TABLES

	Enrolled population (N=278)	Non-randomised population (N=81)	Randomised population (N=197)	LEN arm (N=101)	OBS arm (N=96)
Age, years	57 (51-62)	58 (54-62)	57 (49-61)	57 (51-61)	57 (49-61)
Sex					
Female	60 (22%)	16 (20%)	44 (22%)	19 (18%)	25 (26%)
Male	218 (78%)	65 (80%)	153 (78%)	82 (82%)	71 (74%)
Lactate dehydrogenase>ULN	90 (32%)	38 (47%)	52 (26%)	25 (24%)	27 (28%)
ECOG-PS score >1	61 (22%)	23 (28%)	38 (19%)	17 (17%)	22 (23%)
Ann Arbor Stage III-IV	273 (98%)	81 (100%)	192 (97%)	99 (98%)	93 (97%)
MIPI score					
Low	171 (61.5%)	40 (49%)	131 (66%)	62 (58%)	69 (72%)
Intermediate	67 (24%)	25 (31%)	42 (21%)	27 (28%)	15 (16%)
High	40 (14%)	16 (20%)	24 (12%)	12 (14%)	12 (13%)
Bulky disease (>5cm)	88 (32%)	33 (41%)	55 (28%)	27 (28%)	28 (29%)
Bone marrow involvement	217 (78%)	71 (88%)	146 (74%)	70 (69%)	76 (79%)
Ki67 index >=30%	77/255 (30%)	24/71 (34%)	53/184 (29%)	24/92 (26%)	29/92 (32%)
MIPI-c					
Low risk	128/255 (50%)	31/71 (44%)	97/184 (53%)	44/92 (49%)	53/92 (58%)
Low-intermediate risk	75/255 (27%)	22/71 (31%)	53/184 (29%)	32/92 (34%)	21/92 (23%)
High-intermediate risk	31/255 (12%)	11/71 (15%)	20/184 (11%)	12/92 (13%)	8/92 (9%)
High risk	21/255 (8%)	7/71 (10%)	14/184 (8%)	4/92 (4%)	10/92 (11%)
Blastoid histology	25 (9%)	15 (14%)	13 (7%)	7 (7%)	6 (6%)
$TP53^{mut}$ or del(17p)	36/229 (17%)	16/70 (23%)	20/159 (13%)	10/79 (15%)	10/86 (12%)

Table S1. Clinical characteristics of patients included in the pharmacogenomics study.

PS ECOG, Performance status by Eastern Cooperative Oncology Group; MIPI, Mantle cell Prognostic Index; CF, Flow Cytometry; TP53, Tumor Protein 53; CR, Complete Remission; PR, Partial Remission.

Gene	Polymorphisms	Role	Reference
ABCB1	c.1236 C>T (rs1128503) c.2677G>T/A (rs2032582) c.3435C>T (rs1045642)	Transmembrane transporters (ABC transporter family)	Orsolya Polgar, Robert W Robey & Susan E Bates. Expert Opinion Drug Metab Toxicol, 2008
ABCG2	c.421C>A		
VEGF-A	c.2055C>A	Angiogenic factor and regulator of endothelial cell proliferation	S. Galimberti Acta Haematol. 2010
FCGR2A	c.497A>G	Cellular receptor for Immunoglobulin G (IgG)	Sietse Q. Nagelkerke, David E. Schmidt, Masja de Haas and Taco W. Kuijpers, Frontiers in Immunology, 2019 .
NCF4	c.368G>A	Cytosolic component of the inducible NAD(P)H oxidase	M. Hoffmann CR 010
GSTP1	c.313G>A	• Phase II detoxification enzyme: catalyse the conjugation of glutathione (GSH) to a wide variety of xenobiotics. • ligand-binding protein in the regulation of cell cycle components such as mitogen-activated protein kinases (MAPK) and extracellular-regulated kinases (ERK)	CC Mcllwain Nature 2006
CRBN	rs1714327 G>C rs1705814 T>C – 277	A component of a E3 ubiquitin ligase complex. Molecular target of lenalidomide	P.Chamberlain Nature 2014

Table S2. SNPs investigated in the present population of patients. The role of the gene with respect to the mechanism of action of lenalidomide and its pharmacokinetics is also presented.

Exon	Gene	Locus	Minor allele
12	ABCB1	rs1128503	T
21	ABCB1	rs2032582	T/A
26	ABCB1	rs1045642	T

Table S3a. Haplotype analysis of ABCB1 loci

Loci	**rs1128503**	**rs2032582**	**rs1045642**	
rs1128503	-	0.878	0.744	
rs2032582	0.724	-	0.824	**D'**
rs1045642	0.462	0.532	-	
	r^2			

Table S3b. Haplotype analysis of ABCB1 loci. Pearson's r2 and Lewontin's D' are showed. Both tests confirmed that the three ABCB1 loci were in linkage disequilibrium.

Haplotype		**Loci**		
ID	**Frequency**	**rs1128503**	**rs2032582**	**rs1045642**
#1	266	C	G	C
#2	215	T	T	T
#3	18	T	G	C
#4	7	T	G	T
#5	48	C	G	T
#6	8	C	T	T
#7	12	T	T	C
#8	8	C	T	C

Haplotypes		**Patients**	
A	**B**	**n**	**%**
1 (CGC)	1 (CGC)	61	21.0
1 (CGC)	2-8 (CGT/CTC/…)	144	49.5
2-8 (CGT/CTC/…)	2-8 (CGT/CTC/…)	86	29.5

Table S3c. Haplotype analysis of ABCB1 loci. Frequency of identified haplotypes. The ID#1 was the wildtype haplotype, whereas IDs #2-#8 were polymorphic haplotypes.

