Supplemental Materials for:

Sustained remissions in CLL after frontline FCR treatment with very long-term follow-up

Supplementary methods – Long-term follow-up results

To minimize any bias, our study team attempted to contact all patients who remained alive and in remission at last follow-up. When contactable, patients were asked about remission status, any treatment for CLL, and any other cancers they had been treated for. For patients followed outside MD Anderson, patient reported remission status was confirmed through evaluation of physician notes and CBC results where available. Patients known to have relapsed but not died were also followed for survival.

Of the original 300 patients, 151 were known to be deceased at the time of the previous update (2015). For the remaining 149 patients, the patient record was updated as follows: still following locally at MD Anderson Cancer Center (n=47), calling the patient (n=22), written communication with the patient (n=36), outside hospital records (n=34), and could not be updated (n=10). Of the patients still alive at last follow-up (n=131), 57 (44%) had last follow-up updated within the past 2 years (2021-2022) while 74 (56%) had incomplete follow-up, defined as no contact in the past 2 years.

Supplementary Table 1: Pre-treatment characteristics in the FCR 300 cohort

Characteristic, N=300 unless stated	**MDACC FCR study, n(%) unless stated**
Age, median (range)	57 (17-86)
Age ≥65	72 (24)
β_2-microglobulin ≥4.0mg/l, n=296	128/296 (43)
Binet stage	
A	76 (25)
B	145 (48)
C	78 (26)
Rai stage III-IV	107 (36)
Male gender	211 (70)
ECOG performance status	
0	119 (40)
1	171 (57)
2	10 (3)
IGHV unmutated, n=214	126 (59)
White cell count >/= $200x10^9$/L	27 (9)
LDH >upper limit of normal	108 (36)
ZAP70 positive by IHC, n=209	126 (60)
Del(17p) by karyotyping, n=222	5 (2)

Supplementary Table 2: Summary of other malignancies observed in FCR-treated patients

Malignancy	Number of patients
Hematologic	
Acute myeloid leukemia/myelodysplastic syndrome	19 (6.3)
Richter transformation	29 (9.7)
Other hematologic	6 (2)
T cell lymphoproliferative disorder	3 (1)
Acute lymphoblastic leukemia	1 (0.3)
Myelofibrosis	1 (0.3)
Mantle cell lymphoma	1 (0.3)
Non-hematologic	
Non-melanoma skin cancer	34 (11.3)
Melanoma	5 (1.7)
Other solid tumor (site below)	42 (14)
Prostate	12 (4)
Breast	10 (3.3)
Lung	5 (1.7)
Gastrointestinal	4 (1.3)
Ovaries	2 (0.7)
Renal	2 (0.7)
Thyroid	2 (0.7)
Parotid	1 (0.3)
Adrenal	1 (0.3)
Brain	1 (0.3)
Cervix	1 (0.3)
Soft tissue	1 (0.3)

% displayed as proportion of initial 300 patient cohort.

Supplementary Table 3: Risk of therapy-related myeloid neoplasms according to pre-treatment characteristics

Pre-treatment characteristic (N=300 unless stated)	n (%)	Odds ratio (95% CI), p value
Age		
>/=60	9/114 (7.9%)	1.5 (0.6-3.8), p=0.39
<60	10/186 (5.4%)	
Gender		
Male	15/211 (7.1%)	1.6 (0.5-5.0), p=0.40
Female	4/89 (4.5%)	
Rai Stage		
3-4	13/193 (6.7%)	0.8 (0.3-2.2), p=0.70
0-2	6/107 (5.6%)	
IGHV mutation status (n=214)		
Unmutated	5/88 (5.7%)	1.0 (0.3-3.2), p=0.98
Mutated	7/126 (5.6%)	
B2M (mg/L)		
>/=4.0	10/128 (7.8%)	1.5 (0.6-3.8), p=0.39
<4.0	9/168 (5.4%)	
p53 by Immunohistochemistry (n=223)		
Positive	1/21 (4.8%)	0.9 (0.1-7.1), p=0.87
Negative	11/202 (5.4%)	