Appendix: list of sites with institutional review boards that approved study CALGB 10404.

Albert Einstein College NY
Allan Blair Cancer Centre
Aultman Hospital
Bryn Mawr Hospital
Cancer Institute at Alexian Brothers
Cancer Institute of New Jersey
Cancercare Manitoba
Carolinas Medical Center/Levine Cancer Institute
Christiana Care Health System-Christiana Hospital
Columbus CCOP EPP
Cross Cancer Institute
Danville Regional Medical Center
Dartmouth Hitchcock Medical Center
Decatur Memorial Hospital
Decatur Memorial Hospital EPP
Department of Veterans Affairs Iowa City Health Care System
East Carolina University
Eastern Maine Medical Center
Evanston CCOP-NorthShore University HealthSystem
Fort Wayne Medical Oncology and Hematology Inc-State Boulevard
Fox Chase Cancer Center
Geisinger Medical Center
Geisinger Scenery Park Oncology Clinic
Geisinger Wyoming Valley
Grant Riverside Methodist Hospitals
Greenville CCOP
Gundersen Lutheran
Hartford Hospital
Hematology Oncology Associates of Central New York
Hopital Charles LeMoyne
Hopital de Saint Sacrement-Quebec City
Howard Regional Health System-CCOP
Illinois CancerCare-Peoria
Juravinski Cancer Centre at Hamilton Health Sciences
Kansas City CCOP
Kinston Medical Specialists PA
Lahey Clinic Medical Center
Lankenau Hospital
Long Island Jewish Medical Center
Loyola University
LRGHealthcare-Lakes Region General Hospital
Marshfield Clinic
Marshfield Clinic-Weston Center
Marshfield Clinic Cancer Care at Regional Cancer Center

McGill University
McLeod Regional Medical Center
MD Anderson, Florida
Medical Onc. And Hem. Assoc.- Laurel St.
Medical University of South Carolina
MedStar Georgetown University Hospital
Memorial Hospital of Oconomowoc
Minneapolis Veterans Medical Center
Mission Hospitals, Inc
Montana Cancer Consortium CCOP
Montefiore Hospital
Mount Sinai Medical Center
Mountainview Medical
New Hampshire Oncology-Hematology PA
New Hampshire Oncology-Hematology PA-Hooksett
University of New Mexico
New York University Medical Center
North Shore University Hospital
Northwestern University
OCI/Princess Margaret Hospital
Ohio State University Medical Center
Palo Alto Medical Foundation, Camino Division
Penn State Cancer Institute
Pottstown Memorial Medical Center
Queen Elizabeth II- Health Science Center
Saint Francis Medical Center
Saint Luke's Hospital of Kansas City
Siouxland Hem-Onc Assoc
St John's Hospital/HealthEast
St Louis University
St. Louis CCOP
St. Vincent’s Hospital Regional Cancer Center
State University of New York Upstate Medical University
Swedish American Hospital
Thompson Cancer Survival Center
Tom Baker Cancer Centre
Union Hospital of Cecil County
University Hospitals of Cleveland
University of Chicago
University of Iowa Hospitals and Clinics
University of Nebraska Medical Center
University of New Mexico
University of North Carolina at Chapel Hill
University of Rochester
University of Vermont
UW Cancer Center Johnson Creek

Virginia Commonwealth University
Wake Forest University Health Sciences
Walter Reed Army Medical Center
Washington University School of Medicine
Waukesha Memorial Hospital
Wayne Memorial Hospital
Weill Medical College of Cornell University
Wesley Medical Center
West Michigan Cancer Center
West Virginia University
University of Wisconsin

Methods

Dose modifications for remission induction therapy.

Baseline dose modifications for patients 70 years and older included using fludarabine doses of 20 mg/m^2 and cyclophosphamide doses of 150 mg/m^2 in arms C and D. An absolute neutrophil count of $\geq$ 1 x 10^9/L and platelets $\geq$ 100,000/μL or > 80% of baseline value were required to begin subsequent cycles beyond cycle 2 of therapy. If such recovery did not occur, treatment was delayed and dose reduction occurred.

The following dose modifications were followed for patients of any age treated in arms A and B as well as patients aged less than 70 years and treated in arms C and D.

Dose level	**IV fludarabine dose level**	**Oral fludarabine dose level (Canada only)**	**Cyclophosphamide dose level (arms C and D Only)**
0 (starting level)	25 mg/m2/day	40 mg/m2/day	250 mg/m2/day
-1	18.75 mg/m2/day	30 mg/m2/day	200 mg/m2/day
-2	12.5 mg/m2/day	20 mg/m2/day	150 mg/m2/day

Patients in arms C and D and aged 70 years or older followed the following dose modifications.

Dose level	**IV fludarabine dose level**	**Oral fludarabine dose level (Canada only)**	**Cyclophosphamide dose level (arms C and D Only)**
0 (starting level)	20 mg/m^2/day	32 mg/m^2/day	150 mg/m^2/day
-1	15 mg/m^2/day	24 mg/m^2/day	120 mg/m^2/day
-2	10 mg/m^2/day	16 mg/m^2/day	90 mg/m^2/day

Neutropenia. G-CSF or GM-CSF was not used to avoid dose reductions. G-CSF or GM-CSF was used only in the treatment of febrile neutropenia. For arms A and B, ANC ≥ 1000/μL on day 1 of a cycle was required. For ANC < 1000/μL, fludarabine was held until ANC ≥ 1000/μL and resumed at one dose level lower than previous dose. If dose reduction to less than dose level -2 was required for neutropenia, treatment with fludarabine and rituximab was discontinued. If fludarabine was delayed for neutropenia, rituximab was also delayed. In patients whose baseline ANC was less than 1000/μL, these dose modifications, if required, were not applied until cycle 3. For arms C and D, ANC ≥ 1000/μL on day 1 of a cycle was required. For ANC < 1000/μL, fludarabine and cyclophosphamide was held until ANC ≥ 1000/μL and both resumed at one dose level lower than previous dose. If dose reduction to less than dose level -2 was required for neutropenia, treatment with fludarabine, cyclophosphamide, and rituximab was discontinued. If fludarabine and cyclophosphamide were delayed for neutropenia, rituximab was also delayed. In patients whose baseline ANC was less than 1000/μL, these dose modifications, if required, were not be applied until cycle 3.

