SUPPLEMENTARY

FIGURES

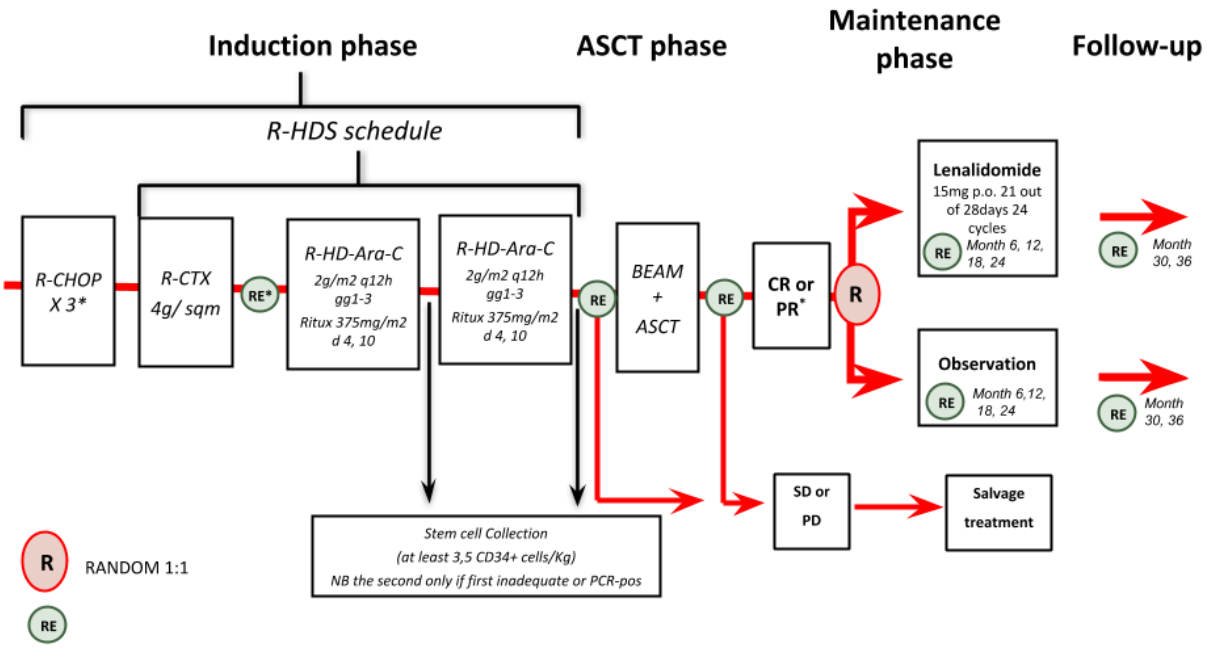

Figure S1. Clinical trial design.

Abbreviations. 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 .

