

Patterns of Care in Medical Oncology

Chronic Lymphocytic Leukemia

CASE 3: A 74-year-old woman is diagnosed with asymptomatic CLL in 2000 with a white blood cell count of 15,000/mm³ and is initially observed. After 7 years of active surveillance, at age 81 she develops progressive fatigue and anemia (Hb 8.0 g/dL). Cytogenetic testing shows CLL with 17p deletion.

The patient undergoes transfusion and receives R-CVP x 4 with a near-complete response and becomes transfusion independent. Consolidation alemtuzumab is administered x 6 weeks. She fares well for approximately 2 years and then develops progressive lymphocytosis and anemia. She is being considered for treatment with rituximab/bendamustine followed by alemtuzumab consolidation.

— Dr Friedberg

For a patient with CLL who is asymptomatic without bulky disease, anemia or thrombocytopenia and has a slow lymphocyte doubling time, is there an absolute white blood cell count that you use to initiate treatment?

	CI	PO
% responding no	96%	80%

Do you routinely order cytogenetic testing for your patients with CLL...

	At first diagnosis?		At time of first relapse?	
	CI	PO	CI	PO
Yes, usually	87%	80%	38%	54%
Yes, occasionally	13%	16%	21%	25%
No	0%	4%	41%	21%

In otherwise healthy younger patients with CLL, which of the following cytogenetics or biomarkers do you consider when making your initial treatment decision?

	CI	PO
del(17p)	76%	75%
del(11q)	40%	39%
ZAP-70	36%	52%
CD38 antigen	32%	49%
del(13q)	32%	41%
IgVH gene status	28%	45%
t (11q;v)	8%	16%
I do not consider cytogenetics/biomarkers	24%	17%

What is your usual preferred initial regimen for a 60-year-old patient with CLL requiring treatment?

	Normal cytogenetics		Chromosome 17p deletion	
	CI	PO	CI	PO
FCR	68%	68%	54%	61%
FR	28%	17%	4%	5%
Rituximab/bendamustine	4%	8%	4%	12%
Alemtuzumab	—	—	25%	20%
Other	0%	7%	12%	2%

Phase III trial of combined immunochemotherapy versus bendamustine and rituximab as up-front treatment for CLL

Protocol IDs: GCLLSG-CLL10, EUDRACT-2007-007587-21, EU-20883

Target Accrual: 550

Eligibility

B-cell CLL with Binet Stage C, or Stage B or A requiring treatment (B symptoms; progressive lymphocytosis; progressive marrow failure; massive, progressive or painful splenomegaly or hypersplenism; massive lymph nodes or lymph node clusters)

R

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graph LR; R((R)) --> A[Fludarabine + cyclophosphamide + rituximab x 6]; R --> B[Bendamustine + rituximab x 6];
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**Fludarabine +
cyclophosphamide +
rituximab x 6**

**Bendamustine +
rituximab x 6**

Primary Endpoint: Progression-free survival rate after 24 months

What is your usual preferred initial regimen for a 75-year-old patient with CLL requiring treatment?

	Normal cytogenetics	
	CI	PO
FR	52%	33%
Rituximab/bendamustine	40%	29%
Chlorambucil	4%	15%
FCR	4%	12%
Single-agent rituximab	0%	9%
Other	0%	2%

What is your usual preferred initial regimen for a 75-year-old patient with CLL requiring treatment? (continued)

	Chromosome 17p deletion	
	CI	PO
FR	17%	21%
Rituximab/bendamustine	33%	31%
Chlorambucil	4%	6%
FCR	13%	23%
Alemtuzumab	25%	15%
Other	8%	4%

Effect of the addition of rituximab (R) to fludarabine (F) and cyclophosphamide (C) on survival for patients with CLL: A Phase III trial

	FCR (n = 408)	FC (n = 409)	Hazard ratio	p-value
3-year progression-free survival	65%	45%	0.56	<0.0001
3-year overall survival	87%	83%	0.67	0.01
Grade 3/4 neutropenia	34%	21%	—	<0.0001
Grade 3/4 leukocytopenia	24%	12%	—	<0.0001

When administering rituximab up front either alone or with chemotherapy for a patient with CLL, what dose and schedule do you generally use?

	CI	PO
375 mg/m² q four-weekly	52%	41%
375 mg/m² initially followed by 500 mg/m² q four-weekly	32%	18%
375 mg/m² q weekly	8%	30%
500 mg/m² q four-weekly	0%	11%
Other	4%	0%
I have not administered rituximab up front alone nor with chemotherapy for patients with CLL	4%	0%

Phase II multicenter trial of bendamustine/rituximab in advanced untreated CLL (N = 117, median age: 64)

OR	CR	PR/nodular PR	SD
90.9%	32.7%	58.2%	9.1%

OR = overall response; CR = complete response; PR = partial response;
SD = stable disease

What second-line treatment would you most often recommend for a patient with CLL who experiences disease progression 18 months after completion of a course of FR?

	CI	PO
Bendamustine with or without rituximab	76%	59%
FCR	12%	12%
PCR	8%	3%
Alemtuzumab	4%	10%
Repeat FR	0%	14%
Ofatumumab	0%	2%

Phase II study of lenalidomide as initial treatment for CLL in elderly patients (N = 60)

	NCI Working Group 2008 response	
	Patients, n	%
Complete response (CR)	6	10
CR with incomplete blood cell count recovery	3	5
Partial response (PR)	25	42
Nodular PR	3	5
Overall response rate	37	62

Phase II study of lenalidomide for patients with relapsed or refractory CLL (N = 45)

Response	Patients, n	%
Overall response	21	47
Complete response	4	9
Partial response	17	38
Stable disease	8	18
Not assessable	12	27
Early for assessment response	4	9

During the past year, have you administered any of the following treatments to your patients with CLL? (Check all that apply)

	CI	PO
Rituximab + chemotherapy	100%	97%
Bendamustine +/- rituximab	92%	88%
Alemtuzumab	68%	60%
Chlorambucil	50%	59%
Ofatumumab	48%	21%
Lenalidomide	40%	34%
Rituximab monotherapy	32%	67%