LENALIDOMIDE CONSOLIDATION IMPROVES PROGRESSION FREE SURVIVAL IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA FOLLOWING INITIAL FCR CHEMOTHERAPY - FINAL ANALYSIS OF CLL6 RESIDUUM STUDY OF THE AUSTRALIAN LEUKAEMIA AND LYMPHOMA GROUP (ALLG) AND THE FRENCH INNOVATIVE LEUKEMIA ORGANIZATION (FILO)

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BACKGROUND

Eradication of residual disease after first line chemoimmunotherapy correlates with longer progression-free survival (PFS) in chronic lymphocytic leukemia (CLL) patients.

Lenalidomide (LEN) has antiproliferative and immunomodulatory effects in CLL.

Here is the **final analysis of the phase III, randomized, CLL6 RESIDUUM trial**, aiming to determine whether lenalidomide is capable of extending remission duration in patients with CLL who have detectable residual disease after induction immunochemotherapy.

OBJECTIVES

To determine whether lenalidomide consolidation **improves PFS in patients with residual CLL after front-line FCR treatment.**

METHODS

Eligibility criteria :

Patients with **identifiable residual disease** after 4-6 cycles of Fludarabine-Cyclophosphamide-Rituximab (FCR)

- Partial remission (iwCLL criteria)

- Complete remission (iwCLL criteria) with measurable residual disease either in peripheral blood (PB) or bone marrow (BM) > 10^{-4} identified by multiparameter flow cytometry (MFC)

Randomization 1:1 ratio

- Lenalidomide 10 mg/d for 2 years (LEN)
- Observation (OBS)

Primary end point : progression free survival (**PFS**).

Hypothesis : Recruitment of **192 patients** in order to detect an increase in 4 y PFS up to 70% in the LEN arm compared with 50% in the OBS arm (two-sided log rank test alpha = 0.05, no competing risks or loss to follow up, power = 0.86)

RESULTS

Baseline demographics population

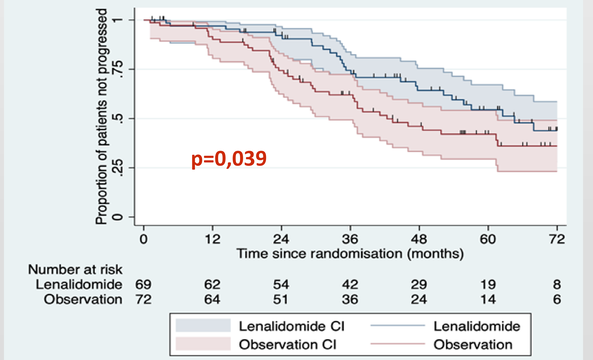
Arm (n)		LEN (71)	OBS (72)	p
Age*		63 (41-78)	60 (26-79)	
Sex ratio F/M		14/57	16/56	
CIRS Score*		1 (0-5)	1(0-5)	0.20
Response Status at Randomization, n (%)	CR	27 (38%)	23 (40%)	0.75
	nPR	9 (49%)	10 (54%)	
	PR	35 (13%)	39 (14%)	
PB MRD >10^{-4} n (%)		49 (69%)	47 (65%)	0.61
BM MRD >10^{-4} n (%)		56 (79%)	58 (81%)	0.73
Creatinine (mg/dL)*		0.8 (0.7-1)	0.83 (0.7-1.2)	0.34
Beta-2-microglobulin*		2.4 (1.2-19)	2.2 (1-23)	0.8

*median (range)

LENALIDOMIDE treatment

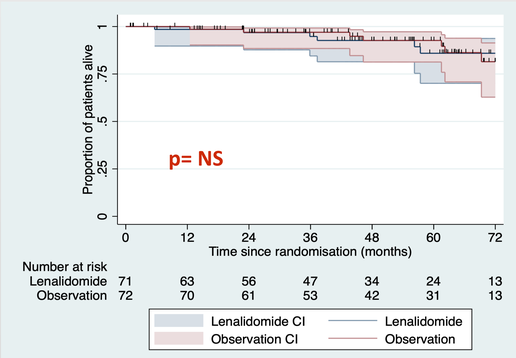
LEN treatment (n)	71
Cycles number median (range)	18 (1-26)
Dose reduction n (%)	37 (52%)
Completed protocol treatment	17 (24%)
Discontinued due to AEs	20 (28%)
Discontinued due to withdrawal of consent / patient refusal	11 (15%)
Discontinued due to other reasons :	19 (27%)

PROGRESSION FREE SURVIVAL



PFS	LEN (N=69)	OBS (N=72)	p-value
Progressions (n)	28	40	
Median M (95%CI)	**64.56** (47.67,NR)	**42.37** (32.28,61.64)	**0.0386**
24M PFS	92.1% (82.1%,96.6%)	74.4% (62.4%,83.0%)	
48M PFS	64.2% (50.0%,75.4%)	46.1% (33.3%,57.9%)	
60M PFS	54.4% (39.5%,67.1%)	42.1% (29.5%,54.1%)	

OVERALL SURVIVAL



ADVERSE EVENTS

Factor	Level	LEN	OBS	Total	p-value
N		71	72	143	
Had an AE?		40 (56.3%)	23 (31.9%)	63 (44.1%)	0.003
Had an SAE?		24 (33.8%)	11 (15.3%)	35 (24.5%)	0.010
Maximum grade of AE	3	29 (81%)	16 (76%)	45 (79%)	0.70
	4	7 (19%)	5 (24%)	12 (21%)	0.52

Second Primary Malignancy

	LEN	OBS
N	**7** (9.8%)	**5** (6.9%)
Squamous Cell Carcinoma	2	2
Colic ADK	3	
Merkel Carcinoma		1
Lung Cancer	1	
Prostate Cancer		1
Myelodysplasic Syndrom	1	
SMZ Lymphoma		1

NO CASE OF ACUTE LYMPHOBLASTIC LEUKEMIA

Severe Adverse Events	LEN		OBS	
by System Organ Class	SAEs (n)	Patients (n)	SAEs (n)	Patients (n)
Blood and lymphatic system	**6**	**4**	**3**	**2**
Gastrointestinal	2	2	1	1
Immune system	0	0	1	1
Infections and infestations	**8**	**8**	**2**	**2**
Metabolism and nutrition	0	0	1	1
Musculoskel	2	2	1	1
Nervous system	**3**	**2**	**0**	**0**
Psychiatric	2	2	0	0
Renal and urinary	3	1	0	0
Reproductive system	1	1	0	0
Resp, thoracic, mediastinal	**8**	**5**	**0**	**0**
Vascular disorders	1	1	0	0
Total (n)	**36**	**28**	**9**	**8**

CONCLUSIONS

In CLL, 2 years of lenalidomide maintenance translated into a significantly longer PFS with no unacceptable toxicity after front line FCR treatment. Specifically, no case of ALL occurred in 69 patients with a minimum 4-year follow-up.

ACKNOWLEDGEMENTS

All patients and their families & all contributing sites & all clinical research assistants