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63rd ASH Annual Meeting Abstracts

POSTER ABSTRACTS

632.CHRONIC MYELOID LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

Analysis of Early Events during the First Year of Tyrosine Kinase Inhibitor Therapy in Patients with Chronic Phase - Chronic Myeloid Leukemia: A "Campus CML" Study

Mario Tiribelli[1], Isabella Capodanno[2], Maria Cristina Miggiano[3], Cristina Bucelli[4], Francesco Cavazzini[5], Sabrina Leonetti Crescenzi[6], Sabina Russo[7], Emilia Scalzulli[8], Andrea Bernardelli[9], Luigiana Luciano[10], Olga Mulas[11], Giuseppina Loglisci[12], Chiara Elena[13], Umberto Pizzano[14], Immacolata Attolico[15], Gianni Binotto[16], Elena Crisà[17], Paolo Sportoletti[18], Ambra Di Veroli[19], Anna Rita Scortechini[20], Annapaola Leporace[21], Maria Basile[22], Monica Crugnola[23], Fabio Stagno[24], Pamela Murgano[25], Davide Rapezzi[26], Alessandra Malato[27], Michele Pizzuti[28], Debora Luzi[29], Malgorzata Monika Trawinska[30], Alessandra Iurlo[4], Monica Bocchia[31], Carmen Fava[32], Giovanni Caocci[33], Massimiliano Bonifacio[34], Giuseppe Nicola Saglio[35], Giorgina Specchia[36], Massimo Breccia[37], Roberto Latagliata[19]

[1] Division of Hematology and BMT, Department of Medical Area, University of Udine, Udine, Italy
[2] Hematology Unit, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[3] Hematology Department, San Bortolo Hospital, Azienda ULSS8 "Berica" di Vicenza, Vicenza, Italy
[4] Hematology Division, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[5] Division of Hematology, Department of Medical Sciences, University of Ferrara, Azienda Ospedaliera-Universitaria, Arcispedale S. Anna, Ferrara, Italy
[6] Hematology Unit, San Giovanni Hospital, Rome, Italy
[7] Division of Hematology, Policlinico "G. Martino", University of Messina, Messina, Italy
[8] Hematology, Department of Translational and Precision Medicine, Policlinico Umberto I, Sapienza University, Rome, Italy
[9] Hematology, University of Verona, Verona, Italy
[10] Hematology Unit, Federico II University of Naples, Napoli, Italy
[11] Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy
[12] Hematology Unit, Vito Fazzi Hospital, Lecce, Italy
[13] Department of Hematology Oncology, Foundation IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy
[14] Hematology, University of Udine, Udine, Italy
[15] Hematology and Stem Cell Transplantation Unit, AOUC Policlinico, Bari, Italy
[16] Department of Medicine, Hematology and Clinical Immunology, Padua School of Medicine, Padua, Italy
[17] Division of Hematology, Department of Translational Medicine, Università del Piemonte Orientale Amedeo Avogadro, AOU Maggiore della Carità, Novara, Italy
[18] Department of Medicine, Division of Hematology and Clinical Immunology, University of Perugia, Perugia, Italy
[19] Hematology, Belcolle Hospital, Viterbo, Italy
[20] Division of Hematology, Azienda Ospedaliero Universitaria Ospedali Riuniti Ancona, Ancona, Italy
[21] Hematology Unit, Azienda Ospedaliero Universitaria Sant' Andrea, Rome, Italy
[22] Hematology, Giuseppe Moscati Hospital, Taranto, Italy
[23] Hematology and BMT Center, Department of Medicine and Surgery, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy
[24] Chair and Hematology Section, Ferrarotto Hospital, Catania, Italy
[25] Division of Hematology, S. Elia Hospital, Caltanissetta, Italy
[26] S.C. Ematologia, ASO S. Croce e Carle, Cuneo, Italy
[27] Department of Hematology, Ospedali Riuniti Villa Sofia-Cervello, Palermo, Italy
[28] Ematologia, Azieda Ospedaliera S. Carlo, Potenza, Italy
[29] Hematology, Azienda Ospedaliera - S. Maria Terni, Terni, ITA
[30] Department of Hematology S. Eugenio Hospital, Rome, Italy
[31] Hematology, Hematology Unit, University of Siena, Azienda Ospedaliero Universitaria Senese, Siena, Italy
[32] Hematology Division, Ospedale Mauriziano, University of Turin, Torino, Italy
[33] Department of Medical Sciences and Public Health, University of Cagliari, Businco Hospital, Cagliari, Italy

