CLLR3: A RANDOMIZED PHASE II TRIAL EVALUATING THE CHEMOTHERAPIES FC/ B COMBINED WITH GA101 FOLLOWED BY GA101 MAINTENANCE IN RELAPSED/ REFRACTORY CLL

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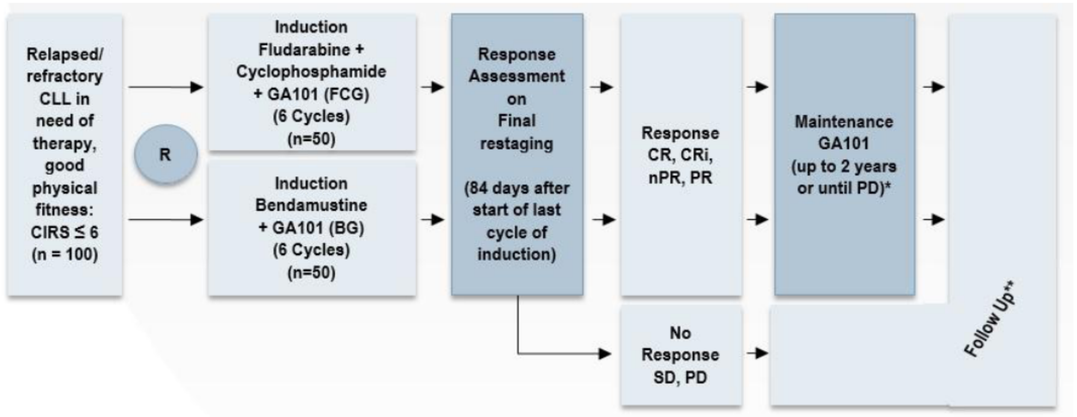
INTRODUCTION

- GA101 has demonstrated high efficacy in relapsed/ refractory (r/r) chronic lymphocytic leukemia (CLL) patients (pts).[1]
- GA101 has also shown superiority to rituximab in combination with chlorambucil.[2]
- FCR (fludarabine + cyclophosphamide + rituximab) and BR (bendamustine + rituximab) are active in patients with r/r CLL .[3,4]
- A combination with FC + GA101 (FCG) or B + GA101 (BG) might further improve the therapeutic outcome in r/r CLL.
- There has been no systematic approach yet to evaluate if GA101 is superior to rituximab in all therapy settings. This underlines the need for further evaluation of GA101-containing regimens in regard to future combination therapies including new substances.

TRIAL DESIGN

- Phase II
- Prospective, multicenter, randomized
- 100 CLL pts
- Relapsed and/or refractory
- Physically fit pts (CIRS score ≤ 6)
- Induction therapy: up to 6 cycles of FCG or BG
- Maintenance therapy for pts in response: GA101 every 3 months for a maximum of 2 years or until progression



CR = complete remission, CRi = CR with incomplete marrow recovery, nPR= nodular partial remission, PR = partial remission, SD = stable disease, PD = progressive disease

*1000mg iv every three months (84 days)

** until death, up to 48 months after final restaging (incl. maintenance) or withdrawal of consent from study whichever occurs first

OBJECTIVES

- Primary objective: evaluation of the efficacy using the best overall response rate (ORR).
- Secondary objectives: safety, other efficacy parameters like progression-free (PFS) and overall survival (OS) as well as minimal residual disease (MRD) levels.

