**BACKGROUND**

- BTK inhibitors (BTKis) have transformed treatment paradigms for several B-cell malignancies. However, BTK resistance follows strategies to identify new targets.
- Mutations in BTK kinase result in resistance to BTKis such as ibrutinib, a population that generally remains BTKi-sensitive.
- Vecabrutinib is a highly selective BTKi with activity against Tec family members (Cys481 and C481x mutation).

**OBJECTIVES**

- To evaluate the safety and pharmacokinetics (PK) of vecabrutinib in patients with B-cell malignancies.
- To assess the preliminary exploratory activity of vecabrutinib.

**METHODS**

- The 3+3 design (Figure 2, Table 2) was performed in 5 cohorts. Cohorts 1 and 2 received vecabrutinib as a single agent while Cohorts 3 to 5 received vecabrutinib in combination with CAR-T, CAR-M, or Venetoclax.

**RESULTS**

- Baseline Characteristics, Phase 1b Cohorts 1 to 5: Twenty-nine patients received evaluable treatment in Cohorts 1 to 5.
- Pharmacodynamics: Vecabrutinib PK profile showed sustained exposure over the dosing interval with an approximate median steady-state trough concentration (C49) of 50 ng/mL (Cohort 4, 350 mg BID).

**CONCLUSIONS**

- The study is currently treating patients at 400 mg BID (Figure 4).

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