**Phase 2 NHL Study Design**

- **Model:** multicenter, open-label study in participants with R-FL or G1 NHL.
- **Participants:** prospectively assigned to cohorts according to EZH2 mutational status: *EZH2* wild-type (WT) or *EZH2* mutant (MT).
- **Duration:** 12 months, with a 1-month follow-up period.
- **Eligibility:** all participants must have a measurable disease, confirmed by prior imaging, and have received a minimum of 1 prior line of therapy.
- **Study drug:** Tazemetostat, 800 mg BID until PD or withdrawal.

**RESULTS**

- **Baseline characteristics:**
  - **Total participants:** 82.
  - **EZH2 WT:** 49.
  - **EZH2 MT:** 33.
  - **Median age:** 61 years.
  - **Primary diagnosis:** FL (n=71), DLBCL (n=60), MM (n=11).
  - **Sex:** 61 (75%) males, 21 (25%) females.
  - **Race:** 78 (95%) White, 2 (2%) African American, 2 (2%) other.

- **Efficacy:**
  - **Objective response rate (ORR):**
    - **EZH2 WT:** 9 (18%)
    - **EZH2 MT:** 20 (60%)
  - **Complete response (CR):**
    - **EZH2 WT:** 3 (6%)
    - **EZH2 MT:** 3 (9%)
  - **Median time from last prior therapy:** 61 weeks.
  - **Median progression-free survival (PFS):**
    - **EZH2 WT:** 11.9 weeks
    - **EZH2 MT:** 15.9 weeks
  - **Median overall survival (OS):**
    - **EZH2 WT:** 28 months
    - **EZH2 MT:** 48.5 months

- **Adverse events:**
  - **Grade ≥ 3:**
    - **EZH2 WT:** 40 (40%)
    - **EZH2 MT:** 30 (29%)
  - **AE leading to dose reduction:**
    - **EZH2 WT:** 4 (5)
    - **EZH2 MT:** 4 (5)
  - **AE leading to discontinuation:**
    - **EZH2 WT:** 3 (6%)
    - **EZH2 MT:** 2 (6%)

**CONCLUSIONS**

- **Tazemetostat demonstrated clinical activity in a phase 2 study in patients with relapsed/refractory follicular lymphoma.**
- **ORR of 40% in EZH2 mutant patients, compared to 18% in EZH2 wild-type patients.**
- **EZH2 MT patients had significantly longer median PFS and OS compared to EZH2 WT patients.**
- **EZH2 MT patients showed a trend towards improved outcomes compared to EZH2 WT patients.**
- **Future studies are needed to further evaluate the role of EZH2 inhibition in follicular lymphoma.**