P700 TREATMENT-FREE REMISSION (TFR) AFTER DASATINIB IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA IN CHRONIC PHASE (CML-CP) AND DEEP MOLECULAR RESPONSE (DMR): FINAL 5-YEAR RESULTS OF DASFREE. Topic: 08. Chronic myeloid leukemia – Clinical Neil P. Shah1, ***Valentín García-Gutiérrez2***, Antonio Jiménez-Velasco3, Susanne Saussele4, Delphine Rea5, François-Xavier Mahon6, Moshe Yair Levy7, ***María Teresa Gómez-Casares8***, Michael J. Mauro9, Oumar Sy10, Patricia Martin-Regueira10, Jeffrey H. Lipton11 1 *UCSF School of Medicine, San Francisco, United States;**2 Servicio Hematología y Hemoterapia, Hospital Universitario Ramón y Cajal, IRYCIS,* **Madrid**, **Spain**;3 *Hospital Universitario Carlos Haya, Malaga, Spain;*4 *Medizinische Fakultät Mannheim der Universität Heidelberg, Mannheim, Germany;*5 *Hôpital Saint-Louis, Paris, France;*6 *Institut Bergonié Cancer Center, Université Bordeaux, Bordeaux, France;*7 *Baylor Charles A. Sammons Cancer Center, Dallas, United States;**8 Hospital Universitario de Gran Canaria Dr. Negrín, Las Palmas de Gran Canaria, Spain;*9 *Memorial Sloan Kettering Cancer Center, New York, United States;*10 *Bristol Myers Squibb, Princeton, United States;*11 *Princess Margaret Cancer Centre, University of Toronto, Toronto, Canada.*

Background: Patients (pts) with CML-CP who have a DMR are eligible to discontinue treatment (Tx) to attempt TFR. DASFREE (NCT01850004) is a single-arm, open-label, phase 2 trial evaluating dasatinib discontinuation in pts with a stable DMR. At the 2-year (y) follow-up, 46% of pts remained in TFR; in a multivariate analysis, longer duration of prior dasatinib, first-line (1L) dasatinib, and older age were significantly associated with TFR maintenance (Shah et al. Leuk Lymphoma 2019).

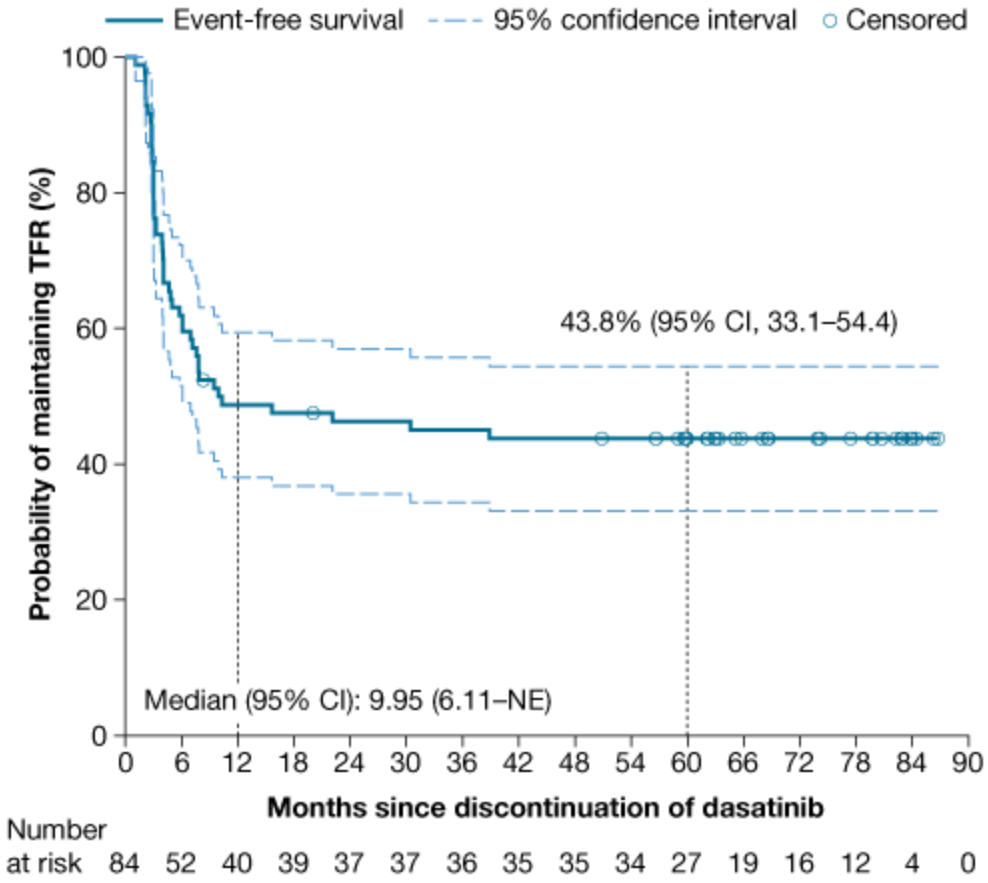
Aims: To report the final 5-y results assessing TFR maintenance after dasatinib discontinuation.

