

Real-world treatment and outcomes among older adults with chronic lymphocytic leukemia before the novel agents era

Anthony Mato,¹ Jordan Jahnke,² Pengxiang Li,^{2,3} Maneesha Mehra,⁴ Vrushabh P. Ladage,² Michelle Mahler,⁵ Scott Huntington⁶ and Jalpa A. Doshi^{2,3}

¹Memorial Sloan Kettering Cancer Center, New York, NY; ²Division of General Internal Medicine, University of Pennsylvania, Philadelphia, PA; ³Leonard Davis Institute of Health Economics, Philadelphia, PA; ⁴Janssen Global Services, LLC, Raritan, NJ; ⁵Janssen Research & Development, Raritan, NJ and ⁶Department of Internal Medicine, Yale School of Medicine, New Haven, CT, USA

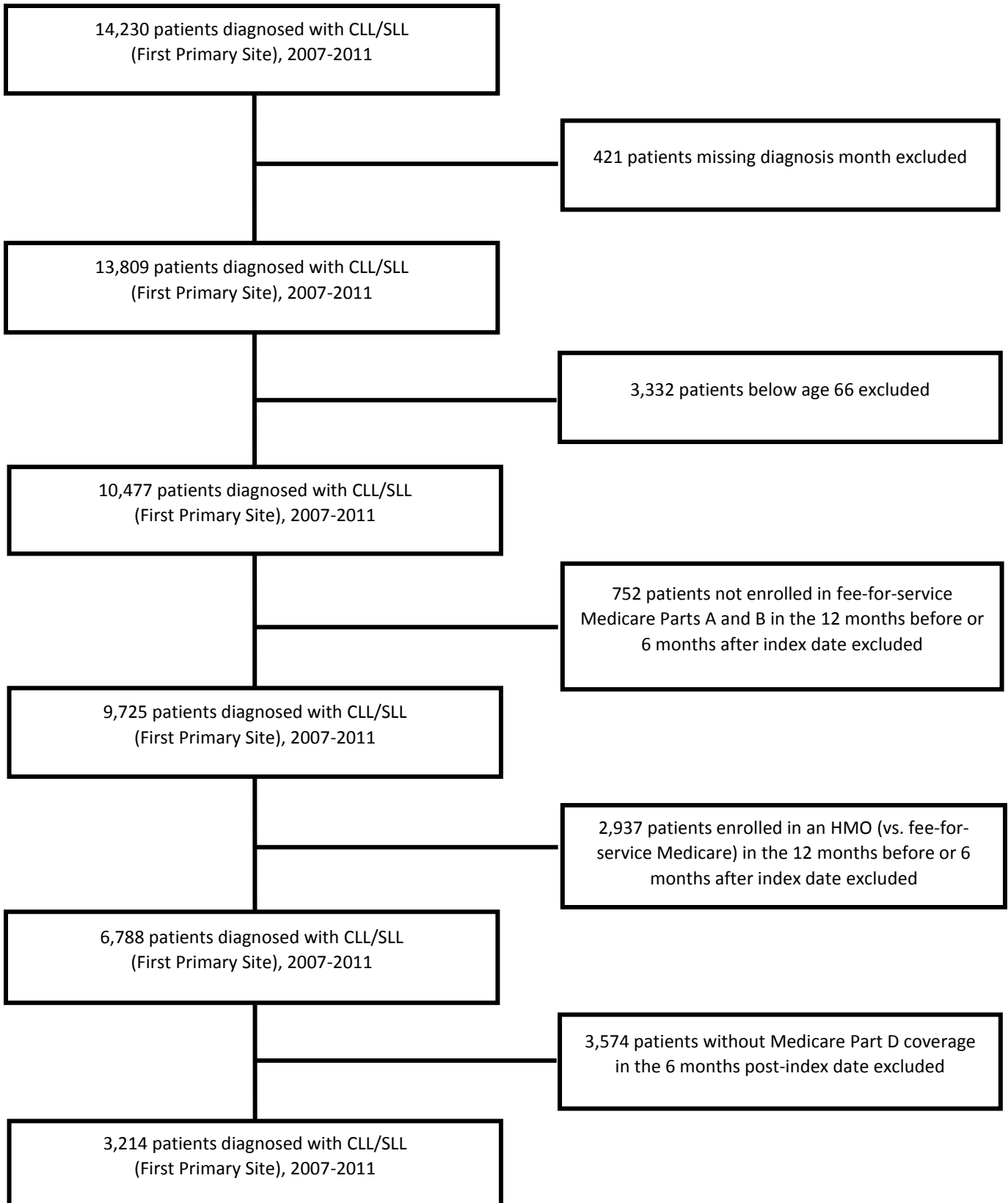
*Correspondence: jdoshi@penmedicine.upenn.edu
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Appendix