	OVERALL POPULATION (N=278)			**LEN ARM (N=101)**			**OBS ARM (N=96)**			**RANDOMIZED POPULATION (N=197)**		
	HoWT	***HePOL***	***HoPOL***	***HoWT***	***HePOL***	***HoPOL***	***HoWT***	***HePOL***	***HoPOL***	***HoWT***	***HePOL***	***HoPOL***
ABCB1 c.1236 C>T (rs1128503)	82 (29.5%)	145 (52.2%)	51 (18.3%)	33 (32.6%)	48 (47.5%)	20 (19.8%)	26 (27.1%)	54 (56.2%)	16 (16.7%)	59 (29.9%)	102 (51.8%)	36 (18.2%)
ABCB1 c.2677G>T/A (rs2032582)	86 (30.9%)	146 (52.5%)	46 (16.5%)	32 (31.7%)	52 (51.5%)	17 (16.8%)	28 (29.2%)	55 (57.3%)	13 (13.5%)	60 (30.5%)	107 (54.3%)	30 (15.2%)
ABCB1 c.3435C>T (rs1045642)	70 (25.1%)	143 (51.4%)	65 (23.4%)	27 (26.7%)	50 (49.5%)	24 (23.7%)	21 (21.9%)	50 (52.1%)	25 (26.0%)	48 (24.4%)	100 (50.8%)	49 (24.9%)
ABCG2 c.421C>A	1 (0.4%)	32 (11.5%)	245 (88.1%)	0	13 (12.9%)	88 (87.1%)	0	7 (7.3%)	89 (92.7%)	0	20 (10.2%)	177 (89.8%)
VEGF-A c.2055A>C	56 (20.1%)	131 (47.1%)	91 (32.7%)	18 (17.8%)	53 (52.5%)	30 (29.7%)	24 (25.0%)	43 (44.8%)	29 (30.2%)	42 (21.3%)	96 (48.7%)	59 (29.9%)
FCGR2A c.497A>G	101 (36.3%)	128 (46.0%)	48 (17.3%)	37 (36.6%)	45 (44.6%)	19 (18.8%)	34 (34.4%)	50 (52.1%)	12 (12.5%)	71 (36.0%)	95 (48.2%)	31 (15.7%)
NCF4 c.368G>A	115 (41.4%)	125 (44.9%)	37 (13.3%)	38 (37.6%)	45 (44.6%)	18 (17.8%)	46 (47.9%)	38 (39.6%)	12 (12.5%)	85 (43.1%)	83 (42.1%)	30 (15.2%)
GSTP1 c.313G>A	124 (44.6%)	126 (45.3%)	28 (10.1%)	50 (49.5%)	38 (37.6%)	13 (12.9%)	47 (48.9%)	39 (40.6%)	10 (10.4%)	97 (49.2%)	77 (39.1%)	23 (11.7%)
CRBN rs1714327 G>C	145 (52.2%)	106 (38.1%)	26 (9.4%)	53 (52.5%)	37 (36.6%)	11 (10.9%)	54 (55.2%)	33 (34.4%)	9 (9.4%)	107 (54.3%)	70 (35.5%)	20 (10.1%)
CRBN rs1705814 T>C	113 (40.6%)	91 (32.7%)	73 (26.2%)	43 (42.6%)	30 (29.7%)	28 (27.7%)	43 (43.7%)	34 (35.4%)	19 (19.8%)	86 (43.7%)	64 (32.5%)	47 (23.8%)

Table S4. Distribution of investigated polymorphisms in the studied population

(A)

	OVERALL POPULATION			RANDOMIZED POPULATION		
ABCB1	**GG (N=86)**	**GW/WW (N=192)**	**P value**	**GG (N=60)**	**GW/WW (N=137)**	**P value**
Age, years	56.50 [51.00, 62.00]	57.00 [52.75, 62.00]	0.845	55.07	54.68	0.755
Gender F	19 (22.1%)	41 (21.4%)	0.890	16 (26.7%)	29 (21.2%)	0.397
Ann Arbor Stage						
II	1 (1.2%)	4 (2.1%)	0.593	1 (1.7%)	4 (2.9%)	0.606
III	4 (4.7%)	8 (4.2%)	0.854	3 (5.0%)	7 (5.0%)	0.974
IV	81 (94.2%)	180 (93.8%)	0.888	56 (93.3%)	126 (91.9%)	0.740
Bulky Disease (>5cm)	24 (27.9%)	64 (33.3%)	0.369	14 (23.3%)	41 (29.9%)	0.342
ECOG-PS score	64 (74.4%)	153 (79.7%)	0.327	45 (75.0%)	114 (83.2%)	0.178
Ki-67 index >=30%	25 (32.5%)	52 (29.2%)	0.603	18 (30%)	35 (25.5%)	0.516
Blastoid Histology	2 (2.3%)	23 (12.0%)	0.011	0	13 (9.5%)	
MIPI score High	15 (17.4%)	25 (13.0%)	0.332	9 (15.0%)	15 (10.9%)	0.423
LDH High	28 (32.6%)	62 (32.3%)	0.965	16 (26.7%)	36 (26.3%)	0.954
TP53^{mut} or del(17p)	8/69 (11,5%)	28/160 (17,5%)	0.259	5/48 (10.4%)	15/111 (13.5%)	0.588
KMT2D^{mut}	10/56 (17,8%)	13/124 (10,5%)	0 .170	5/38 (13.1%)	6/83 (7.2%)	0.292

(B)

