

Insights From the informCLL Registry: Real-World Application of NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)

Nilanjan Ghosh, MD, PhD¹; Danielle Brander, MD²; Anthony R. Mato, MD³; Jeff P. Sharman, MD⁴; Meghan Gutierrez, BA⁵; Maoko Naganuma, MSc⁶; Sandhya Upasani, MS⁶; Divi Alagappan, PhD⁷; Qing Huang, PhD⁷; Alex Young, PharmD⁶; Jacqueline C. Barrientos, MD, MS⁸

¹Levine Cancer Institute, Charlotte, NC, USA; ²Duke University Health System, Durham, NC, USA; ³Memorial Sloan Kettering Cancer Center, New York, NY, USA; ⁴Willamette Valley Cancer Institute & Research Center/US Oncology Research, Eugene, OR, USA;

⁵Lymphoma Research Foundation, New York, NY, USA; ⁶PharmacyClics LLC, an AbbVie Company, Sunnyvale, CA, USA; ⁷Janssen Scientific Affairs, LLC, Horsham, PA, USA; ⁸Division of Medical Oncology and Hematology, Northwell Health Cancer Institute, Donald & Barbara Zucker School of Medicine at Hofstra/Northwell, Lake Success, NY, USA

INTRODUCTION

- Treatment paradigms for patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) have evolved with the approval of novel agents and an increased understanding of prognostic biomarkers that impact patient outcomes.
- The NCCN Guidelines® provide recommendations on evolving treatment options to inform treatment decisions.¹
 - Results from clinical trials provide information on outcomes with new agents or updates to existing therapies, which may be used as evidence to support a change in clinical practice standards.
 - Prognostic biomarker testing, including FISH cytogenetics (eg, del(17p)), *TP53* mutational status, and IGHV mutation, is a critical part of guiding optimal treatment decisions for patients with CLL/SLL.
- The informCLL registry, a prospective, observational registry of patients who received treatment for CLL/SLL, provides a valuable and unique opportunity to evaluate real-world CLL treatment practices in the novel agent era.