Appendix Table 1. FDA-Approved Drugs for Chronic Lymphocytic Leukemia Included in the Study

	Generic Name	Brand Name	Route(s) of Administration	Medicare Coverage	First FDA Approval Date
1	alemtuzumab	Campath	IV	B	May 2001
2	bendamustine	Treanda	IV	B/D	October 2008
3	chlorambucil	Luekeran	Oral	D	March 1957
4	cladribine	Leustatin	IV	B	February 1993
5	cyclophosphamide	Cytoxan	IV/Oral	B/D	November 1959
6	cytarabine	Depocyt	IV	B	August 1999
7	doxorubicin	Doxil	IV	B	June 1999
8	fludarabine	Fludara	IV	B	April 1991
9	ibrutinib	Impruvica	Oral	D	November 2013
10	idelalisib	Zydelig	Oral	D	July 2014
11	lenalidomide	Revlimid	Oral	D	October 2005
12	obinutuzumab	Gazyva	IV	B	November 2013
13	ofatumumab	Arzerra	IV	B	October 2009
14	oxaliplatin	Eloxatin	IV	B	August 2002
15	pentostatin	Nipent	IV	B	October 1991
16	rituximab	Rituxan	IV	B	November 1997
17	vincristine	Oncovin	IV	B	July 1963

Appendix Figure 1. Sample Selection Flowchart



Appendix Table 2. Sample Characteristics for Elderly Medicare Patients Newly Diagnosed with Chronic Lymphocytic Leukemia, by Age Group

Characteristic	All CLL patients (N = 3,214)		Age <75 (n = 1,243)		Age ≥75 (n = 1,971)		P
	n	%	n	%	n	%	
Age, mean (SD)	78.0	8.0	70.0	2.6	83.0	5.7	
Male	1,567	48.8	706	56.8	861	43.2	<.001
Race							.547
White	2,873	89.4	1,106	89.0	1,767	89.7	
Non-white	341	10.6	137	11.0	204	10.4	
Region							<.001
Northeast	725	22.6	238	19.2	487	24.7	
Midwest	434	13.5	156	12.6	278	14.1	
South	779	24.2	311	25.0	468	23.7	
West	1,276	39.7	538	42.2	738	37.4	
Part D Low-Income Subsidy status							.003
None	2,306	71.7	929	74.7	1,377	69.9	
Full or Partial	908	27.2	314	25.3	594	30.1	
Specific comorbidities							
Anemia/thrombocytopenia	964	30.0	295	23.7	669	33.9	<.001
Cognitive	758	23.6	237	19.1	521	26.4	<.001
Cardiovascular	2,609	81.2	943	75.9	1,666	84.5	<.001
Infection	329	10.2	96	7.7	233	11.8	<.001
Musculoskeletal	1,034	32.2	362	29.1	672	34.1	.003
Renal failure	175	5.4	53	4.3	122	6.2	.019
NCI comorbidity index, mean (SD)	0.79	1.2	0.65	1.1	0.87	1.3	<.001
Claims-based disability status*	500	15.6	102	8.2	398	12.4	<.001
Year of CLL diagnosis							.289
2007	648	20.2	250	20.1	398	20.1	
2008	684	21.3	253	20.4	431	20.4	
2009	662	20.6	242	19.5	420	19.5	
2010	640	19.9	255	20.5	385	20.5	
2011	580	18.0	243	19.6	337	19.6	

