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Pirtobrutinib (LOXO-305), a Next-Generation, Highly Selective, Non-Covalent Bruton's Tyrosine Kinase Inhibitor in Previously Treated Mantle Cell Lymphoma and Other Non-Hodgkin Lymphomas: Phase 1/2 BRUIN Study

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patients continued treatment. Patients received a mean of 4.6 Lonca cycles (std 4.1; range 1–22). ORR was 48.3% (complete response [CR]: 24.8%; partial response [PR]: 23.4%). Median DoR was 12.6 months for patients with CR or PR (n=70); not reached for patients with CR. Median PFS and OS were 4.9 and 9.5 months, respectively. Post-Lonca treatment, 15 patients received CD19-directed chimeric antigen receptor T-cell therapy with an investigator-assessed ORR of 46.7%, and 11 patients proceeded to SCT as consolidation after Lonca response. Most common (≥25.0%) all-grade TEAEs were increased gamma-glutamyltransferase (41.4%), neutropenia (40.0%), thrombocytopenia (33.1%), fatigue (27.6%), and anemia (26.2%). Grade ≥3 TEAEs occurred in 107 (73.8%) patients. Treatment-related TEAEs leading to treatment discontinuation and dose delays occurred in 26 (17.9%) and 62 (42.8%) patients, respectively. **Conclusions:** After longer follow-up of patients in LOTIS-2, durable responses to Lonca continue to be observed in heavily pre-treated patients with R/R DLBCL. No new safety concerns occurred. **Research funding:** ADC Therapeutics SA. **Keywords:** non-Hodgkin lymphoma, diffuse large B-cell lymphoma, antibody-drug conjugate, loncastuximab tesirine, Phase 2

ABCL-030

Safety of Ambulatory High-Dose Methotrexate (HDMTX) Administration Among Hematological Malignancies Patients in a Tertiary Care Center

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Context: The utilization of HDMTX is commonly used in solid malignancies such as osteosarcoma and hematological malignancies such as acute lymphoblastic leukemia and non-Hodgkin lymphoma. Urine alkalinization using intravenous sodium bicarbonate and calcium folinate to facilitate clearance of MTX are two crucial steps in MTX clearance and avoiding or minimizing side effects such as nephrotoxicity and hepatotoxicity. **Objective:** To assess the safety of ambulatory HDMTX administration among adult patients with hematological malignancies in a tertiary care center. **Design:** This is an open-label, single-arm trial that aims to evaluate the safety of HDMTX administration in an outpatient setting among patients with hematological malignancies in a tertiary care center. **Setting:** Tertiary care center. **Patients or Other Participants:** IRB approved. Inclusion criteria: Adult patients from 14 to 60 years of age; normal baseline kidney and liver function; cooperative and fully compliant patients; living nearby the hospital and has access to medical service. Exclusion criteria: Pregnant or breastfeeding women. **Interventions:** Urine alkalinization with sodium bicarbonate and acetazolamide as per protocol, starting the day prior to methotrexate infusion. Good hydration. Daily serum MTX until below 0.1 micromol/L. **Main Outcomes Measures:** The safety of ambulatory HDMTX administration. **Results:** Thirty-four (n=34) cycles for 16 patients have been completed thus far. Approximately 67.65% of cycles were for patients diagnosed with DLBCL. Sixteen (47.1%) of the total cycles achieved MTX level less than 0.1 micromol/L by 48 hours, and 30 cycles (91.2%) achieved the same level by 72 hours. By 72 hours, 23.5% had reversible asymptomatic elevation of creatinine, and all were Grade 1. By 72 hours, approximately 35.3% had reversible asymptomatic hepatotoxicity, and all were Grade 1. **Conclusions:** Our preliminary results suggest that ambulatory HDMTX is safe, cost-effective, and more comfortable for patients. These results encourage the use of this approach more frequently, as it decreases hospitalization and thus reduces cost, increases patient satisfaction, and helps to solve the issue of bed crisis. **Keywords:** ABCL, lymphoma, folinate, therapy, CHOP, DLBCL

ABCL-040

Pirtobrutinib (LOXO-305), a Next-Generation, Highly Selective, Non-Covalent Bruton's Tyrosine Kinase Inhibitor in Previously Treated Mantle Cell Lymphoma and Other Non-Hodgkin Lymphomas: Phase 1/2 BRUIN Study Results

Jonathon B. Cohen[1], Nirav N. Shah[2], Alvaro J. Alencar[3], James N. Gerson[4], Manish R. Patel[5], Bita Fahkri[6], Wojciech Jurczak[7], Xuan N. Tan[8], Katharine L. Lewis[8], Timothy S. Fenske[2], Catherine C. Coombs[9], Ian Flinn[10], David J. Lewis[11], Stephen Le Gouill[12], M Lia Palomba[13], Jennifer A. Woyach[14], John M. Pagel[15], Nicole Lamanna[16], Minal A. Barve[17], Paolo Ghia[18], Toby A. Eyre[19], Ming Yin[20], Binoj Nair[20], Donald E. Tsai[20], Nora C. Ku[20], Anthony R. Mato[13], Chan Y. Cheah[8], Michael L. Wang[21]*

