Response-Adapted Therapy with Copanlisib and Rituximab in Untreated Follicular Lymphoma: a Phase II Study

Gonca Ozcan[1], Rahul Lakhotia[1], Christopher Melani[1], Max J. Gordon[1], Jagan R. Muppidi[1], Stefania Pittaluga[2], James D Phelan[1], Colleen Ramsower[3], Lisa M. Rimsza[4], Ryan S Robertorye[5], George Wright[6], Mark Meerson[7], Ekaterina Postovalova[7], Alexander Bagaev[7], Nathan Fowler[7], Liza Lindenberg[8], Esther Mena[8], Ethan Bergvall[8], Atekelt Tadese[1], Sarah Evans[1], Sumaya Berg[1], Seth M. Steinberg[9], William Figg[10], Elaine S. Jaffe[2], Louis M. Staudt[1], Wyndham H. Wilson[1], Mark Roschewski[1]

[1]Lymphoid Malignancies Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD
[2]Laboratory of Pathology, Center for Cancer Research, National Cancer Institute, Bethesda, MD
[3]Department of Research, Mayo Clinic, Scottsdale, AZ
[4]Department of Laboratory Medicine and Pathology, University of Arizona, Tucson, AZ
[5]Department of Laboratory Medicine and Pathology, Mayo Clinic, Phoenix, AZ
[6]Biometric Research Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, National Institutes of Health, Bethesda, MD
[7]BostonGene Corporation, Waltham, MA
[8]Molecular Imaging Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD
[9]Biostatistics and Data Management Section, National Cancer Institute, National Institutes of Health, Bethesda, MD
[10]Molecular Pharmacology Section, Genitourinary Malignancies Section, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD

Introduction

- Frontline therapy for follicular lymphoma (FL) is not based on molecular biology.
- BCR signaling via the PI3K pathway is a major survival mechanism and can be targeted with copanlisib.

Hypothesis

- Fixed-duration therapy with copanlisib and rituximab can achieve complete responses (CR)

Objectives

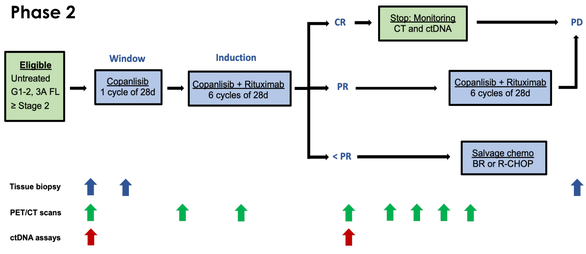
Primary: CR rate

Secondary: Assess tumor response to 1 cycle of copanlisib monotherapy (copanlisib window)
Duration of complete response (DOCR)
Progression-free survival (PFS)
Complete molecular remission (CMR) rate
Safety including autoimmune toxicity and infections

Exploratory: To identify mutational or gene expression signature that predicts clinical response

Methods

Phase 2

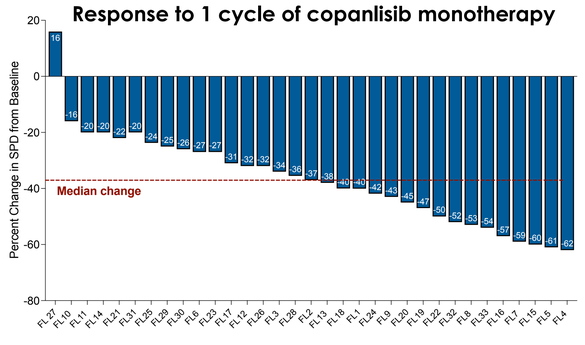


- Copanlisib 60mg weekly for the first 3 weeks of each cycle followed by 1-week break
- Rituximab 375mg/m2 weekly for the first 4 weeks of Cycle 1 of induction, then on Day 1 of each cycle
- Circulating tumor DNA (ctDNA) was analyzed using targeted, panel-based, deep sequencing