	OVERALL POPULATION			RANDOMIZED POPULATION		
VEGF-A	**AA (N=56)**	**AC/CC (N=222)**	**P value**	**AA (N=42)**	**AC/CC (N=155)**	**P value**
Age, years	58.50 [52.00, 62.00]	57.00 [51.00, 61.00]	0.272	55.54	54.59	0.496
Gender F	13 (23.2%)	47 (21.2%)	0.740	7 (16.7%)	37 (23.9%)	0.320
Ann Arbor Stage						
II	2 (3.6%)	3 (1.4%)	0.263	2 (4.8%)	3 (1.9%)	0.301
III	2 (3.6%)	10 (4.5%)	0.758	2 (4.8%)	8 (5.2%)	0.916
IV	52 (92.9%)	209 (94.1%)	0.719	38 (90.5%)	144 (92.9%)	0.598
Bulky Disease (>5cm)	17 (30.4%)	71 (32.0%)	0.815	12 (28.6%)	43 (27.7%)	0.915
ECOG-PS score	41 (73.2%)	176 (79.3%)	0.327	32 (76.2%)	127 (81.9%)	0.402
Ki-67 index >=30%	18 (36.7%)	59 (28.6%)	0.267	14 (33.3%)	39 (25.2%)	0.289
Blastoid Histology	2 (3.6%)	23 (10.4%)	0.187	1 (2.4%)	12 (7.7%)	0.214
MIPI score High	8 (14.3%)	32 (14.4%)	0.980	4 (9.5%)	20 (12.9%)	0.552
LDH High	18 (32.1%)	72 (32.4%)	0.967	9 (21.4%)	43 (27.7%)	0.410
TP53^{mut} or del(17p)	7/47 (14.9%)	29/182 (15.9%)	0.861	3/35 (8.6%)	17/125 (13.6%)	0.426
KMT2D^{mut}	4/35 (11.4%)	19/144 (13.1%)	0.779	2/27 (7.4%)	9/94 (9.6%)	0.729

Table S4. Clinical characteristics of patients carrying either ABCB1 or VEGF-A polymorphism.

Patient ID	Tissue	Timepoint	Tumor infiltration	Quantification technique
101	PB	Baseline	1,00E-03	Flow cytometry
102	PB	FU	Neg	ASO RQ-PCR
103	PB	Baseline	8,00E-03	Flow cytometry
104	PB	Baseline	3,00E-02	Flow cytometry
106	PB	FU	Neg	ASO RQ-PCR
201	PB	FU	5,00E-02	ASO RQ-PCR
203	PB	FU	5,00E-03	ASO RQ-PCR
204	PB	Baseline	2,00E-03	Flow cytometry
301	PB	Baseline	8,00E-01	Flow cytometry
302	PB	FU	4,50E+00	ASO RQ-PCR
304	PB	FU	Neg	ASO RQ-PCR
305	PB	FU	Neg	ASO RQ-PCR
306	PB	FU	PNQ	ASO RQ-PCR
401	PB	FU	Neg	ASO RQ-PCR
402	PB	FU	Neg	ASO RQ-PCR
403	PB	FU	Neg	ASO RQ-PCR
404	PB	FU	Neg	ASO RQ-PCR
405	PB	FU	Neg	ASO RQ-PCR
406	PB	FU	Neg	ASO RQ-PCR
407	PB	FU	Neg	ASO RQ-PCR
408	PB	FU	Neg	ASO RQ-PCR
409	PB	FU	1,02E-04	ASO RQ-PCR
410	PB	FU	Neg	ASO RQ-PCR
411	PB	FU	Neg	ASO RQ-PCR
413	PB	FU	Neg	ASO RQ-PCR
414	PB	FU	Neg	ASO RQ-PCR
415	PB	FU	Neg	ASO RQ-PCR
416	PB	FU	Neg	ASO RQ-PCR
417	PB	FU	Neg	ASO RQ-PCR
418	PB	FU	Neg	ASO RQ-PCR
419	PB	Baseline	4,60E-02	Flow cytometry
420	PB	FU	Neg	ASO RQ-PCR
501	PB	FU	Neg	ASO RQ-PCR
502	PB	Baseline	1,00E-03	Flow cytometry
503	PB	FU	PNQ	ASO RQ-PCR
504	PB	FU	Neg	ASO RQ-PCR

505	PB	FU	1,00E-06	ASO RQ-PCR
506	PB	FU	Neg	ASO RQ-PCR
507	PB	FU	Neg	ASO RQ-PCR
508	PB	FU	Neg	ASO RQ-PCR
509	PB	FU	Neg	ASO RQ-PCR
510	PB	Baseline	2,90E-02	Flow cytometry
511	PB	FU	*NaN*	*NaN*
512	PB	Baseline	2,10E-01	Flow cytometry
513	PB	FU	Neg	ASO RQ-PCR
514	PB	FU	Neg	ASO RQ-PCR
515	PB	FU	Neg	ASO RQ-PCR
516	PB	FU	*NaN*	*NaN*
517	PB	FU	Neg	ASO RQ-PCR
518	PB	Baseline	1,10E-02	Flow cytometry
519	PB	FU	*NaN*	*NaN*
520	PB	Baseline	5,00E-03	Flow cytometry
521	PB	FU	Neg	ASO RQ-PCR
522	PB	FU	Neg	ASO RQ-PCR
523	PB	FU	PNQ	ASO RQ-PCR
524	PB	FU	Neg	ASO RQ-PCR
525	PB	FU	Neg	ASO RQ-PCR
526	PB	Baseline	1,10E-02	Flow cytometry
601	PB	FU	1,00E-06	ASO RQ-PCR
602	PB	FU	Neg	ASO RQ-PCR
603	PB	FU	Neg	ASO RQ-PCR
604	PB	Baseline	1,40E-01	Flow cytometry
605	PB	Baseline	2,00E-03	Flow cytometry
606	PB	FU	Neg	ASO RQ-PCR
607	PB	FU	Neg	ASO RQ-PCR
608	PB	FU	Neg	ASO RQ-PCR
609	PB	FU	Neg	ASO RQ-PCR
610	PB	Baseline	4,21E-01	Flow cytometry
611	PB	FU	Neg	ASO RQ-PCR
701	PB	FU	Neg	ASO RQ-PCR
702	PB	Baseline	6,00E-03	Flow cytometry
703	PB	Baseline	3,23E-01	Flow cytometry
704	PB	Baseline	*NaN*	*NaN*
705	PB	Baseline	2,00E-03	Flow cytometry

