Long-term treatment-free remission (TFR) in patients (pts) with chronic myeloid leukemia in chronic phase (CML-CP) after stopping second-line (2L) nilotinib: ENESTop 144-wk results.

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Background:TFR is a new treatment goal in CML. In the ENESTop study (NCT01698905) in pts with CML-CP who sustained a deep molecular response with 2L nilotinib, 57.9% and 53.2% remained in TFR 48 wk (primary endpoint) and 96 wk after stopping treatment, respectively. We report an analysis of longer-term durability of TFR in ENESTop.**Methods:**Pts treated with ≥ 2 y of nilotinib following > 4 wk of imatinib (≥ 3 y total) and achieving $MR^{4.5}$ (*BCR-ABL1*≤ 0.0032% on the International Scale [$BCR\text{-}ABL1^{IS}$] by quantitative real-time PCR) on nilotinib were eligible. Following a 1-y consolidation phase, pts with no confirmed loss of $MR^{4.5}$ could attempt TFR; nilotinib was restarted upon loss of major molecular response (MMR; $BCR\text{-}ABL1^{IS}$≤ 0.1%) or confirmed loss of MR^{4} ($BCR\text{-}ABL1^{IS}$≤ 0.01%). The data cutoff for this analysis was Oct 18, 2017, when all pts had completed ≥ 144 wk of TFR, restarted nilotinib, or discontinued the

study.**Results:**Of 126 pts entering TFR, 61 remained in TFR at data cutoff, 58 restarted nilotinib (loss of MMR, n = 34; confirmed loss of MR^4, n = 24), and 7 discontinued the study in this phase. The TFR rate at 144 wk was 48.4% (95% CI, 39.4%-57.5%). Of 67 pts in TFR at 96 wk, 6 were no longer in TFR at 144 wk due to confirmed loss of MR^4 (n = 3; at 108, 120, and 144 wk), death (n = 2), or study discontinuation (n = 1; pt/guardian decision). Of 34 pts restarting nilotinib due to loss of MMR, 33 (97.1%) and 31 (91.2%) regained MMR and $MR^{4.5}$, respectively; of 24 pts restarting due to confirmed loss of MR^4, 23 (95.8%) regained $MR^{4.5}$. Stable $MR^{4.5}$ for 48 wk was achieved by 42 of 54 pts who regained $MR^{4.5}$ (77.8%). No disease progression or deaths due to CML were reported; 144-wk treatment-free survival rate was 52.0% (95% CI, 42.9%-60.4%). Of 68 pts who remained in TFR for > 96 wk, 10.3%, 51.5%, 19.1%, and 11.8% experienced any-grade musculoskeletal pain–related adverse events in the consolidation phase and first, second, and third 48 wk of TFR, respectively.**Conclusions:**These results demonstrate the long-term durability of TFR following 2L nilotinib and show that most pts restarting nilotinib regained stable $MR^{4.5}$. Pts should be routinely monitored for late loss of response. Clinical trial information: NCT01698905