Febrile neutropenia. For arms A and B, fludarabine was held until fever resolved and ANC ≥ 1000/μL and then resumed at one dose level lower than the previous dose. If dose reduction to less than dose level -2 was required for febrile neutropenia, treatment with fludarabine and rituximab was discontinued. If fludarabine was delayed for febrile neutropenia, rituximab was also delayed. For arms C and D, fludarabine and cyclophosphamide was held until fever resolved and ANC ≥ 1000/μL and then both resumed at one dose level lower than the previous dose. If dose reduction to less than dose level -2 was required for febrile neutropenia, treatment with fludarabine, cyclophosphamide, and rituximab was discontinued. If fludarabine and cyclophosphamide were delayed for febrile neutropenia, rituximab also was delayed.

Thrombocytopenia. For arms A and B, platelets ≥ 100,000/μL or > 80% of baseline value on day 1 of a cycle were required. For platelets < 100,000/μL or < 80% of baseline, fludarabine was held until platelets were ≥ 100,000/μL or > 80% of baseline, and then then resumed at one dose level lower than the previous dose. If dose reduction to less than dose level -2 was required for thrombocytopenia, treatment with fludarabine and rituximab was discontinued. If fludarabine was delayed for thrombocytopenia, rituximab was also delayed. In patients whose baseline platelet count was <100,000/μL, these dose modifications, if required, were not applied until cycle 3. For arms C and D, platelets must be ≥ 100,000/μL or > 80% of baseline value on day 1 of a cycle. For platelets < 100,000/μL or < 80% of baseline, fludarabine and cyclophosphamide were held until platelets ≥ 100,000/μL or > 80% of baseline, and then both resumed at one dose level lower than the previous dose. If dose reduction to less than dose level -2 was required for thrombocytopenia, treatment with fludarabine, cyclophosphamide, and rituximab was discontinued. If fludarabine was delayed for thrombocytopenia, rituximab was also delayed. In patients whose baseline platelet count <100,000/μL, these dose modifications, if required, were not applied until cycle 3.

Patients developing autoimmune hemolytic anemia (AIHA) or autoimmune thrombocytopenia (AIT) during fludarabine therapy were removed from protocol therapy, and treated at the discretion of the local physician. For non-hematologic toxicity (not including nausea, vomiting, diarrhea, drug-related chills and hair loss) ≥ grade 2 attributable to fludarabine, fludarabine was reduced by 50%. For non-hematologic toxicity ≥ grade 2 attributable to cyclophosphamide, cyclophosphamide was reduced by 50%. If cough, dyspnea, and other pulmonary symptoms occurred, a chest x-ray, high-resolution chest CT scan and incentive

spirometry studies were obtained, and pneumocystis pneumonia or viral pneumonitis was considered.

Dose modifications for consolidation therapy with lenalidomide.

If a toxicity resulted in withholding a dose, the missed dose was not made up. No dose reductions below dose level -2, as shown below, were permitted.

Lenalidomide dose levels (month 1)	
Starting dose	5 mg/day
Dose level -1	2.5 mg/day
Lenalidomide dose levels (month 2-6)	
Starting Dose	10 mg/day
Dose Level -1	5 mg/day
Dose Level -2	2.5 mg/day

Neutropenia. In the instance of grade 3 neutropenia on day 1 of a cycle, lenalidomide therapy was held and CBC was monitored weekly. If neutropenia resolved to ≤ grade 2, then lenalidomide was resumed at the next lower dose level. Upon patient evaluations, re-escalation after 2 weeks on the reduced dose was attempted. If neutropenia occurred on day 1 of a cycle, the cycle could be delayed. In the instance of grade 4 neutropenia, lenalidomide therapy was held until toxicity resolved to ≤ grade 2. Treatment was resumed with one dose level reduction for subsequent cycles. If treatment was delayed for 4 weeks, all protocol therapy was discontinued and the study chair notified. G-CSF or GM-CSF was not used to avoid dose reductions. G-CSF or GM-CSF was used only in the treatment of febrile neutropenia.

Febrile neutropenia. In the instance of febrile neutropenia occurring at any time, lenalidomide therapy was held and appropriate antibiotics and G-CSF or GM-CSF were administered until recovery (ANC ≥ 1500/μL + absence of fever). If fever resolved and ANC was ≤ grade 2, then lenalidomide resumed at one dose level reduction for subsequent cycles. If treatment was held for 4 weeks, all protocol therapy was discontinued and the study chair notified.

Thrombocytopenia. In the instance of grade 3 or 4 thrombocytopenia, lenalidomide therapy was held until platelets were ≥ 50,000/μL (≤ grade 2). Lenalidomide therapy then resumed with a one dose level reduction. Upon patient evaluation, re-escalation after 2 weeks on the reduced dose was attempted.

Anemia. In the instance of grade 3 anemia, lenalidomide therapy was continued with a one dose level reduction. Upon patient evaluation, re-escalation after 2 weeks on the reduced dose was attempted. In the instance of grade 4 anemia, lenalidomide was held until hemoglobin ≤ grade 3 (post-transfusion). Lenalidomide therapy then resumed with a one dose level reduction. Upon patient evaluation, re-escalation after 2 weeks on the reduced dose was attempted. Epoetin or darbepoetin was not used concurrent with lenalidomide therapy due to potential increased risk of venous thrombosis with co-administration of these agents.

Allergic reaction. In the instance of grade 2 allergic reaction, lenalidomide therapy was held and toxicity was monitored weekly. If toxicity resolved to ≤ grade 1, then lenalidomide therapy was resumed. In the instance of ≥ grade 3 allergic reaction, protocol therapy was discontinued.

Dermatologic toxicity. In the instance of ≥ grade 3 desquamating rash, protocol therapy was discontinued.

Cardiac, thyroid and other non-hematologic toxicity: In the instance of grade 2 or 3 cardiac, thyroid or other non-hematologic toxicity, lenalidomide therapy was held, the study chair notified, and toxicity monitored at least weekly. If toxicity resolved to ≤ grade 1, then lenalidomide resumed at the next lower dose level. Upon patient evaluation, re-escalation after 2 weeks on the reduced dose was attempted. In the instance of grade 4 non-hematologic toxicity, protocol therapy was discontinued.

Tumor lysis syndrome. In the instance of grade 3 tumor lysis syndrome with electrolyte abnormalities, treatment was discontinued until values returned to ≤ grade 1. Treatment resumed at the same lenalidomide dose level.

