shown in Figure 1). Serious TEAEs occurred in 42.4% (arm A) and 51.5% (arm B) of pts. There were three deaths unrelated to tafasitamab and/or LEN (sepsis, urosepsis, and COVID-19 pneumonia). Dose intensity of R-CHOP was maintained in both arms.

Among 60 pts who completed tumor assessments after cycle 3, ORR was 89.7% (arm A) and 93.5% (arm B).

Conclusion: These data suggest that R-CHOP + tafasitamab or tafasitamab + LEN is tolerable in pts with Tx-naïve DLBCL. Dosing of R-CHOP is unaffected by the addition of tafasitamab. Toxicities were similar to those expected with R-CHOP alone or with LEN. Updated safety and early efficacy data will be presented at the conference.

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Conflicts of interests pertinent to the abstract

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238 | CLINICAL ACTIVITY OF LONCASTUXIMAB TESIRINE PLUS IBRUTINIB IN NON-HODGKIN LYMPHOMA: UPDATED LOTIS 3 PHASE 1 RESULTS

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Introduction: The treatment of relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL) remains an area of unmet need. Combination therapy using agents with different mechanisms of action may improve upon therapeutic outcomes. We investigated the combination of loncastuximab tesirine (Lonca; an antibody-drug conjugate composed of a humanized anti-CD19 monoclonal antibody conjugated to a pyrrolobenzodiazepine dimer toxin) with ibrutinib (a small-molecule inhibitor of Bruton's tyrosine kinase). Here we present updated safety and efficacy data from the Phase 1 portion of a Phase 1/2 study (NCT03684694).

Methods: The protocol is a dose escalation and dose expansion, open label, single-arm, combination study in patients (≥18 years) with R/R DLBCL or R/R MCL. The primary objectives of Phase 1 are to characterize the safety and tolerability of Lonca plus ibrutinib, and identify the recommended Phase 2 dose and schedule. Secondary objectives include evaluation of antitumor effects. The maximum tolerated dose

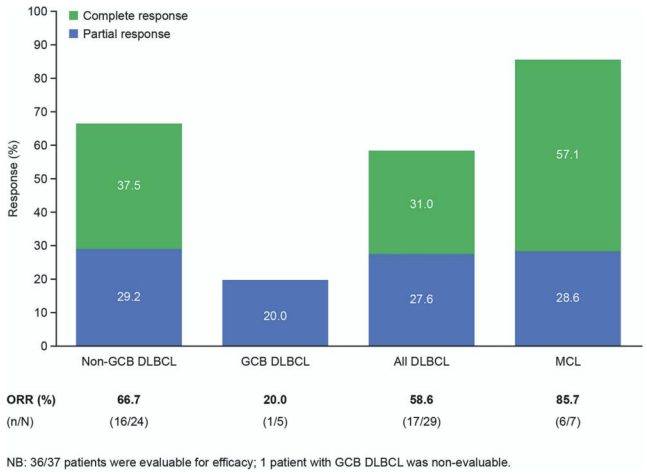

FIGURE 1 ORR by histology

(MTD) was determined during the dose escalation part as Lonca 60 μg/kg IV every 3 weeks (Q3W) for 2 cycles and oral ibrutinib 560 mg/day po for up to 1 year. After disease assessment at Week 14, patients with partial response or stable disease may receive 2 additional cycles of Lonca every 4 weeks at Cycles 5 and 6.

Results: At data cut-off (January 4, 2021), 30 patients with DLBCL (24 with non-germinal center B-cell [non-GCB] DLBCL and 6 with GCB DLBCL) and 7 patients with MCL had received the MTD. Median patient age was 72 years (range 40–91) and 28 (75.7%) had Stage 4 disease. Patients received a median of 2 (range 1–6) prior therapies. Eight (21.6%) patients were primary refractory and 18 (48.6%) were refractory to their last-line of therapy; 24 (64.9%) and 17 (45.9%) had relapsed with first-line and last-line therapy, respectively.

Patients received a median of 2 Lonca cycles (range 1–4) and 4 (range 1–14) ibrutinib cycles. Median treatment duration was 105 days (range 18–379).

Treatment-emergent adverse events (TEAEs) were reported in 37/37 (100%) patients; most common (≥20%) were thrombocytopenia (11 [29.7%]), anemia (9 [24.3%]), fatigue, diarrhea, and rash (all 8 [21.6%]). Grade ≥3 TEAEs were reported in 24/37 (64.9%) patients; most common (≥5%) were anemia (4 [10.8%]), neutropenia (4 [10.8%]), thrombocytopenia (2 [5.4%]), and fatigue (2 [5.4%]). TEAEs leading to treatment discontinuation occurred in 3 (8.1%) patients.

Overall response rate (ORR; in 36 evaluable patients) was 63.9% (36.1% and 27.8% for complete and partial response, respectively). ORR for patients with non-GCB DLBCL, GCB DLBCL, all DLBCL, and MCL was 66.7%, 20.0%, 58.6%, and 85.7%, respectively (Figure 1).

Conclusions: Results indicate that Lonca 60 μg/kg plus ibrutinib 560 mg has encouraging antitumor activity, with manageable toxicity in R/R DLBCL or R/R MCL.