Results

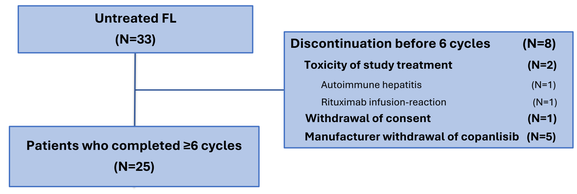
Characteristics	N = 33
Median Age (range)	55 (24-80)
Preexisting Conditions of Interest	
Prediabetes	10 (30)
Diabetes	2 (6)
Hypertension	11 (33)
FLIPI Score	
0 or 1	2 (6)
2	11 (33)
3 to 5	20 (61)
FL24Cx risk category (N=24)	
Good	20 (67)
Poor	10 (33)
Stage	
1-2	1 (3)
3 or 4	32 (97)

Response to 1 cycle of copanlisib monotherapy

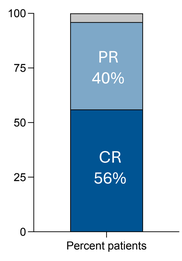


Results

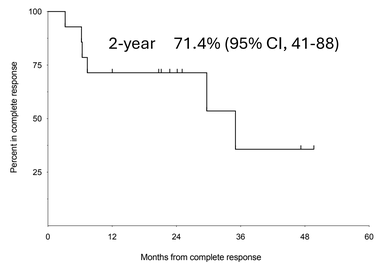
Patient disposition



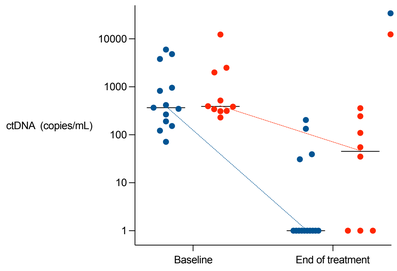
Response rate



Duration of CR



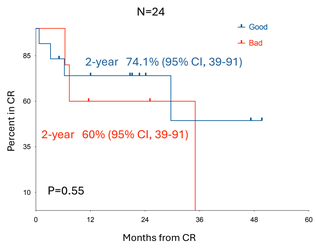
Quantitative ctDNA response after induction



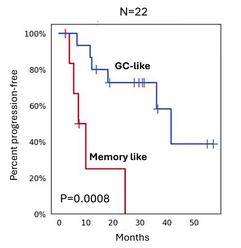
CMR rate 59%

Detectable ctDNA		
Complete response (n/N)	13/13	4/14
No complete response (n/N)	10/10	5/8

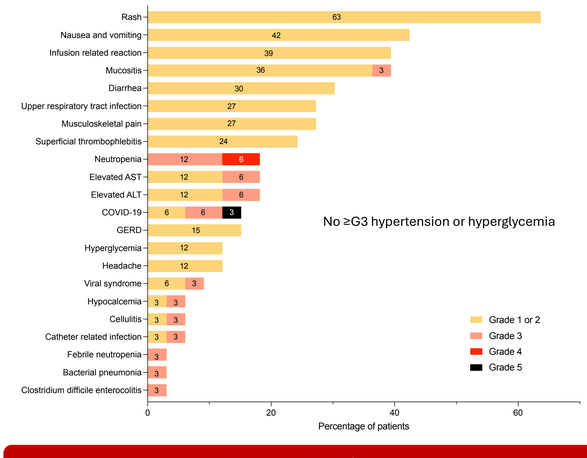
PFS by FL24Cx gene-predictor



PFS by FL20 gene-predictor



Adverse events in >10% patients including all Grade ≥3



Conclusion

- PI3K-inhibition shows activity in nearly all patients with untreated FL including high-risk patients by FL24Cx
- Fixed-duration copanlisib and rituximab shows good tolerability and achieves durable, MRD-negative remissions in patients with untreated FL

SOHO2025