Renal toxicity. For creatinine clearance (CrCl) < 30 mL/min on day 1 of a consolidation cycle, interrupt lenalidomide was interrupted for two weeks and reassessed. If CrCl remained < 30 mL/min, then lenalidomide was interrupted for the remainder of the consolidation cycle and reassessed. If CrCl was not improved to ≥ 30 mL/min by start of the next consolidation cycle, then the patient was removed from protocol therapy. For CrCl < 60 mL/min but ≥ 30 mL/min, lenalidomide was decreased to the next lower dose level for remainder of the cycle. Upon patient evaluation, re-escalation of lenalidomide at the next cycle was attempted.

Pregnancy or suspected pregnancy. For pregnancy or suspected pregnancy in females taking lenalidomide, lenalidomide was discontinued. For pregnancy occurring in the female partner of a male taking lenalidomide, the female partner was advised to seek further evaluation and counseling as appropriate.

Dose modification for obese patients. There was no clearly documented adverse impact of treatment of obese patients when dosing was performed according to actual body weight, and therefore, all dosing was determined solely by the patient's BSA as calculated from actual weight or the actual weight without any modification unless explicitly described in the protocol. This eliminated the risk of calculation error and the possible introduction of variability in dose administration. Failure to use actual body weight in the calculation of drug dosages was considered a major protocol deviation. Physicians who were uncomfortable with administering chemotherapy dose based on actual body weight were advised not to enroll obese patients.

Response assessment

Patients in all arms underwent response assessment approximately 10 months after beginning induction therapy and patients in arms B and D who had stable disease or better with an absolute neutrophil count of $\geq$ 1 x 10^9/L, platelets $\geq$ 100,000/μL, and estimated glomerular filtration rate $\geq$ 30 mL/min proceeded to receive up to six lenalidomide consolidation cycles. These patients in arms B and D underwent an additional full staging and response evaluation to assess the effectiveness of lenalidomide consolidation approximately 18 months after beginning induction therapy. Patients in all arms who had not already progressed underwent a full staging evaluation approximately 24 months after beginning induction therapy. All patients were followed for progression and survival every 3 months following induction therapy for the first year and every 6 months thereafter.

Statistics

Chi-square or Fisher's exact and Kruskal-Wallis tests were used to compare categoric and continuous baseline characteristics, respectively, between patient groups[1,2]. Best overall and complete response rates were estimated with exact 90% confidence intervals per protocol. Probabilities for PFS and OS were estimated using the method of Kaplan-Meier. According to protocol, differences in curves were tested using the log-rank test, which is optimal when the hazard rates in the groups are proportional to each other over time. If there was evidence of non-proportional hazards, then this was accounted for in univariable and multivariable models by allowing the hazard ratio to change over time, as described below.

Logistic regression and proportional hazard models were used to model response and PFS/OS, respectively, as a function of baseline characteristics for patients with non-del(11q).[3,4] Univariable models were fit and variables with $p<0.20$ were included in a multivariable model. Models were fit using patients with complete data for all variables considered. In the univariable

models for PFS/OS, if any baseline variable violated the assumption of proportional hazards, a time-dependent covariate model was used in the subsequent modeling. In this situation, hazard ratios with 95% confidence intervals were presented at specific time points. All multivariable models stratified on Rai stage and included treatment arm. Due to the limited sample size for patients with del(11q), modeling of response and PFS/OS in this subgroup of patients was not performed.

All secondary analyses were hypothesis generating and served to provide information and support for the planning of future studies. Therefore, no control for multiple comparisons or other adjustments were considered. All p-values were two-sided and p-values less than 0.05 were considered statistically significant.

Table S1: Baseline characteristics according to del(11q) status.

Variable	Non-del(11q) N = 342	del(11q) N = 58	P*
Median age, years (range)	61 (28-81)	60 (30-78)	0.35
Sex, no. (%)			0.77
Male	222 (65)	39 (67)	
Female	120 (35)	19 (33)	
Rai stage, no. (%)			0.83
I	72 (21)	12 (21)	
II	108 (32)	22 (38)	
III	68 (20)	10 (17)	
IV	94 (27)	14 (24)	
ECOG PS, no. (%)			0.84
0	181 (53)	33 (57)	
1	149 (44)	23 (40)	
2	12 (4)	2 (3)	
Median hemoglobin, g/dL (range)	12.2 (5.9-17.3)	12.1 (3.5-15.4)	0.98
Median platelets, $x10^3$/uL (range)	141 (12-486)	144 (37-375)	0.76
Median WBC, $x10^3$/uL (range)	79.1 (1.2-899.8)	70.3 (6.3-289.0)	0.97
B2M above normal, no. (%)			0.33
No	55 (17)	12 (23)	
Yes	273 (83)	40 (77)	
LDH above normal, no. (%)			0.77
No	169 (50)	29 (53)	
Yes	171 (50)	26 (47)	
Serum creatinine above normal, no. (%)			0.33
No	304 (89)	53 (95)	
Yes	36 (11)	3 (5)	
Palpable splenomegaly, no. (%)			1.00
No	182 (54)	32 (55)	
Yes	152 (46)	26 (45)	
Palpable hepatomegaly, no. (%)			0.56
No	307 (94)	52 (91)	
Yes	21 (6)	5 (9)	
Adenopathy, no. (%)			0.003
No adenopathy	9 (3)	0 (0)	
Yes, lymph node <5cm	234 (72)	27 (51)	
Yes, lymph node 5-10cm	62 (19)	22 (42)	
Yes, lymph node >10cm	21 (6)	4 (8)	
del(17p), no. (%)			0.33
Absent	294 (90)	55 (95)	
Present	33 (10)	3 (5)	
Trisomy 12, no. (%)			0.19
Absent	243 (74)	48 (83)	
Present	84 (26)	10 (17)	
del(13q), no. (%)			0.25
Absent	153 (47)	22 (38)	
Present	174 (53)	36 (62)	

NOTE: (%) values are calculated out of the number of patients with non-missing data in each category.
Abbreviations: ECOG PS indicates Eastern Cooperative Oncology Group Performance Status; WBC, white blood cell count; B2M, beta-2 microglobulin; and LDH, lactate dehydrogenase.
*Fisher's exact and Kruskal-Wallis p-values are presented for categoric and continuous variables, respectively.

