AC676, an Orally Bioavailable BTK Chimeric Degrader in Patients with B-cell Malignances

IBCL-147

Manish R Patel[1,3], Michael Tees[2,3], Nadia Khan[4], Farrukh Awan[5], David Bond[6], Qiming Xu[7], Gladys Brown[7], Hui Zhang[7], Su Young Kim[7], Jennifer Woyach[6]

[1]Florida Cancer Specialists, Sarasota, FL; [2]Colorado Blood Cancer Institute, Denver, Colorado; [3]Sarah Cannon Research Institute, Nashville, TN; [4]Swedish Cancer Institute, Seattle, WA, USA; [5]University of Texas Southwestern Medical Center, Dallas, TX, USA; [6]Ohio State University, Columbus, Ohio; [7]Accutar Biotechnology, Cranbury, NJ

STUDY RATIONALE

- Bruton tyrosine kinase (BTK) is an intracellular molecule that plays a central role in B-cell receptor transduction
- Approved BTK inhibitors can result in resistance due to the development of mutations in BTK residues (including C481 and L528)
- The Protein-Protein Interaction Targeting Chimeras (PPI-TAC) platform informed the design of AC676 as a chimeric degrader to target and degrade the protein of interest, BTK, irrespective of mutations
- AC676 contains ligands for BTK and cereblon E3-ligase, bringing BTK in proximity to E3 ligase, which subsequently induces robust ubiquitination and degradation of BTK (Figure 1)

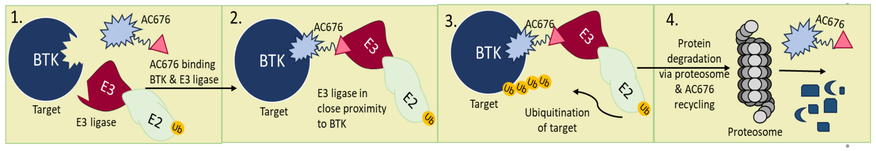


Figure 1. AC676 Mechanism of action

KEY ELIGIBILITY CRITERIA

Inclusion criteria

- Adults with histologically confirmed B-cell malignancies (see Figure 2)
- Must have received at least two prior systemic therapies or have no other standard of care therapies to provide significant clinical benefit
- Must have measurable disease

Exclusion criteria

- Small molecule drugs within 5 half-lives or 2 days, which is longer
- Chemotherapy, investigational agents, radiation within 14 days
- History of central nervous system lymphoma/leukemia in remission for < 2 years

STUDY OBJECTIVES

Primary

- Evaluate safety and tolerability of AC676

Secondary

- Evaluate the anti-tumor activity
- Characterize PK profile of a single dose and multiple doses of AC676

Exploratory

- Evaluate relationship between gene mutation status and anti-tumor activity of AC676
- Evaluate the pharmacodynamic effect of AC676 on BTK levels in B-cells

B-CELL MALIGNANCIES

- Patients with B-cell malignancies listed in Figure 2 are eligible to participate.

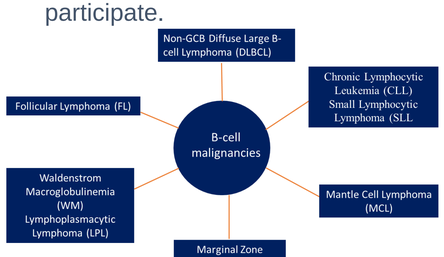


Figure 2. B-cell malignancies accepted for enrollment

STUDY DESIGN

- Phase I, first-in-human, open-label, dose-escalation study of AC676 monotherapy (Figure 3)
- AC676 is administered orally, once daily, in 28-day cycles
- Dose escalation follows a 3+3 design, to identify dose limiting toxicities and potentially a maximum tolerated dose

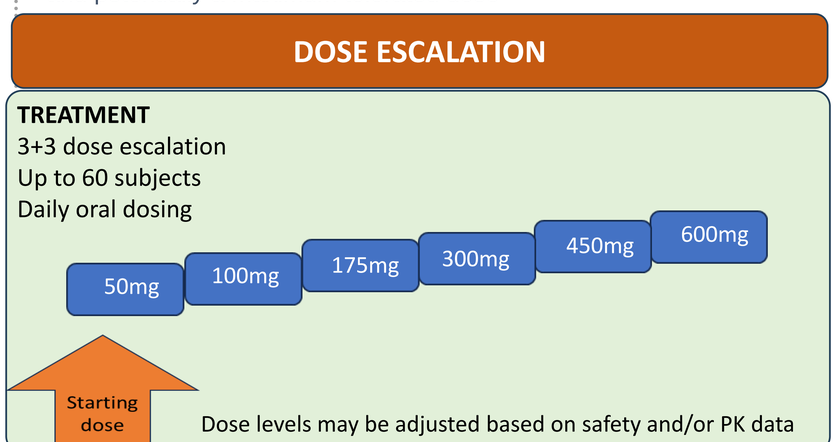


Figure 3. Study schema for dose escalation

ENROLLMENT

- The trial was initiated in April 2023
- 6 sites in the US are currently activated and enrolling patients
- NCT05780034

Medical@accutarbio.com
908-340-0879

Accutar Biotech