EZH2 Gain-of-Function Mutations Are Not Associated With More Favorable Prognosis in Relapsed/Refractory Lymphoma: A Preliminary Analysis on 908 Patients

**PS1247**

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**BACKGROUND**

- EZH2 is an epigenetic regulator of gene expression and plays a critical role in multiple forms of cancer.
- Activating mutations of EZH2 are an oncogenic driver, especially in follicular lymphomas (FL), and are present in ~20–25% of patients.7

**METHODS**

- Retrospective data on therapy types and clinical outcomes were collected from 4 academic sites:
  - Barts Cancer Institute, London
  - Institute Gustave Roussy, Paris
  - Memorial Sloan Kettering Cancer Center, New York
  - Semmelweis University, Budapest

- Tumor tissues collected at the time of diagnosis, in most cases, were analyzed for activating mutations of EZH2 (1L) in FL patients treated with immunochemotherapy regimens3,4

- The vast majority of patients received systemic anticancer therapy (Table 1), including a range of chemotherapeutic regimens. Use of combination chemotherapy alone was >40% in 2L+ regimen. Use of immunochemotherapy decreased in second line therapy (2L) and beyond (2L+) such that only 22% of 4L patients treated for R/R FL patients did not include as therapy lines in the analysis

**CONCLUSIONS**

- ORR was similar between patients with MT EZH2 compared with WT EZH2 in all lines of therapy
- Analysis of OS indicates that there are no significant differences between MT and WT EZH2 R/R FL patients followed for more than 30 years
- Improved PFS was observed in 1L patients with MT EZH2 compared with WT EZH2, similar to results reported by Pastore et al.3 and Huet et al.4

**REFERENCES**


**RESULTS**

- Table 1. Baseline Demographics

**Table 2. Systemic anti-cancer therapy types by line of therapy**

**Table 3. PFS of FL patients with MT and WT EZH2 resolving systemic anticancer therapy by line of therapy**

**Table 4. ORR of FL patients with MT and WT EZH2 across lines of therapy**

**Figure 1. PFS by line of therapy for FL patients with MT vs WT EZH2**

**Figure 2. OS for FL patients with MT vs WT EZH2**

**Figure 3. ORR for FL patients with MT vs WT EZH2 across lines of therapy**

**Figure 4. Progression-Free Survival Probability by FL patients with MT vs WT EZH2**

**Table 5. Characteristics of Patients with MT vs WT EZH2**

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**Patient characteristics**

- Data from 908 R/R FL patients (MT-EZH2, n=331; WT-EZH2, n=577; EZH2 status unknown, n=2) treated with systemic anti-cancer therapy before December 1972 and December 2017 at 4 academic centers were included for analyses
- Median follow-up from diagnosis to last follow up or death in patients was 8.92 years (range, 0.03–38.52 years) (Table 1)
- The frequency of EZH2 activating mutations was 21%. The mutation frequency at each hotspot residue was:
  - 83% for 1898/FL (L7)
  - 11% for 4629
  - 8% for 4673
- The vast majority of patients received systemic anti-cancer therapy (Table 1), including a range of chemotherapeutic regimens that often included rituximab (immunohistochemical) (Table 2)
  - In some cases, patients may have also received radiotherapy and/or stem cell transplantation. These chemotherapeutic regimens were not included as therapy lines in the analysis.
  - In 1L, most patients received combination immunotherapy (50%). A substantial number of patients received combination chemotherapy (27%) (Table 2)
  - Use of immunotherapy decreased in second line therapy (2L) and beyond (2L+) such that only 22% of 4L patients received rituximab-based chemotherapy
  - Use of combination chemotherapy alone was >40% in 2L
  - Other therapy types, including anti-CO20-monotherapy and various targeted therapies, were employed in later lines of therapy