706	PB	FU	Neg	ASO RQ-PCR
707	PB	FU	5,49E-03	ASO RQ-PCR
708	PB	FU	*NaN*	*NaN*
709	PB	Baseline	6,00E-03	Flow cytometry
710	PB	Baseline	7,88E-01	Flow cytometry
711	PB	FU	Neg	ASO RQ-PCR
801	PB	FU	Neg	ASO RQ-PCR
802	PB	FU	1,00E-06	ASO RQ-PCR
803	PB	Baseline	8,00E-03	Flow cytometry
804	PB	FU	*NaN*	*NaN*
805	PB	FU	Neg	ASO RQ-PCR
806	PB	FU	Neg	ASO RQ-PCR
807	PB	Baseline	*NaN*	*NaN*
808	PB	Baseline	2,60E-02	Flow cytometry
809	PB	FU	Neg	ASO RQ-PCR
810	PB	FU	Neg	ASO RQ-PCR
901	PB	FU	Neg	ASO RQ-PCR
902	PB	FU	Neg	ASO RQ-PCR
903	PB	FU	Neg	ASO RQ-PCR
904	PB	FU	Neg	ASO RQ-PCR
905	PB	FU	Neg	ASO RQ-PCR
906	PB	Baseline	1,38E-01	Flow cytometry
907	PB	Baseline	1,32E-01	Flow cytometry
908	PB	Baseline	9,50E-02	Flow cytometry
1001	PB	FU	Neg	ASO RQ-PCR
1002	PB	FU	*NaN*	*NaN*
1101	PB	Baseline	5,10E-02	Flow cytometry
1103	PB	FU	Neg	ASO RQ-PCR
1104	PB	Baseline	1,90E-02	Flow cytometry
1201	PB	Baseline	3,39E-01	Flow cytometry
1202	PB	FU	PNQ	ASO RQ-PCR
1203	PB	Baseline	2,00E-02	Flow cytometry
1204	PB	FU	Neg	ASO RQ-PCR
1205	PB	FU	Neg	ASO RQ-PCR
1301	PB	FU	Neg	ASO RQ-PCR
1302	PB	FU	*NaN*	*NaN*
1303	PB	FU	Neg	ASO RQ-PCR
1304	PB	FU	1,60E-04	ASO RQ-PCR

1305	PB	FU	PNQ	ASO RQ-PCR
1306	PB	FU	Neg	ASO RQ-PCR
1307	PB	FU	1,21E-02	ASO RQ-PCR
1308	PB	FU	Neg	ASO RQ-PCR
1309	PB	FU	Neg	ASO RQ-PCR
1310	PB	FU	Neg	ASO RQ-PCR
1311	PB	Baseline	1,40E-02	Flow cytometry
1401	PB	FU	Neg	ASO RQ-PCR
1402	PB	Baseline	5,00E-04	Flow cytometry
1403	PB	FU	Neg	ASO RQ-PCR
1404	PB	Baseline	6,20E-02	Flow cytometry
1405	PB	FU	Neg	ASO RQ-PCR
1406	PB	FU	Neg	ASO RQ-PCR
1407	PB	FU	Neg	ASO RQ-PCR
1408	PB	Baseline	9,00E-03	Flow cytometry
1409	PB	FU	Neg	ASO RQ-PCR
1410	PB	FU	Neg	ASO RQ-PCR
1411	PB	Baseline	1,20E-02	Flow cytometry
1501	PB	Baseline	6,00E-03	Flow cytometry
1502	PB	FU	*NaN*	*NaN*
1503	PB	FU	Neg	ASO RQ-PCR
1504	PB	Baseline	7,00E-03	Flow cytometry
1505	PB	FU	Neg	ASO RQ-PCR
1506	PB	FU	Neg	ASO RQ-PCR
1507	PB	Baseline	4,50E-02	Flow cytometry
1508	PB	FU	Neg	ASO RQ-PCR
1509	PB	FU	Neg	ASO RQ-PCR
1510	PB	FU	*NaN*	*NaN*
1511	PB	Baseline	7,30E-01	Flow cytometry
1512	PB	Baseline	9,40E-02	Flow cytometry
1513	PB	FU	*NaN*	*NaN*
1601	PB	FU	Neg	ASO RQ-PCR
1602	PB	FU	Neg	ASO RQ-PCR
1603	PB	FU	Neg	ASO RQ-PCR
1604	PB	FU	Neg	ASO RQ-PCR
1605	PB	FU	Neg	ASO RQ-PCR
1606	PB	Baseline	8,28E-01	Flow cytometry
1607	PB	Baseline	1,38E-01	Flow cytometry