Table S2: Treatment received by treatment arm and del(11q) status.

Induction	**Arm A: FR Non-del(11q) N = 123**	**Arm B: FR+L Non-del(11q) N = 109**	**Arm C: FCR Non-del(11q) N = 110**	**Arm C: FCR del(11q) N = 27**	**Arm D: FCR+L del(11q) N = 31**
Cycles Received, no. (%)					
1	2 (2)	1 (1)	7 (6)	2 (7)	2 (6)
2	6 (5)	13 (12)	9 (8)	3 (11)	1 (3)
3	9 (7)	13 (12)	4 (4)	4 (15)	3 (10)
4	15 (12)	6 (6)	16 (15)	5 (19)	4 (13)
5	4 (3)	4 (4)	7 (6)	5 (19)	1 (3)
6	87 (71)	72 (66)	67 (61)	8 (30)	20 (65)
Consolidation	**Arm A: FR Non-del(11q) N = 0**	**Arm B: FR+L Non-del(11q) N = 69**	**Arm C: FCR Non-del(11q) N = 0**	**Arm C: FCR del(11q) N = 0**	**Arm D: FCR+L del(11q) N = 18**
Cycles Received, no. (%)	NA		NA	NA	
1		3 (4)			1 (6)
2		5 (7)			1 (6)
3		5 (7)			2 (11)
4		2 (3)			1 (6)
5		0 (0)			2 (11)
6		54 (78)			11 (61)

Abbreviations: FR indicates fludarabine in combination with rituximab; FR+L, fludarabine in combination with rituximab followed by lenalidomide consolidation; FCR, fludarabine in combination with cyclophosphamide and rituximab; FCR+L, fludarabine in combination with cyclophosphamide and rituximab followed by lenalidomide consolidation; and NA, not applicable.

Table S3: Grade 3-5 adverse events by treatment arm and del(11q) status.

Adverse event type	Group	Grade 3 no. (%)	Grade 4 no. (%)	Grade 5 no. (%)
Hematologic				
Blood/bone marrow - other	Arm A: FR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	2 (2)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	1 (3)	0 (0)	0 (0)
CD4 count	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	3 (3)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	1 (3)	0 (0)
Hemoglobin	Arm A: FR, non-del(11q)	15 (13)	3 (3)	0 (0)
	Arm B: FR+L, non-del(11q)	12 (11)	4 (4)	0 (0)
	Arm C: FCR, non-del(11q)	22 (21)	4 (4)	0 (0)
	Arm C: FCR, del(11q)	4 (15)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	2 (6)	2 (6)	0 (0)
Hemolysis	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	3 (3)	0 (0)	1 (1)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	2 (6)	1 (3)	0 (0)
Leukocytes (total WBC)	Arm A: FR, non-del(11q)	29 (25)	7 (6)	0 (0)
	Arm B: FR+L, non-del(11q)	22 (20)	12 (11)	0 (0)
	Arm C: FCR, non-del(11q)	22 (21)	11 (10)	0 (0)
	Arm C: FCR, del(11q)	6 (23)	3 (12)	0 (0)
	Arm D: FCR+L, del(11q)	6 (19)	3 (10)	0 (0)
Lymphopenia	Arm A: FR, non-del(11q)	25 (21)	11 (9)	0 (0)
	Arm B: FR+L, non-del(11q)	19 (18)	13 (12)	0 (0)
	Arm C: FCR, non-del(11q)	23 (22)	18 (17)	0 (0)
	Arm C: FCR, del(11q)	2 (8)	6 (23)	0 (0)
	Arm D: FCR+L, del(11q)	5 (16)	4 (13)	0 (0)
Neutrophils/granulocytes (ANC/AGC)	Arm A: FR, non-del(11q)	43 (37)	33 (28)	0 (0)
	Arm B: FR+L, non-del(11q)	35 (32)	42 (39)	0 (0)
	Arm C: FCR, non-del(11q)	30 (28)	44 (42)	0 (0)
	Arm C: FCR, del(11q)	9 (35)	13 (50)	0 (0)
	Arm D: FCR+L, del(11q)	8 (26)	14 (45)	0 (0)
Platelets	Arm A: FR, non-del(11q)	9 (8)	1 (1)	0 (0)
	Arm B: FR+L, non-del(11q)	9 (8)	4 (4)	0 (0)

	Arm C: FCR, non-del(11q)	15 (14)	7 (7)	0 (0)
	Arm C: FCR, del(11q)	3 (12)	1 (4)	0 (0)
	Arm D: FCR+L, del(11q)	3 (10)	1 (3)	0 (0)
Non-Hematologic				
Allergic reaction/hypersensitivity	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Autoimmune reaction	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Hearing loss	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Cardiac ischemia/infarction	Arm A: FR, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Cardiac troponin I (cTnI)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Hypertension	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	6 (6)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Hypotension	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	1 (1)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	1 (3)	0 (0)	0 (0)
Left ventricular diastolic dysfunction	Arm A: FR, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)

	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Left ventricular systolic dysfunction	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	1 (4)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Prolonged QTc interval	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Supraventricular and nodal arrhythmia	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	1 (4)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
INR	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
PTT (partial thromboplastin time)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	1 (4)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Fatigue (asthenia, lethargy, malaise)	Arm A: FR, non-del(11q)	4 (3)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	15 (14)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	11 (10)	1 (1)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Fever	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Insomnia	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)

	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Obesity	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	3 (3)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Rigors/chills	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Weight gain	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Death not associated with CTCAE term	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	1 (1)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	1 (1)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	1 (4)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Pruritus/itching	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Rash/desquamation	Arm A: FR, non-del(11q)	6 (5)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	4 (4)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	7 (7)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	2 (6)	0 (0)	0 (0)
Urticaria (hives, welts, wheals)	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Wound complication, non-infectious	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)

	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Anorexia	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Ascites (non-malignant)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Colitis	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Constipation	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	1 (4)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Dehydration	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Dental: periodontal disease	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q	0 (0)	0 (0)	0 (0)
Diarrhea	Arm A: FR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	5 (5)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Fistula, GI	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)

	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Heartburn/dyspepsia	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Hemorrhoids	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Nausea	Arm A: FR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	4 (4)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Perforation, GI	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Ulcer, GI	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Vomiting	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	1 (3)	0 (0)	0 (0)
Hemorrhage, GI	Arm A: FR, non-del(11q)	1 (1)	1 (1)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Cholecystitis	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)