*Claims-based prediction for disability status, a proxy measure for the Eastern Cooperative Oncology Group (ECOG) performance status scale

Appendix Table 3. Characteristics of Medicare Patients Newly Diagnosed with Chronic Lymphocytic Leukemia, by Treatment Status

Characteristics	All CLL Patients (N = 3,214)		CLL Patients Initiating First-Line Treatment (n = 1,047)		CLL Patients Initiating Second-Line Treatment (n = 387)	
	n	%	n	%	n	%
Age						
<75 years	1,243	38.6	476	45.5	176	45.5
≥75 years	1,971	61.4	571	54.5	211	54.5
Gender, male	1,567	48.8	541	51.7	187	48.3
Race						
White	2,873	89.4	926	88.4	342	88.4
Non-white	341	6.0	121	6.1	45	11.6
Region						
Midwest	434	13.5	135	12.9	51	13.2
Northeast	725	22.6	214	20.4	78	20.2
South	779	24.2	278	26.6	98	25.3
West	1,276	39.7	420	40.1	160	41.3
Part D Low-Income Subsidy Status						
None	2,306	71.7	778	74.3	294	76.0
Full or Partial	908	27.2	269	24.7	93	24.0
Specific comorbidities						
Cognitive	758	23.6	181	17.3	60	15.5
Cardiovascular	2,609	81.2	826	74.3	300	77.5
Infection	329	10.2	79	7.5	23	5.9
Musculoskeletal	1,034	32.2	319	27.4	108	27.9
Renal failure	175	5.4	49	4.7	14	3.6
Anemia/Thrombocytopenia	964	30.0	314	27.4	115	29.7
NCI comorbidity index, mean (SD)	0.79	1.2	0.65	37.9	0.55	36.2
Claims-based disability status*	500	15.6	75	74.3	20	5.2
Year of CLL diagnosis						
2007	648	20.2	245	23.4	118	30.5
2008	684	21.3	231	22.1	87	22.5
2009	662	20.6	230	22.0	91	23.5
2010	640	19.9	191	18.2	56	14.5
2011	580	18.0	150	14.3	35	9.0
First-line treatment						
Chlorambucil only	N/A		163	15.6	63	16.3
Rituximab only	N/A		268	25.6	125	32.3
Rituximab containing chemoimmunotherapy combination	N/A		510	48.7	155	40.0
Other chemotherapy	N/A		106	10.1	44	11.4
Second-line treatment						

Chlorambucil only	N/A	N/A	35	9.0
Rituximab only	N/A	N/A	118	30.5
Rituximab containing chemoimmunotherapy combination	N/A	N/A	158	40.8
Other chemotherapy	N/A	N/A	76	19.6

*Claims-based prediction for disability status, a proxy measure for the Eastern Cooperative Oncology Group (ECOG) performance status scale

Appendix Table 4. Multivariate Cox Regression Results for Overall and CLL-Specific Survival

