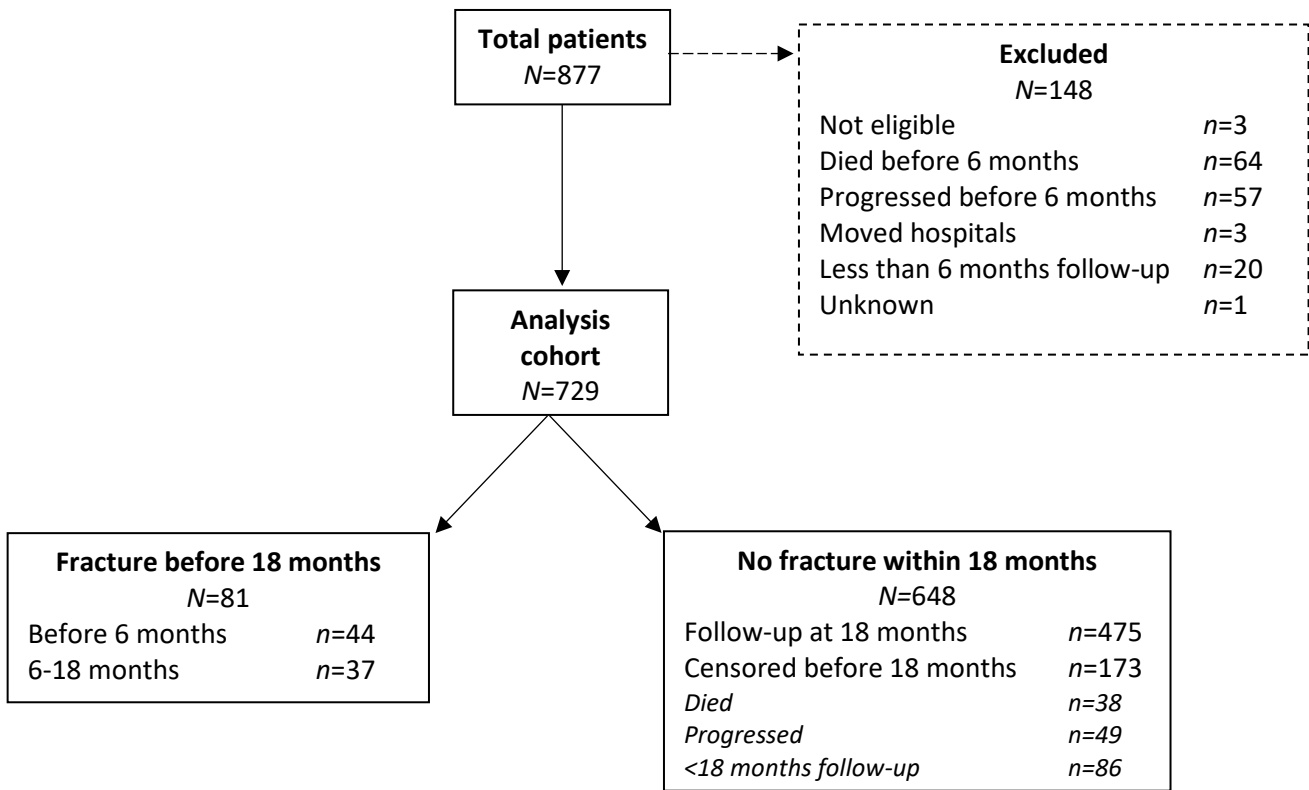


Supplementary Figure 1: Consort diagram



Supplementary Table 1. Fractures according to R-CHOP cycles and use of pre-phase steroids.

	All patients N = 729 N (%)	Fracture N = 81 N (%)	No fracture N = 648 N (%)
R-CHOP Cycles, N (%)			
1	11 (1.5)	0 (0.0)	11 (1.7)
2	11 (1.5)	2 (2.5)	9 (1.4)
3	39 (5.3)	2 (2.5)	37 (5.7)
4	71 (9.7)	5 (6.2)	66 (10.2)
5	24 (3.3)	3 (3.7)	21 (3.2)
6	540 (74.1)	66 (81.5)	474 (73.1)
7	3 (0.4)	0 (0.0)	3 (0.5)
8	30 (4.1)	3 (3.7)	27 (4.2)
R-CHOP cycles, median (range)	6 (1- 8)	6 (2- 8)	6(1- 8)
Steroid Pre-phase, N (%)			
No	526 (73.9)	53 (65.4)	473 (75.0)
Yes	186 (26.1)	28 (34.6)	158 (25.0)
Unknown	17	0	17

Abbreviations: R-CHOP rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone.

Supplementary Table 2. Fractures according to history of bone-protective medication.

	All patients N = 729 N (%)	Fracture N = 81 N (%)	No fracture N = 648 N (%)
Vitamin D supplements, N (%)			
No	614 (95.5)	76 (98.7)	538 (95.1)
Yes	29 (4.5)	1 (1.3)	28 (4.9)
Unknown	86	4	82
Calcium supplements, N (%)			
No	632 (88.8)	64 (82.1)	568 (89.6)
Yes	80 (11.2)	14 (17.9)	66 (10.4)
Missing	17	3	14
Bisphosphonates, N (%)			
No	669 (94.0)	69 (88.5)	600 (94.6)
Yes	43 (6.0)	9 (11.5)	34 (5.4)
Unknown	17	3	14

Supplementary Table 3. Univariable analysis of risk factors for fracture.