	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Colitis, infectious	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Febrile neutropenia	Arm A: FR, non-del(11q)	14 (12)	1 (1)	0 (0)
	Arm B: FR+L, non-del(11q)	16 (15)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	17 (16)	2 (2)	0 (0)
	Arm C: FCR, del(11q)	3 (12)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	5 (16)	0 (0)	0 (0)
Infection - other	Arm A: FR, non-del(11q)	1 (1)	1 (1)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Infection w/ normal or Grade 1/2 ANC	Arm A: FR, non-del(11q)	4 (3)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	5 (5)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	4 (4)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Infection with Grade 3 or 4 ANC	Arm A: FR, non-del(11q)	5 (4)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	12 (11)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	7 (7)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Infection with unknown ANC	Arm A: FR, non-del(11q)	3 (3)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	3 (3)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	1 (4)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Opportunistic infection	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Edema: limb	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)

	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Edema: trunk/genital	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Lymphatics - other	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Lymphocele	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
ALT, SGPT	Arm A: FR, non-del(11q)	4 (3)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	6 (6)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	1 (1)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	1 (3)	0 (0)
AST, SGOT	Arm A: FR, non-del(11q)	4 (3)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	4 (4)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	1 (1)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	1 (3)	0 (0)
Acidosis (metabolic or respiratory)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Albumin, serum-low (hypoalbuminemia)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Alkaline phosphatase	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)

	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Amylase	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Bilirubin (hyperbilirubinemia)	Arm A: FR, non-del(11q)	1 (1)	1 (1)	0 (0)
	Arm B: FR+L, non-del(11q)	4 (4)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Calcium, serum-high (hypercalcemia)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Calcium, serum-low (hypocalcemia)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Cholesterol, serum-high	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Creatinine	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
GGT (gamma-glutamyl transpeptidase)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Glomerular filtration rate	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)

	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Glucose, serum-high (hyperglycemia)	Arm A: FR, non-del(11q)	3 (3)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	8 (7)	2 (2)	0 (0)
	Arm C: FCR, non-del(11q)	11 (10)	3 (3)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	1 (3)	0 (0)	0 (0)
Glucose, serum-low (hypoglycemia)	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Lipase	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Phosphate, serum-low (hypophosphatemia)	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	6 (6)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	1 (4)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	1 (3)	0 (0)	0 (0)
Potassium, serum-high (hyperkalemia)	Arm A: FR, non-del(11q)	1 (1)	1 (1)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Potassium, serum-low (hypokalemia)	Arm A: FR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	2 (6)	0 (0)	0 (0)
Sodium, serum-low (hyponatremia)	Arm A: FR, non-del(11q)	3 (3)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	4 (4)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	5 (5)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	2 (8)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Triglyceride, serum-high	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)

	Arm C: FCR, non-del(11q)	0 (0)	2 (2)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Uric acid, serum-high (hyperuricemia)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Arthritis (non-septic)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Fracture	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Muscle weakness (not due to neuropathy)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	1 (3)	0 (0)	0 (0)
Osteoporosis	FR in non-del(11q22.3)	0 (0)	0 (0)	0 (0)
	FR+L in non-del(11q22.3)	0 (0)	0 (0)	0 (0)
	FCR in non-del(11q22.3)	1 (1)	0 (0)	0 (0)
	FCR in del(11q22.3)	0 (0)	0 (0)	0 (0)
	FCR+L in del(11q22.3)	0 (0)	0 (0)	0 (0)
Cognitive disturbance	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Confusion	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Encephalopathy	Arm A: FR, non-del(11q)	0 (0)	0 (0)	1 (1)
	Arm B: FR+L, non-del(11q)	0 (0)	1 (1)	0 (0)

	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Mood alteration	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Neurology - other	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Neuropathy: sensory	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Personality/behavioral	Arm A: FR, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Seizure	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Speech impairment	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Syncope (fainting)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	3 (3)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Cataract	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)

	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Treatment related secondary malignancy	Arm A: FR, non-del(11q)	0 (0)	2 (2)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	2 (2)	2 (2)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	2 (6)	1 (3)	0 (0)
Pain	Arm A: FR, non-del(11q)	8 (7)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	12 (11)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	13 (12)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	2 (8)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Pain - other	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Aspiration	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Bronchospasm, wheezing	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Carbon monoxide diffusion capacity	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Cough	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Dyspnea (shortness of breath)	Arm A: FR, non-del(11q)	3 (3)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	4 (4)	2 (2)	0 (0)

	Arm C: FCR, non-del(11q)	3 (3)	2 (2)	0 (0)
	Arm C: FCR, del(11q)	2 (8)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Hypoxia	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	1 (1)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	2 (6)	0 (0)	0 (0)
Pneumonitis/pulmonary infiltrates	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	3 (3)	0 (0)	1 (1)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Pulmonary/upper respiratory - other	Arm A: FR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Cystitis	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	1 (1)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Renal failure	Arm A: FR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	3 (3)	1 (1)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Erectile dysfunction	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Cytokine release syndrome	Arm A: FR, non-del(11q)	2 (2)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Tumor lysis syndrome	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	1 (1)	0 (0)	0 (0)

	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Thrombosis/embolism (vascular access-relate)	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	1 (1)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	0 (0)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)
Thrombosis/thrombus/embolism	Arm A: FR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm B: FR+L, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, non-del(11q)	0 (0)	0 (0)	0 (0)
	Arm C: FCR, del(11q)	0 (0)	1 (4)	0 (0)
	Arm D: FCR+L, del(11q)	0 (0)	0 (0)	0 (0)

NOTE: (%) values are calculated out of the number of patients who started treatment and submitted at least one adverse event form for each group: FR in non-del(11q) (n=117), FR+L in non-del(11q) (n=109), FCR in non-del(11q) (n=106), FCR in del(11q) (n=26), FCR+L in del(11q) (n=31).
Abbreviations: FR indicates fludarabine in combination with rituximab; FR+L, fludarabine in combination with rituximab followed by lenalidomide consolidation; FCR, fludarabine in combination with cyclophosphamide and rituximab; and FCR+L, fludarabine in combination with cyclophosphamide and rituximab followed by lenalidomide consolidation.

