THE DECLINE OF BCR-ABL/GUS RATIO IN CML PATIENTS TREATED UPFRONT WITH NILOTINIB SHOWS A RAPID DESCENT DURING THE FIRST TRIMESTER, AND THE RESPONSES ARE SIMILAR TO THOSE ACHIEVED WITH ABL AS CONTROL

Friday, June 13, 2014 / 17:45 - 19:00

Abstract:

ABSSUB-5879: MGUS DIAGNOSED CML

J. L. Steegmann*L. F. Casado MonteroM. T. Gómez-CasaresM. RozmanM. A. EchevesteV. Garcia-GutierrezJ. L. SastreA. Ramirez PayerE. OlavarriaF. ValB. XicoyP. GiraldoE. CondeR. Omar VallansotJ. L. LorenzoL. PalomeraS. RuizL. CasasC. WalasekD. ColomerL. F. Casado Montero*M. T. Gómez-CasaresD. ColomerM. RozmanM. A. EchevesteV. Garcia-GutierrezJ. L. SastreA. Ramirez PayerE. OlavarriaF. ValB. XicoyP. GiraldoE. CondeR. Omar VallansotJ. L. LorenzoL. PalomeraS. RuizC. WalasekL. CasasJ. L. SteegmannL. F. Casado Montero*M. T. Gómez-Casares D. ColomerM. RozmanM. A. EchevesteV. Garcia-GutierrezJ. L. SastreA. Ramirez PayerE. OlavarriaF. ValB. XicoyP. GiraldoE. CondeR. Omar VallansotJ. L. LorenzoL. PalomeraS. RuizC. WalasekL. CasasJ. L. SteegmannL. F. Casado Montero [1,*]M. T. Gómez-Casares [2]D. Colomer [3]M.

Rozman [4]M. A. Echeveste [5]V. Garcia-Gutierrez [6]J. L. Sastre [7]A. Ramirez Payer [8]E. Olavarria [9]F. Val [10]B. Xicoy [11]P. Giraldo [12]E. Conde [13]R. Omar Vallansot [14]J. L. Lorenzo [15]L. Palomera [16]S. Ruiz [17]C. Walasek [18]L. Casas [19]J. L. Steegmann [20]

[1]Hematology Dept, Hospital Virgen de la Salud, Toledo, [2]Hematology Dept, Hospital Universitario Gran Canaria Dr Negrin, Las Palmas de Gran Canaria, [3]Hematology Dept, Hospital Clinic, [4] Hematology Dept, Hospital Clínico de Barcelona, Barcelona, [5]Hematology Dept, Hospital Universitario de Donostia, San Sebastian, [6]Servicio Hematología y Hemoterapia, Hospital Universitario Ramón y Cajal, Madrid, [7]Hematology Dept, Complejo Hospitalario de Orense, Orense, [8]Hematology Dept, Hospital Central de Asturias, Oviedo, [9]Hematology Dept, Hospital de Navarra, Pamplona, [10]Hematology Dept, Hospital Mutua de Terrassa, Terrassa, [11]Hematology Dept, Hosptial Germans Trias i Pujol, Barcelona, [12]Servicio Hematología y Hemoterapia, Hospital Miguel Servet, Zaragoza, [13]Hematology and Stem Cell Transplantation, Hospital and investigational Institute Marques de Valdecilla, Santander, [14]Hematology Dept, Hospital Joan XXIII, Tarragona, [15]Hematology Dept, Fundación Jimenez Diaz, Madrid, [16]Hematology Dept, Hospital Lozano Blesa, Zaragoza, [17]Novartis Oncology, Novartis, Madrid, Spain, [18]Novartis, Novartis Oncology Region Europe, Vienna, Austria, [19]Dynamic Solutions, [20]Servicio Hematología y Hemoterapia, Hospital Universitario de la Princesa, Madrid, Spain

Abstract topic: 8. Chronic myeloid leukemia - Clinical

Background: The exact decline of BCR-ABL ratios during the first trimester of therapy has not been previously reported in CML patients treated upfront with Nilotinib

Aims: To analyze the kinetic of the descent, and the molecular response , using BCR-ABL/GUS ratios during the during the first trimester of therapy, and at 6, 12 and 18 months (m).

Methods: BCR-ABL/GUS ratios were measured prior to nilotinib, and subsequently every 2 weeks until the 3rd month (m), and at 6, 12 and 18 m. Sokal scores were calculated with data at diagnosis. Kinetics of changes were calculated using the slopes of the curves of interest. Molecular response was classified according to ELN2013 recommendations.