1701	PB	Baseline	5,85E-01	Flow cytometry
1702	PB	FU	4,82E-05	ASO RQ-PCR
1703	PB	FU	Neg	ASO RQ-PCR
1801	PB	FU	PNQ	ASO RQ-PCR
1802	PB	FU	*NaN*	*NaN*
1803	PB	FU	*NaN*	*NaN*
1804	PB	FU	Neg	ASO RQ-PCR
1805	PB	FU	Neg	ASO RQ-PCR
1806	PB	FU	*NaN*	*NaN*
1807	PB	Baseline	9,00E-04	Flow cytometry
1808	PB	FU	Neg	ASO RQ-PCR
1809	PB	FU	Neg	ASO RQ-PCR
1901	PB	FU	1,00E-06	ASO RQ-PCR
1903	PB	FU	2,41E-05	ASO RQ-PCR
1904	PB	FU	Neg	ASO RQ-PCR
2001	PB	FU	Neg	ASO RQ-PCR
2101	PB	Baseline	3,90E-02	Flow cytometry
2102	PB	FU	Neg	ASO RQ-PCR
2103	PB	FU	PNQ	ASO RQ-PCR
2201	PB	FU	1,00E-06	ASO RQ-PCR
2203	PB	FU	Neg	ASO RQ-PCR
2204	PB	FU	Neg	ASO RQ-PCR
2301	PB	FU	Neg	ASO RQ-PCR
2302	PB	FU	Neg	ASO RQ-PCR
2303	PB	FU	Neg	ASO RQ-PCR
2304	PB	FU	Neg	ASO RQ-PCR
2305	PB	FU	1,54E-01	ASO RQ-PCR
2306	PB	FU	Neg	ASO RQ-PCR
2307	PB	FU	Neg	ASO RQ-PCR
2308	PB	FU	Neg	ASO RQ-PCR
2309	PB	FU	Neg	ASO RQ-PCR
2401	PB	FU	1,00E-06	ASO RQ-PCR
2402	PB	FU	PNQ	ASO RQ-PCR
2403	PB	FU	Neg	ASO RQ-PCR
2404	PB	FU	Neg	ASO RQ-PCR
2405	PB	Baseline	*NaN*	*NaN*
2406	PB	FU	Neg	ASO RQ-PCR
2503	PB	Baseline	9,00E-04	Flow cytometry

2601	PB	FU	PNQ	ASO RQ-PCR
2602	PB	FU	4,46E-03	ASO RQ-PCR
2603	PB	FU	Neg	ASO RQ-PCR
2604	PB	Baseline	3,90E-02	Flow cytometry
2701	PB	FU	Neg	ASO RQ-PCR
2702	PB	FU	Neg	ASO RQ-PCR
2802	PB	FU	Neg	ASO RQ-PCR
2803	PB	FU	Neg	ASO RQ-PCR
2804	PB	Baseline	4,30E-02	Flow cytometry
2805	PB	Baseline	7,19E-01	Flow cytometry
2901	PB	FU	1,00E-06	ASO RQ-PCR
2902	PB	Baseline	2,32E-01	Flow cytometry
3001	PB	FU	Neg	ASO RQ-PCR
3002	PB	FU	Neg	ASO RQ-PCR
3003	PB	FU	Neg	ASO RQ-PCR
3004	PB	FU	Neg	ASO RQ-PCR
3007	PB	FU	*NaN*	*NaN*
3008	PB	FU	Neg	ASO RQ-PCR
3009	PB	FU	Neg	ASO RQ-PCR
3010	PB	FU	Neg	ASO RQ-PCR
3011	PB	Baseline	2,10E-02	Flow cytometry
3101	PB	FU	Neg	ASO RQ-PCR
3102	PB	FU	Neg	ASO RQ-PCR
3201	PB	FU	5,89E-04	ASO RQ-PCR
3202	PB	FU	*NaN*	*NaN*
3203	PB	FU	Neg	ASO RQ-PCR
3204	PB	FU	Neg	ASO RQ-PCR
3301	PB	FU	Neg	ASO RQ-PCR
3304	PB	FU	Neg	ASO RQ-PCR
3306	PB	FU	Neg	ASO RQ-PCR
3307	PB	FU	PNQ	ASO RQ-PCR
3308	PB	Baseline	3,00E-04	Flow cytometry
3309	PB	Baseline	9,30E-02	Flow cytometry
3401	PB	FU	Neg	ASO RQ-PCR
3501	PB	FU	Neg	ASO RQ-PCR
3502	PB	FU	*NaN*	*NaN*
3503	PB	FU	Neg	ASO RQ-PCR
3504	PB	FU	Neg	ASO RQ-PCR

