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POSTER ABSTRACTS

642.CHRONIC LYMPHOCYTIC LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

Ibrutinib As First Line Therapy in Chronic Lymphocytic Leukemia Patients over 80 Years Old: A Retrospective Real-Life Multicenter Italian Cohort

Enrica Antonia Martino, MD[1], Francesca Romana Mauro[2], Gianluigi Reda, MD[3], Luca Laurenti, MD[4], Andrea Visentin, MDPhD[5], Annamaria Frustaci[6], Ernesto Vigna, MD[7], Sara Pepe, MD PhD[8], Gioacchino Catania, MD[9], Giacomo Loseto, MD[10], Roberta Murru, MD[11], Annalisa Chiarenza, MD[12], Paolo Sportoletti, MD[13], Maria Ilaria Del Principe, MD[14], Marta Coscia, MD PhD[15], Sara Galimberti[16], Alessandra Tedeschi[17], Davide Rossi[18,19], Livio Trentin[20], Fortunato Morabito[21], Valter Gattei, MD[22], Massimo Gentile, MD[23]

[1] UOC Ematologia Cosenza, Cosenza, Italy
[2] Department of Translational and Precision Medicine, Hematology unit, 'Sapienza' University, Roma, Italy
[3] Hematology Department, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan, Milan, Italy
[4] S. Ematologia, Dipartimento Scienze Radiologiche Radioterapiche ed Ematologiche, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
[5] Hematology unit, Department of Medicine, University of Padova, Padova, Italy
[6] Department of Hematology, ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy
[7] U.O. Di Ematologia, Ospedale L'Annunziata, Cosenza, ITA
[8] Hematology, Department of Translational and Precision Medicine, Sapienza University, Rome, Italy
[9] Hematology and Marrow Transplant„ A.O. SS Antonio e Biagio e Cesare Arrigo, Alessandria, Alessandria, ITA
[10] IRCCS Istituto Tumori "Giovanni Paolo II", Hematology Unit, Bari, Italy
[11] Hematology and Stem Cell Transplantation Unit, Ospedale Oncologico A. Businco, ARNAS "G. Brotzu", Cagliari, Italy
[12] Division of Hematology, Policlinico, Department of Surgery and Medical Specialties, University of Catania, Catania, Catania, Italy
[13] Department of Medicine and Surgery, Institute of Hematology, Centro di Ricerca Emato-Oncologica (CREO), University of Perugia, Perugia, Italy
[14] Hematology, Department of Biomedicine and Prevention, University Tor Vergata, Roma, Italy
[15] A.O.U. Città della Salute e della Scienza di Torino, Torino, Torino, ITA
[16] Ematologia di Pisa, Pisa, ITA
[17] Niguarda Ca' Granda Hospital, Milano, ITA
[18] Clinic of Hematology, Oncology Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Bellinzona, Switzerland
[19] Oncology Institute of Southern Switzerland, Bellinzona, Switzerland
[20] Hematology Unit, Department of Medicine, University of Padova, Padova, Italy
[21] Biothecnology Research Unit, AO of Cosenza, Cosenza, ITA
[22] Centro Di Riferimento Oncologico, Aviano, Italy
[23] Haematology, Azienda Ospedaliera di Cosenza, Cosenza, Italy, Cosenza, Italy

Background: Although CLL primarily affects older adults (median age 71 years), limited data exist about the outcomes of adults who are ≥80 years old because they are under-enrolled in clinical trials.
Methods: We performed a multicenter national study enrolling consecutive treatment-naïve CLL patients ≥80 years at the time of frontline CLL therapy, treated with ibrutinib. Kaplan-Meier analyses were used to plot progression-free survival (PFS) and overall survival (OS).
Results: Our study included 79 patients with CLL who were aged ≥80 years at the time of frontline CLL therapy starting between 1/2014 and 3/2021; the clinical features of these patients are summarized in Table 1.
A total of 13 (16.5%) patients achieved a nodal clinical response (CR; bone marrow evaluation was not performed), 58 (73.4%) a partial response (PR) or PR + lymphocytosis (PR+L), 3 (3.8%) a stable disease (SD), and 5 (6.3%) were not evaluated since they early withdrew ibrutinib. Discontinuation because of progressive disease (PD) occurred in 9 cases (11%), whereas discontinuation due to toxicity in 11 patients (13.9%).