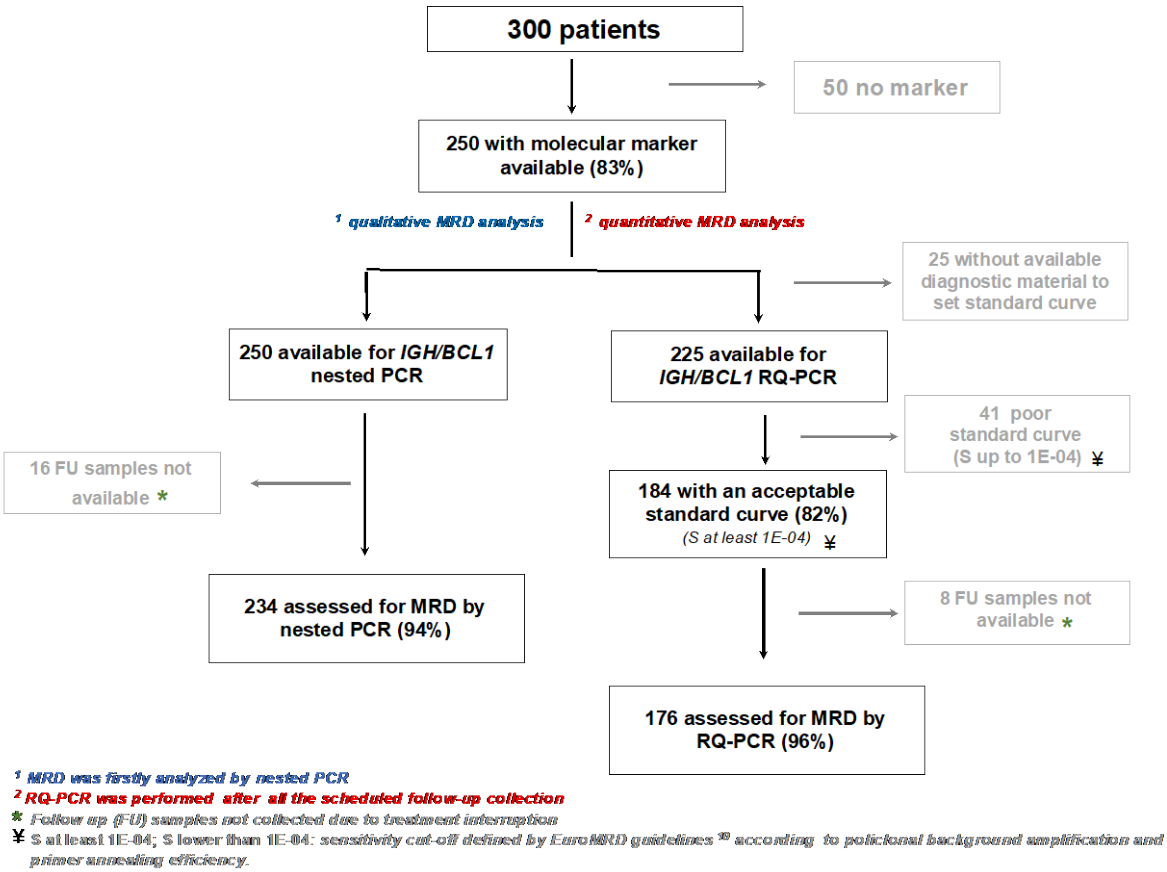

Figure S2. **Samples flow for MRD detection.**

Abbreviations. MRD: Minimal Residual Disease; RQ-PCR: Real Time Quantitative Polymerase Chain Reaction; S: sensitivity; FU: follow up.

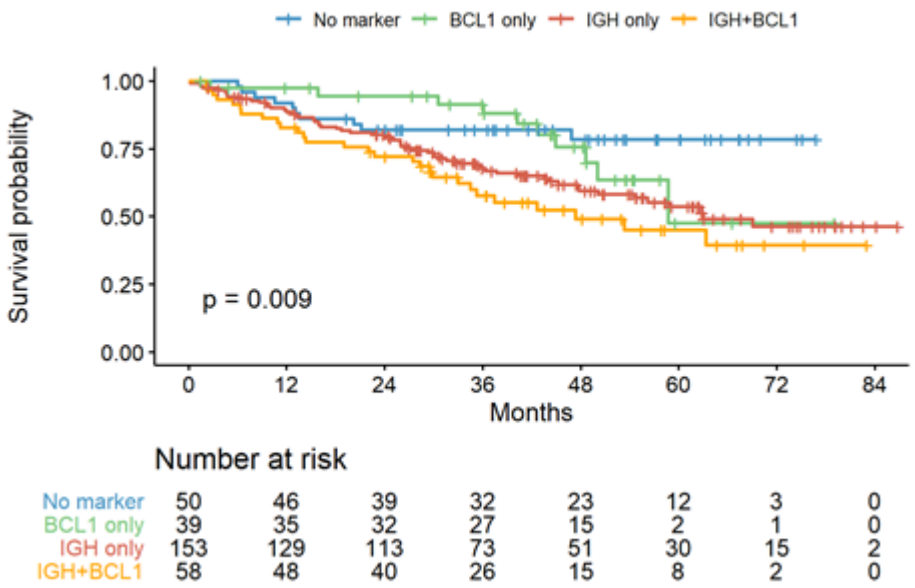

Figure S3. Impact on TTP of molecular marker detection.

Abbreviations. TTP, time to progression; No marker: no marker detected at diagnosis; BCL1 only: patients with only *BCL1/IGH* marker available; IGH only: patients with only *IGH* marker available; IGH+BCL1: patients with both markers.

