F. Morschhauser
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110 | ATEZOLIZUMAB + OBINUTUZUMAB + VENETOCLAX IN PATIENTS WITH RELAPSED OR REFRACTORY FOLLICULAR LYMPHOMA: PRIMARY ANALYSIS OF A PHASE 2 TRIAL FROM LYSA

G. Cartron[1], E. Bachy[2], S. Guidez[3], E. Gyan[4], R. Gressin[5], N. Morineau[6], D. Sibon[7], O. Casasnovas[8], S. Le Gouill[9], H. Tilly[10], L. Ysebaert[11], J. M. Schiano de Colella[12], P. Feugier[13], E. Nicolas Virelizier[14], C. Haioun[15], G. Damaj[16], K. Tarte[17], C. Laurent[18], R. Houot[19], C. Thieblemont[20], F. Morschhauser[21], C. Herbaux[1]
[1]*CHU Montpellier, Hématologie Clinique, Montpellier, France*, [2]*CHU, Hematology, Lyon, France*, [3]*CHU, Hematology, Poitiers, France*, [4]*CHU, Hematology, Tours, France*, [5]*CHU, Hematology, Grenoble, France*, [6]*CHD Vendée, Hematology, La Roche sur Yon, France*, [7]*Necker, Hematology, Paris, France*, [8]*CHU, Hematology, Dijon, France*, [9]*CHU, Hematology, Nantes, France*, [10]*CHB Unicancer, Hematology, Rouen, France*, [11]*Oncopole, Hematology, Toulouse, France*, [12]*IPC, Hematology, Marseille, France*, [13]*CHU, Hematology, Nancy, France*, [14]*CLB, Hematology, Lyon, France*, [15]*Mondor, Hematology, Paris, France*, [16]*CHU, Hematology, Caen, France*, [17]*CHU, Pathology, Rennes, France*, [18]*Oncopole, Pathology, Toulouse, France*, [19]*CHU, Hematology, Rennes, France*, [20]*St Louis, Hematology, Paris, France*, [21]*CHU, Hematology, Lille, France*

Introduction: Relapsed and refractory (R/R) Follicular Lymphoma (FL) treatment remains challenging. Atezolizumab (ATE) and obinutuzumab (OBI) are monoclonal antibodies acting respectively to inhibit T-lymphocyte exhaustion or by inducing lymphoma cells cytotoxicity, whereas venetoclax (VEN) is a small molecule inhibiting BCL-2. Combining tumor-targeted therapies with agents that enhance anti-tumor immunity represents an attractive treatment paradigm. This LYSA sponsored multicenter phase 2 trial (NCT03276468) evaluated ATE, OBI and VEN combination in R/R B-cell lymphomas. Herein, we present primary efficacy and safety data from the FL cohort.
Methods: Patients ≥18 years with biopsy-confirmed R/R FL who failed at least one line of therapy were eligible. OBI was given IV at 1 g on day (D) 1, 8 and 15 of cycle (C) 1 and on D1 from C2 to C8 every 3 weeks. ATE was given IV, 1.2 g every 3 weeks, started at D2 of C1, then administered at D2 of each cycle for 24 cycles. VEN was given orally at 800 mg/D at full dose, starting on D8C1 for 24 cycles. The primary endpoint was the Overall Response Rate (ORR) evaluated by Lugano criteria at the end of induction (EOI) after 8 cycles of ATE, OBI and VEN (M6) or at premature treatment discontinuation.
Results: At the time of the primary analysis (08 Jan 2021), 58 FL patients were enrolled. The median follow-up was 14.5 months, 45 patients completed induction phase and 34 patients started maintenance. Baseline characteristics were: median age, 56 years (38-83); male, 66.1%; Ann Arbor Stage III/IV, 85.7%; FLIPI HR, 47.3%; > 2 prior lines of therapy, 32.1%; refractory to last line of prior regimen, 26.8%; and exposed to ASCT, 30.4%. The OMRR at EOI was measured at 53.6% [41.8%-65.1%], including 30.4% of CMR whereas OMRR at C4 was 75.0% [61.6%-85.6%], including 28.6% of CMR. Best of Response Rate (BOR) was 80.4% [69.6%-88.6%] including 35.7% of CMR. To date, 23 patients relapsed after an initial response (51% of the 45 responders). Thirty-seven patients (63%) received the full induction treatment. At the time of analysis, a median of 8 cycles [1-8] has been administered. A total of 41 (70.7%) patients experienced grade 3–4 adverse event (AE) and 1 had an AE that led to discontinuation of any drug. AE of grade 3 or more reported in at least 10% of patients were neutropenia (41.4%), thrombocytopenia (24.1%) and lymphopenia (22.4%). Of note, two patients experienced autoimmune colitis (grade 2 and 3) and one patient experience a grade 2 immune-related pancreatitis during induction.
Conclusion: ATE, OBI and VEN combo appears to be well tolerated, with no unexpected toxicity brought by the combination. The ORR at EOI seems to be comparable to other innovative regiments in this setting, with durable responses to date.
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Keywords: Indolent non-Hodgkin lymphoma, Combination Therapies, Immunotherapy

No conflicts of interest pertinent to the abstract.

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R. Bannerji[1], S. Yuen[2], T. Phillips[3], C. Arthur[4], I. Isufi[5], P. Marlton[6], J. F. Seymour[7], P. Corradini[8], A. Molinari[9], G. Gritti[10], R. Emmons[11], J. Hirata[12], L. Musick[12], S. Saha[13], B. Croft[12], C. Flowers[14]
[1]*Rutgers Cancer Institute of New Jersey, Section of Hematologic Malignancies, New Brunswick, New Jersey, USA*, [2]*The Calvary Mater Newcastle Hospital, Waratah, Australia*, [3]*University of Michigan Medical School, Division of Hematology and Oncology, Ann Arbor, USA*, [4]*Royal North Shore Hospital, Sydney, Australia*, [5]*Yale University, Smilow Cancer Hospital, Section of Hematology, New Haven, USA*, [6]*Princess Alexandra Hospital and University of Queensland, Department of Haematology, Brisbane, Australia*, [7]*Peter MacCallum Cancer Centre & Royal Melbourne Hospital, Department of Haematology, Melbourne, Australia*, [8]*University of Milan, Istituto Nazionale dei Tumori, Medical Oncology and Hematology Department, Milan, Italy*, [9]*AUSL Romagna, Ospedale degli Infirmi, Dirigente Medico Ematologia, Rimini, Italy*, [10]*ASST Papa Giovanni XXIII, UOC Ematologia, Bergamo, Italy*, [11]*James Graham Brown Cancer Center, Louisville, USA*, [12]*Genentech, Inc., Product Development Oncology, South San Francisco, USA*, [13]*F. Hoffmann-La Roche Ltd, Product Development Biometrics, Welwyn Garden City, UK*, [14]*M.D. Anderson Cancer Center, Department of Lymphoma/Myeloma, Houston, USA*