Results: 61 patients. Age : 51,8 y (19-81), M/F: 67%/33%. Risk: Sokal (L,I,H):60%, 28.3%, 11.7%. Ten patients abandoned during the first 18 m because of AE's. They have been classified as non-responders after the time they went off-study. **Outcomes:** No patient died or had transformation. The kinetic of the descent showed a fast decline of BCR-ABL/GUS ratios during the first trimester. We compared the slopes of the BCR-ABL/GUS ratio in the intervals Baseline-D90 and D90 (3m)-18m. The slopes of the values of Log(BCR-ABL/GUS) before and after the 3rd m were ignificantly different (-0,78±0,34 vs -0,1 ±0,11) ($p<0,001$). (Figure 1). The responses were fast. Of note, the proportion of patients having a ratio of 10% or less at 1 month was 70%. The frequencies of optimal responses (ITT method) at 3, 6 and 12 m were 90%, 80% and 70% respectively. The frequencies of MR^4 and $MR^{4.5}$ at 18 m were 48% and 18%, respectively. **Discussion.** Using frequent measures during the first trimester of Nilotinib therapy, our results show that the curve of descent of BCR-ABL /GUS ratios has a biphasic shape, with a steeper descent during the first 3 months of therapy, and a significant slower decrease thereafter. The frequencies of MMR at 12m, and MR^4 and $MR^{4.5}$ at 18 m (70%, 40%, and 18%, respectively) are equivalent to those reported in the ENEST1st core study, in which ABL was used as control (68%, 36.3% and 19.8%, respectively) (Giles, F. et al Blood 2013 122:4030). In summary, in CML-CP patients treated upfront with NIlotinib, the molecular response using BCR-ABL/GUS shows a rapid decline during the first trimester of therapy, and the frequency of responses are similar to those reported using ABL as gene control.

Summary/Conclusion: Using frequent measures during the first trimester of Nilotinib therapy, our results show that the curve of descent of BCR-ABL /GUS ratios has a biphasic shape, with a steeper descent during the first 3 months of therapy, and a significant slower decrease thereafter. The frequencies of MMR at 12m, and MR^4 and $MR^{4.5}$ at 18 m (70%, 40%, and 18%, respectively) are equivalent to those reported in the ENEST1st core study, in which ABL was used as control (68%, 36.3% and 19.8%, respectively) (Giles, F. et al Blood 2013 122:4030). In summary, in CML-CP patients treated upfront with NIlotinib, the molecular response using BCR-ABL/GUS shows a rapid decline during the first trimester of therapy, and the frequency of responses are similar to those reported using ABL as gene control.

Background: The exact decline of BCR-ABL ratios during the first trimester of therapy has not been previously reported in CML patients treated upfront with Nilotinib

Aims: To analyze the kinetic of the descent, and the molecular response , using BCR-ABL/GUS ratios during the during the first trimester of therapy, and at 6, 12 and 18 months (m).

Methods: BCR-ABL/GUS ratios were measured prior to nilotinib, and subsequently every 2 weeks until the 3rd month (m), and at 6, 12 and 18 m. Sokal scores were calculated with data at diagnosis. Kinetics of changes were calculated using the slopes of the curves of interest. Molecular response was classified according to ELN2013 recommendations.

Results: 61 patients. Age : 51,8 y (19-81), M/F: 67%/33%. Risk: Sokal (L,I,H):60%, 28.3%, 11.7%. Ten patients abandoned during the first 18 m because of AE's. They have been classified as non-responders after the time they went off-study. **Outcomes:** No patient died or had transformation. The kinetic of the descent showed a fast decline of BCR-ABL/GUS ratios during the first trimester. We compared the slopes of the BCR-ABL/GUS ratio in the intervals Baseline-D90 and D90 (3m)-18m. The slopes of the values of Log(BCR-ABL/GUS) before and after the 3rd m were ignificantly different (-0,78±0,34 vs -0,1 ±0,11) ($p<0,001$). (Figure 1). The responses were fast. Of note, the proportion of patients having a ratio of 10% or less at 1 month was 70%. The frequencies of optimal responses (ITT method) at 3, 6 and 12 m were 90%, 80% and 70% respectively. The frequencies of MR^4 and $MR^{4.5}$ at 18 m were 48% and 18%, respectively. **Discussion.** Using frequent measures during the first trimester of Nilotinib therapy, our results show that the curve of descent of BCR-ABL /GUS ratios has a biphasic shape, with a steeper descent during the first 3 months of therapy, and a significant slower decrease thereafter. The frequencies of MMR at 12m, and MR^4 and $MR^{4.5}$ at 18 m (70%, 40%, and 18%, respectively) are equivalent to those reported in the ENEST1st core study, in which ABL was used as control (68%, 36.3% and 19.8%, respectively) (Giles, F. et al Blood 2013 122:4030). In summary, in CML-CP patients treated upfront with NIlotinib, the molecular response using BCR-ABL/GUS shows a rapid decline during the first trimester of therapy, and the frequency of responses are similar to those reported using ABL as gene control.

