DO CHRONIC MYELOID LEUKEMIA PATIENTS WITH LATE "WARNING" RESPONSES BENEFIT FROM SWITCHING THERAPY TO A SECOND GENERATION TYROSINE KINASE INHIBITOR?

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Abstract:

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V. García-Gutiérrez*V. García-Gutiérrez*J. M. PuertaB. MaestroL. F. Casado MonteroJ. R. Molina HurtadoM. Perez-EncinasM. V. Moreno RomeroI. MassagueR. Sola GarciaR. De PazM. J. Ramirez SanchezS. OsorioM. I. Mata VazquezJ. MartinezJ. L. SastreM. D. L. A. PorteroG. Bautista M. S. Duran NietoP. GiraldoM. Jimenez JambrinaC. BurgaletaJ. Ruiz AredondoM. J. PeñarrubiaV. García-Gutiérrez*J. M. PuertaB. MaestroL. F. Casado MonteroJ. R. Molina HurtadoM. Perez-EncinasM. V. Moreno RomeroI. MassagueR. Sola GarciaR. De PazM. J. Ramirez SanchezS. OsorioM. I. Mata VazquezJ. MartinezJ. L. SastreM. D. L. A. PorteroG. BautistaM. S. Duran NietoP. GiraldoM. Jimenez JambrinaC. BurgaletaJ. Ruiz AredondoM. J. PeñarrubiaV. García-Gutiérrez*J. M. PuertaB. MaestroL. F. Casado MonteroJ. R. Molina HurtadoM. Perez-EncinasM. V. Moreno RomeroI. MassagueR. Sola GarciaR. De PazM. J. Ramirez SanchezS. OsorioM. I. Mata Vazquez J. MartinezJ. L. SastreM. D. L. A. PorteroG. BautistaM. S. Duran NietoP. GiraldoM. Jimenez JambrinaC. BurgaletaJ. Ruiz AredondoM. J. PeñarrubiaM. J. RequenaM. D. C. Fernández ValleC. CalleA. Paz CollJ. Á. Hernández-RivasR. Franco OsorioP. CanoD. Tallón PérezM. Fernández de la MataP. López GarridoJ. L. SteegmannV. García-Gutiérrez [1,*] J. M. Puerta [2] B. Maestro [3] L. F. Casado Montero [4] J. R. Molina Hurtado [5] M. Perez-Encinas [6] M. V. Moreno Romero [7] I. Massague [8] R. Sola Garcia [9] R. De Paz [10] M. J. Ramirez Sanchez [11] S. Osorio [12] M. I. Mata Vazquez [13] J. Martinez [14] J. L. Sastre [15] M. D. L. A. Portero [16] G. Bautista [17] M. S. Duran Nieto [18] P. Giraldo [19] M. Jimenez Jambrina [20] C. Burgaleta [21] J. Ruiz Aredondo [22] M. J. Peñarrubia [23] M. J. Requena [24] M. D. C. Fernández Valle [25] C. Calle [26] A. Paz Coll [27] J. Á. Hernández-Rivas [28] R. Franco Osorio [29] P. Cano [30] D. Tallón Pérez [31] M. Fernández de la Mata [32] P. López Garrido [2] J. L. Steegmann [33]

[1]Servicio Hematología y Hemoterapia, Hospital Universitario Ramón y Cajal, Madrid, [2]Servicio Hematología y Hemoterapia, Hospital Universitario Virgen de las Nieves, Granada, [3]Registro Español de Investigación y Tratamiento de Leucemia Mieloide Crónica (RELMC), , Madrid, [4] Hematology Dept, Hospital Virgen de la Salud, Toledo, [5]Hematology Dept, Hospital Reina Sofía, Cordoba, [6]Servicio Hematología y Hemoterapia, Hospital Clinico U. de Santiago de Compostela, Santiago de Compostela, [7]Servicio Hematología y Hemoterapia, Hospital Juan Ramón Jiménez, Huelva, [8]Servicio Hematología y Hemoterapia, Hospital Vall de Hebron, Barcelona, [9]Servicio Hematología y Hemoterapia, Hospital Clínico San Cecilio, Granada, [10]Servicio Hematología y Hemoterapia, Hospital Universitario La Paz, Madrid, [11]Servicio Hematología y Hemoterapia, Hospital de Jerez, Jerez, [12]Servicio Hematología y Hemoterapia, Hospital Universitario Gregorio Marañon, Madrid, [13]Servicio Hematología y Hemoterapia, Hospital Costa del Sol, Malaga, [14] Servicio Hematología y Hemoterapia, Hospital Universitario 12 de Octubre, Madrid, [15]Hematology

