with azacitidine in patients with AdvSM, including high-risk and very high-risk SM-AHN.

**Study objectives and design**

**AZURE (NCT05669482)** is an international, phase 1/2, open-label, 2-arm study designed to evaluate the safety and efficacy of BLU-263 as monotherapy and in combination with azacitidine in patients with AdvSM, including those with high-risk and very high-risk SM-AHN in whom HMAs, including azacitidine, are the standard of care.

**Study design**

**Arm 1: BLU-263 monotherapy**
- Dose escalation will involve a cohort-based administration of incremental doses of BLU-263 to identify the recommended dose (RD) of BLU-263 monotherapy (RDmono) in Arm 1, and the RD of BLU-263 + azacitidine (RD combo) in Arm 2.
- Dose escalation will further characterize the safety and preliminary efficacy of BLU-263 RDmono and RD combo in patients with SM-AHN.
- After determining RDmono in Arm 1 dose escalation and RD combo in Arm 2 dose escalation, patients may be enrolled in the respective dose expansion phases.
- Once safety has been established in the BLU-263 monotherapy dose escalation, BLU-263 + azacitidine combination dose escalation will be initiated.
- Patients will receive azacitidine 75 mg/m² orally on days 1–7 (or 1–5, and days 8 and 9 if [2+2 schedule]) of each 28-day cycle.
- Patients with SM-AHN receiving BLU-263 monotherapy who experience AHN progression may be considered to receive azacitidine, in addition to BLU-263 at the RD combo.
- Dose escalation of monotherapy and combination therapy in both arms will follow the rules of Bayesian optimal interval design (BOIN).

**Arm 2: BLU-263 + azacitidine combination therapy**
- The study has 2 arms: Arm 1 will evaluate BLU-263 monotherapy in all patients with AdvSM, while Arm 2 will evaluate BLU-263 in combination with azacitidine in a selected population of high- and very high-risk SM-AHN patients.
- Each study arm will involve a dose escalation and expansion phase.
- Dose escalation will involve a cohort-based administration of incremental doses of BLU-263 to identify the recommended dose (RD) of BLU-263 monotherapy (RDmono) in Arm 1, and the RD of BLU-263 + azacitidine (RD combo) in Arm 2.
- Dose escalation will further characterize the safety and preliminary efficacy of BLU-263 RDmono and RD combo in patients with AdvSM.
- After determining RDmono in Arm 1 dose escalation and RD combo in Arm 2 dose escalation, patients may be enrolled in the respective dose expansion phases.
- Once safety has been established in the BLU-263 monotherapy dose escalation, BLU-263 + azacitidine combination dose escalation will be initiated.
- Patients will receive azacitidine 75 mg/m² orally on days 1–7 (or 1–5, and days 8 and 9 if [2+2 schedule]) of each 28-day cycle.
- Patients with SM-AHN receiving BLU-263 monotherapy who experience AHN progression may be considered to receive azacitidine, in addition to BLU-263 at the RD combo.
- Dose escalation of monotherapy and combination therapy in both arms will follow the rules of Bayesian optimal interval design (BOIN).

**Combination Arm 2: BLU-263 + azacitidine**
- The study has arms: Arm 1 will evaluate BLU-263 monotherapy in all patients with AdvSM, while Arm 2 will evaluate BLU-263 in combination with azacitidine in a selected population of high- and very high-risk SM-AHN patients.
- Each study arm will involve a dose escalation and expansion phase.
- Dose escalation will involve a cohort-based administration of incremental doses of BLU-263 to identify the recommended dose (RD) of BLU-263 monotherapy (RDmono) in Arm 1, and the RD of BLU-263 + azacitidine (RD combo) in Arm 2.
- Dose escalation will further characterize the safety and preliminary efficacy of BLU-263 RDmono and RD combo in patients with AdvSM.
- After determining RDmono in Arm 1 dose escalation and RD combo in Arm 2 dose escalation, patients may be enrolled in the respective dose expansion phases.
- Once safety has been established in the BLU-263 monotherapy dose escalation, BLU-263 + azacitidine combination dose escalation will be initiated.
- Patients will receive azacitidine 75 mg/m² orally on days 1–7 (or 1–5, and days 8 and 9 if [2+2 schedule]) of each 28-day cycle.
- Patients with SM-AHN receiving BLU-263 monotherapy who experience AHN progression may be considered to receive azacitidine, in addition to BLU-263 at the RD combo.
- Dose escalation of monotherapy and combination therapy in both arms will follow the rules of Bayesian optimal interval design (BOIN).

**BOIN dose escalation design**

**Sponsorship**

BLU-263 is also being studied in HARBOR, a phase 2/3 study comparing the efficacy and safety of BLU-263 + best supportive care (BSC) with placebo + BSC in patients with indolent SM whose symptoms are not adequately controlled by BSC.

**To learn more about our clinical trials in the USA, visit blueprintclinicaltrials.com or contact us in the USA at maditainfo@blueprintmedicines.com or 1-888-BLU-PRINT (1-888-258-7768), and in Europe at medinfoeurope@blueprintmedicines.com or +31 85 044 0154.**

**For more information visit:**

https://www.blueprintmedicines.com/clinical_trial_details?study_id=3058

**References**


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