Treatment and Prognostic Testing Patterns in Patients With Chronic Lymphocytic Leukemia: The InformCLL™ Real-World Registry Interim Analysis

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INTRODUCTION

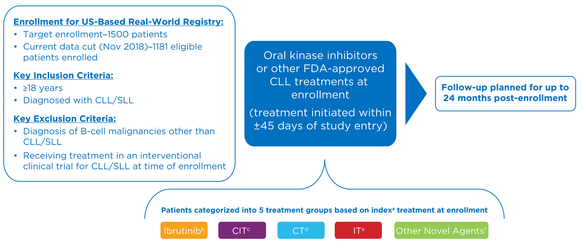
- The approach to chronic lymphocytic leukemia (CLL) treatment has evolved with the approval of novel targeted agents and a greater appreciation for the prognostic nature of biomarkers on patient outcomes.[1-6]
- Observational registries provide valuable insights into how data from clinical trials translate to daily clinical practice.
- Initiating enrollment in October 2015, informCLL (NCT02582879) is the first US-based, prospective, observational registry to characterize previously untreated and relapsed/refractory (R/R) patients receiving treatment for CLL/small lymphocytic lymphoma (SLL) in the era of novel targeted therapies.

OBJECTIVE

- To describe prognostic testing rates, CLL treatment patterns, and dosing for the first 1181 patients enrolled in the informCLL registry as of the November 30, 2018, data cut.

METHODS

Figure 1. Study Design



CIT, chemoimmunotherapy; CT, chemotherapy; IT, immunotherapy.
[a]Index treatment defined as treatment received at registry enrollment. [b]Single agent or in combination. [c]Single-agent anti-CD20 monoclonal antibodies, such as rituximab, obinutuzumab, or ofatumumab in combination with chemotherapy (eg, bendamustine+rituximab [BR]; obinutuzumab+chlorambucil [GC]; fludarabine+cyclophosphamide+rituximab [FCR]). [d]Chlorambucil, bendamustine, fludarabine, cyclophosphamide, doxorubicin, gemcitabine, vincristine, or any other chemotherapy (as single agent or in combination). [e]Single-agent anti-CD20 monoclonal antibodies, including rituximab, obinutuzumab, or ofatumumab (with or without steroids). [f]Idelalisib, venetoclax, or other drugs (single agent or in combination).

- Any changes to a patient's CLL treatment regimen were recorded; a new treatment regimen was defined as (1) stoppage of 1 regimen and the initiation of a new regimen, or (2) the addition (but not discontinuation) of a new agent to the active line.
  - Any treatment given after a gap of ≥6 months was considered a new regimen, even if similar or identical to previous treatment, but retreatment following a gap of <6 months would be considered due to toxicity and part of the previous regimen.

RESULTS

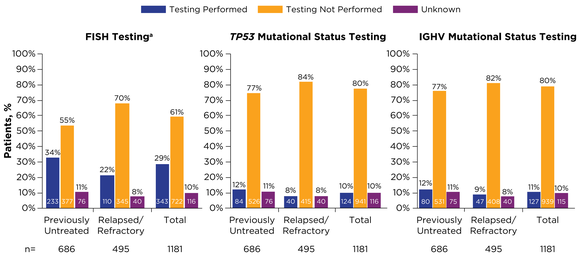
Table 1. Patient Demographics and Clinical Characteristics at Enrollment

		Previously Untreated (n=686)	R/R (n=495)	Total (N=1181)
Age, years	Median (range)	69 (37–95)	71 (34–95)	70 (34–95)
Gender, n (%)	Male	441 (64)	327 (66)	768 (65)
Race, n (%)	White	625 (91)	450 (91)	1075 (91)
	African American	45 (7)	37 (7)	82 (7)
Institution type, n (%)	Community[a]	145 (95)	130 (96)	156 (95)
	Academic	8 (5)	6 (4)	8 (5)
Insurance, n (%)[b]	Private[c]	208 (30)	134 (27)	342 (29)
	Public[d]	481 (70)	382 (77)	863 (73)
US region, n (%)	Midwest	128 (19)	79 (16)	207 (18)
	Northeast	117 (17)	96 (19)	213 (18)
	South	332 (48)	246 (50)	578 (49)
	West	109 (16)	74 (15)	183 (15)
ECOG status, n (%)	0	316 (46)	208 (42)	524 (44)
	1	295 (43)	221 (45)	516 (44)
	≥2	45 (7)	48 (10)	93 (8)
Staging done at enrollment, n (%)	No	203 (30)	205 (41)	408 (35)
	Missing/Not Specified	38 (6)	32 (6)	70 (6)
	Yes	445 (65)	258 (52)	703 (60)
Rai staging at enrollment, n (%)[e]	Stage 0	56 (13)	20 (8)	76 (11)
	Stage I	88 (20)	39 (15)	127 (18)
	Stage II	84 (19)	39 (15)	123 (17)
	Stage III	98 (22)	52 (20)	150 (21)
	Stage IV	109 (24)	85 (33)	194 (28)