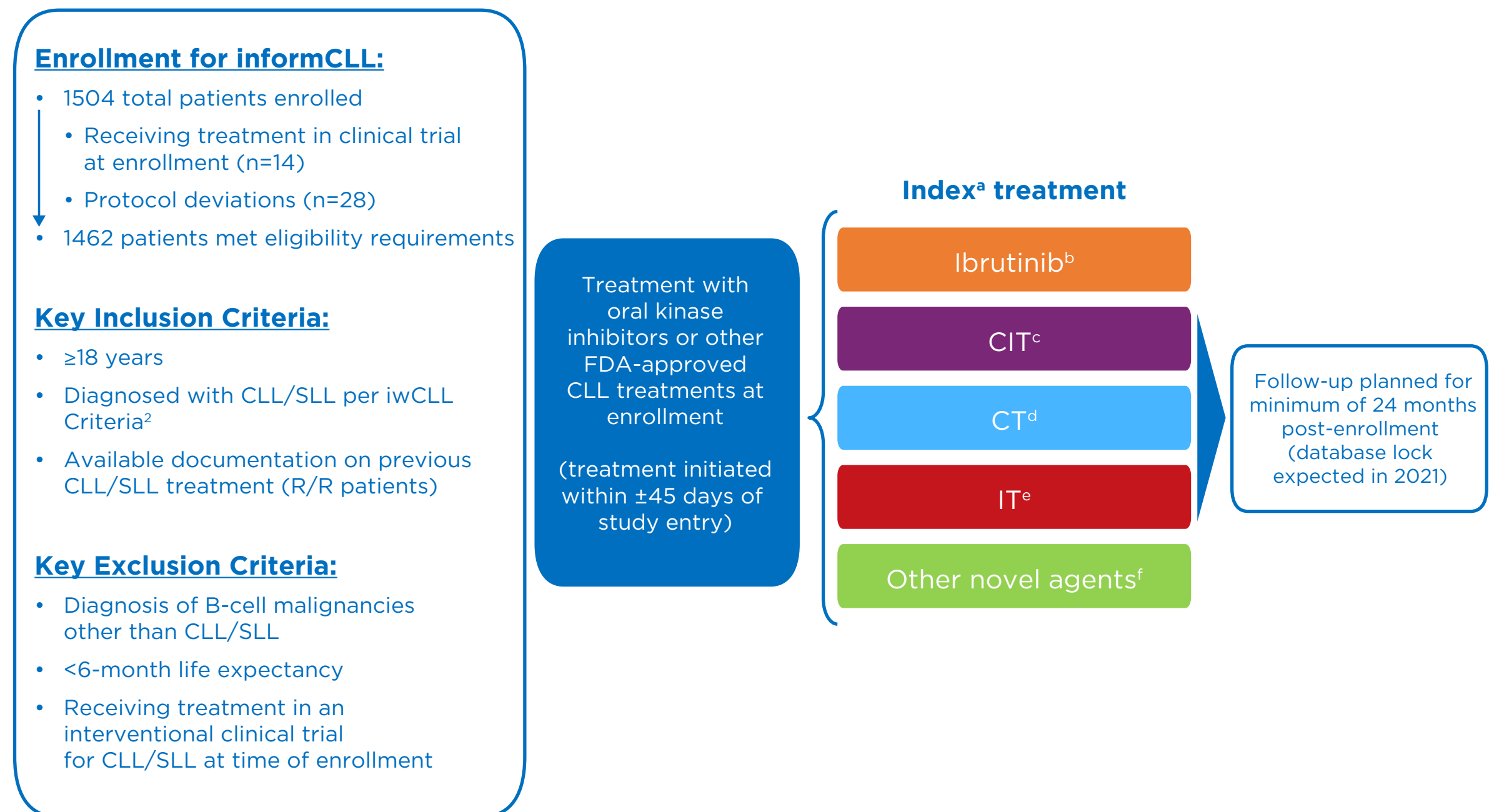
OBJECTIVE

- To understand the application of guidelines in routine clinical practice, we assessed how treatment regimens that patients received in the informCLL registry aligned with National Comprehensive Cancer Network® (NCCN®)-recommended regimens for CLL/SLL.

METHODS

- informCLL (NCT02582879) is a US-based, multicenter, real-world registry (Figure 1).
 - Patients were enrolled from October 2015 to June 2019.

Figure 1. Study Design



*Index treatment defined as treatment received at registry enrollment. [†]Single agent or in combination. [‡]Single-agent anti-CD20 monoclonal antibodies such as R, G, or ofat in combination with CT (eg, BR, G-Cib, FCR). [§]Cib, B, F, C, doxorubicin, gemtacinine, vincristine, or any other CT (as single agent or in combination). ¹Single-agent anti-CD20 monoclonal antibodies, including R, C, ofat (with or without steroids). ²Ideia, ven, or other drugs (single agent or in combination). ³B, bendamustine, C, cyclophosphamide, CT, chemoimmunotherapy, Cib, chlorambucil, CT, chemotherapy, F, fludarabine, G, obinutuzumab, ideia, idealisib, IT, immunotherapy, ofat, ofatumumab, R, rituximab, R/R, relapsed/refractory, ven, venetoclax.

- Results from prognostic biomarker testing (eg, FISH, *TP53* mutational status, IGHV mutation status), if performed, were captured from patient records at registry enrollment.
- For the current analysis, the NCCN Guidelines for CLL/SLL V.2.2017 were chosen, given 74% of patients were enrolled in informCLL in 2017 or later.
 - NCCN Guidelines for CLL/SLL V.2.2017 provided treatment recommendations by line of therapy (LOT) and del(17p)/*TP53* mutation status; for patients without del(17p)/*TP53* mutation status, additional recommendations were provided based on age (≥65 years or <65 years) and comorbidity status.
- The Charlson comorbidity index (CCI) was chosen for evaluating comorbidity burden as CCI is widely used for real-world studies.
 - CCI ≥3 was used as the threshold for defining “significant comorbidities” in this analysis, consistent with a prior publication from a large, CLL registry.³
- For patients without del(17p)/*TP53* mutation, 3 age/comorbidity sub-groups were defined as follows:
 - Elderly and frail with significant comorbidities (≥65 years and CCI ≥3)
 - Elderly without significant comorbidities (≥65 years and CCI <3), or younger with significant comorbidities (<65 years and CCI ≥3)
 - Younger without significant comorbidities (<65 years and CCI <3)
- Treatment patterns were assessed based on LOT, del(17p), and *TP53* mutation status, and further categorized by age/comorbidity groups per the guidelines.

