**BACKGROUND**

Drugs that have benefited a subset of patients but discovered for development may be rescued through identification of a biomarker predictive of response.

1. **Enzastaurin:** a potent and selective inhibitor of protein kinase C (PKC), also suppresses tumor growth, proliferation, and angiogenesis.

2. **DGM1:** is the major transcript expressed in normal and malignant B cells and is required for B cell receptor signaling, activation of NFκB, and angiogenesis.

**METHODS**

- **Enzastaurin** was assessed as a potential biomarker in the phase 2 trial when combined with R-CHOP.
- **Confirmation of the biomarker identified in the phase 3 study was performed by independent analysis of the biomarker in a separate randomized (1:1) multinational study of patients with DLBCL, randomized to treatment with R-CHOP plus enzastaurin, and achieving a CR/CRu after induction were eligible to continue with single agent enzastaurin or placebo maintenance for up to three years.

**RESULTS**

- **The original analysis of the phase 2 study found a trend toward improved, but not statistically significant OS in patients with high-risk (IPI≥3) DLBCL receiving R-CHOP plus enzastaurin, an area of significant unmet need.**

**CONCLUSION**

- **These data are supportive of DGM1 as a potentially predictive biomarker for enzastaurin response in patients with treatment naïve high-risk DLBCL.**

**REFERENCES**

- Hainsworth, JD, et al. A randomized, phase 2 study of R-CHOP plus enzastaurin for treatment naïve high-risk DLBCL patients with newly diagnosed high-risk DLBCL was initiated and is currently enrolling patients. Leukemia. 2018;32(3):562-563.

**ENGINE STUDY KEY ELIGIBILITY**

- **CBOP-0171 (R-CHOP) C:
  - Treatment naïve
  - Daclizumab (Eli Lilly and Company) positive DLBCL**

**ENGINE STUDY DESIGN**

- **Randomized (1:1) double blind, placebo controlled, multicenter study in patients with treatment naïve high-risk DLBCL.**

**ACKNOWLEDGMENTS**

- **The phase 2 study was supported by Peking University Cancer Hospital & Institute, Beijing, China;**
- **Primary Objective is to compare the effect of R-CHOP plus enzastaurin or R-CHOP plus placebo maintenance (OS) in treatment naïve patients with newly diagnosed high-risk DLBCL who possess the DGM1 biomarker.**

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