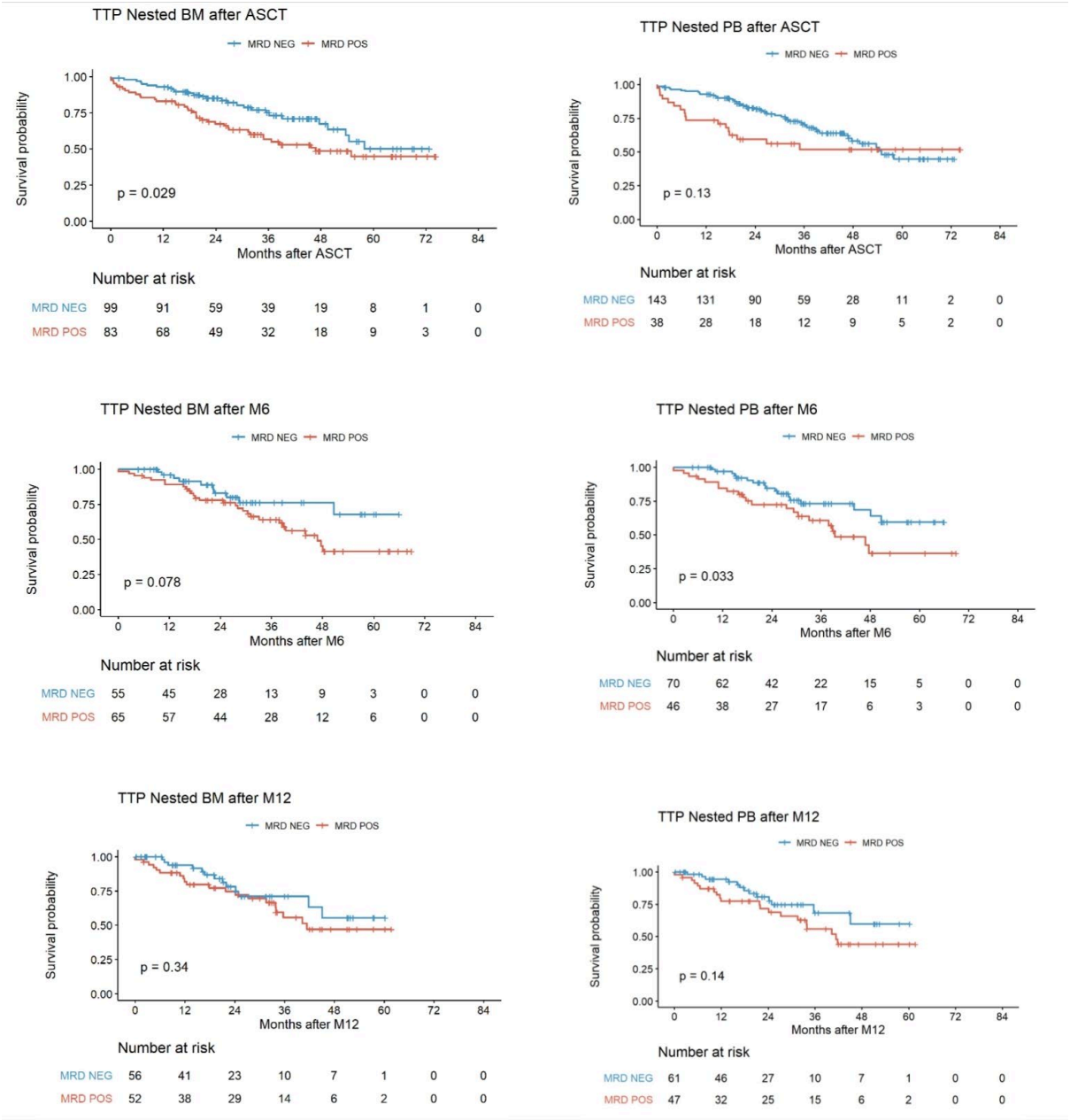

Figure S4. MRD impact on TTP, measured by nested PCR. Timepoints after ASCT, M6 and M12 measured in BM (left) and in PB (right). Abbreviations. MRD, minimal residual disease; TTP, time to progression; ASCT, autologous stem cell transplant; M6, six months from transplant; M12, twelve months from transplant; Nested, nested polymerase chain reaction; NEG, negative; POS, positive; BM, bone marrow; PB, peripheral blood.