REFERENCES

- Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma V.2.2017. February 21, 2017. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
- Haike M, et al. *Blood* 2008;111(2):444-56.
- Mato A, et al. *Blood Adv* 2020;4(7):1407-18.

RESULTS

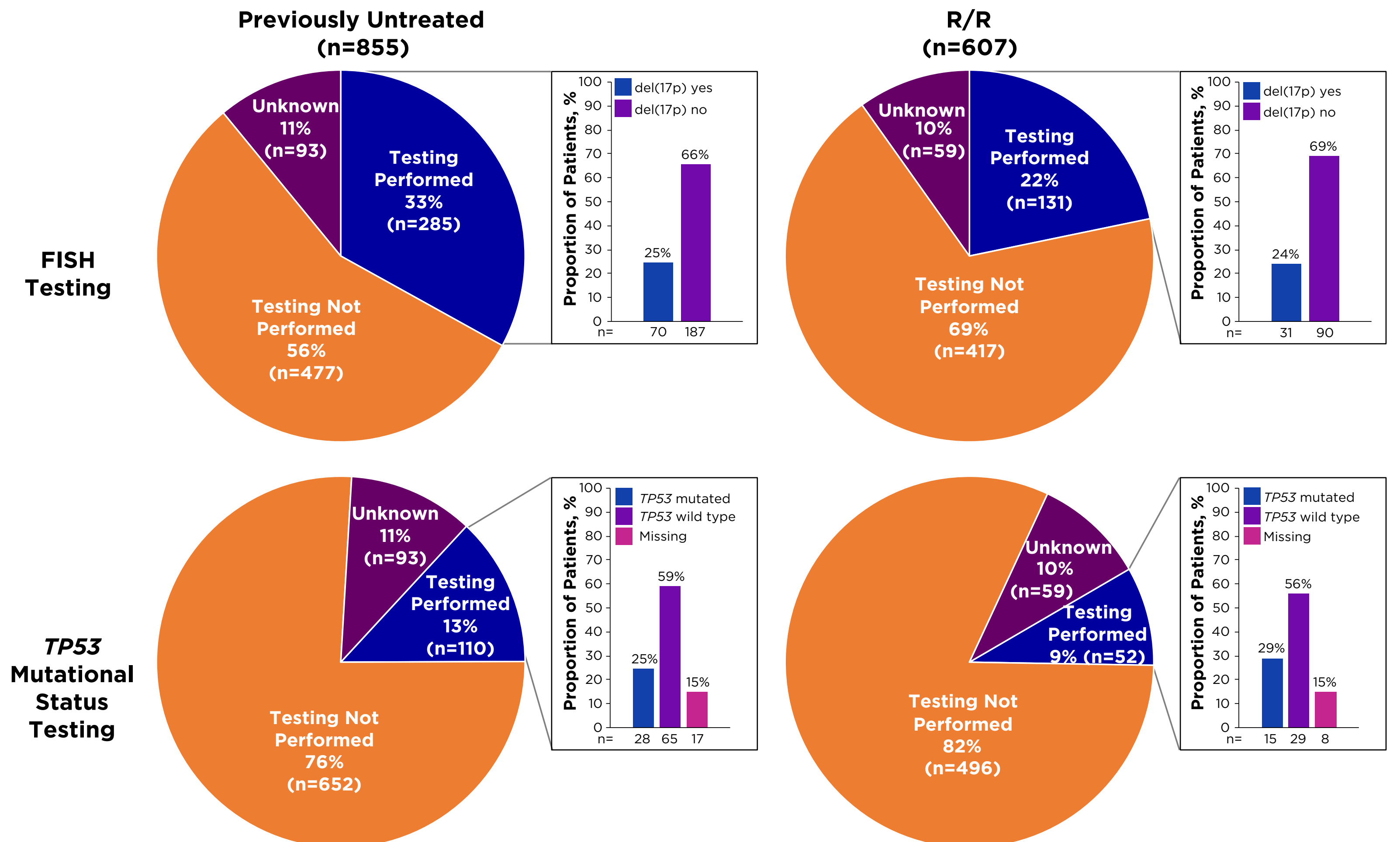
Table 1. Baseline Demographics and Clinical Characteristics at Enrollment

