Treatment-Free Remission in Patients with CML-CP Treated with Frontline Nilotinib: Results From the ENESTfreedom Study.

2016 ASCO Annual Meeting. Oral Abstract Session. Presented Saturday, June 4, 2016

Authors:

Andreas Hochhaus, Tamas Masszi, Francis J. Giles, Jerald P. Radich, David M. Ross, **María Teresa Gómez Casares**, Andrzej Hellmann, Jesper Stentoft, Eibhlin Conneally, **Valentin García Gutierrez**, Norbert Gattermann, Wieslaw Wiktor-Jedrzejczak, Philipp D. Le Coutre, Bruno Martino, Susanne Saussele, Hans D. Menssen, Weiping Deng, Nancy Krunic, Veronique Bedoucha, Giuseppe Saglio; Jena University Hospital, Jena, Germany; Fovarosi Onkormanyzat Szent Laszlo Korhaza, Hematologia, Budapest, Hungary; Northwestern Medicine Developmental Therapeutics Institute, Chicago, IL; Seattle Cancer Care Alliance/Fred Hutchinson Cancer Research Center, Seattle, WA; SA Pathology, Flinders Medical Centre, Adelaide, Australia; Hospital Universitario Doctor Negrin, Las Palmas De Gran Canaria, Spain; Akadeia Medyczna w Gdansku, Gdansk, Poland; Aarhus University Hospital, Aarhus, Denmark; St. James's Hospital, Dublin, Ireland; Hospital Universitario Ramón y Cajal, Madrid, Spain; Universitatsklinikum Dusseldorf, Duesseldorf, Germany; Medical University of Warsaw, Warsaw, Poland; Charité-Universitätsmedizin Berlin, Berlin, Germany; Azienda Ospedaliera Bianchi Melacrino Morelli, Reggio Calabria, Italy; III. Med. Klinik, Medizinische Fakultät Mannheim der Universität Heidelberg, Mannheim, Germany; Novartis Pharma AG, Basel, Switzerland; Novartis Pharmaceuticals Corporation, East Hanover, NJ; Novartis Institute for Biomedical Research, Cambridge, MA; University of Turin, Orbassano, ItalyView Less

Abstract Disclosures

Research Funding:

None

Background: In prior clinical trials, ≈40-60% of pts with CML-CP and sustained deep molecular response (MR) maintained TFR after stopping long-term imatinib (median duration: ≈ 5-7 y). The single-arm phase 2 ENESTfreedom study (NCT01784068) is the first to specifically investigate TFR following frontline nilotinib.**Methods:**Pts with CML-CP with typical b2a2 or b3a2 *BCR-ABL1* transcripts, ≥ 2 y of frontline nilotinib, and $MR^{4.5}$(*BCR-ABL1*^{IS}≤ 0.0032%) at prescreening were eligible. Upon enrollment, pts continued nilotinib for 1 y, with RQ-PCR assessments every 12 wk (consolidation [CONS] phase) at a central standardized laboratory. Pts with no assessment worse than MR^4 (*BCR-ABL1*^{IS}≤ 0.01%), ≤ 2 assessments between MR^4 and $MR^{4.5}$, and $MR^{4.5}$ in the last assessment of the CONS phase were eligible to stop treatment (TFR phase). Loss of major MR (MMR [*BCR-ABL1*^{IS}≤ 0.1%]) triggered re-initiation of nilotinib (ReRx phase). The data cutoff for this analysis was 30 Nov 2015, when all pts who entered the TFR phase had completed 48 wk of TFR, entered the ReRx phase, or discontinued from the study.**Results:**A total of 215 pts entered the CONS phase.

Of these, 190 stopped nilotinib and entered the TFR phase (median age at baseline: 55 y; median time from first $MR^{4.5}$ to study entry: 18 mo; median nilotinib duration prior to TFR: 43 mo [range: 33-89 mo]). At wk 48 of the TFR phase, 51.6% (95% CI: 44.2-58.9%) of these 190 pts were in MMR and had not re-initiated treatment (primary endpoint). Of 86 pts who entered the ReRx phase due to loss of MMR by the data cutoff, 85 regained MMR (1 pt discontinued from the study [pt decision] without MMR 7.1 wk after entering the ReRx phase) and 76 regained $MR^{4.5}$ (median time to MMR and $MR^{4.5}$ among all pts who entered the ReRx phase: 7.9 wk and 13.1 wk, respectively). No new safety signals were observed on treatment. During the TFR phase, 24.7% of pts experienced musculoskeletal pain (grade 3/4 in 1.1%).**Conclusions:**These data demonstrate the feasibility of TFR following frontline nilotinib. Nilotinib is the first tyrosine kinase inhibitor to demonstrate successful TFR in a large proportion of eligible pts after relatively short exposure (median: ≈ 3.6 y) Clinical trial information: NCT01784068