109 | CHARACTERISTICS OF PATIENTS ACHIEVING COMPLETE OR PARTIAL RESPONSE (CR/PR) WITH TAZEMETOSTAT (TAZ) IN WILD-TYPE RELAPSED/REFRACTORY (R/R) FOLLICULAR LYMPHOMA (FL)

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Introduction: Enhancer of zeste homolog 2 (EZH2) epigenetic modifier expressed within germinal centers is an important regulator of FL growth and survival. TAZ is an EZH2 inhibitor approved for R/R FL with heightened overall response rates (ORRs) in mutant (MT) *EZH2* but similar progression-free survival (PFS) in wild-type (WT) and MT *EZH2* cohorts. Pivotal phase 2 study identified ORRs (CR/PR) of 35% (19/54) and 69% (31/45) in WT and MT *EZH2* cohorts, respectively; PFS was 11.1 mo in WT and 13.8 mo in MT *EZH2* cohorts. This exploratory analysis assessed if baseline demographics or disease characteristics correlate with response to TAZ in the WT *EZH2* FL cohort.

Methods: Detailed methods of this open-label multicenter phase 2 study (NCT01897571) are described in Morchhauser et al. *Lancet Oncol* 2020. Oral TAZ 800 mg twice daily was assessed in adults with FL after ≥2 prior systemic therapies. Baseline demographics and disease characteristics were summarized using descriptive statistics.

Results: Of 99 patients (pts) with WT or MT *EZH2*, 19 pts with WT EZH2 who received a median of 3 prior lines of therapy responded (2 CR, 17 PR). In general, WT *EZH2* group had more pts with high-risk features than the MT *EZH2* group. Baseline characteristics of pts in the WT *EZH2* group who achieved a response were similar to pts with MT *EZH2* who responded, as well as the general population (Table). The number of pts with high-risk features, such as progression of disease within 24 mos (POD24), refractory to rituximab-containing regimen, and double refractory, were similar in the WT and MT *EZH2* responder groups, respectively. Pts with refractoriness to last therapy represented 26.3% and 51.6% of WT and MT *EZH2* responders, but the populations were small.

Conclusions: Characteristics of responders in the WT *EZH2* FL cohort were reflective of the overall population, with a broad distribution of disease severity at baseline. Responders with WT *EZH2* included pts with high-risk features, such as POD24, refractoriness to rituximab-based regimens, or double refractory disease. Response to TAZ in pts with WT *EZH2* R/R FL appears to be independent of baseline clinical factors; however, small numbers preclude a definitive assessment. Additional correlative molecular analyses are in progress.

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Conflicts of interests pertinent to the abstract

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TABLE: Baseline Disease Characteristics of Responders

Characteristic	Patients With CR/PR (WT *EZH2*) (n=19)	Total Population, WT *EZH2* (n=54)	Patients with CR/PR, MT *EZH2* (n=31)	Total Population, MT *EZH2* (n=45)
POD24, n (%)	8 (42.1)	32 (59.3)	12 (38.7)	19 (42.2)
Refractory to rituximab-containing regimen, n (%)	10 (52.6)	32 (59.3)	13 (41.9)	22 (48.9)
Refractory to last therapy, n (%)	5 (26.3)	22 (40.7)	16 (51.6)	22 (48.9)
Double refractory, n (%)[a]	4 (21.1)	15 (27.8)	7 (22.6)	9 (20.0)
Prior hematopoietic stem cell transplant, n (%)	7 (36.8)	21 (38.9)	3 (9.7)	4 (8.9)

[a]Refractory to rituximab-containing regimen and an alkylating agent-containing regimen.

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

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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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