RESULTS

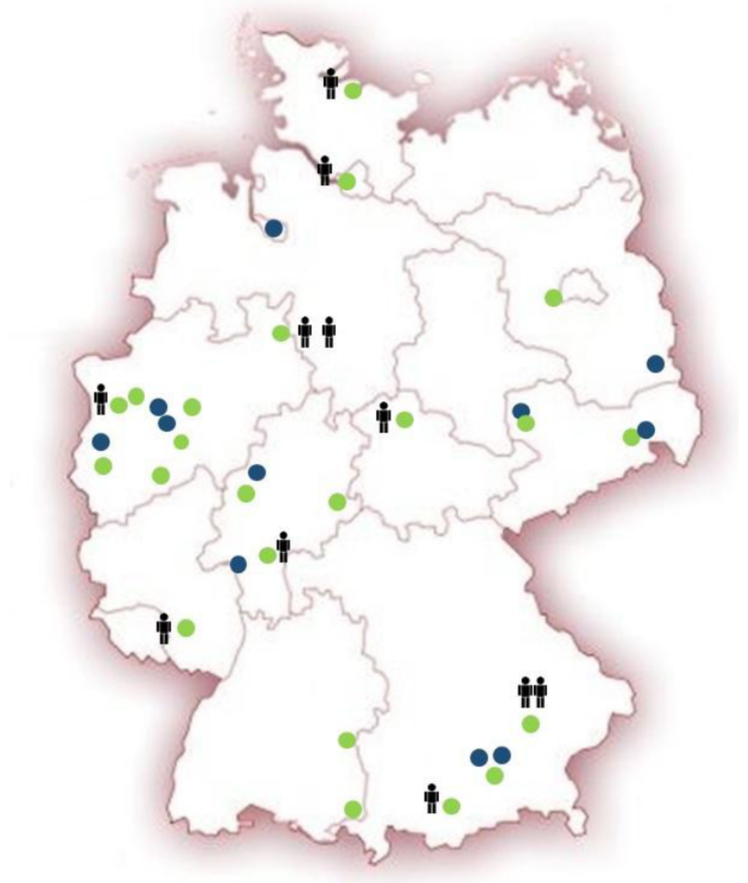
- Actively recruiting
- 22 of 33 centers have been initiated
- a total of 35 centers are planned
- Serious adverse events (SAEs): 1 pt experienced a grade 3 IRR at first dose of GA101, 2 pts experienced a grade 3-4 TLS. Grade 3-4 cytopenias were seen in 4 pts, 4 pts had a grade 3-4 infection.

Baseline characteristics	FCG N (%)	BG N (%)
All patients, N (%)	6 (60.0)	4 (40.0)
Age (y), median (range)	63.5 (55-71)	73 (71-80)
Sex, N (%): Male	5 (83.3)	4 (100.0)
Time since diagnosis (y), median (range)	8.5 (5.2-13.2)	6.6 (4.5-30.0)
Binet stage, N (%)		
A	1 (16.7)	1 (25.0)
B	2 (33.3)	0 (0.0)
C	3 (50.0)	3 (75.0)
ECOG performance status, N (%)		
0	5 (83.3)	2 (50.0)
1	2 (16.7)	2 (50.0
2	0 (0.0)	0 (0.0)
B-symptoms, N (%): yes	2 (33.3)	1 (25.0)
Number of prior therapies, N (%)		
1	3 (50.0)	2 (50.0)
2	3 (50.0)	1 (25.0)
3	0 (0.0)	1 (25.0)
Total CIRS score, median (range)	4 (0-6)	0.5 (0-5)
Number of involved CIRS categories, N (%)		
≤ 1	2 (33.3)	3 (75.0)
> 1	4 (66.7)	1 (25.0)

CONCLUSIONS

- 2 standard chemotherapies for fit pts with r/r CLL are combined with GA101.
- GA101 has not yet been evaluated in combination with chemotherapy for physically fit pts.
- We expect to improve responses and prolong remissions with an adequate safety profile.
- GA101 will be explored as maintenance treatment in responding pts with r/r CLL while other trials have shown benefits of alternative anti-CD20 antibodies (rituximab, ofatumumab) in this setting.[5,6]
- These data will be of great interest for future therapy concepts.

SITE ACTIVATION & RECRUITMENT



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CONFLICTS OF INTEREST STATEMENT

NK: travel grants by Mundipharma. - SB: research funding, honoraria, travel grants by Roche. - StSt: research grants, advisory boards, honoraria by Roche, Mundipharma. - K-A K: honoraria, research support by Roche, Mundipharma. – MH: honoraria by Roche, Mundipharma - MB: honoraria by Roche, Munidpharma; advisory role, travel grants by Roche. - CMW: honoraria, advisory boards, research funding, travel grants by Roche, Mundipharma

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Ongoing trials

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