3601	PB	FU	Neg	ASO RQ-PCR
3602	PB	FU	6,31E-01	ASO RQ-PCR
3704	PB	Baseline	4,50E-02	Flow cytometry
3705	PB	FU	Neg	ASO RQ-PCR
3706	PB	FU	1,00E-06	ASO RQ-PCR
3707	PB	FU	Neg	ASO RQ-PCR
3708	PB	FU	*NaN*	*NaN*
3801	PB	FU	Neg	ASO RQ-PCR
3802	PB	FU	PNQ	ASO RQ-PCR
3901	PB	FU	Neg	ASO RQ-PCR
3902	PB	FU	Neg	ASO RQ-PCR
4002	PB	Baseline	5,00E-03	Flow cytometry
4003	PB	FU	Neg	ASO RQ-PCR
4004	PB	FU	Neg	ASO RQ-PCR
4101	PB	FU	Neg	ASO RQ-PCR
4102	PB	FU	Neg	ASO RQ-PCR
4103	PB	FU	Neg	ASO RQ-PCR
4301	PB	Baseline	8,81E-01	Flow cytometry
4303	PB	FU	Neg	ASO RQ-PCR
4304	PB	FU	Neg	ASO RQ-PCR
4401	PB	FU	Neg	ASO RQ-PCR
4403	PB	FU	Neg	ASO RQ-PCR
4501	PB	Baseline	1,20E-02	Flow cytometry
4503	PB	Baseline	1,70E-03	Flow cytometry
4504	PB	FU	Neg	ASO RQ-PCR
4702	PB	FU	Neg	ASO RQ-PCR
4703	PB	FU	Neg	ASO RQ-PCR
4704	PB	Baseline	1,52E-01	Flow cytometry
4705	PB	FU	Neg	ASO RQ-PCR
4901	PB	Baseline	1,00E-03	Flow cytometry
5101	PB	FU	Neg	ASO RQ-PCR
5102	PB	FU	Neg	ASO RQ-PCR
5201	PB	FU	Neg	ASO RQ-PCR
5202	PB	FU	Neg	ASO RQ-PCR
5203	PB	FU	Neg	ASO RQ-PCR
5205	PB	Baseline	4,00E-03	Flow cytometry

Table S5. Purity information of the samples analyzed for the pharmacogenomic study.

FU, follow up; PB, peripheral blood; NaN, not a number; Neg, negative; ASO-RQ-PCR, allele-specific oligonucleotide real-time quantitative polymerase chain reaction.

FIGURES

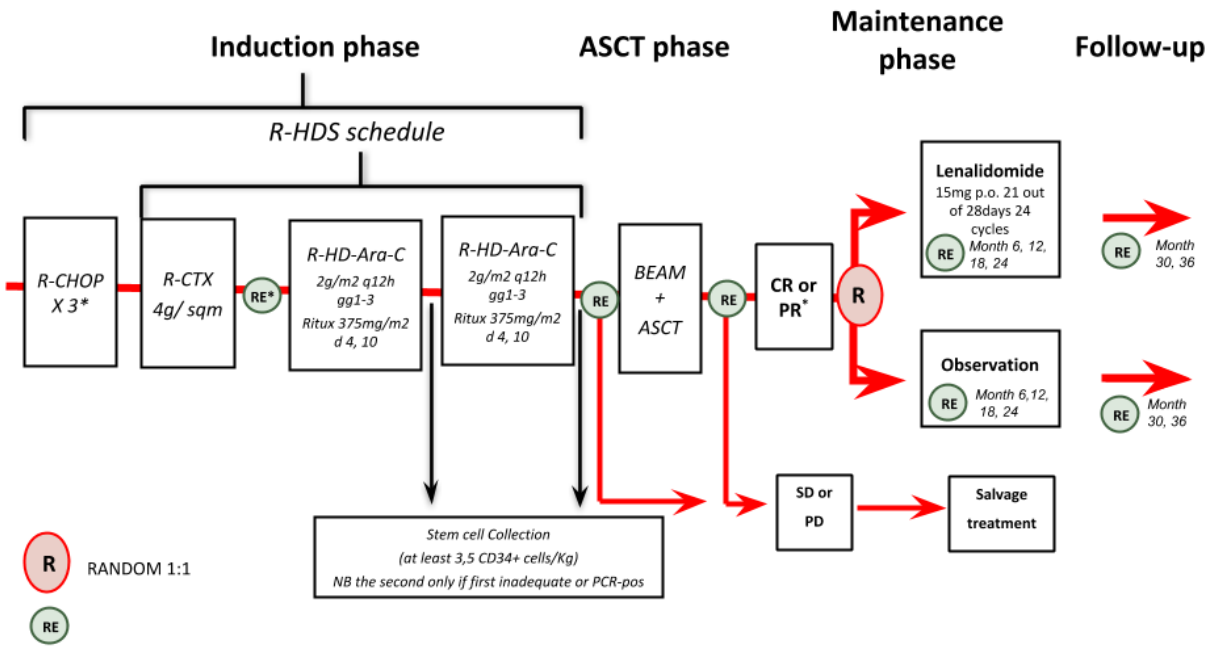

Figure S1. Clinical trial design.

R-HDS, Rituximab- high dose schedule; R-CHOP, Rituximab- Cyclophosphamide Doxorubicin Vincristine and Prednisone; R-CTX, Rituximab-Cyclophosphamide; R-HD-ARAC, Rituximab- High Dose- Citarabine; BEAM, Carmustine, Eteposide, Cytarabine, Melphalan; ASTC, Autologous Stem Cell Transplant; CR, Complete remission; PR, Partial Remission; SD, Stable Disease; PD, Progression Disease; RE, Restaging.

