LymphomaHub

DLBCL

ASCO 2016 | No Improved DFS, But Improved OS and LSS, Observed with Adjuvant Everolimus Therapy Versus Placebo for Poor-Risk DLBCL

Terri Penfold | Nov 15, 2016

This ASCO 2016 oral abstract presentation took place on Sunday June 5, 9:45am–12:45pm, during the 'Hematologic Malignancies-Lymphoma and Chronic Lymphocytic Leukemia' session. This session was chaired by Pr Gilles Salles, Head of the Hematology Department in South Lyon hospitals, Lyon, France.

The abstract (#*7506*) was presented by Dr Thomas E Witzig of the Mayo Clinic Cancer Center in Rochester, MN.

PILLAR2 (NCT00790036) is a randomized, double-blind, multicenter, phase III study investigating everolimus (EVE) adjuvant therapy *versus* placebo (PBO) in patients with stage III/IV poor-risk (IPI ≥3) Diffuse Large B-Cell Lymphoma (DLBCL) who have achieved a complete response with first-line rituximab-chemotherapy.

Patients were randomized 1:1 to receive either EVE 10mg/day or PBO for 12 months or until disease relapse, unacceptable toxicity, or death.

The primary outcome measure of PILLAR2 was Disease Free Survival (DFS). The secondary outcome measures were Overall Survival (OS), Lymphoma-Specific Survival (LSS), and a comparison of the safety profiles of EVE *versus* PBO. LSS is the time from randomization to death caused by lymphoma. The trial began in July 2009, and 742 patients were randomized.

- Aged ≥65 years = 47% pts; male = 50%; IPI of 4–5 = 42%
- Median follow-up = 50.4 months (range, 24.0–76.9 months)
- Completed study treatment per protocol: EVE = 177 (48%); PBO = 249 (67%)
- Adjuvant EVE did not improve DFS vs. PBO (*P* = 0.276)
- 2-yr DFS rate: EVE = 78% (95% CI, 73–82%); PBO = 77% (95% CI, 72–81%)
- Trends favoring EVE were observed for OS and LSS, and for exploratory analyses of DFS and OS in males and those with IPI 4–5
- Frequent Grade 3–4 AEs with >3% difference between EVE and PBO arms included neutropenia, stomatitis, CD4 lymphocytes decreased, lymphopenia and anemia

	EVE vs PBO **Hazard ratio (95% confidence interval)**
DFS*	
Overall (n = 742)	0.92 (0.69–1.22)†
IPI 4–5 (n = 313)	0.65 (0.42–1.01)
Male (n = 372)	0.68 (0.45–1.05)
OS*	
Overall (n = 742)	0.75 (0.51–1.10)
IPI 4–5 (n = 313)	0.63 (0.37–1.07)
Male (n = 372)	0.55 (0.32–0.94)
LSS* (n = 742)	0.64 (0.39–1.04)

Adjuvant EVE for 1 year did not improve DFS when compared to PBO in IPI 4–5 PET-CR after R-CHOP patients with DLBCL. However, improved OS and LSS were observed with adjuvant EVE compared with PBO. Moreover, adjuvant EVE demonstrated its known safety profile; no new safety concerns were observed. Thomas E Witzig concluded that additional exploration into adjuvant EVE therapy for high-risk DLBCL should be undertaken; as well as other studies investigating the risk-benefit of other adjuvants. Lastly, it was hypothesized that a potential new therapeutic approach would be to combine front-line R-CHOP with everolimus.

Reference

1. Witzig TE, *et al.* PILLAR-2: a randomized, double-blind, placebo-controlled, phase III study of adjuvant everolimus (EVE) in patients (pts) with poor-risk diffuse large B-cell lymphoma (DLBCL). J Clin Oncol 34, 2016 (suppl; abstr 7506).