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Keywords: CombinationTherapies

Conflicts of interests pertinent to the abstract

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239 | FINAL ANALYSIS OF A NORDIC LYMPHOMA GROUP PHASE IB/IIA TRIAL OF PIXANTRONE, ETOPOSIDE, BENDAMUSTINE AND, IN CD20-POSITIVE TUMORS, RITUXIMAB IN RELAPSED AGGRESSIVE B- OR T-CELL LYMPHOMAS

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Introduction: Multiply relapsed aggressive lymphomas still represent an unmet clinical need, particularly, if they occur in frail patients (pts). We developed an out-patient based salvage regimen consisting of pixantrone, etoposide, bendamustine and, in CD20+ lymphomas, rituximab (P[R]EBEN). Here we present the final analysis of a phase 1b/2a trial testing this regimen in relapsed aggressive B- or T-cell lymphomas. Treatment refractory pts, i.e. duration of response (DoR) since last treatment <6 months (mo), were excluded.

Methods and Results: *Phase 1b:* Five pts were included (median age: 60 yrs; range 39-68 yrs). Four had diffuse large cell B-cell (DLBCL) and 1 peripheral T-cell lymphoma (PTCL). All had progressed after autologous transplant. The pharmacokinetics for pixantrone given in combination (Fig.1a) resembled those of pixantrone monotherapy. Six serious adverse events (SAEs) were reported among 4 pts: grade 1 (transitory asymptomatic troponin T elevation), grade 2 (non-neutropenic airways infection), grade 3 (non-neutropenic fever, neutropenic fever + anemia, pneumonia), grade 4 (septicemia). Two dose-limiting toxicities (DLTs; neutropenic infection and neutropenia $<0.5 \times 10^9$/l of >5 days duration) occurred within cycle 2 at baseline level, meeting the criteria for maximum tolerated dose (MTD; primary endpoint, phase1), and defining the phase 2 dose level (P 50 mg/m^2 i.v. day 1+8, R 375 mg/m^2 i.v. day 1, E 100 mg/m^2 i.v. day 1, Ben 90 mg/m^2 i.v. day 1).

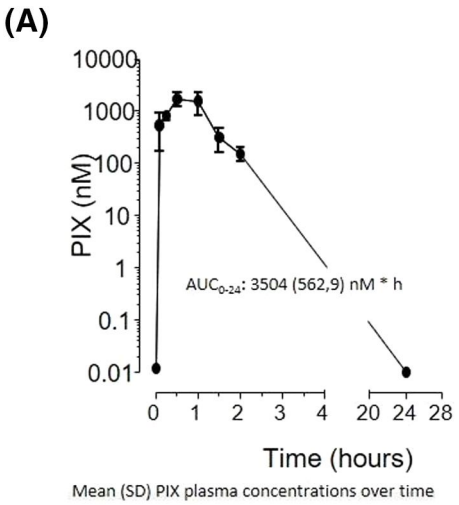
Phase 2: Sixty pts (M/F ratio:1.3; age range:39-84 yrs, median:71 yrs; 37 DLBCL and 23 PTCL) were enrolled and 58 were evaluable. Median follow-up was 33 mo (range 8-53 mo). Grade 3-4 hematologic AEs included neutropenia 33%, thrombocytopenia 16%, and anemia 13%. Grade 3-4 non-hematological AEs included infections 33%, cardiac 13% and other causes 27%. There were 31 deaths due to: lymphoma (22;71%), sepsis (2; 6%) and other causes (7; 23%: 1 lung carcinoma, 1 acute leukemia, 1 myelodysplasia, 1 lung embolism, 1 allotransplant related and 2 unknown). Of 58 evaluable pts, 38 (66%) had a complete (CR) and 1 (2%) a partial response, with an overall response rate (primary endpoint, phase 2) of 68% (B: 51%; T: 70%) . The median DoR (co-primary endpoint, phase 2) of the 34 pts in CR at end of treatment was 13 mo (range 0.5-53+ mo; B: 13 mo; T: 12,5 mo). Three pts were bridged to allogeneic transplant. The 3-yr overall and progression-free survival (PFS) rates were 39% and 28%, respectively. Pts with early metabolic response had a significantly better PFS than those with active disease (Fig.1b). A correlative analysis on pre-therapeutic biopsies is ongoing to identify gene expression signatures in DLBCL and PTCL related to treatment response.

Conclusion: The P[R]EBEN regimen is a feasible out-patient based treatment, applicable in frail, heavily pre-treated aggressive lymphoma pts and shows encouraging CR rates and DoR, particularly in early responders.

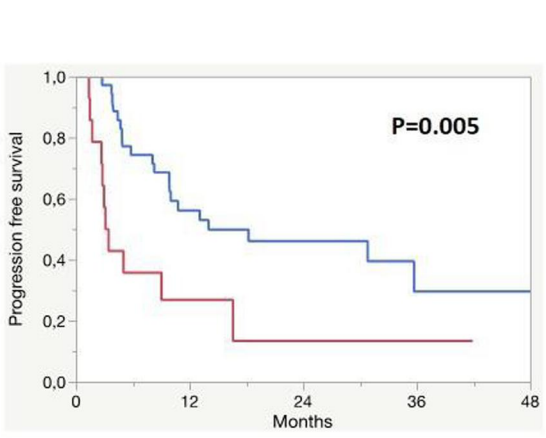
The research was funded by: CTI Life Sciences Limited and Servier Affaires Médicales

Keywords: Aggressive B-cell non-Hodgkin lymphoma, Aggressive T-cell non-Hodgkin lymphoma, Combination Therapies

No conflicts of interest pertinent to the abstract.



Mean (SD) PIX plasma concentrations over time



PFS for pts with metabolic response (Deauville score 1-4 - blue line) vs no response (Deauville score 5 – red line) at first interim PET/CT evaluation