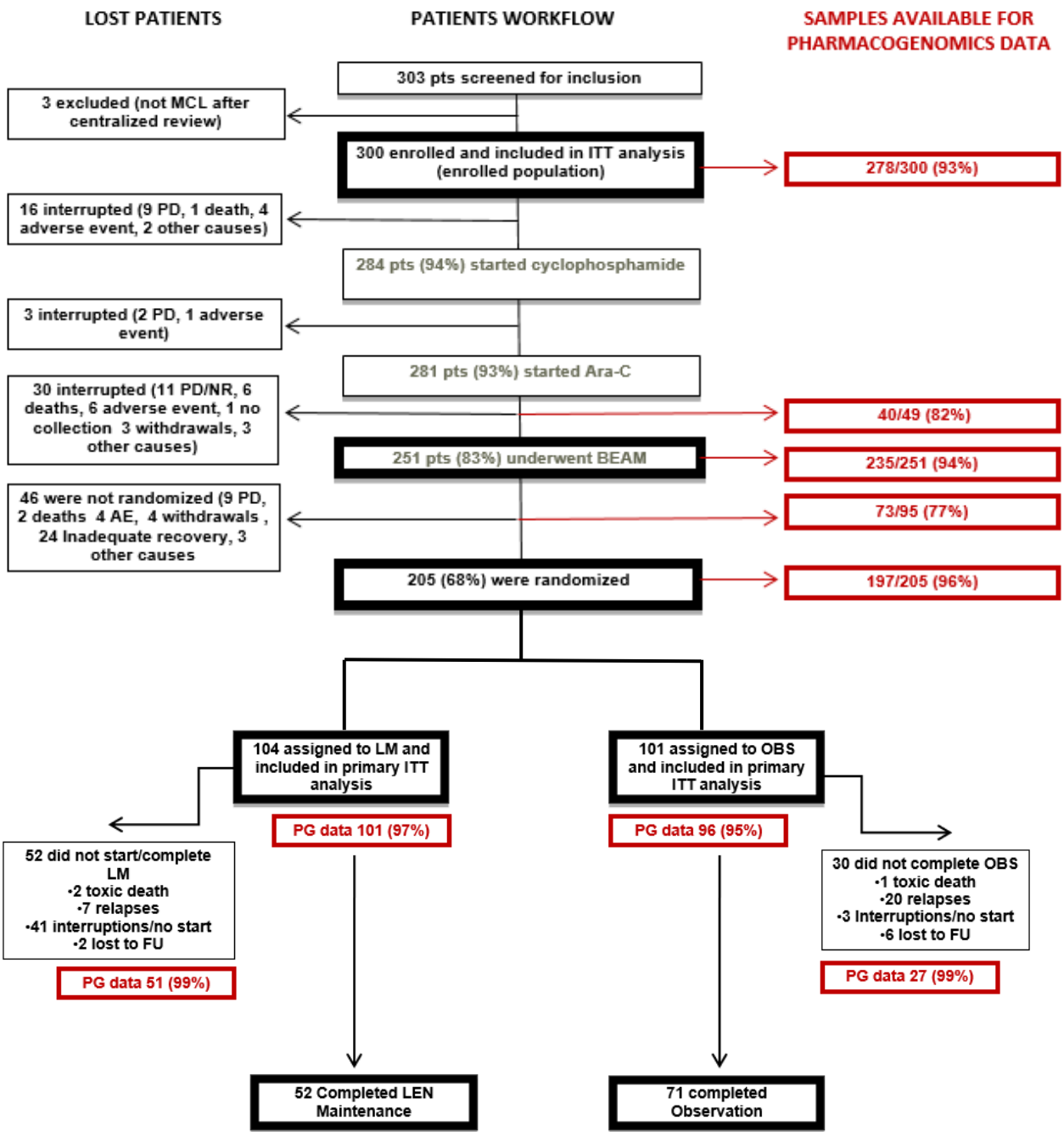

Figure S2. Workflow of patients and samples included in the pharmacogenomics study.

PS ECOG, Performance status by Eastern Cooperative Oncology Group; MIPI, Mantle cell Prognostic Index; CF, Flow Cytometry.

