Presented at EHA 2024

Response-adapted treatment with mosunetuzumab with or without obinutuzumab and polatuzumab vedotin in treatment naïve follicular and marginal zone lymphoma: interim results and PhasED-Seq MRD analysis

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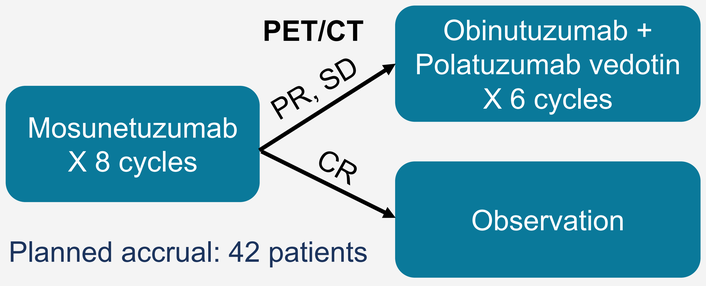
Background

- Mosunetuzumab (mosun) is a CD3:CD20 bispecific antibody FDA-approved for R/R follicular lymphoma after two prior lines
- Outpatient fixed-duration dosing yields durable remissions in ~50% of patients[1].
- We hypothesized that mosun would be even more active in patients without prior lymphotoxic chemotherapy[2,3].
- There is limited data utilizing ultra-sensitive MRD testing (PhasED-Seq)[4] in untreated FL, and no current data in any setting utilizing this technology in patients treated with bispecific antibodies

Schema



- Planned accrual: 42 patients
- Single Center IIT
- Primary endpoint: CR as best reponse (Lugano[5])
- Secondary Endpoint: ORR as best response
- Exploratory analysis: Correlation of results with MRD assessments by PhasED-Seq

Results: Safety

Demographics

Patient Characteristic	N = 38
Age, median (range)	59 (36-83)
Baseline disease characteristics, n (%)	
Stage 3 or 4 at Diagnosis, n (%)	36 (95%)
Histology	
Follicular lymphoma, grade 1-2	27 (71%)
Follicular lymphoma, grade 3a	7 (18%)
Marginal zone lymphoma	4 (11%)
B symptoms	5 (13%)
Extranodal disease	20 (53%)
Elevated LDH	6 (16%)
FLIPI 3-5 (FL only)	12 (35%)
Indications for treatment (can have more than 1)	
Symptomatic disease	30 (79%)
Threatened organ function	4 (11%)
Cytopenias	0 (0%)
Steady progression	11 (29%)
Bulk > 7 cm	13 (34%)
Hepatomegaly	0 (0%)
Splenomegaly	4 (11%)

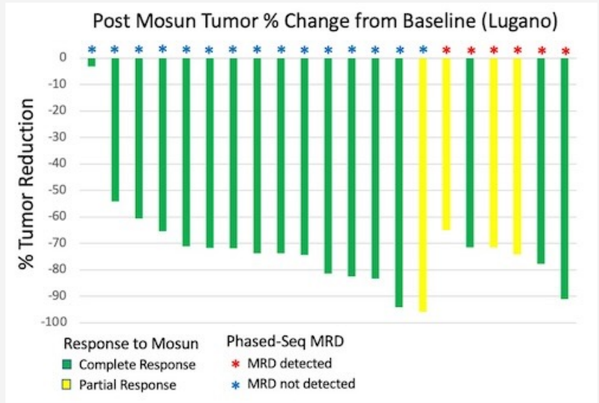
Grade 3-4 AEs

CTCAE Category	Grade 3-4
Neutropenia	4 (11%)
ALT Elevation	2 (5%)
Hypertension	2 (5%)
Abdominal pain	1 (3%)
Diarrhea	1 (3%)
Edema	1 (3%)
Hypertryglyceridemia	1 (3%)
Lung infection	1 (3%)
Malabsorption	1 (3%)
Syncope	1 (3%)
Thrombocytopenia	1 (3%)
Zoster	1 (3%)

- 4 pts with SAEs: (G3 pneumonia + shingles, G2 URI, G1 CRS, G3 Abdominal pain and malabsorption)
- CRS: G1 25 (66%), No G2
- Headache: Any 20 (53%), G2 2 (5%)
- Rash: Any 13 (%), G2 3 (8%)
- Injection site reaction: 33 (87%), G2 2 (5%)
- 10 (26%) patients with mosun delay
  - Two patients with mulitple delays
    - Infection, Neutropenia, Bone pain
  - Infection: 5
  - Neutropenia: 4
  - ALT elevation, hyperglycemia: 1
- One patient permanently discontinued mosun after C1 due to persistent G1 CRS and G3 ALT elevation, subsequent PET in CR
- 8 (21%) patients required additional steroid pre-meds beyond C2
- No patient required tocilizumab

- No G3+ AEs experienced in those in Part B
- Infections were common (17, 45%), but only one patient experienced G3+ infection
  - COVID-19: 4, 11%, All G2 with no hospitalization
- Liver toxicity uncommon
  - ALT ↑: Any 15 (39%)
  - AST ↑: Any 6 (16%)
  - Bili ↑: Any 6 (16%)

Results: Efficacy + MRD



- Mosun EOT CR: 25/31 (81%)
- 4 patients have completed Obinutuzumab/polatuzumab vedotin
  - All achieved a CR

- 21/22 patients with detectable baseline ctDNA
- Undetectable MRD rate: 15/21 (71%)
- Two PD events to date – all transformations to large cell lymphoma

Conclusion

- Fixed-duration mosun monotherapy achieves a high CR rate in untreated pts with follicular and marginal zone lymphoma
- No G2+ CRS and no ICANS of any grade.
- Injection site reactions and headaches were common but reversible.
- Most patients had detectable baseline ctDNA, and most cleared with 8 cycles of mosun monotherapy

Acknowledgements

- We acknowledge our UW Medical Oncology Heme Malignancy research team, IFLI, Washington University in STL, our clinical support staff, and our PATIENTS.

References 1: Budde LE et al. Blood 2021, 2: Marcus R et al. NEJM 2017, 3: Phillips T et al. ASH 2016, 4: Kurtz et al. Nat Biotech 2022 5: Cheson BD et al. JCO 2014

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