Summary/Conclusion: Using frequent measures during the first trimester of Nilotinib therapy, our results show that the curve of descent of BCR-ABL /GUS ratios has a biphasic shape, with a steeper descent during the first 3 months of therapy, and a significant slower decrease thereafter. The frequencies of MMR at 12m, and MR^4 and $MR^{4.5}$ at 18 m (70%, 40%, and 18%, respectively) are equivalent to those reported in the ENEST1st core study, in which ABL was used as control (68%, 36.3% and 19.8%, respectively) (Giles, F. et al Blood 2013 122:4030). In summary, in CML-CP patients treated upfront with NIlotinib, the molecular response using BCR-ABL/GUS shows a rapid decline during the first trimester of therapy, and the frequency of responses are similar to those reported using ABL as gene control.

Background: The exact decline of BCR-ABL ratios during the first trimester of therapy has not been previously reported in CML patients treated upfront with Nilotinib

Aims: To analyze the kinetic of the descent, and the molecular response , using BCR-ABL/GUS ratios during the during the first trimester of therapy, and at 6, 12 and 18 months (m).

Methods: BCR-ABL/GUS ratios were measured prior to nilotinib, and subsequently every 2 weeks until the 3rd month (m), and at 6, 12 and 18 m. Sokal scores were calculated with data at diagnosis. Kinetics of changes were calculated using the slopes of the curves of interest. Molecular response was classified according to ELN2013 recommendations.

Results: 61 patients. Age : 51,8 y (19-81), M/F: 67%/33%. Risk: Sokal (L,I,H):60%, 28.3%, 11.7%. Ten patients abandoned during the first 18 m because of AE's. They have been classified as non-responders after the time they went off-study. **Outcomes:** No patient died or had transformation. The kinetic of the descent showed a fast decline of BCR-ABL/GUS ratios during the first trimester. We compared the slopes of the BCR-ABL/GUS ratio in the intervals Baseline-D90 and D90 (3m)-18m. The slopes of the values of Log(BCR-ABL/GUS) before and after the 3rd m were ignificantly different (-0,78±0,34 vs -0,1 ±0,11) ($p<0,001$). (Figure 1). The responses were fast. Of note, the proportion of patients having a ratio of 10% or less at 1 month was 70%. The frequencies of optimal responses (ITT method) at 3, 6 and 12 m were 90%, 80% and 70% respectively. The frequencies of MR^4 and $MR^{4.5}$ at 18 m were 48% and 18%, respectively.

Image/Pictures:

	N[1]	% BCR-ABL/GUS	MR1 ≤ 10%	MR2 ≤ 1%	MR3 ≤ 0.1%	MR4 ≤ 0.01%*	MR4.5 ≤ 0.0032%
Baseline	57	33.5±33.7					
D15	56	22.1 ±21.2	30/60 (50%)	2/60 (3.3%)	0/60 (0%)	0/60 (0%)	0/60 (0%)
D30 (M1)	56	13 ±13.2	42/60 (70%)	9/60 (15%)	1/60 (1.7%)	0/60 (0%)	0/60 (0%)
D45	57	9 ±16.1	56/60 (93.3%)	45/60 (75%)	23/60 (38.3%)	9/60 (15%)	5/60 (8.3%)
D60 (M2)	56	4.10 ±8.05	50/60 (83.3%)	25/60 (41.7%)	2/60 (3.3%)	0/60 (0%)	0/60 (0%)
D90 (M3)	56	0.72±1.48	54/60 (90%)	50/60 (83.3%)	35/60 (58.3%)	19/60 (31.7%)	10/60 (16.7%)
Month 6	54	0,45±1.39	50/60 (83.3%)	48/60 (80%)	42/60 (70%)	31/60 (51.7%)	20/60 (33.3%)
Month 12	50	0,08±0.29	50/60 (83.3%)	48/60 (80%)	42/60 (70%)	31/60 (51.7%)	20/60 (33.3%)
Month 18	46	0.049±0.1	46/60 (76.7%)	46/60 (76.7%)	41/60 (68.3%)	29/60 (48.3%)	11/60 (18.3%)

1. *Molecularly evaluated.*
2. *For MR^4 and $MR^{4.5}$, in the case of 0% ratio, , a requisite of 24.000 and 77.000 copies was necessary, respectively*

Summary/Conclusion: Using frequent measures during the first trimester of Nilotinib therapy, our results show that the curve of descent of BCR-ABL /GUS ratios has a biphasic shape, with a steeper descent during the first 3 months of therapy, and a significant slower decrease thereafter. The frequencies of MMR at 12m, and MR^4 and $MR^{4.5}$ at 18 m (70%, 40%, and 18%, respectively) are equivalent to those reported in the ENEST1st core study, in which ABL was used as control (68%, 36.3% and 19.8%, respectively) (Giles, F. et al Blood 2013 122:4030). In summary, in CML-CP patients treated upfront with NIlotinib, the molecular response using BCR-ABL/GUS shows a rapid decline during the first trimester of therapy, and the frequency of responses are similar to those reported using ABL as gene control.

Disclosure of Interest: None Declared

Keywords: Chronic myeloid leukemia