Methods: Eligible pts were aged ≥18 y, received dasatinib Tx as 1L or subsequent therapy for ≥ 2 y, and had a DMR (MR4.5 or BCR-ABL ≥0.0032% on the international scale, confirmed during pre-screening and with 2 central lab assessments 3 months [mo] apart) for ≥1 y prior to study entry. Pts discontinued dasatinib and were monitored for up to 5 y. All pts provided written informed consent. If loss of major molecular response (MMR) occurred, pts restarted dasatinib at the same dose as at enrollment. A univariate analysis was conducted to identify baseline correlates of maintaining TFR. Rate of TFR maintenance (event-free survival) in the extended follow-up, rate of MMR recapture after relapse, identification of predictive factors for TFR maintenance, and safety were all key secondary or exploratory endpoints.

Results: A total of 84 pts discontinued dasatinib. At a minimum follow-up of 60 mo (database lock, Dec 2021), 44% (n=37) of pts remained in TFR and the remaining 56% (n=47) had lost MMR and restarted Tx. No relapses occurred later than 39 mo after discontinuation. Baseline characteristics were balanced between pts who remained in TFR versus those who restarted Tx, except for age (65% of pts who remained in TFR vs 85% who restarted Tx were aged <65 y). Among enrolled pts, 24 discontinued the study early (4 due to drug-related adverse events [AEs]; none due to death); 60 discontinued as planned per protocol (end of study). Patients who discontinued from the study were evaluated for response regained before discontinuation. All evaluable pts (n=46; one patient withdrew from the study 1 month after restarting Tx and did not undergo molecular assessment) who restarted Tx regained MMR and MR4.5 in a median (range) time of 1.9 mo (0.9‑3.7) and 3.3 mo (1.5‑29.6), respectively. The 5-

y TFR rate was 43.8% (95% CI, 33.1‑54.4; Figure). A univariate analysis of baseline correlates identified older age and 1L dasatinib as significantly associated with maintaining TFR. Musculoskeletal and connective tissue disorders (any grade) were experienced by 39% of pts (n=33). The most common any-grade AEs were arthralgia (18%) and hypertension (13%). There were no deaths due to CML. Withdrawal events (n=15) were experienced by 9 pts (11%) after a median (range) of 3.7 (<1‑18) mo from dasatinib discontinuation, with no new events beyond 18 months of study follow-up; 10 events resolved in a median (range) of 5.98 (<1‑70) mo.

Figure. Five-year TFR rate



CI, confidence interval; NE, not evaluable; TFR, treatment-free remission.

Summary/Conclusion: Discontinuation of dasatinib after 1L therapy and beyond is a viable option for pts with CMLCP in sustained DMR. About half of the pts who discontinued dasatinib maintained TFR at 5 y. Re-treatment after relapse was successful; all evaluable pts who lost MMR regained MMR and MR4.5 after therapy was reinitiated. The overall safety profile was consistent with the known safety profile of dasatinib and with the 2-y results.