ECOG, Eastern Cooperative Oncology Group. [a]Centers not affiliated with teaching/academic institutions. [b]In some instances, patients may have had both private and public insurance; therefore, the sum of the total may be more than 100%. [c]Includes employer-based, American Association of Retired Persons (AARP), self-pay, private insurance, and exchange-based coverage (through the Health Insurance Marketplace or state-based exchanges that were established as part of the Affordable Care Act of 2010). [d]Includes Medicare, Medicaid, and military-based. [e]Data not reported for all enrolled patients; some patients underwent Binet staging.

- Median follow-up times were 11.8 months (range, 0.03–35.88) for all patients, 11.5 months (0.03–35.88) for previously untreated, and 12.0 months (0.03–33.74) for R/R patients.
- Of all enrolling sites, most (95%) were community settings and 5% were considered academic institutions (**Table 1**).

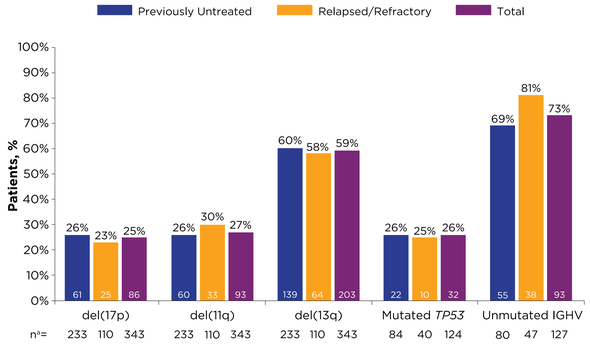
Figure 2. Frequency of Consensus Guideline-Recommended Prognostic/Predictive Biomarker Testing by Treatment Line



Due to rounding, some totals may not add up to 100%. [a]Includes chromosome 17p deletion (del[17p]), chromosome 11q deletion (del[11q]), chromosome 13q deletion (del[13q]), and trisomy 12.

- Across all lines of therapy, prognostic biomarker testing rates were low: 29% of patients had FISH testing, 10% had *TP53* testing, and 11% had IGHV testing performed (**Figure 2**).

Figure 3. Proportion of Tested Patients With Genetic Abnormality and/or Molecular Mutation



[a]Number of patients with testing results available/acquired.

- Similar rates of abnormalities were found between previously untreated and R/R patients for all high-risk prognostic/predictive features tested (**Figure 3**).

Table 2. Index Treatment Groups and Dosing of Common Index Treatment Regimens

	Previously Untreated (n=686)	R/R (n=495)	Total (N=1181)
Ibrutinib – single agent or in combination, n (%)	280 (41)	238 (48)	518 (44)
Starting at 420 mg daily dose, n/N[a] (%)	244/280 (87)	212/238 (89)	456/518 (88)
No dose modifications,[b] n/N (%)	167/205 (81)	123/154 (80)	290/359 (81)
Chemoimmunotherapy, n (%)	296 (43)	109 (22)	405 (34)
BR	163 (55)	81 (74)	244 (60)
Received <6 cycles of treatment,[c] n/N (%)	59/78 (76)	26/31 (84)	85/109 (78)
Received ≥6 cycles of treatment,[c] n/N (%)	19/78 (24)	5/31 (16)	24/109 (22)
Median number of cycles received[c]	5	5	5
Still receiving treatment, n/N (%)	50/163 (31)	24/81 (30)	74/244 (30)
FCR	65 (22)	8 (7)	73 (18)
Received <6 cycles of treatment,[c] n/N (%)	26/31 (84)	2/2 (100)	28/33 (85)
Received ≥6 cycles of treatment,[c] n/N (%)	5/31 (16)	0	5/33 (15)
Median number of cycles received[c]	5	3	5
Still receiving treatment, n/N (%)	14/65 (22)	1/8 (13)	15/73 (21)
GC	52 (18)	13 (12)	65 (16)
Received <6 cycles of treatment,[c] n/N (%)	12/35 (34)	6/9 (67)	18/44 (41)
Received ≥6 cycles of treatment,[c] n/N (%)	2335 (66)	3/9 (33)	26/44 (59)
Median number of cycles received[c]	6	5	6
Still receiving treatment, n/N (%)	4/52 (8)	3/13 (23)	7/65 (11)
CT, n (%)	12 (2)	12 (2)	24 (2)
IT, n (%)	95 (14)	84 (17)	179 (15)
Other Novel Agents, n (%)	3 (<1)	52 (11)	55 (5)