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Context: Despite the marked efficacy of covalent BTK inhibitors (BTKi) in MCL, WM, and MZL, the development of resistance and discontinuation for adverse events can lead to treatment failure. Low oral bioavailability or short half-life of these agents can lead to suboptimal BTK target coverage and ultimately result in acquired resistance in some patients (pts). Pirtobrutinib (LOXO-305) is a highly selective, non-covalent BTKi that inhibits both WT and C481-mutated BTK with equal, low nM potency. **Objective:** To evaluate safety and efficacy of pirtobrutinib in pts with MCL/NHLs. **Design:** BRUIN is an ongoing multi-center phase 1/2 trial (NCT03740529). Enrollment was initiated 21 March 2019. **Setting:** Global: community hospitals, academic medical centers. **Patients:** Previously treated pts with advanced B-cell malignancies. **Interventions:** Oral pirtobrutinib (7 dose escalation levels: 25–300mg once daily) in 28-day cycles. **Main Outcomes Measures:** Determining the maximum tolerated dose/recommended phase 2 dose (RP2D), safety profile, and efficacy based on response assessment using disease-specific criteria per protocol. **Results:** As of 27 September 2020, 323 pts with B-cell malignancies (170 CLL/SLL, 61 MCL, 26 WM, and 66 other B-cell lymphomas) were treated on 7 dose levels (25–300mg QD). Pirtobrutinib demonstrated high oral exposures, with doses ≥100 mg QD exceeding the BTK IC90 for the entirety of the dosing interval. No DLTs occurred. The only TEAEs, regardless of attribution or grade in ≥10% of pts (n=323), were fatigue (20%), diarrhea (17%) and contusion (13%). A RP2D of 200mg QD was selected. At the efficacy cutoff date, 35 (57%) MCL pts, 18 (69%) WM pts, and 34 (52%) other NHL pts remained on therapy. Among the 52 efficacy evaluable prior BTKi treated MCL pts, the ORR was 52%. Among the 19 efficacy evaluable pts with WM, the ORR was 68%. For the other 55 efficacy evaluable NHL pts, ORR was 24% (DLBCL), 50% (FL), 22% (MZL), and 75% (Richter's transformation). **Conclusion:** Pirtobrutinib demonstrated promising efficacy in MCL and other NHL pts, was well-tolerated and exhibited a wide therapeutic index. **Keywords:** ABCL, MCL, NHL, non-covalent, BTK inhibitor, BRUIN

ABCL-062

Primary Effusion Lymphoma: Clinical Characteristics and Natural History

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Introduction: Primary effusion lymphoma (PEL) is a very rare type of non-Hodgkin lymphoma (NHL), accounting for less than 4% of HIV-related NHL and frequently occurring in the context of HIV or other states of immunosuppression infection. Large-scale studies describing the natural history of this entity are lacking. **Materials and Methods:** The National Cancer Database (NCDB) was queried for patients diagnosed with PEL between 2004 and 2017. All patients aged ≥18 years diagnosed with PEL were included. We excluded patients with multiple primary malignancies or lost to follow-up. Kaplan-Meier and multivariate Cox regression were used in the analyses. **Results:** Of the 219 PEL patients included in the analysis, 179 (82%) were males, 161 (74%) Caucasian, and 49 (22%) African American. The median age at diagnosis was 60±19 years. One hundred fifteen (53%) were HIV-positive, and 63 (29%) HIV-negative. One hundred eleven (51%) received chemotherapy; 101 (46%) did not receive chemotherapy. The time to treat (TTT) from diagnosis to chemotherapy start was ≤8 days in 27 patients, within 9–15 days in 24 patients, within 16–32 days in 24 patients, and ≥32 days in 25 patients. The median OS for each group was 6 months, 13 months, 41 months, and 16 months, respectively, and the differences were not statistically significant. Compared to HIV-negative patients, HIV-positive patients were younger (mean age 47 *vs* 77 years, P<0.001), with no significant difference in the stage or IPI score and had better OS (median OS 13 *vs* 8 months, P=0.015). Patients who received chemotherapy had better OS compared to patients who did not receive chemotherapy (median OS 13 *vs* 3 months, P<0.001) and that was found in HIV-positive patients (median OS 22.97 *vs* 1.97 months, P=0.006), but not in HIV-negative patients (median OS 6 *vs* 8 months, P=0.752). By multivariate analysis, chemotherapy was associated with better OS (HR 0.502, 95% CI 0.324–0.777; P=0.002), whereas HIV status did not affect the OS (HR 0.6, 95% CI 0.3–1.4; P=0.258). **Conclusions:** In contrast to the impression that HIV positivity might confer poorer outcomes, these data suggest that HIV-positive patients with PEL have comparable outcomes to HIV-negative patients, possibly due to improvement in antiretroviral therapy. **Keywords:** ABCL, non-Hodgkin lymphoma, overall survival, chemotherapy, HIV

ABCL-064

"DA-EPOCH+/-R" Protocol in High-Grade Lymphoma: An Analysis

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Context: DA-EPOCH (dose-adjusted etoposide, doxorubicin, cyclophosphamide, vincristine, and prednisolone) +/- R (rituximab) is one of the standard chemotherapeutic regimens for high-grade lymphomas. **Objective:** This study aimed to evaluate the safety and efficacy of DA-EPOCH+/-R in an Indian context. **Design and Setting:** This retrospective study included 47 patients with high-grade lymphoma who received uniform DA-EPOCH+/-R protocol with GCSF prophylaxis in the Department of Medical Oncology at All India Institute of Medical Sciences, New Delhi, India, from May 1, 2013 to April 30, 2021. **Results:** The median age was 35 years