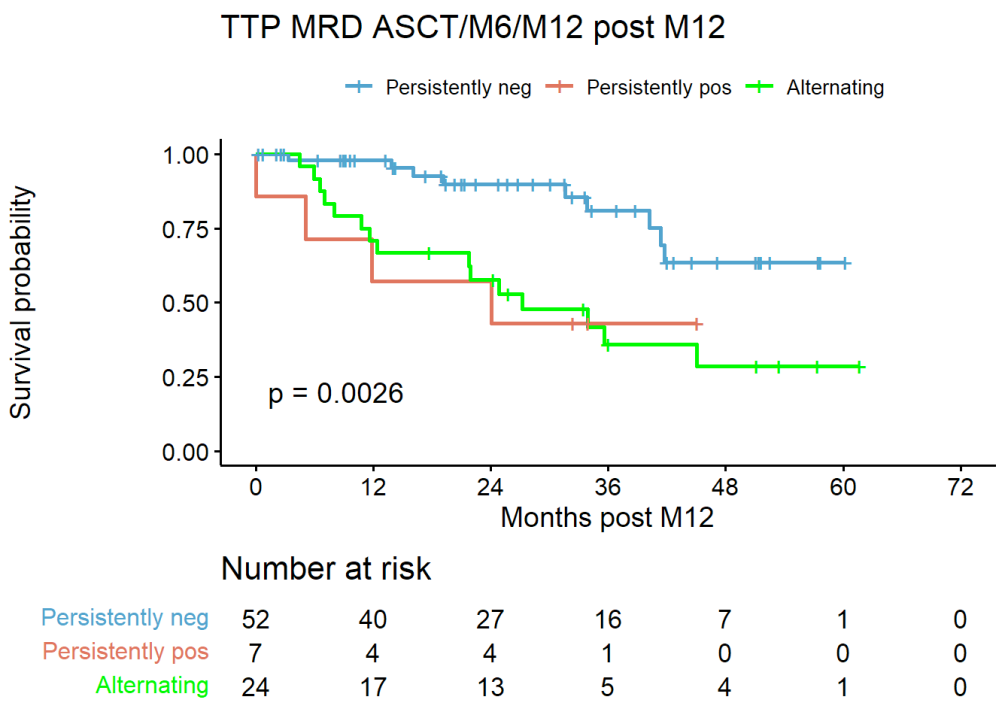

Figure S5. Impact of MRD kinetics on TTP. MRD results by RQ-PCR in BM between ASCT and M12 were considered. Landmark analysis starting from the date of M12 MRD determination.
Abbreviations. MRD, minimal residual disease; RQ-PCR, Real Time quantitative polimerase chain reaction; BM, bone marrow; ASCT: Autologous stem cell transplant; M, months after ASCT Neg: negative. Pos: positive. Alternating: at least one positive and one negative time point in the first year post ASCT.