[34] Department of Medicine, Section of Hematology, University of Verona, Verona, Italy
[35] Divisione Universitaria di Ematologia e Terapie Cellulari, A.O. Ordine Mauriziano, Turin, Italy
[36] Hematology Section, Department of Emergency and Transplantation - GIMEMA WP CML, University of Bari Aldo Moro, Bari, Italy
[37] Division of Hematology, Department of Translational and Precision Medicine, Azienda Policlinico Umberto I, Sapienza University, Rome, Italy

Abstract Background Tyrosine kinase inhibitors (TKIs) revolutionized treatment of chronic myeloid leukemia (CML). However, the first months of therapy are crucial, as optimal response is defined as the achievement of molecular milestones at 3, 6 and 12 months (mo.) and as many toxicities, also causing a TKI switch, are more frequent in the 1st year.
Methods To evaluate achievement of early molecular response (MR) and incidence of events leading to a TKI change during the 1st year of therapy, we retrospectively studied 1650 CP-CML patients diagnosed from 2012 and 2019 at 31 Hematology Centres and treated with frontline imatinib (IM) or second-generation (2G) TKIs dasatinib or nilotinib. Optimal MR at 3, 6 and 12 mo. were assessed according to 2020 ELN recommendations.
Results Frontline TKI was IM in 926 (56.1%) and 2G-TKIs in 724 (43.9%) cases: the main clinical features at diagnosis of the entire cohort and according to frontline treatment is reported in the Table 1. Commonest comorbidities were arterial hypertension (38.7%), previous neoplasm (13.6%), diabetes (11.3%), peripheral vascular diseases (7.8%), COPD (7.5%) and ischemic heart disease (6.8%). IM-treated patients were older ($p<0.001$), with higher ELTS score (int/high 47.6% vs 35.6%, $p<0.001$) and more comorbidities ($p<0.005$ for all diseases).
Optimal MR was achieved at 3 mo. by 1186/1430 (82.9%), at 6 mo. by 1025/1352 (75.8%) and at 12 mo. by 826/1264 patients (65.3%), respectively.
Total number of patients discontinuing TKI in the 1st year was 321/1650 (19.4%), being higher with IM (237/926, 25.5%) than 2G-TKIs (84/724, 11.6%) ($p<0.001$). Main causes were primary resistance (8.7%, 12.3% IM vs 4.2% 2G-TKIs, $p<0.001$), extra-hematologic toxicity (6.4%, 8.2% IM vs 4.2% 2G-TKIs, $p>0.001$), hematologic toxicity (1.7%, 2.0% IM vs 1.4% 2G-TKIs, $p=0.25$) and progression (1.0%, 1.2% IM vs 0.8% 2G-TKIs, $p=0.56$). Cumulative incidence of discontinuation at 3, 6 and 12 mo. were 5.6%, 10.7% and 19.3%, respectively; values for IM and 2G-TKIs at the three timepoints were 8.1%, 15.0%, 25.5% and 2.5%, 5.3%, 11.5% ($p<0.001$) (Fig. 1).
Conclusions This real-world study on over 1600 CML patients shows that almost 20% discontinue frontline TKI during the 1st year, mostly for primary resistance or toxicity. Discontinuation rates are higher with IM compared to 2G-TKIs, mostly at 3 mo. and are probably due to a lower attainment of early MR. The impact of older age, higher risks and heavier burden of comorbidities in IM patients should be considered and need deeper investigation.

