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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

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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.
The research was funded by: Roche, Abbvie

Keywords: Indolent non-Hodgkin lymphoma, Combination Therapies, Immunotherapy

No conflicts of interest pertinent to the abstract.

111 | POLATUZUMAB VEDOTIN + OBINUTUZUMAB + VENETOCLAX IN PATIENTS WITH RELAPSED/REFRACTORY (R/R) FOLLICULAR LYMPHOMA (FL): PRIMARY ANALYSIS OF A PHASE 1B/2 TRIAL

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Introduction: Polatuzumab vedotin (Pola) + obinutuzumab (G) demonstrated activity and tolerability in a Phase 1b/2 trial of patients (pts) with R/R FL (Phillips, et al. Blood 2016). Preclinical studies with venetoclax (Ven) showed that concurrent treatment with Pola promotes MCL-1 degradation, a known mechanism of resistance to Ven, and enhances *in vivo* anti-tumor efficacy (Amin, et al. AACR 2020). Here, we report the primary safety/efficacy analysis with Pola-G-Ven in a Phase 1b/2 study of pts with R/R FL (GO29833; NCT02611323).
Methods: Pts received induction treatment every 21 days (D) x six cycles (C) of: Pola 1.4–1.8mg/kg intravenously (IV) in dose escalation (DE) or recommended Phase II dose (RP2D) on D1; G 1000mg IV (C1: D1, D8, D15; C2–6: D1); and oral Ven 200–800mg (DE or RP2D; D1–21). Pts with complete response/partial response/stable disease (CR/PR/SD) at end of induction (EOI) received maintenance with G (1000mg on D1 every 2 months [mo] for 24 mo) and Ven (200–800mg daily) for 8 mo. Primary endpoints were safety/tolerability and positron emission tomography (PET)-CR rate at EOI by independent review committee (IRC) using modified Lugano criteria.
Results: At the primary analysis (Oct 05, 2020), 74 pts were enrolled. Median pt age was 64 years (range 36–78); male (57%); Ann Arbor Stage III–IV (86%); FL International Prognostic Index high risk ≥3 (55%); bulky disease ≥7cm (16%); prior lines of therapy ≥2 (74%); refractory to: last prior therapy (51%), any prior anti-CD20 therapy (55%), both anti-CD20 therapy and an alkylating agent (double refractory; 55%). Grade 3–4 adverse events (AEs) were experienced by 73% of pts; most commonly, neutropenia (39%), thrombocytopenia (19%), and infections (16%; mainly pneumonia). AEs led to dose reduction in 38% and interruption in 68% of pts (mainly modifications to Ven). One fatal AE was reported (pneumonia). In total, 49 pts were treated at RP2D (Pola 1.8mg/kg + Ven 800mg) and were evaluable for efficacy. PET-CR rate at EOI by IRC was 57% (**Table**). With a median follow-up of 14.4 mo (range 8.2–28.4), the 12-mo progression-free survival (PFS) was 73% (95% confidence interval: 59.4–86.9). Median PFS was not reached.
Conclusions: The safety profile of Pola-G-Ven is consistent with the known profiles of the individual drugs. Response rates at EOI with Pola-G-Ven are encouraging in this R/R FL patient population. Additional follow-up is needed to assess PFS benefit during maintenance treatment and beyond.

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Keywords: Indolent non-Hodgkin lymphoma, Molecular Targeted Therapies, Combination Therapies

Conflicts of interests pertinent to the abstract

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TABLE: Responses at EOI by modified Lugano criteria (RP2D; =49)

N (%)	INV	IRC
ORR	38 (78)	35 (71)
CR	28 (57)	28 (57)
PR	10 (20)	7 (14)
SD	6 (12)	8 (16)
PD	3 (6)	4 (8)
Missing/unevaluable	2 (4)	2 (4)

CR, complete response; INV, investigator-assessed; IRC, independent review committee-assessed; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

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112 | CHRONOS-3: RANDOMIZED PHASE III STUDY OF COPANLISIB PLUS RITUXIMAB *VS* RITUXIMAB/PLACEBO IN RELAPSED INDOLENT NON-HODGKIN LYMPHOMA (INHL)

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