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The most common grade >3 adverse events (AEs) were infections (25.5%), neutropenia (10.1%), and anemia (2.5%).
Eighteen patients (22.8%) experienced cardiovascular events: 9 (11%) had atrial fibrillation (AF), 5 hypertension (6%), 3 heart failure (3%), and 1 acute coronary syndrome (1%). All cases of AF and hypertension were of grade 2. Patients with AF received anticoagulation and no thrombotic stroke were recorded. Bleeding events were observed in 27 (34.2%) patients but were mild, of grade 1-2 in 24 and grade 3 in 3. Patients who received anticoagulants or anti-platelets drugs did not experienced a significantly higher rate of hemorrhagic events than those not assuming anticoagulation. Secondary malignancies were reported in 6 patients (7.8%) and Richter's transformation in five.
Temporary drug withdrawal (7-30 days) occurred in 33 patients (41.8%): in 17 (21.5%) due to infections, 5 (6.3%) cardiovascular events, 10 (12.7%) hemorrhagic events, and 4 (5.1%) hematologic toxicity. Ibrutinib was permanently discontinued in 26 patients (32%): in 9 with PD (Richter's syndrome, 5), 6 with secondary malignancies, 5 with infections, 3 with cardiac failure, 2 due to severe bleeding and a sudden death was reported in 1.
After a median follow-up of 24 months, the median PFS was 49.3 months (95% CI 39.9-58.7) and the median OS 51.8 (95% CI 50.1-53.5). Age, sex, creatinine clearance, Binet stage, del17p, *TP53* and *IGHV* mutational status did not significantly impact PFS. Conversely, CIRS >6 was associated with a significantly shorter PFS (median PFS: 33.1 months, 95% CI 25.3-40.9 vs. not reached, p=0.016). A significantly longer PFS (p=0.03) was observed in the 46 patients who never discontinued ibrutinib or stopped the drug for less than 7 days (median PFS 66.3 months, 95% CI 50.5-82.1) compared to those with a transient treatment discontinuation, between 7 and 30 days, (median PFS; 32.7 months, 95% CI 23.2-42.3) (Figure 1).
Sex, creatinine clearance, Binet stage, *IGHV*, del17p, and *TP53* mutational status, as well as CIRS, did not significantly impact OS. Conversely, a trend toward a statistically significant longer OS (P=0.07) was observed for patients who discontinued ibrutinib <7 days (67.2 months, 95% CI 43.5-90.9) compared with those who discontinued for 7-30 days (51.8 months, 95% CI 34.4-69.2).
Conclusions: To our knowledge, this is the largest real-world study examining treatment-naive elderly patients receiving ibrutinib as first-line therapy.
Ibrutinib represents a suitable therapeutic choice even for patients aged >80 years with comorbidities. In this setting of patients, the drug was well tolerated and no new side effects were recorded.

Disclosures Mauro: *Abbvie, Janssen, Beigene, Astra Zeneca, Takeda:* Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau. **Reda:** *AbbVie:* Consultancy; *Astrazeneca:* Consultancy, Current Employment; *Jannsen:* Consultancy; *BeiGene:* Consultancy. **Laurenti:** *Janssen:* Membership on an entity's Board of Directors or advisory committees; *Beigene:* Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Membership on an entity's Board of Directors or advisory committees; *AstraZeneca:* Membership on an entity's Board of Directors or advisory committees. **Visentin:** *AstraZeneca:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Abbvie:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Membership on an entity's Board of Directors or advisory committees; *BeiGene:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Takeda:* Speakers Bureau; *CSL behring:* Membership on an entity's Board of Directors or advisory committees. **Pepe:** *Abbvie, Astra-Zeneca, Beigene:* Membership on an entity's Board of Directors or advisory committees, Other: travel grant. **Murru:** *Abbvie, Janssen, Astra Zeneca:* Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau. **Sportoletti:** *Abbvie, Janssen, Beigene, Astra Zeneca, Takeda, Novartis:* Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau. **Tedeschi:** *Beigene:* Speakers Bureau; *Janssen:* Speakers Bureau; *Abbvie:* Speakers Bureau; *Astrazeneca:* Speakers Bureau. **Rossi:** *AbbVie, AstraZeneca, Gilead, BeiGene, BMS, Janssen, Lilly, Kyte:* Honoraria, Research Funding.

Table 1. Clinical features of patients treated with new drugs in a real-world setting.

Features	N° of cases treated with ibrutinib (%)
Median age, y (range)	81 (80-87)
Sex	
Male	36 (45.6)
Female	43 (54.4)
CIRS	
0-6	29 (36.7)
>6	50 (63.3)
Median creatinine clearance (mL/min)	45 (25-65)
Binet stage	
A	5 (6.3)
B	37 (46.8)
C	37 (46.8)
17p deletion	
No	54 (68.4)
Yes	25 (31.6)
TP53	
Wild type	48 (61.8)
Mutated	31 (39.2)
IGHV mutational status	
Mutated	42 (51.9)
Unmutated	37 (48.1)

Figure 1. PFS according to ibrutinib temporary withdrawal (yes, more than 7 consecutive days and less than 30 days; no, no drug suspension or less than 7 days).

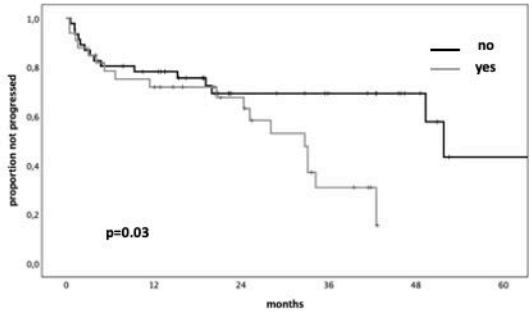

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Figure 1

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