Characteristic	Previously Untreated (n=855)	R/R (n=607)	Overall (N=1462)
Median age (range), years	70 (37–95)	72 (34–95)	71 (34–95)
≥65 years, n (%)	579 (68)	458 (75)	1037 (71)
Male gender, n (%)	547 (64)	392 (65)	939 (64)
Race, n (%)			
White	780 (91)	545 (90)	1325 (91)
African American	58 (7)	48 (8)	106 (7)
Other	17 (2)	14 (2)	31 (2)
Institution type, number of sites (%)			
Community*	156 (94)	138 (93)	166 (93)
Academic	10 (6)	10 (7)	12 (7)
US regions, n (%)			
Midwest	172 (20)	119 (20)	291 (20)
Northeast	131 (15)	110 (18)	241 (16)
South	414 (48)	286 (47)	700 (48)
West	138 (16)	92 (15)	230 (16)
Insurance, n (%)[‡]			
Private*	322 (38)	213 (35)	535 (37)
Public [‡]	601 (70)	473 (78)	1074 (73)
Other*	7 (1)	4 (1)	11 (1)
None	8 (1)	2 (<1)	10 (1)
ECOG status, n/N (%)[§]			
0	393/823 (48)	271/580 (47)	664/1403 (47)
1	375/823 (45)	247/580 (42)	622/1403 (44)
≥2	55/823 (7)	62/580 (11)	117/1403 (8)
Rai staging at enrollment, n/N (%)[¶]			
Stage 0	66/547 (12)	25/305 (8)	91/852 (11)
Stage I	111/547 (20)	49/305 (16)	159/852 (19)
Stage II	105/547 (19)	47/305 (15)	152/852 (18)
Stage III	125/547 (23)	63/305 (21)	188/852 (22)
Stage IV	133/547 (24)	111/305 (36)	244/852 (29)
Missing	7/547 (1)	11/305 (4)	18/852 (2)
Charlson Comorbidity Index, n (%)			
0–2	723 (85)	507 (84)	1230 (84)
≥3	132 (15)	100 (16)	232 (16)
Index Treatment, n (%)			
Ibrutinib	382 (45)	296 (49)	678 (46)
CIT	361 (42)	124 (20)	485 (33)
CT	9 (1)	12 (2)	21 (1)
IT	99 (12)	97 (16)	196 (13)
Other novel agents	4 (<1)	78 (13)	82 (6)

*Centers not affiliated with teaching/academic institutions. [‡]Patients may have had both private and public insurance; therefore, the sum of the total may be more than 100%. [§]Includes employer-based, 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). [¶]Includes Medicare, Medicaid, and military-based. [‡]Both private and public insurance. [§]Data not reported for all enrolled patients. [¶]AARP, American Association of Retired Persons; ECOG, Eastern Cooperative Oncology Group.

- informCLL enrolled 1462 eligible patients (58% previously untreated, 42% R/R) from 178 sites (Table 1).
 - The median age of patients was 71 years (range 34–95).
 - The median CCI was 1.0 (range 0–11), with 16% having a CCI ≥3.
 - Community-based practices enrolled 93% of patients.
 - Single-agent ibrutinib was the most common index treatment across LOT at enrollment.

Figure 2. FISH^a and *TP53* Mutational Status Testing Were Performed Infrequently



^aIncludes del(17p), del(11q), del(13q), trisomy 12. The “Unknown” category includes patients whose testing status (ie, whether testing was performed or not) was missing.

- Overall, prognostic biomarker testing was performed in less than one third of all patients (Figure 2).