Dept, Complejo Hospitalario de Orense, Orense, [16]Servicio Hematología y Hemoterapia, Hospital Virgen de la Macarena, Sevilla, [17]Servicio Hematología y Hemoterapia, Hospital Universitario Puerta de Hierro, Madrid, [18]Servicio Hematología y Hemoterapia, Hospital de Jaen, Jaen, [19] Servicio Hematología y Hemoterapia, Hospital Miguel Servet, Zaragoza, [20]Servicio Hematología y Hemoterapia, Hospital de Rio Tinto, Huelva, [21]Servicio Hematología y Hemoterapia, Hospital Universitario Principe de Asturias, Madrid, [22]Servicio Hematología y Hemoterapia, Hospital de Antequera, Malaga, [23]Servicio Hematología y Hemoterapia, Hospital Clinico Universitario de Valladolid, Valladolid, [24]Servicio Hematología y Hemoterapia, Hispital Severo Ochoa, Madrid, [25] Servicio Hematología y Hemoterapia, Hospital Puerta del Mar, Cadiz, [26]Servicio Hematología y Hemoterapia, Hospital General de Ciudad Real, Ciudad Real, [27]Servicio Hematología y Hemoterapia, Hospital de Puerto Real, Cadiz, [28]Servicio Hematología y Hemoterapia, Hospital Infanta Leonor, Madrid, [29]Servicio Hematología y Hemoterapia, Hospital Punta de Europa, Cadiz, [30]Servicio Hematología y Hemoterapia, Hospital La Mancha Centro, Ciudad Real, [31]Servicio Hematología y Hemoterapia, Hospital San Agustín, Jaén, [32]Servicio Hematología y Hemoterapia, Hospital Infanta Margarita, Córdoba, [33]Servicio Hematología y Hemoterapia, Hospital Universitario de la Princesa, Madrid, Spain

Abstract topic: 8. Chronic myeloid leukemia - Clinical

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Aims: The aim of this study was to describe outcomes of late warning patients, classified by the latest ELN recommendations, in order to explore the potential benefit of treatment switching in these patients.

Methods: Our registry includes a cohort of 945 CP-CML patients that are treated with first-line imatinib and are not involved in clinical trials. Registries were approved by the corresponding Ethical committees, and all the procedures were performed in accordance with international legislation. The monitoring and treatment strategies were chosen at the hematologist's discretion and thus reflect the actual treatment of CML patients outside clinical trials. All data was recorded by data managers that operated independently from the physicians taking care of the patients. From this cohort we identified 198 patients with a warning response after 12 months of treatment (patients with a complete cytogenetic response but no major molecular response [MMR]). patients who underwent treatment change due to intolerance were identified but not categorized as late warning responders

Results: One hundred and fourty six patients (group 1) remained on imatinib, while 52 patients (group 2) changed treatment to a Second Generation Tyrosine Kinase Inhibitor (2GTKI). The overall probabilities of obtaining MMR and $MR^{4.5}$ by 24 months on an intention-to-treat basis were 10% vs. 21 % respectively, whereas by 48 months the corresponding probabilities were: 21% vs. 44%. Overall survival was 97% vs. 92% by 24 and 48 months respectively, whereas PFS was 98% vs. 96% for the same periods of time. Changing therapy resulted in a significant improvement in the probability of a MMR: 24% vs. 42% by 12 months and 43% vs. 64% by 24 months (p=.002); as well as the probability of achieving a deep molecular responses ($MR^{4.5}$): 1% vs. 19% and 7% vs. 23% by 12 and 24 months respectively (p=<0.001). Treatment

change was also associated with an increased stability of cytogenetic responses, reflected by the observation that 17 patients (11%) in group 1 lost CCyR, compared to 2 patients (3%) in group 2 (p=.001). Similarly, treatment change significantly influenced the probability of remaining in MMR and $MR^{4.5}$ at the last follow-up: 36% vs. 49% and 14% vs. 25% implying a relative risk of 1.5 (1.2; 1.9) for MMR and a relative risk of 1.8(1.0; 3.3) for $MR^{4.5}$ in the group of patients who changed treatment vs. patients continuing imatinib. These improvements did not correlate with an increase in overall survival (OS) or progression-free survival (PFS)

Summary/Conclusion: To our knowledge our study represents the largest study of late warning patients treated with imatinib (including the published data regarding outcomes of late suboptimal responders under the old classification scheme). Our study shows how late warning responders had an excellent prognosis in terms of PFS and OS, and offers an empirical demonstration of the adequacy of classifying these responses as a warning, if survival outcomes are the objectives of the treatment. However, if the objectives include lowering (mitigating) the probability of treatment failure as well as obtaining deeper molecular responses, our study demonstrates that switching to a 2GTKI is the preferred option.

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Disclosure of Interest: None Declared