Table S4: New primary or new secondary malignancies by treatment arm and del(11q) status

Malignancies	Arm A: FR Non-del(11q) N = 123	Arm B: FR+L Non-del(11q) N = 109	Arm C: FCR Non-del(11q) N = 110	Arm C: FCR del(11q) N = 27	Arm D: FCR+L del(11q22.3) N = 31
Any Occurrence, no. (%)					
No	98 (80)	91 (83)	88 (80)	21 (78)	23 (74)
Yes	25 (20)	18 (17)	22 (20)	6 (22)	8 (26)
Type, no. of patients*					
Bladder cancer	2	0	0	0	0
Breast cancer	1	0	0	0	0
Endometrial cancer	1	0	0	0	0
GI cancer	1	1	3	1	1
Head and neck cancer	1	1	0	0	0
Kidney cancer	1	0	0	0	1
Lung cancer	1	3	1	0	1
Melanoma	2	2	4	0	1
Prostate cancer	0	2	2	0	0
Squamous/basal cell skin cancer	11	8	8	3	3
Sarcoma cancer	0	0	1	0	0
Treatment-related AML/MDS	3	1	1	1	2
Richter's transformation	4	2	1	1	0
Other blood cancers	1	0	1	0	0

*Not mutually exclusive as 7 patients had two types of secondary malignancies. Non-del(11q22.3) FR: AML/MDS transformation and squamous/ basal cell skin cancer in 1, AML/MDS and Richter's transformation in 1, melanoma and squamous/ basal cell skin cancer in 1, GI and breast cancer in 1; Non-del(11q22.3) FR+L: prostate and squamous/basal cell skin cancer in 2; del(11q22.3) FCR+L: melanoma and squamous/ basal cell skin cancer in 1. Abbreviations: FR indicates fludarabine in combination with rituximab; FR+L, fludarabine in combination with rituximab followed by lenalidomide consolidation; FCR, fludarabine in combination with cyclophosphamide and rituximab; and FCR+L, fludarabine in combination with cyclophosphamide and rituximab followed by lenalidomide consolidation.

Table S5: Best response by treatment arm and del(11q) status.

Group	N	Overall Response Rate	Exact 90% Confidence Interval	Complete Response Rate	Exact 90% Confidence Interval
Arm A: FR, non-del(11q)	123	75%	68-81%	32%	25-39%
Arm B: FR+L, non-del(11q)	109	69%	61-76%	32%	25-40%
Arm C: FCR, non-del(11q)	110	71%	63-78%	51%	43-59%
Arm C: FCR, del(11q)	27	59%	42-75%	19%	8-35%
Arm D: FCR+L, del(11q)	31	74%	58-86%	35%	21-52%

Abbreviations: FR indicates fludarabine in combination with rituximab; FR+L, fludarabine in combination with rituximab followed by lenalidomide consolidation; FCR, fludarabine in combination with cyclophosphamide and rituximab; and FCR+L, fludarabine in combination with cyclophosphamide and rituximab followed by lenalidomide consolidation.

TABLE S6 Univariable and multivariable logistic regression models for overall response.

Number of Evaluable Patients N = 273	Univariable Models*			Multivariable Model†		
Modeling the effect of:	**Odds Ratio**	**95% CI**	**P**	**Odds Ratio**	**95% CI**	**P‡**
Age at study entry, years (≥ 65 vs < 65)	0.68	(0.39-1.17)	0.16	0.81	(0.42-1.56)	0.52
Sex (female vs male)	2.03	(1.11-3.70)	0.02	2.00	(0.97-4.13)	0.06
Rai stage						
II vs I	0.46	(0.18-1.16)	0.10	---	---	---
III vs I	0.25	(0.09-0.66)	0.005			
IV vs I	0.29	(0.11-0.72)	0.008			
ECOG PS (1/2 vs 0)	1.14	(0.67-1.96)	0.63	---	---	---
Prior cancer treatment (yes vs no)	1.08	(0.21-5.46)	0.93	---	---	---
Hemoglobin, 1 unit increase	1.15	(1.01-1.32)	0.03	1.03	(0.84-1.26)	0.78
Platelet, 50 unit increase	1.27	(1.02-1.60)	0.04	1.07	(0.79-1.44)	0.68
Log_2(WBC), 2-fold increase	0.88	(0.74-1.05)	0.15	1.02	(0.82-1.25)	0.89
Abnormal B2M (yes vs no)	0.45	(0.19-1.05)	0.07	0.70	(0.25-1.98)	0.51
Abnormal LDH (yes vs no)	1.37	(0.80-2.36)	0.25	---	---	---
Abnormal serum creatinine (yes vs no)	0.69	(0.29-1.61)	0.39	---	---	---
Spleen involvement (yes vs no)	0.78	(0.45-1.34)	0.36	---	---	---
Liver involvement (yes vs no)	0.58	(0.20-1.65)	0.30	---	---	---
Bulky lymphadenopathy > 5 cm (yes vs no)	1.10	(0.59-2.04)	0.76	---	---	---
Hierarchical cytogenetic classification						
del(17p) vs del(13q)	0.24	(0.10-0.56)	0.001	0.20	(0.08-0.50)	0.0007
del(11q)§ vs del(13q)	1.39	(0.36-5.39)	0.63	1.36	(0.33-5.62)	0.67
Trisomy12 vs del(13q)	2.82	(1.21-6.57)	0.02	3.24	(1.33-7.89)	0.01
None vs del(13q)	2.18	(0.96-4.96)	0.06	2.60	(1.08-6.22)	0.03
Treatment Group						
FR+L vs FR	0.68	(0.36-1.31)	0.25	0.64	(0.30-1.33)	0.23
FCR vs FR	0.92	(0.47-1.80)	0.81	0.71	(0.33-1.55)	0.39

* Univariable logistic regression models were constructed for each predictor.

† One multivariable logistic regression model, stratifying on Rai stage and containing treatement arm and all predictors with $p < 0.20$ from the univariable models was constructed, with each predictor adjusted for all others in the model.

‡ Two-sided Wald χ^2 p-values.

§ The del(11q) category includes patients without del(17p) in accordance with the Dohner hierarchical classification for cytogenetics, but only for those patients with del(11q) detected in more than 2.3% of cells (above background) and in less than 20% of cells.

Abbreviations: CI indicates confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; WBC, white blood cell count; B2M, beta-2 microglobulin; LDH, lactate dehydrogenase; FR, fludarabine in combination with rituximab; FR+L, fludarabine in combination with rituximab followed by lenalidomide consolidation; and FCR, fludarabine in combination with cyclophosphamide and rituximab.