Risk factor	All data			Complete cases only		
	Event	HR (95% CI)	p-value	Events/	HR (95% CI)	p-value
Age (increase of 10 years)	81/72	1.03 (0.68-1.58)	0.88	67/554	0.85 (0.52-1.37)	0.50
Sex						
Male	29/35	1.00	0.019	24/268	1.00	0.033
Female	52/37	1.71 (1.09-2.70)		43/286	1.71 (1.04-2.82)	
ECOG						
ECOG 0	29/35	1.00	0.53*	24/268	1.00	0.43*
ECOG 1	37/32	1.25 (1.11-1.41)		34/245	1.39 (1.22-1.57)	
ECOG 2	14/14	0.85 (0.73-0.99)		11/105	0.87 (0.74-1.03)	
ECOG 3-4	8/91	1.16 (0.99-1.37)		6/69	1.04 (0.87-1.25)	
IPI						
0-2	34/32	1.00	0.50	29/245	1.00	0.47
3-5	45/37	1.16 (0.75-1.82)		38/295	1.11 (0.68-1.79)	
BMI group						
Underweight	32/31	1.60 (0.62-4.11)		28/238	1.79 (0.69-4.63)	
Normal	5/32	1.00	0.56	5/25	1.00	0.46
Overweight	25/23	1.03 (0.61-1.74)		19/185	0.86 (0.48-1.54)	
Obese	19/13	1.39 (0.79-2.46)		15/106	1.21 (0.65-2.27)	
Current smoker						
No	72/61	1.00	0.89	63/530	1.00	0.48
Yes	4/32	1.07 (0.39-2.94)		4/24	1.44 (0.53-3.97)	
Known osteoporosis or osteopenia						
No	65/65	1.00	<0.001	53/497	1.00	0.0005
Yes	16/63	2.74 (1.58-4.73)		14/51	2.75 (1.52-4.95)	
Rheumatoid arthritis						
No	74/69	1.00	0.036	60/531	1.00	0.0041
Yes	7/30	2.24 (1.03-4.87)		7/22	2.98 (1.36-6.52)	
Type 2 Diabetes						
No	70/63	1.00	0.54	56/493	1.00	0.13
Yes	11/84	1.22 (0.64-2.30)		11/61	1.65 (0.86-3.15)	
Inflammatory Bowel Disease						
No	81/70	1.00	0.55	67/545	1.00	0.31
Yes	0/10	_*		0/8	_*	
History of alcohol abuse						
No	76/61	1.00	0.15	66/529	1.00	0.21
Yes	1/29	0.26 (0.04-1.90)		1/25	0.31 (0.04-2.20)	
Steroids within last 12 months						
No	70/65	1.00	0.59	61/507	1.00	0.95
Yes	8/60	1.23 (0.59-2.55)		6/47	1.03 (0.44-2.38)	
Raised ALP						
No	65/59	1.00	0.70	53/456	1.00	0.48
Yes	15/12	1.12 (0.64-1.96)		14/98	1.23 (0.68-2.22)	
Calcium level						
Low	69/60	0.98 (0.14-7.03)		59/484	1.04 (0.14, 7.50)	
Normal	1/9	1.00	0.75*	1/8	1.00	0.85*
High	8/80	0.88 (0.42-1.83)		7/62	0.93 (0.42-2.03)	
Bone-protective medication*						
No medication, no predisposing history [†]	48/53	1.00	0.0015	40/411	1.00	0.0014
No medication, predisposing history	12/69	2.02 (1.07-3.81)		11/56	2.11 (1.08-4.12)	
Medication, no predisposing history	4/48	0.89 (0.32-2.48)		4/44	0.90 (0.32-2.50)	
Medication and predisposing history	13/53	2.86 (1.55-5.28)		12/43	3.02 (1.58-5.76)	
Bone involvement						
No	46/55	1.00	<0.001	39/423	1.00	<0.001
Yes, without fracture	23/12	2.41 (1.46-3.98)		18/94	2.23 (1.27-3.90)	
Yes, with fracture	12/47	3.51 (1.86-6.63)		10/37	3.31 (1.65-6.63)	
Prior Fracture						
No	62/61	1.00	0.0014	50/465	1.00	0.0066
Yes, not at baseline	4/44	0.88 (0.32-2.42)		4/37	0.97 (0.35-2.70)	
Yes, at baseline	15/62	2.68 (1.52-4.71)		13/52	2.57 (1.39-4.73)	
Non-Lymphoma fracture at baseline						
No	77/70	1.00	0.16	63/535	1.00	0.19
Yes	4/20	2.01 (0.74-5.49)		4/19	1.96 (0.71-5.37)	
Steroid pre-phase						
No	53/52	1.00	0.064	43/415	1.00	0.030
Yes	28/18	1.54 (0.97-2.43)		24/139	1.73 (1.05-2.84)	

Abbreviations: ALP alkaline phosphatase; BMI bone mass index; CI confidence interval; ECOG eastern cooperative oncology group; HR hazard ratio; IPI international prognostic index. *Bone-protective medication includes vitamin D, calcium, and / or bisphosphonates. †Predisposing history includes: osteoporosis, osteopenia, previous fracture and/or rheumatoid arthritis