

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 chemoimmur correlates with longer progression-free survival (PFS) in chro 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 impro patients with residual CLL after front-line FCR treatment.

METHODS

Eligibility criteria :

Patients with identifiable residual disease after 4-6 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)

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Baseline demographics population					PROGRESSION FREE SURVIVAL					
Arm (n)		LEN (71)	OBS (72)) p						
Δσe*		63 (41-78)	60 (26-79)						
Sex ratio F/M		14/57	16/56		gge			·		
CIRS Score*		1 (0-5)	1(0-5)	0.20						
Posponso Status at	CP			0.20	L Is					
Response Status at	CR	27 (50%)	25 (40%)) 0.75	patie					
Randomization, n (%)		0 (4 0 0 ()				p=0,039				
	nPK	9 (49%)	10 (54%))	i, ario					_
	PR	35 (13%)	39 (14%)		d d d					
PB MRD >10 ⁻⁴ n (%)		49 (69%)	47 (65%)) 0.61	- j	12 _ 2	24	36 48	60 7	72
BM MRD >10 ⁻⁴ n (%)		56 (79%)	58 (81%)) 0.73	Number at risk	Time s	ince rando	omisation (months)		
Creatinine (mg/dL)*		0.8 (0.7-1)	0.83 (0.7-1	.2) 0.34	Lenalidomide 69 Observation 72	62 5 64 5	54 51	42 29 36 24	19 14	8 6
Beta-2-microglobulin*	k	2.4 (1.2-19)	2.2 (1-23) 0.8		Lenali	domide C	Lenali	domide	
*median (range)					Observation CI — Observation					
					PFS	LEN (N=6	9)	OBS (N=72)	p-va	alue
LEN	NALIC	OMIDE treati	ment		PFS Progressions (n)	<mark>LEN (N=6</mark> 28	9)	<mark>OBS (N=72)</mark> 40	p-va	alue
LEN LEN treatment (n)	NALIC	OMIDE treat	ment	71	PFS Progressions (n) Median M (95%CI)	LEN (N=6 28 64.56 (47.6)	9) 7,NR)	OBS (N=72) 40 42.37 (32.28,61	p-va 64) 0.03	alue 386
LEN LEN treatment (n) Cycles number mediar	NALIC n (rang	DOMIDE treati	ment	71 18 (1-26)	PFSProgressions (n)Median M (95%CI)24M PFS	LEN (N=6 28 64.56 (47.6 92.1% (82.1%	9) 7,NR) ,96.6%)	OBS (N=72) 40 42.37 (32.28,61 74.4% (62.4%,83	p-va 64) 0.03	alue 386
LEN LEN treatment (n) Cycles number mediat	NALIC n (ran	DOMIDE treati ge)	ment	71 18 (1-26)	PFSProgressions (n)Median M (95%CI)24M PFS48M PFS	LEN (N=6 28 64.56 (47.6 92.1% (82.1% 64.2% (50.0%	9) 7,NR) ,96.6%) ,75.4%)	OBS (N=72) 40 42.37 (32.28,61 74.4% (62.4%,83 46.1% (33.3%,57	p-va 64) 0.03 3.0%) 7.9%)	alue 386
LEN treatment (n) Cycles number mediat Dose reduction n (%)	NALIC n (rana	DOMIDE treat	ment	71 18 (1-26) 37 (52%)	PFSProgressions (n)Median M (95%CI)24M PFS48M PFS60M PFS	LEN (N=6 28 64.56 (47.6 92.1% (82.1% 64.2% (50.0% 54.4% (39.5%	9) 7,NR) ,96.6%) ,75.4%) ,67.1%)	OBS (N=72) 40 42.37 (32.28,61 74.4% (62.4%,83 46.1% (33.3%,57 42.1% (29.5%,54	p-va 64) 0.03 3.0%) 7.9%) 4.1%)	alue 386
LEN treatment (n) Cycles number mediae Dose reduction n (%) Completed protocol tr	NALIC n (rana reatmo	oomide treatures and the second secon	ment	71 18 (1-26) 37 (52%) 17 (24%)	PFSProgressions (n)Median M (95%CI)24M PFS48M PFS60M PFS	LEN (N=6 28 64.56 (47.6 92.1% (82.1% 64.2% (50.0% 54.4% (39.5%	9) 7,NR) ,96.6%) ,75.4%) ,67.1%)	OBS (N=72) 40 42.37 (32.28,61 74.4% (62.4%,83 46.1% (33.3%,57 42.1% (29.5%,54	p-va 64) 0.03 3.0%) 7.9%) 4.1%)	alue 386
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LEN treatment (n)
Cycles number median (range)
Dose reduction n (%)
Completed protocol treatment
Discontinued due to AEs
Discontinued due to withdrawal of consent / patier
refusal
Discontinued due to other reasons :

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.

RESULTS

CONCLUSIONS

SMZ Lymphoma





ADVERSE EVENTS									
Factor	Level	LEN	OBS	Total	p-value				
Ν		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				

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	

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