TABLE S7. Univariable and multivariable Cox models for progression-free survival

Number of Evaluable Patients N = 273	**Univariable Models***			**Multivariable Model†**		
Modeling the effect of:	**Hazard Ratio**	**95% CI**	**P‡**	**Hazard Ratio**	**95% CI**	**P‡**
Age at study entry, years (≥ 65 vs < 65)	0.99	(0.69-1.41)	0.95	---	---	---
Sex (female vs male)	0.69	(0.48-0.99)	0.04	0.77	(0.51-1.15)	0.21
Rai stage						
II vs I	1.03	(0.64-1.65)	0.92	---	---	---
III vs I	1.25	(0.72-2.17)	0.43			
IV vs I	1.23	(0.76-1.99)	0.40			
ECOG PS (1/2 vs 0)	1.19	(0.85-1.67)	0.31	---	---	---
Prior cancer treatment (yes vs no)	1.08	(0.40-2.92)	0.88	---	---	---
Hemoglobin, 1 unit increase	0.98	(0.90-1.07)	0.63	---	---	---
Platelet, 50 unit increase	0.93	(0.82-1.06)	0.27	---	---	---
Log_2(WBC), 2-fold increase	1.26	(1.12-1.41)	<0.0001	1.24	(1.08-1.42)	0.002
Abnormal B2M (yes vs no)	2.01	(1.19-3.39)	0.009	1.37	(0.70-2.69)	0.12
Abnormal LDH (yes vs no)	1.32	(0.94-1.85)	0.11	1.12	(0.74-1.69)	0.61
Abnormal serum creatinine (yes vs no)	1.57	(0.96-2.58)	0.08	1.78	(0.99-3.19)	0.05
Spleen involvement (yes vs no)	1.12	(0.80-1.56)	0.52	---	---	---
Liver involvement (yes vs no)	1.55	(0.84-2.87)	0.17	1.11	(0.53-2.31)	0.79
Bulky lymphadenopathy > 5 cm (yes vs no)	1.38	(0.96-1.98)	0.08	1.65	(1.11-2.45)	0.01
Hierarchical cytogenetic classification						
del(17p) vs del(13q)			<0.0001			<0.0001
at 1 year	3.75	(2.16-6.50)		3.81	(2.10-6.91)	
at 2 years	2.48	(1.36-4.52)		2.39	(1.24-4.61)	
at 3 years	1.95	(0.95-4.00)		1.82	(0.83-3.99	
at 4 years	1.64	(0.72-3.75)		1.50	(0.61-3.69)	
at 5 years	1.44	(0.57-3.60)		1.29	(0.48-3.50)	
del(11q)§ vs del(13q)			0.001			0.0004
at 1 year	1.14	(0.34-3.79)		1.27	(0.36-4.44)	
at 2 years	2.38	(1.20-4.73)		2.85	(1.39-5.82)	
at 3 years	3.67	(1.81-7.43)		4.56	(2.15-9.68)	
at 4 years	4.98	(2.05-12.09)		6.37	(2.46-16.49)	
at 5 years	6.31	(2.15-18.56)		8.26	(2.60-26.27)	
Trisomy 12 vs del(13q)			0.28			0.34
at 1 year	0.55	(0.25-1.18)		0.57	(0.27-1.22)	
at 2 years	0.77	(0.48-1.25)		0.69	(0.41-1.18)	
at 3 years	0.94	(0.59-1.51)		0.77	(0.45-1.33)	
at 4 years	1.09	(0.63-1.88)		0.83	(0.45-1.55)	
at 5 years	1.21	(0.64-2.30)		0.89	(0.44-1.79)	
None vs del(13q)			0.03			0.01
at 1 year	0.19	(0.06-0.64)		0.19	(0.06-0.61)	
at 2 years	0.41	(0.21-0.81)		0.37	(0.18-0.73)	
at 3 years	0.64	(0.37-1.10)		0.55	(0.31-0.96)	
at 4 years	0.88	(0.49-1.59)		0.72	(0.39-1.35)	
at 5 years	1.13	(0.56-2.30)		0.90	(0.43-1.88)	

Number of Evaluable Patients N = 273	**Univariable Models***			**Multivariable Model†**		
Modeling the effect of:	**Hazard Ratio**	**95% CI**	**P‡**	**Hazard Ratio**	**95% CI**	**P‡**
Treatment Group						
FR+L vs FR			0.14			0.02
at 1 year	0.93	(0.55-1.57)		0.84	(0.48-1.47)	
at 2 years	0.76	(0.51-1.12)		0.63	(0.41-0.97)	
at 3 years	0.67	(0.44-1.02)		0.53	(0.34-0.85)	
at 4 years	0.62	(0.38-0.99)		0.48	(0.28-0.81)	
at 5 years	0.58	(0.34-0.99)		0.43	(0.24-0.79)	
FCR vs FR			0.0002			<0.0001
at 1 year	0.73	(0.43-1.23)		0.77	(0.44-1.35)	
at 2 years	0.48	(0.31-0.74)		0.44	(0.28-0.71)	
at 3 years	0.38	(0.23-0.61)		0.32	(0.19-0.53)	
at 4 years	0.32	(0.18-0.55)		0.26	(0.14-0.46)	
at 5 years	0.28	(0.15-0.51)		0.21	(0.11-0.41)	

*Univariable Cox models were constructed for each predictor. If a variable violated the assumption of proportional hazards, the hazard ratio was allowed to vary over time and hazard ratio estimates are provided with 95% confidence intervals are provided at specific time points.

† One multivariable Cox model, stratifying on Rai stage and containing all predictors with $p < 0.20$ from the univariable models was constructed, with each predictor adjusted for all others in the model.

‡Two-sided Wald χ^2 p-values.

§ The del(11q) category includes patients without del(17p) in accordance with the Dohner hierarchical classification for cytogenetics, but only for those patients with del(11q) detected in more than 2.3% of cells (above background) and in less than 20% of cells.

Abbreviations: CI indicates confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; WBC, white blood cell count; B2M, beta-2 microglobulin; LDH, lactate dehydrogenase; FR, fludarabine in combination with rituximab; FR+L, fludarabine in combination with rituximab followed by lenalidomide consolidation; and FCR, fludarabine in combination with cyclophosphamide and rituximab.