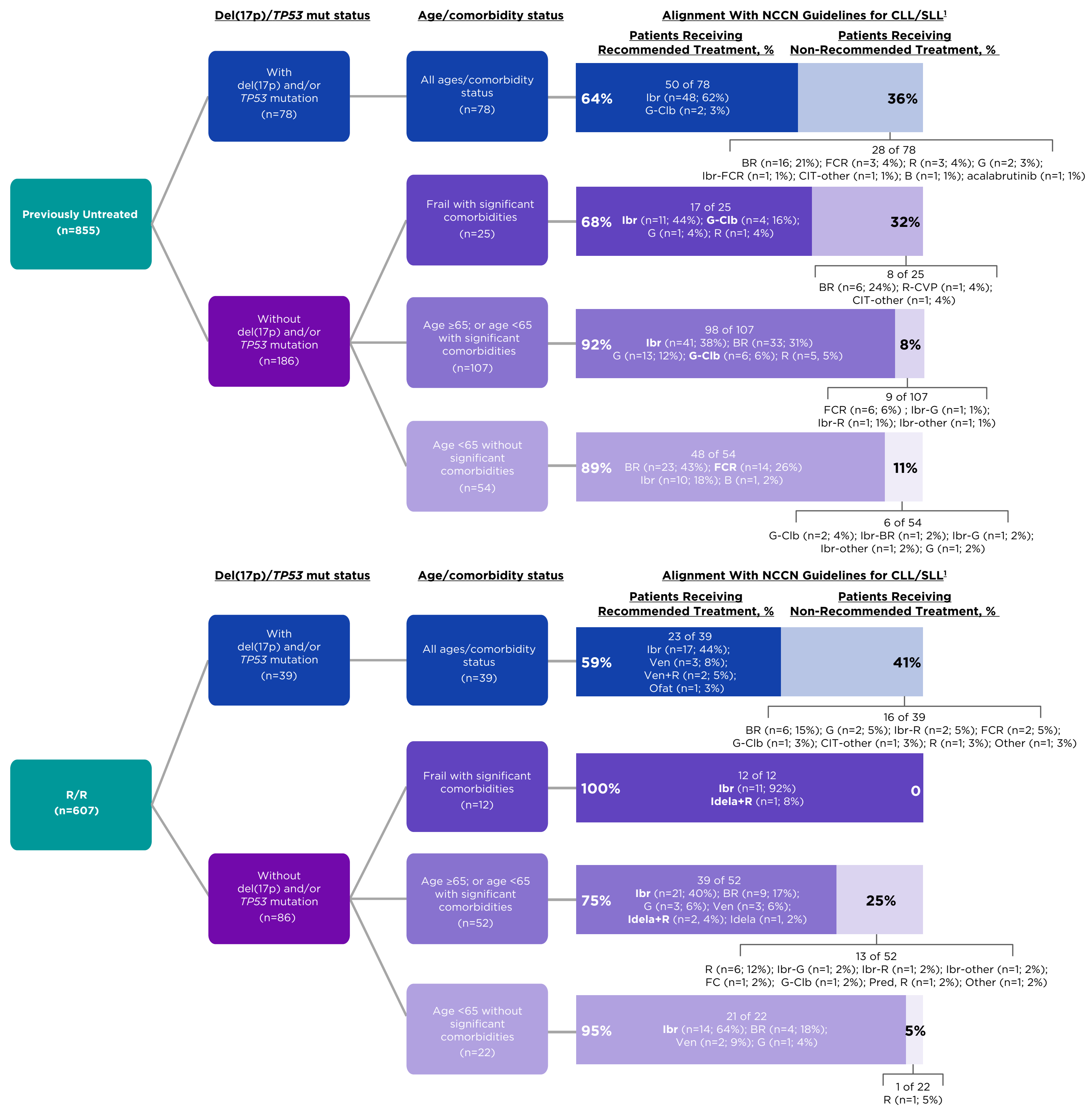
DISCLOSURES

ND: honoraria from AbbVie, Adisvivo Biotech, ADC Therapeutics, AstraZeneca, Bristol Myers Squibb, Epizyme, Genzyme, Gilead, Incyte, Karyopharma, Janssen, PharmacyClics LLC, an AbbVie Company, Seattle Genetics, and TG Therapeutics; consultancy/advisory role with Adisvivo Biotech, ADC Therapeutics, AstraZeneca, Bristol Myers Squibb, Genzyme, Gilead, Incyte, Karyopharma, Janssen, PharmacyClics LLC, an AbbVie Company, Seattle Genetics, and TG Therapeutics; research funding from Bristol Myers Squibb, Genentech, Gilead, PharmacyClics LLC, an AbbVie Company, and TG Therapeutics; speakers’ bureau for AbbVie, AstraZeneca, Bristol Myers Squibb, Epizyme, Gilead, Janssen, PharmacyClics LLC, an AbbVie Company, and Seattle Genetics; **DB:** consultancy/advisory role with AbbVie, Genentech, Pfizer, PharmacyClics LLC, an AbbVie Company, TG Therapeutics, and Verastem; research funding paid to institution from AbbVie, ArQule, Ascentage, AstraZeneca, Celgene, DTRM, Genentech, Juno Therapeutics/Celgene/BMS, LOXO, MEI Pharma, Novartis, PharmacyClics LLC, an AbbVie Company, and TG Therapeutics; other relationships with NCCN (panel member); **AM:** consultancy/advisory role with AbbVie, Adisvivo Biotech, AstraZeneca, Celgene, Genentech, Janssen, LOXO, PharmacyClics LLC, an AbbVie Company, and TG Therapeutics; research funding from AbbVie, Adisvivo Biotech, Genentech, Gilead, Janssen, LOXO, Nune, PharmacyClics LLC, an AbbVie Company, and TG Therapeutics; other relationships with TG Therapeutics (DSMR); **JS:** honoraria from AbbVie, Acerta, AstraZeneca, Celgene, Genentech, Gilead, PharmacyClics LLC, an AbbVie Company, Roche, and TG Therapeutics; consultancy/advisory role with AbbVie, Acerta, AstraZeneca, Celgene, Genentech, Gilead, PharmacyClics LLC, an AbbVie Company, Roche, and TG Therapeutics; research funding from AbbVie, Acerta, AstraZeneca, Celgene, Genentech, Gilead, PharmacyClics LLC, an AbbVie Company, Roche, and TG Therapeutics; **MD:** no relevant disclosure; **MG:** employment with PharmacyClics LLC, an AbbVie Company; stock ownership in AbbVie; **SD:** employment with PharmacyClics LLC, an AbbVie Company, and Protagonist Therapeutics; stock