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ORAL ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Subcutaneous (SC) Mosunetuzumab (mosun) As First-Line Therapy for Patients (pts) with High Tumor-Burden Follicular Lymphoma (FL): First Results of a Multicenter Phase 2 Study

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Introduction:
Cytotoxic chemotherapy plus anti-CD20 antibodies is the current standard of care for pts with newly diagnosed high-burden FL. While effective, this approach is burdened by toxicities, including infections and second cancers, and up to 20% of pts progress within 2 years and have poor outcomes. Intravenous (IV) mosun is a CD20xCD3 bispecific antibody recently approved for the treatment of pts with relapsed or refractory FL based on remarkable efficacy data, and its activity may be even greater in chemotherapy-naïve patients. Furthermore, SC mosun proved as effective as, and possibly better tolerated than, the IV formulation while increasing administration efficiency and convenience. Here, we present the first results of a phase 2 multicenter trial of SC mosun in patients with untreated high-burden FL.

Methods:
Key eligibility criteria included: Age ≥18 years, stage 2-4 FL in need of therapy per GELF criteria, being fit for chemoimmunotherapy, adequate bone marrow and organ function. SC mosun was administered at the dose of 5 mg on D1 and 45 mg on D8 and D15 of C1, and 45 mg on D1 of each subsequent 21-day cycle. Premedication consisted of dexamethasone, diphenhydramine, and acetaminophen before each mosun dose during C1 and on C2D1 if cytokine release syndrome (CRS) occurred in C1. Subjects with ≥3 CRS risk factors (stage 3-4, bulky disease, bone marrow (BM) involvement, elevated LDH) received dexamethasone 10 mg for 3 days with each mosun dose in C1 and C2. Prophylactic hospitalization was not required. Treatment lasted 8 cycles in pts who achieved complete response (CR), and up to 17 in those with partial response. Response was assessed per the Lugano 2014 and LYRIC 2016 criteria. BM evaluation was mandated in pts with baseline BM involvement who achieved radiographic CR. CRS and neurotoxicity were graded per the 2019 ASTCT criteria.

Results:
Between July 2022 and July 2023, 43 pts were enrolled. Median age was 55 years (range 26-77), 40% of pts had bulky disease (≥7 cm), 25% had grade 3A FL, and 27% had a FLIPI score ≥3. The median SUV_{max} was 11.5 (range 3.7-41.1)(Table). At the cutoff date of 07/21/2023, 4 pts were in screening, 22 were on treatment, and 13 completed treatment. Four pts discontinued therapy early due to progressive disease (1), or adverse events (AE) (3, one related to study drug). Out of 230 patient-cycles administered, 9 (4%) were delayed due to AEs, by a median of 13 days (range 7-17).
Among 39 safety-evaluable pts, the most common treatment-emergent AE were injection site reaction (72%, all G1), CRS (51%), fatigue (33%), dry skin (33%), skin rash (26%), ALT elevation (23%), and AST elevation (21%). G≥3 neutropenia occurred in 4 pts (10%), while infections occurred in 10 pts (26%), and were G1-2 in 8 cases and G3 in 2 cases. One pt died of cardiac arrhythmia in the setting of COVID19-associated pneumonia. CRS occurred most commonly after C1D1 and was G1 in 18 pts (90%) and G2 in 2 (10%). Median time to onset of the first CRS episode was 31h (2-91). Hospitalization and tocilizumab were only required in the two pts who experienced G2 CRS.

Twenty-six pts were evaluable for response (1 had concurrent neoplasm at first response assessment, 1 had indeterminate response (IR)3 per LYRIC criteria, and 15 are yet to be evaluated). The best overall response rate was 96% and the CR rate was 81%. All 22 CR were seen at the first response assessment (Figure). Similar response rates were observed among higher-risk subgroups, including pts with high-risk FLIPI (figure), grade 3A FL (ORR 100%, CR 75%), bulky disease (ORR 100%, CR 82%), or SUVmax ≥13 (ORR 83%, CR 83%)). At a median follow-up for response-evaluable pts of 6.0 months, 2 pts have experienced progression, one with CD20-negative FL at the end of therapy, the other with DLBCL diagnosed 6 weeks after treatment initiation on a left axillary lymph node with baseline SUV 41 and not previously biopsied.

Conclusion:

SC mosun demonstrated a manageable safety profile and highly encouraging efficacy in pts with newly diagnosed high-burden FL, including those with higher-risk disease. Assessment of durability of responses will require additional follow-up. Enrollment continues and updated data will be presented.

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OffLabel Disclosure: Mosunetuzumab is a CD20xCD3 bispecific antibody approved by the FDA for use in patients with follicular lymphoma (FL) after 2 or more lines of systemic therapy. Frontline use of subcutaneous mosunetuzumab in FL is experimental.

Table. Patient characteristics

Characteristic	All Patients (N=43)
Age, years, median (range)	55 (26 - 77)
Gender, n (%)	
Male	22 (51.2%)
Female	21 (48.8%)
Race, n (%)	
White	35 (81.4%)
Asian	6 (14.0%)
Black	1 (2.3%)
Unknown	1 (4.7%)
Ethnicity, n (%)	
Non-Hispanic	38 (88.4%)
Unknown	5 (11.6%)
Grade, n (%)	
1-2	32 (74.4%)
3A	11 (25.6%)
ECOG performance status, n (%)	
0	35 (81.4%)
1	8 (18.6%)
Stage, n (%)	
II	4 (9.3%)
III	7 (16.3%)
IV	32 (74.4%)
FLIPI, n (%)	
0-1	8 (18.6%)
2	23 (53.5%)
3	8 (18.6%)
4	4 (9.3%)
Bulky disease (≥7 cm), n (%)	17 (39.5%)
B symptoms, n (%)	9 (20.9%)
ALC, median (range)	1.2 (0.6 - 7.1*)
Elevated LDH, n (%)	7 (16.3%)
Time to Treatment Initiation, months, median (range)	3.2 (0.9 - 72.7)

ECOG, eastern cooperative oncology group; FLIPI, follicular lymphoma international prognostic index; ALC, absolute lymphocyte count; LDH, lactate dehydrogenase; *Clonal B-cells = 1700/µL

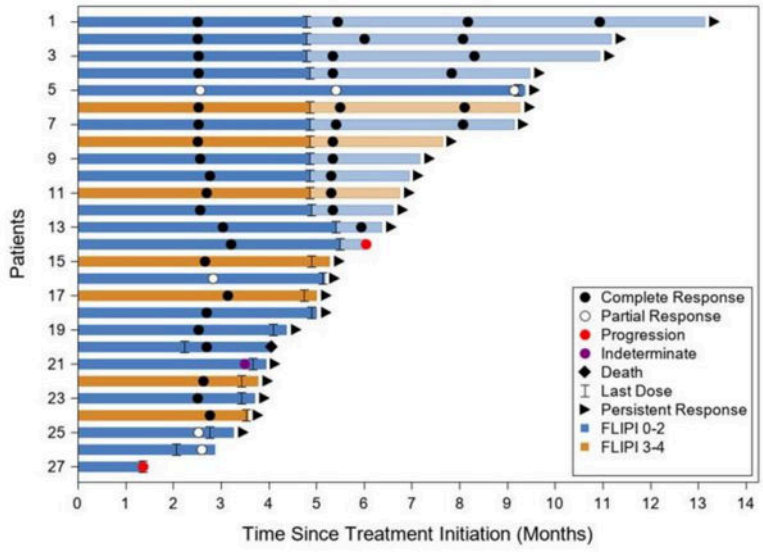

Figure 1

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