Bruton’s tyrosine kinase (BTK) plays a key role in B-cell receptor-mediated pathways. M7583 is a potent, highly selective BTK inhibitor (BTKi) that has shown activity against several B-cell malignancies, including chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), B cell lymphoma, MCL, or Waldenstrom’s macroglobulinemia (WM) who had received 1–3 lines of prior therapy.

**METHODS**

- **Study design:** Study conducted in patients with relapsed/refractory B-cell malignancies who had failed 1–3 lines of prior therapy.
  - M7583 given once daily (QD) in 28-day cycles in ascending dose cohorts until disease progression, unacceptable toxicity, or withdrawal of consent.
  - Treatment was continued until disease progression, unacceptable toxicity, or discontinuation by the investigator.

- **Assessment:** Parameters assessed included disease response, overall survival, progression-free survival, and safety endpoints. The primary objective was to evaluate the efficacy and safety of M7583 across the tumor types investigated (80/160 mg QD, 300 mg QD, 600 mg QD, 300 mg BID, and 600 mg BID doses).

**RESULTS**

- **Maximum tolerated dose (MTD):** M7583 was 600 mg QD (Table 1).

- **Objective response rate:** The objective response rate (ORR) was 50% and disease control rate was 78% (Table 5).

- **Median time to response:** The median time to the observed responses was 7.1 weeks (range, 7.1, 50.0 weeks).

- **Duration of response:** The duration of response was unknown due to ongoing treatment at the time of analysis.

- **Safety profile:** The most common treatment-emergent adverse events (TEAEs) were diarrhea, fatigue, and vomiting (Table 4).

**DISCUSSION**

- **Efficacy:** Activity against several B-cell malignancies, including CLL, SLL, DLBCL, MCL, and WM.

- **Safety:** Treatment-related serious adverse events (SAEs) were neutropenia, febrile neutropenia, and pneumonia.

- **Conclusion:** M7583 demonstrated efficacy and a manageable safety profile in patients with relapsed/refractory B-cell malignancies, supporting further investigation in 300 mg QD, with 900 mg QD as a supporting daily dose.