Zanubrutinib plus obinutuzumab vs obinutuzumab in patients with relapsed/refractory follicular lymphoma: updated analysis of the ROSEWOOD study

Authors: Sam Yuen[1], Judith Trotman[2], Peter S. Ganly[3], Pier Luigi Zinzani[4], Jiří Mayer[5], Fontanet Bijou[6], Ana C. de Oliveira[7], Yuqin Song[8], Rebecca Auer[9], Pil Kim[10], Sha Huang[11], Richard Delarue[12], Christopher R. Flowers[13]

Institutions: [1]Calvary Mater Newcastle, Waratah, NSW, Australia; [2]Concord Repatriation General Hospital, University of Sydney, Concord, NSW, Australia; [3]Department of Haematology, Christchurch Hospital, Christchurch, New Zealand; [4]Institute of Hematology "Seràgnoli", University of Bologna, Bologna, Italy; [5]Department of Internal Medicine-Hematology and Oncology, Masaryk University and University Hospital Brno, Brno, Czech Republic; [6]Institut Bergonié, Bordeaux, France; [7]Institut Català d'Oncologia (ICO) - Hospital Duran i Reynals, Barcelona, Spain; [8]Peking University Cancer Hospital and Institute, Beijing, China; [9]St Bartholomew's Hospital, Barts Health NHS Trust, London, UK; [10]BeiGene USA, Inc, San Mateo, CA, USA; [11]BeiGene (Shanghai) Co, Ltd, Shanghai, China; [12]BeiGene International GmbH, Basel, Switzerland; [13]Department of Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Aim: In an early-phase study, the combination of zanubrutinib plus obinutuzumab (ZO) was well tolerated and showed a signal of efficacy in patients with follicular lymphoma (FL) (Tam. *Blood Adv.* 2020). ROSEWOOD (NCT03332017) is a phase 2 study designed to assess the efficacy and safety of ZO vs obinutuzumab (O) in patients with relapsed/refractory (R/R) FL. An updated analysis with a median follow-up of 20.2 months is reported.

Method: Patients (N=217) with R/R FL (grade 1-3a) who received ≥2 lines of therapy including an anti-CD20 antibody and alkylating agent were randomized 2:1 to receive ZO (n=145) or O (n=72). Zanubrutinib was given at 160 mg twice daily until progression or unacceptable toxicity. The primary endpoint was overall response rate (ORR) by independent central review. Other endpoints included duration of response (DOR), progression-free survival (PFS), overall survival, and safety. Time to next treatment was also assessed.

Result: In the study population (median age, 64 years; median prior lines, 3 [range, 2-11]), 52.5% of patients were refractory to rituximab; 98.6% received prior immunochemotherapy. ORR was 69.0% (ZO) vs 45.8% (O). DOR at 18 months was 69.3% (ZO) vs 41.9% (O). Median PFS was 28.0 months (ZO) vs 10.4 months (O) (hazard ratio, 0.50; 95% CI, 0.33-0.75; *P*=.0007). Additional efficacy results are in the **Table**. Nonhematologic treatment-emergent adverse events (any grade) that occurred more frequently with ZO vs O (>5% difference) were petechiae and herpes zoster infection (6.3% vs 0% for both); in patients receiving O, pyrexia (13.3% vs 19.7%) and infusion-related reactions (2.8% vs 9.9%) occurred more frequently. Exposure-adjusted incidences of infection and cytopenia were similar; incidence of hemorrhage (all grade) was 2.4 (ZO) vs 1.3 (O) persons/100 person-months.

Conclusion: ZO demonstrated meaningful efficacy and a manageable safety profile in patients with heavily pretreated R/R FL and represents a potential novel therapy.

Table. Efficacy Results

	ZO	O	HR (95% CI)	2-sided *P* value
Primary endpoint				
ORR by ICR, %	69.0	45.8	-	.0012
Other endpoints				
Complete response rate by ICR, %[a]	39.3	19.4	-	.0035
18-month DOR rate by ICR, %[a]	69.3	41.9	-	-
PFS by ICR, median, months[a]	28.0	10.4	0.50 (0.33-0.75)	.0007
TTNT, median, months	NE	12.2	0.34 (0.22-0.52)	<.0001
OS rate at 24 months, %[a]	77.3	71.4	-	-
OS, median, months[a]	NE	34.6	0.62 (0.35-1.07)	.0845

DOR, duration of response; HR, hazard ratio; ICR, independent central review; NE, not estimable; O, obinutuzumab; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; TTNT, time to next treatment; ZO, zanubrutinib plus obinutuzumab.
[a] Secondary endpoint.