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FL

ASCO 2016 | E2408 Phase II Trial – Addition of Bortezomib to Bendamustine-Rituximab Greatly Improves CR Rates in Patients with Untreated High-Risk Follicular Lymphoma

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 presentation (*abstract #7507*) was given by Dr Andrew M Evens, Director of the Tufts Cancer Center, Chief of the Division of Hematology/Oncology, Director of the Lymphoma Program and Professor at Tufts University School of Medicine, Boston, MA, USA.

High Risk (HR) Follicular Lymphoma (FL) is an area on great unmet clinical need. The E2408 phase IIa, open-label, multicenter study, conducted by the ECOG-ACRIN Cancer Research Group, began in May 2013 and the primary outcome measure was Overall Response Rate (ORR). It aimed to assess if bortezomib (V) can improve the CR rate achieved by standard bendamustine-rituximab (BR) induction in untreated HR stage I/II or IIIa FL. Moreover, it was investigated if the addition of lenalidomide (len) to maintenance rituximab (MR) improves rates of remission.

HR was defined as high tumor burden by GELF and/or FLIPI 3–5. Patients were randomized to one of three different treatment arms in a 1:2:2 ratio:

A) BR x 6 followed by MR x 2 years (yrs)

B) BVR x 6 (V 1.3 mg/m^2 IV/SQ days 1, 4, 8, 11) then MR x 2 yrs

C) BR x 6 then MR x 2 yrs + len 20 mg/day x 1 yr

The data presented in this abstract reports on the first primary objective of CR rate with induction therapy (Tx) with arms A + C combined for induction comparison (90% power at 1-sided α of 0.15).

- Overall, 250 pts were randomized HR FL pts; 28 were excluded for not starting Tx (n=5), ineligibility (n=8), or central pathology review (n=15)
- Analyses are based on 236 evaluable pts
- Among all pts, high GELF = 92%; FLIPI 3–5 = 55%; ECOG PS 0 = 55%, 1 = 42%, 2 = 3%; marrow involvement = 55%; and stages II = 7%, III = 27%, IV = 66%
- 6 cycles of induction = 86%; no differences between arms

- ORR: BVR = 91%; BR = 90% (*P* = 0.008)
- CR: BVR = 74%; BR = 58% (*P* = 0.016)
- The most frequent Grade 3–4 toxicities (n=241) for BVR vs. BR were neutropenia (35% vs. 30%), sensory neuropathy (12% vs. 1%), thrombocytopenia (10% vs. 5%), fatigue (6% vs. 7%), febrile neutropenia (3% vs. 5%), and diarrhea (5% vs. 1%)
- Incidence of Grade 3 sensory neuropathy occurred in 14% IV vs. 4% subcutaneous administration of bortezomib (OR, 3.7; *P* = 0.2)
- During induction, 3 deaths were reported all in arm C (2 were attributed to disease)

	BR		**BVR**	
FLIPI	**N**	**CR %**	**N**	**CR %**
0–2	40	65%	77	72%
3–5	28	53%	35	76%

In conclusion, this initial report demonstrated that adding bortezomib to front-line induction with BR is feasible in high tumor burden FL patients. The CR rate for BVR was significantly superior versus BR alone. Overall, BVR was also well tolerated (neurotoxicity was less common when bortezomib was administered subcutaneously).

Reference

1. Evens A.M. *et al.* Effect of bortezomib on complete remission (CR) rate when added to bendamustine-rituximab (BR) in previously untreated high-risk (HR) follicular lymphoma (FL): a randomized phase II trial of the ECOG-ACRIN Cancer Research Group (E2408). J Clin Oncol 34, 2016 (suppl; abstr 7507).