Characteristics	Overall Mortality from First-Line Treatment Date (N = 1,047)	Overall Mortality from Second-Line Treatment Date (N = 387)	CLL-Specific Mortality from First-Line Treatment Date (N = 1,047)	CLL-Specific Mortality from Second-Line Treatment Date (N = 387)
Age, years				
<75	Reference	Reference	Reference	Reference
≥75	1.81 (1.46 to 2.24)	1.53 (1.1 to 2.13)	1.81 (1.34 to 2.44)	1.86 (1.15 to 2.99)
Male	1.56 (1.28 to 1.91)	1.47 (1.06 to 2.03)	1.42 (1.07 to 1.88)	1.40 (0.89 to 2.19)
Race				
White	Reference	Reference	Reference	Reference
Non-white	1.01 (0.74 to 1.38)	0.88 (0.53 to 1.47)	1.14 (0.75 to 1.75)	0.79 (0.37 to 1.66)
Region				
Midwest	1.17 (0.85 to 1.60)	1.07 (0.64 to 1.77)	1.27 (0.84 to 1.92)	1.26 (0.66 to 2.41)
Northeast	1.52 (1.18 to 1.96)	1.68 (1.13 to 2.51)	1.21 (0.83 to 1.75)	1.28 (0.69 to 2.38)
South	1.08 (0.84 to 1.39)	1.06 (0.70 to 1.61)	1.05 (0.74 to 1.49)	1.33 (0.77 to 2.32)
West	Reference	Reference	Reference	Reference
Part D Low-Income Subsidy status				
None	Reference	Reference	Reference	Reference
Full or partial	1.31 (1.03 to 1.67)	1.33 (0.89 to 1.98)	1.21 (0.86 to 1.68)	1.32 (0.77 to 2.25)
NCI comorbidity score	1.15 (1.05 to 1.27)	1.11 (0.94 to 1.30)	1.13 (0.99 to 1.29)	1.18 (0.96 to 1.46)
Disabled	1.66 (1.16 to 2.37)	1.68 (0.83 to 3.42)	1.62 (0.99 to 2.65)	1.83 (0.72 to 4.63)
Comorbidities				
Anemia/thrombocytopenia	1.00 (0.80 to 1.24)	1.07 (0.74 to 1.55)	1.01 (0.75 to 1.37)	1.09 (0.65 to 1.81)
Cognitive	1.03 (0.79 to 1.34)	0.77 (0.49 to 1.23)	1.04 (0.73 to 1.50)	0.53 (0.27 to 1.07)
Cardiovascular	1.31 (1.00 to 1.71)	1.11 (0.73 to 1.68)	1.37 (0.94 to 2.00)	1.17 (0.66 to 2.07)
Infection	1.04 (0.73 to 1.48)	1.20 (0.64 to 2.23)	1.09 (0.68 to 1.75)	1.58 (0.73 to 3.44)
Musculoskeletal	1.24 (0.79 to 1.94)	0.66 (0.45 to 0.98)	0.80 (0.59 to 1.08)	0.64 (0.37 to 1.12)
Renal failure	1.25 (0.80 to 1.97)	1.23 (0.50 to 3.03)	0.92 (0.45 to 1.85)	0.40 (0.05 to 3.27)
Time to treatment (months)	1.00 (0.99 to 1.01)	1.01 (1.00 to 1.02)	0.98 (0.97 to 0.99)	0.98 (0.96 to 1.00)
First line treatment group				
Chlorambucil only	Reference	Reference	Reference	Reference
Rituximab only	0.69 (0.51 to 0.91)	0.96 (0.58 to 1.60)	0.56 (0.38 to 0.84)	0.92 (0.44 to 1.90)
Rituximab containing chemoimmunotherapy combination	0.64 (0.49 to 0.84)	1.39 (0.85 to 2.27)	0.64 (0.44 to 0.92)	1.74 (0.89 to 3.41)
Other chemotherapy	0.86 (0.61 to 1.21)	1.19 (0.66 to 2.16)	0.90 (0.57 to 1.42)	1.14 (0.50 to 2.57)
Second line treatment group				
Chlorambucil only	N/A	Reference	N/A	Reference
Rituximab only	N/A	0.73 (0.39 to 1.35)	N/A	0.70 (0.30 to 1.61)
Rituximab containing chemoimmunotherapy combination	N/A	1.00 (0.54 to 1.85)	N/A	1.10 (0.48 to 2.49)
Other chemotherapy	N/A	1.41 (0.75 to 2.63)	N/A	1.79 (0.80 to 4.03)
Year of diagnosis				
2007	Reference	Reference	Reference	Reference
2008	1.05 (0.80 to 1.37)	1.31 (0.85 to 2.04)	0.89 (0.62 to 1.27)	1.01 (0.57 to 1.80)
2009	0.83 (0.63 to 1.11)	1.18 (0.74 to 1.88)	0.59 (0.40 to 0.87)	0.68 (0.36 to 1.28)
2010	0.88 (0.64 to 1.21)	1.32 (0.75 to 2.31)	0.56 (0.36 to 0.87)	0.73 (0.35 to 1.54)
2011	0.71 (0.47 to 1.06)	2.16 (1.12 to 4.15)	0.35 (0.19 to 0.65)	0.66 (0.22 to 1.99)