TABLE S8. Univariable and multivariable Cox models for overall survival

Number of evaluable patients N = 273	**Univariable Models***			**Multivariable Model†**		
Modeling the effect of:	**Hazard Ratio**	**95% CI**	**P‡**	**Hazard Ratio**	**95% CI**	**P‡**
Age at study entry, years (≥ 65 vs < 65)	2.89	(1.77-4.73)	<0.0001	2.76	(1.58-4.83)	0.0004
Sex (female vs male)	0.53	(0.30-0.95)	0.03	0.70	(0.36-1.33)	0.27
Rai stage						
II vs I	1.93	(0.87-4.27)	0.11	---	---	---
III vs I	2.38	(1.01-5.63)	0.05			
IV vs I	1.68	(0.73-3.86)	0.22			
ECOG PS (1/2 vs 0)	1.60	(0.98-2.60)	0.06	1.58	(0.92-2.71)	0.10
Prior cancer treatment (yes vs no)	1.09	(0.27-4.45)	0.91	---	---	---
Hemoglobin, 1 unit increase	0.90	(0.80-1.02)	0.09	0.99	(0.82-1.19)	0.88
Platelet, 50 unit increase	0.92	(0.76-1.11)	0.37	---	---	---
Log_2(WBC), 2-fold increase	1.10	(0.94-1.29)	0.22	---	---	---
Abnormal B2M (yes vs no)	3.40	(1.24-9.35)	0.02	1.29	(0.43-3.83)	0.65
Abnormal LDH (yes vs no)	1.63	(0.99-2.68)	0.06	1.47	(0.83-2.62)	0.19
Abnormal serum creatinine (yes vs no)	2.47	(1.34-4.54)	0.004	1.38	(0.66-2.86)	0.39
Spleen involvement (yes vs no)	1.17	(0.72-1.90)	0.52	---	---	---
Liver involvement (yes vs no)	2.00	(0.91-4.40)	0.08	1.07	(0.40-2.86)	0.89
Bulky lymphadenopathy > 5 cm (yes vs no)	1.41	(0.84-2.37)	0.19	1.74	(0.97-3.12)	0.07
Hierarchical cytogenetic classification						
del(17p) vs del(13q)	3.65	(1.96-6.81)	<0.0001	3.70	(1.86-7.33)	0.0002
del(11q)§ vs del(13q)	0.75	(0.18-3.16)	0.69	1.23	(0.28-5.43)	0.79
Trisomy 12 vs del(13q)	0.99	(0.51-1.95)	0.98	0.72	(0.34-1.53)	0.40
None vs del(13q)	0.84	(0.40-1.76)	0.65	0.76	(0.35-1.63)	0.47
Treatment Group						
FR+L vs FR			0.03			0.01
at 1 year	2.34	(0.65-8.37)		2.53	(0.63-10.06)	
at 2 years	1.08	(0.48-2.43)		1.03	(0.44-2.45)	
at 3 years	0.69	(0.35-1.36)		0.61	(0.30-1.26)	
at 4 years	0.50	(0.25-1.02)		0.42	(0.20-0.89)	
at 5 years	0.39	(0.18-0.86)		0.32	(0.14-0.73)	
FCR vs FR			0.16			0.12
at 1 year	2.83	(0.81-9.90)		3.57	(0.91-13.98)	
at 2 years	1.54	(0.72-3.29)		1.76	(0.76-4.06)	
at 3 years	1.08	(0.60-1.96)		1.16	(0.60-2.25)	
at 4 years	0.84	(0.46-1.53)		0.87	(0.45-1.67)	
at 5 years	0.69	(0.35-1.36)		0.69	(0.33-1.44)	

*Univariable Cox models were constructed for each predictor. If a variable violated the assumption of proportional hazards, the hazard ratio was allowed to vary over time and hazard ratio estimates are provided with 95% confidence intervals are provided at specific time points.

† One multivariable Cox model, statifying on Rai stage and containing all predictors with $p < 0.20$ from the univariable models was constructed, with each predictor adjusted for all others in the model.

‡Two-sided Wald χ^2 p-values.

§ The del(11q) category includes patients without del(17p) in accordance with the Dohner hierarchical classification for cytogenetics, but only for those patients with del(11q) detected in more than 2.3% of cells (above background) and in less than 20% of cells.

Abbreviations: CI indicates confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; WBC, white blood cell count; B2M, beta-2 microglobulin; LDH, lactate dehydrogenase; FR, fludarabine in combination with rituximab; FR+L, fludarabine in combination with rituximab followed by lenalidomide consolidation; and FCR, fludarabine in combination with cyclophosphamide and rituximab.

TABLE S9: Best response, progression-free survival (PFS), and overall survival (OS) by treatment arm and del(11q) status for patients aged 65 years or older.

Endpoint	Arm A: FR Non-del(11q) N = 43	Arm B: FR+L Non-del(11q) N = 42	Arm C: FCR Non-del(11q) N = 40	Arm C: FCR del(11q) N = 9	Arm D: FCR+L del(11q) N = 10
CR rate (95% CI)	37% (23-53%)	31% (18-47%)	48% (32-64%)	11% (<1-48%)	50% (19-81%)
ORR (95% CI)	72% (56-85%)	67% (50-80%)	60% (43-75%)	44% (14-79%)	80% (44-97%)
PFS					
Number of events	21	19	23	5	6
Median, mo. (95% CI)	58 (29-NR)	66 (40-NR)	55 (26-97)	61 (1-NR)	36 (3-NR)
% at 5 years (95% CI)	48 (30-63)	50 (32-66)	41 (25-57)	62 (21-86)	29 (5-60)
OS					
Number of events	18	13	16	4	6
Median, mo. (95% CI)	85 (59-NR)	NR	101 (54-NR)	70 (2-NR)	37 (7-NR)
% at 5 years (95% CI)	66 (50-78)	73 (57-84)	66 (49-79)	78 (36-94)	40 (12-67)

Abbreviations: FR indicates fludarabine in combination with rituximab; FR+L, fludarabine in combination with rituximab followed by lenalidomide consolidation; FCR, fludarabine in combination with cyclophosphamide and rituximab; FCR+L, fludarabine in combination with cyclophosphamide and rituximab followed by lenalidomide consolidation; CR, complete response, ORR, overall response rate; mo, months; and NR, not reached.

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