ownership in AbbVie; **DA:** employment with Janssen; stock ownership in Janssen; **QH:** employment with Janssen Scientific Affairs, LLC; stock ownership in Janssen; **JB:** employment with PharmacyClics LLC, an AbbVie Company; stock ownership in AbbVie; **JCB:** honoraria from Janssen; consultancy/advisory role with AstraZeneca, Genentech, Innate, Kite, and Verastem; research funding from Oncental Therapeutics and Velocidio.

- FISH testing was performed in 28% of patients.
 - Of the patients who had FISH testing performed, 24% (101/416) had del(17p).
- TP53* mutation testing was performed in 11% of patients.
 - Of those who were tested, 27% (43/162) had *TP53* mutation.
- IGHV mutational testing was performed in 12% of patients.
 - Of those who were tested, 70% (121/172) had unmutated IGHV.

Application of NCCN Guidelines in informCLL

Figure 3. Alignment With NCCN Guidelines for CLL/SLL¹ in Patients With del(17p) and *TP53* Mutation Status Available in informCLL



CVP, cyclophosphamide, vincristine, and prednisolone; Ibr, ibrutinib; Pred, prednisone. Regimens in bold font indicate Category 1 treatment per NCCN Guidelines for CLL/SLL V.2.2017.

CONCLUSIONS

- Within informCLL, most patients who had prognostic testing results available received NCCN-recommended regimens.
 - However, a third of the patients with del(17p)/*TP53* mutation, a high-risk population with poor outcomes after CIT, did not receive NCCN-recommended regimens.
 - Most patients without del(17p)/*TP53* mutation received recommended treatments across age/comorbidity groups.
- Overall, prognostic biomarker testing was performed infrequently in informCLL, with more than two thirds of patients not having testing performed.
 - The most common regimen received for patients with no del(17p)/*TP53* mutation data available was single-agent ibrutinib.
 - One-third of patients in the registry with no data available on del(17p)/*TP53* mutation may have received suboptimal treatment with CIT.
- These results underscore the need for awareness of NCCN Guidelines recommendations and increased testing to better inform treatment decisions, particularly in the community setting.

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