

3764 Outcomes of Chronic Myeloid Leukemia (CML) Patients Who Stopped Second Generation Tyrosine Kinase Inhibitors (2GTKIs) As Second Line Treatment. Results of the CML Spanish National Registry (RELMC).

Program: Oral and Poster Abstracts

Session: 632. Chronic Myeloid Leukemia - Therapy: Poster III

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J Valentin Garcia-Gutierrez, MD, PhD^{1*}, Begoña Maestro^{2*}, Luis Felipe Casado, MD, PhD^{3*}, Manuel Perez-Encinas^{4*}, Isabel Massague^{5*}, Raquel de Paz^{6,7*}, Santiago Osorio^{8*}, Joaquin Martinez, MD^{9*}, Guiomar Bautista, MD^{10*}, Pilar Giraldo¹¹, Carmen Burgaleta^{12*}, Maria Jesús Peñarrubia^{13*}, Maria José Requena^{14*}, Carmen Calle^{15*}, Jose Ángel Hernández-Rivas^{16*}, Pilar Cano^{17*} and Juan Luis Steegmann, MD, PhD¹⁸

¹*Servicio Hematología y Hemoterapia, Hospital Universitario Ramon y Cajal, Madrid, Spain*

²*Registro Español de Investigación y Tratamiento de Leucemia Mieloide Crónica (RELMC), Madrid, Spain*

³*Hematology, Hospital Virgen de la Salud, Toledo, Spain*

⁴*Servicio de Hematología, Hospital Clínico U. de Santiago de Compostela, Santiago de Compostela, Spain*

⁵*Servicio de Hematología, Hospital Valle de Hebron, Barcelona, Spain*

⁶*Hospital Universitario La Paz, Madrid, Spain*

⁷*Dept. Hematology, Hospital Universitario La Paz-IDIPaz, Madrid, Spain*

⁸*Hospital General Universitario Gregorio Marañón, Hematology, Madrid, Spain*

⁹*Hospital 12 de Octubre, Madrid, Spain*

¹⁰*Hematology, Hospital Puerta de Hierro Majadahonda, Majadahonda, Spain*

¹¹*Haematology, Hospital Universitario Miguel Servet, Zaragoza, Spain*

¹²*Hematology, Hospital Universitario Principe de Asturias, Madrid, Spain*

¹³*Clinical Hematology Department, Hospital Clínico Universitario de Valladolid*

¹⁴*Hematology, Hospital Universitario Severo Ochoa, Leganés*

¹⁵*Servicio de Hematología, Hospital General de Ciudad Real, Ciudad Real, Spain*

¹⁶*Servicio de Hematología, Hospital Infanta Leonor, Madrid*

¹⁷*Servicio de Hematología, Hospital La Mancha Centro, Ciudad Real*

¹⁸*Dept. of Hematology, Hospital Universitario de la Princesa, Madrid, Spain*

Introduction: In CML-CP patients showing resistance or intolerance to imatinib, rescue therapy with second generation 2GTKIs produced nearly 50% of complete cytogenetic responses (CCyR). However, in the long term, a high percentage (roughly 70%) of patients abandoned the targeted treatment. The information about the outcome of patients treated in third line with TKI's is scarce, and come mostly from clinical trials. In these experiences CCyR were obtained in approximately 20%, and the duration of MCyR was around 18 months.

Aims: To describe the evolution of patients who interrupted 2GTKI, given as 2nd line treatment, outside clinical trials.

Patients and methods: In our registry, we have identified 105 patients treated with second generation TKI in second line out of 487 patients treated with imatinib as first TKI. Reasons for treatment change were failure in 53%, intolerant in 33% and suboptimal in 14%. Sokal risk indexes were 40%, 47% and 13% for low, intermediate and high risk, respectively. 33% of patients had received interferon prior to imatinib. Cumulative incidence of CCyR and major molecular responses (MMR) with a median follow up of 85.59 (8.93-130) months, were 65% and 49%. Fifty two (49%) withdrew treatment because of failure (22%), intolerance (18%), suboptimal response (7%) and exitus (8%).

Results: A total of 31 patients started third-line therapy with a third TKI, representing 29% of patients who started second-line treatment and 78% of patients who discontinued the treatment. The reasons for starting the 3rd line treatment was failure in 55% and intolerance, in 44%. With a median follow up of 9 months, probabilities of achievement a complete hematological response (CHR) and CCR was 93% and 30%. These responses were influenced depending on the indication of treatment, with cumulative incidence of CCyR of 18% and 50% for resistant and intolerant patients, respectively ($p = 0.031$). The corresponding figures for transformation-free survival and overall survival were 61% vs 76, and 72% vs 88% for failure and intolerance settings, respectively.

Conclusions: In this registry-based experience, outside clinical trials, 2GTKI have offered a substantial benefit to patients resistant or intolerant to Imatinib. However, the experience in 3rd line in patients resistant to 2GTKI in 2nd line, has been dismal, with less than 20% of CCyR. In this particular subgroup, BMT must be considered, and new experimental therapeutic schemes are necessary for those patients who are not suitable candidates for BMT.

Disclosures: Casado: *Novartis*: Consultancy, Speakers Bureau; *BMS*: Consultancy, Speakers Bureau; *Pfizer*: Consultancy, Speakers Bureau. Steegmann: *Pfizer*: Consultancy, Research Funding, Speakers Bureau; *Bristol-Myers Squibb*: Consultancy, Research Funding, Speakers Bureau; *Novartis*: Consultancy, Research Funding, Speakers Bureau.