Disclosures Elena: *GILEAD:* Membership on an entity's Board of Directors or advisory committees; *NOVARTIS:* Membership on an entity's Board of Directors or advisory committees; *PFIZER:* Membership on an entity's Board of Directors or advisory committees; *CELGENE:* Other: funding for meeting participation. **Sportoletti:** *AstraZeneca:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria; *AbbVie:* Consultancy, Honoraria. **Stagno:** *InCyte:* Consultancy, Honoraria; *Pfizer:* Consultancy, Honoraria, Other: Support for attending meetings and/or travel; *Novartis:* Consultancy, Honoraria, Other: Support for attending meetings and/or travel, Research Funding. **Iurlo:** *Pfizer:* Speakers Bureau; *Incyte:* Speakers Bureau; *Novartis:* Speakers Bureau; *Bristol Myers Squibb:* Speakers Bureau. **Bonifacio:** *Novartis:* Honoraria; *Pfizer:* Honoraria; *Amgen:* Honoraria; *Bristol Myers Squibb:* Honoraria. **Breccia:** *Pfizer:* Honoraria; *Incyte:* Honoraria; *Abbvie:* Honoraria; *Bristol Myers Squibb/Celgene:* Honoraria; *Novartis:* Honoraria. **Latagliata:** *Novartis:* Honoraria; *Pfizer:* Honoraria; *BMS Cellgene:* Honoraria.

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Table 1 - Clinical features at diagnosis of the whole cohort and according frontline TKI

	All patients (1650)	Frontline imatinib (926)	Frontline 2G-TKIs (724)	p
Gender, M/F (%)	962/688 (58.3 – 41.7)	551/375 (59.5 – 40.5)	411/313 (56.8 – 43.2)	0.271
Median age (years) (IQR)	60.0 (47.1 – 71.4)	66.6 (55.8 – 75.7)	50.9 (40.6 – 62.2)	<0.001
Hb, g/dl (IQR)	12.7 (11.0 – 14.2)	12.8 (11.3 – 14.1)	12.6 (10.6 – 14.3)	0.251
WBC, x 10^9/l (IQR)	58.2 (28.7 – 133.0)	50.4 (26.5 – 102.8)	76.8 (33.9 – 174.1)	<0.001
PLTS, x 10^9/l (IQR)	357 (244 – 562)	350 (240 – 551)	362 (246 – 576)	0.335
Spleen, n° evaluable (%):	1605	894	710	
< 5 cm below costal margin	1341 (83.5)	802 (89.7)	538 (75.8)	<0.001
≥ 5 cm below costal margin	264 (16.5)	92 (10.3)	172 (24.2)	
Sokal score, n° evaluable (%):	1598	885	712	
Low	619 (38.7)	306 (34.6)	313 (44.0)	
Intermediate	749 (46.9)	460 (52.0)	288 (40.4)	<0.001
High	230 (14.4)	119 (13.4)	111 (15.6)	
ELTS score, n° evaluable (%):	1555	855	699	
Low	898 (57.7)	448 (52.4)	450 (64.4)	
Intermediate	477 (30.7)	289 (33.8)	187 (26.8)	<0.001
High	180 (11.6)	118 (13.8)	62 (8.8)	

Figure 1 – Cumulative incidence of TKI treatment discontinuation according to frontline TKI

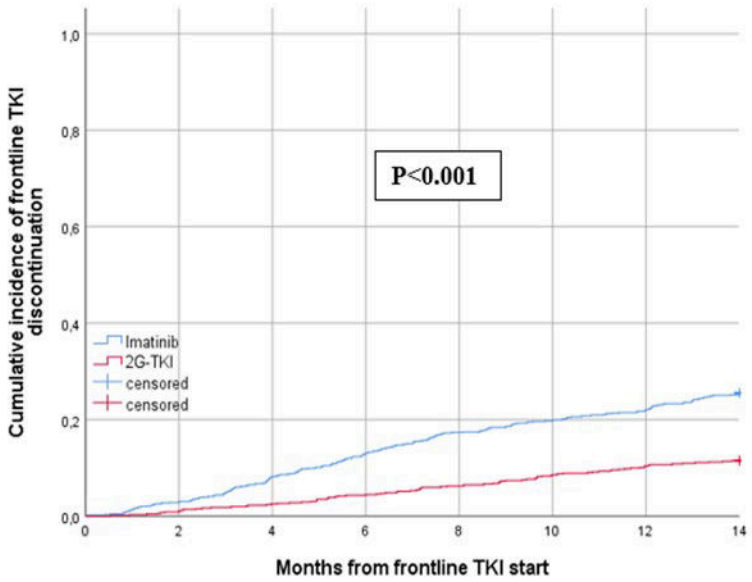

Figure 1