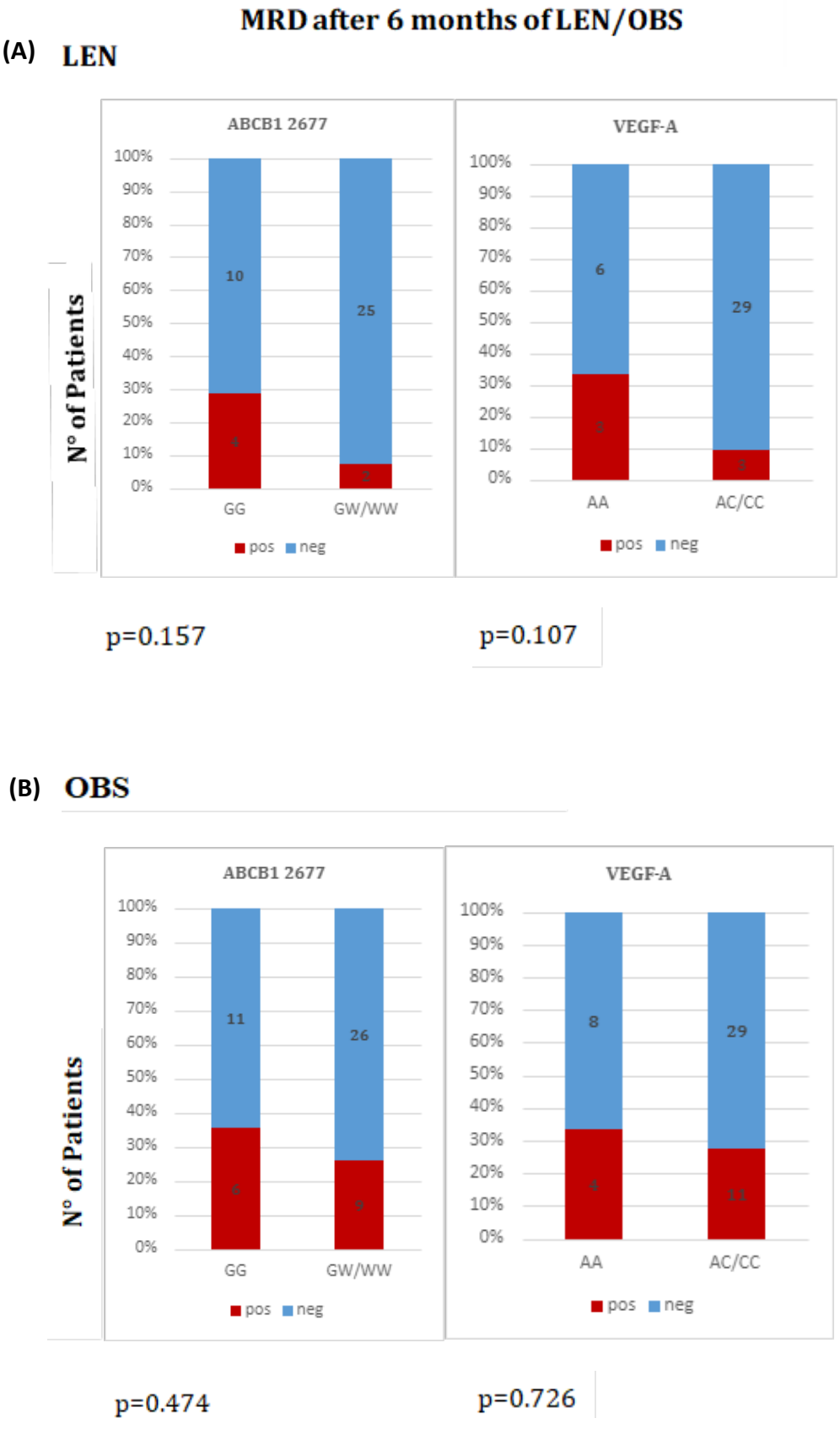

Figure S3. MRD evaluation by RQ-PCR in BM after six months in LEN (A) and OBS (B) arms.

MRD, Minimal Residual Disease; LEN, Lenalidomide; OBS, Observation.

RQ-PCR: Real-time Quantitative Polymerase Chain Reaction.

ABCB1: HoWT=GG, HePOL=GW, HoPOL=WW; ***VEGF-A***: HoWT=AA, HePOL=AC, HoPOL=CC

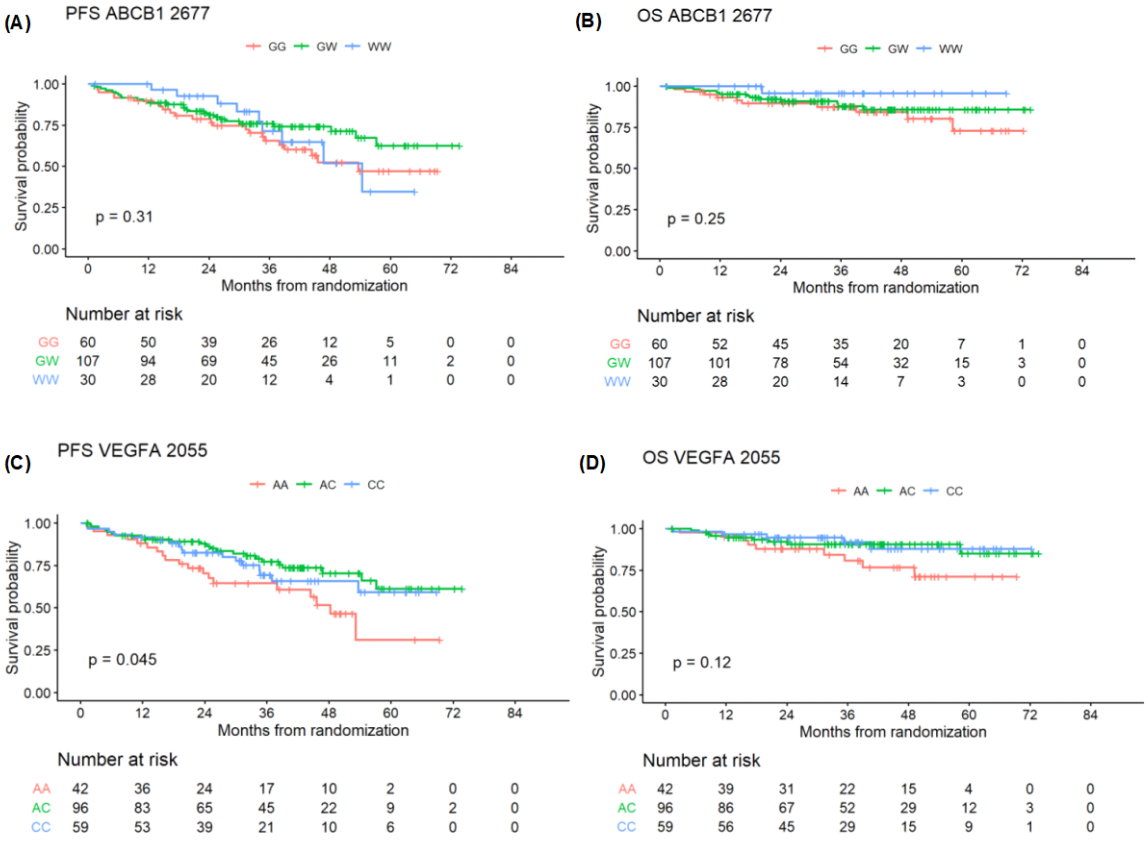

Figure S4. Association between *ABCB1* or *VEGF-A* single genotypes and survival in randomized population.

PFS stratified by *ABCB1* (A) or *VEGF-A* (C) genotypes; OS stratified by *ABCB1* (B) or *VEGF-A* (D) genotypes.

PFS, Progression Free Survival; OS, Overall Survival.

ABCB1: HoWT=GG, HePOL=GW, HoPOL=WW; ***VEGF-A***: HoWT=AA, HePOL=AC, HoPOL=CC