[a]Label-recommended dose of ibrutinib for CLL treatment is 420 mg orally once daily.
[b]Patients with ongoing treatment at time of analysis. [c]Patients who completed course per physician discretion.

- A comparable percentage of previously untreated patients received ibrutinib (41%) and CIT (43%), while ibrutinib was the most common treatment for R/R patients (48%) (**Table 2**).
  - In all patients completing CIT treatment, median cycles received were 5 BR, 5 FCR, and 6 GC, with 85/109 (78%), 28/33 (85%), and 18/44 (41%), respectively, receiving <6 cycles.

SUMMARY OF RESULTS

- Current treatment guidelines note decreased efficacy of CIT in patients with high-risk prognostic/predictive features (eg, del[17p], *TP53* mutation, unmutated IGHV).
- Despite the well-established role of cytogenetic abnormalities and *TP53*/IGHV mutation status in CLL prognosis and guideline recommendations to test for those, our results show that these prognostic/predictive tests were performed in less than one-third of all patients.
- Results from our real-world registry study show approximately one-third of all patients who tested positive for high-risk prognostic/predictive features received CIT.
- In this study, ibrutinib and CIT were commonly used in previously untreated and R/R patients, while ibrutinib was the most common treatment for R/R patients.
  - The majority (88%) of ibrutinib-treated patients received the FDA-recommended once-daily dose of 420 mg, with only 19% of patients experiencing dose modifications (**Table 2**).
  - In previously untreated and R/R patients who received BR or FCR, most received <6 cycles of treatment (78% and 85%, respectively).

CONCLUSIONS

- Although prognostic/predictive testing is recommended by oncology clinical practice guidelines, it is infrequently performed in US community clinical practices, and our results show that many high-risk patients still received CIT despite current treatment guidelines, in which CIT regimens are not recommended.
- Data from prospective registry studies such as informCLL represent an opportunity to educate about the necessity of prognostic testing to guide optimal CLL treatment decisions for patients and real-world outcomes for payors.

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DISCLOSURES

MS: former employment with Johnson & Johnson; stock ownership in AbbVie, Bristol-Myers Squibb, and Johnson & Johnson; **NG:** consultancy/advisory role with Juno/Celgene/Bristol-Myers Squibb, Kite/Gilead, Janssen, Pharmacyclics LLC, an AbbVie Company, Seattle Genetics, and TG Therapeutics; research funding from Forty Seven Inc, Janssen, Juno/Celgene/BMS, Roche/Genentech, Pharmacyclics LLC, an AbbVie Company, Seattle Genetics, and TG Therapeutics; speakers' bureau for AbbVie, Astra Zeneca, Celgene/Bristol-Myers Squibb, Kite/Gilead, Janssen, and Seattle Genetics; **KK:** stock ownership in AbbVie, Agios, and Celgene; speakers' bureau for Celgene and Takeda; **SU:** employment with Pharmacyclics LLC, an AbbVie Company, Protagonist Therapeutics; stock ownership in AbbVie; **JH:** employment with Janssen Biotech; stock ownership in Johnson and Johnson; **CAC:** former employment with Pharmacyclics LLC, an AbbVie Company; stock ownership in AbbVie; **RI:** employment with Pharmacyclics LLC, an AbbVie Company; stock ownership in AbbVie; patents, royalties, or other intellectual property with Express Scripts.

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