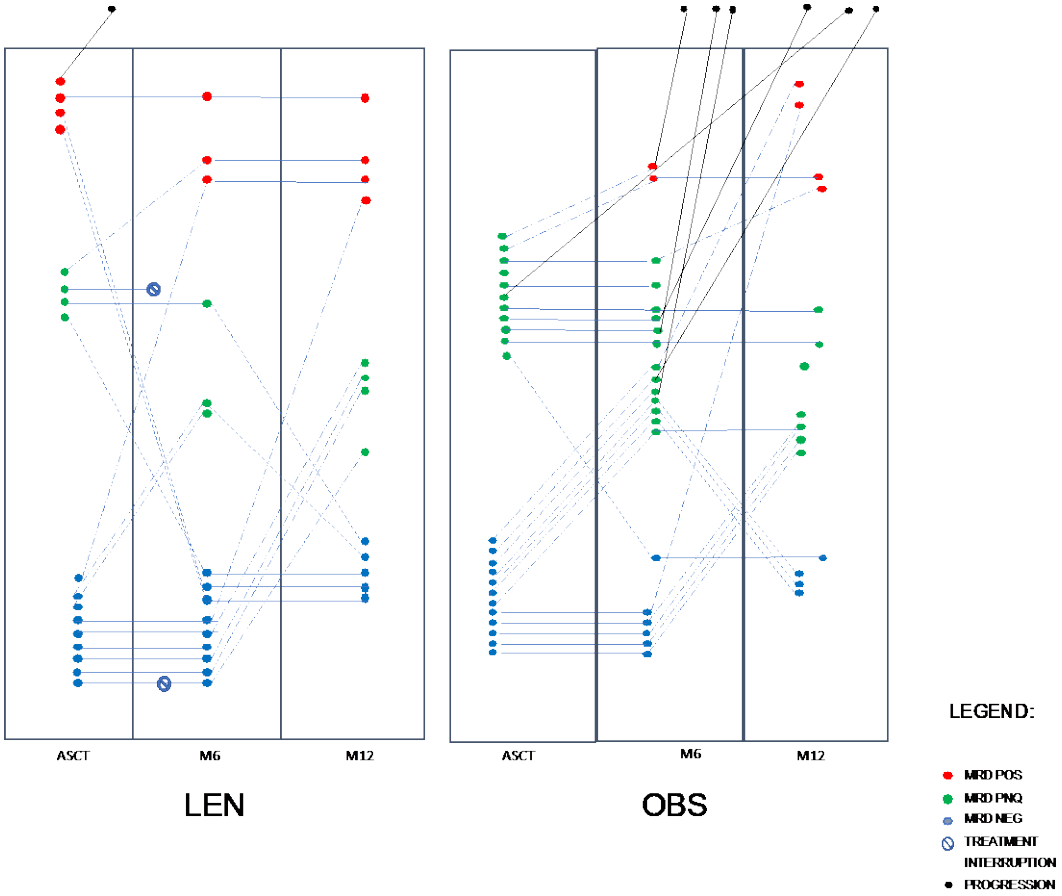

Figure S6. MRD kinetics in the randomized population during the first year after ASCT. Only patients with alternating MRD results are represented here in detail. Abbreviations. LEN: Lenalidomide arm. OBS: observation arm. ASCT: Autologous stem cell transplant. M6: six months from ASCT. M12: twelve months from ASCT. MRD Pos: MRD positive. MRD Neg: MRD negative. MRD PNQ: MRD positive non quantifiable.

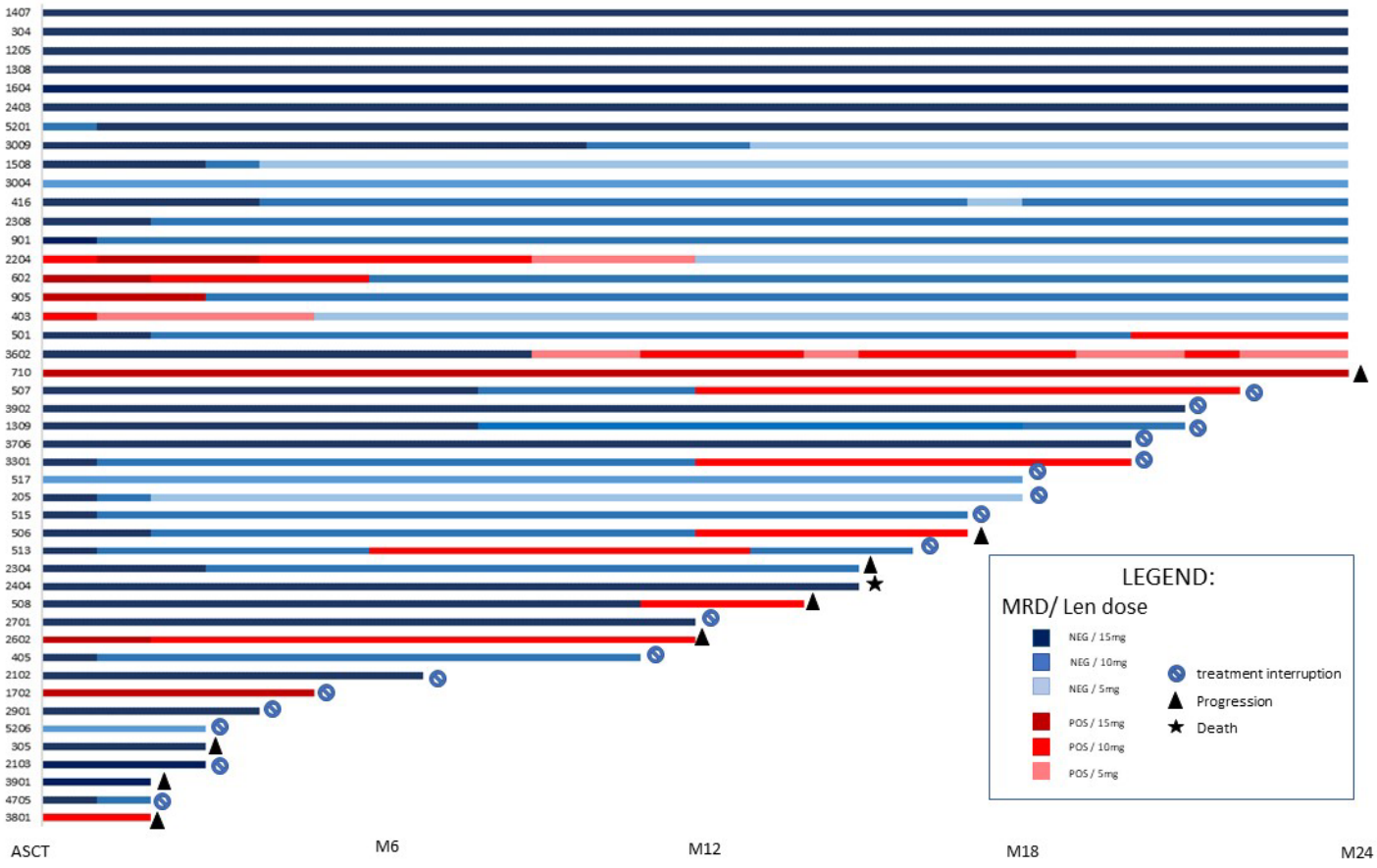

Figure S7. MRD status and lenalidomide dose in the randomized population from ASCT to M24.

Abbreviations. LEN: lenalidomide. ASCT: autologous stem cell transplant. M: months from ASCT. MRD Pos: MRD positive. MRD Neg: MRD negative.

TABLES

MRD Timepoint	Expected samples	Compliance	On treatment	Compliance	Treatment interruption	Compliance
BASELINE	300					
R-CTX	236	95%	234	96%	2	0%
R-HD-ARAC	215	85%	205	87%	10	50%
ASCT	203	89%	168	93%	35	69%
M6	192	70%	144	83%	48	31%
M12	179	70%	130	86%	49	27%
M18	169	57%	119	67%	50	34%
M24	151	63%	102	79%	49	29%
M30	142	50%	95	59%	47	32%
M36	140	51%	94	63%	46	26%

(A)

MRD Timepoint	Expected samples	Compliance	On treatment	Compliance	Treatment interruption	Compliance
BASELINE	300					
R-CTX	236	93%	234	94%	2	0%
R-HD-ARAC	215	86%	205	88%	10	50%
ASCT	203	88%	168	93%	35	66%
M6	192	67%	144	80%	48	29%
M12	179	70%	130	86%	49	27%
M18	169	54%	119	62%	50	34%
M24	151	64%	102	81%	49	29%
M30	142	51%	95	58%	47	32%
M36	140	51%	94	66%	46	26%

(B)

Table S1. Sample collection compliance. BM (A) and PB (B) samples.

Abbreviations: R-CTX: Rituximab-Cyclophosphamide. R-HD-ARA-C: Rituximab-High dose Cytarabine. ASCT: Autologous Stem Cell Transplant. MRD: minimal residual disease.

Baseline features	No marker (50)	*BCL1* only (39)	*IGH* only (153)	*IGH+BCL1* (58)	Sign.
Female, no. (%)	11 (22%)	5 (12%)	35 (23%)	14 (24%)	P= 0.5
Ann Arbor stage Stage IV, no. (%)	40 (80%)	35 (89%)	149 (97%)	58 (100%)	P< 0.001*
Bulky disease (>5 cm), no. (%)	11 (22%)	14 (36%)	45 (29%)	28 (48%)	P= 0.019*
PS ECOG > 0, no. (%)	7 (14%)	6 (15%)	33 (21%)	23 (39%)	P= 0.005*
Ki67>30%, no. (%)	15 (32%)	10 (27%)	41 (30%)	18 (35%)	P= 0.83
Blastoid histology, no. (%)	4 (8%)	3 (7%)	15 (9%)	4 (7%)	P= 0.95
High risk MIPI, no. (%)	3 (6%)	1 (3%)	28 (18%)	14 (24%)	P= 0.003*
Tumor infiltration by CF > median value, no. (%)	7 (16%)	8 (23%)	73 (59%)	38 (74%)	P< 0.001*

Table S2. Clinical characteristics and molecular markers at the time of enrollment.

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

	BM			PB		
TTP	**HR**	**95%CI**	**p**	**HR**	**95%CI**	**p**
Positive (ref)	1	-	-	1	-	-
1 cumulative negativity	0.42	0.21,0.85	0.015	0.82	0.44,1.54	0.541
2 cumulative negativities	0.39	0.19,0.79	0.009	0.58	0.31,1.08	0.087
3 or more negativities	0.16	0.08,0.32	0.000	0.23	0.12,0.42	0.000

Table S3. TTP analysis according to cumulative negativity results of RQ-PCR in BM and PB. PCR evaluations were included as time-dependent covariate in a Cox model.
Abbreviations: TTP, time to progression; HR, hazard ratio; CI, confidence interval; ref, reference; RQ-PCR, Real Time quantitative polimerase chain reaction; BM, bone marrow; PB, peripheral blood.