P696 SUBTHERAPEUTIC TKI DOSES FOR THE MAINTENANCE OF CML PATIENTS WITH INTOLERANCE OR REFUSAL TO DISCONTINUE: A SINGLE CENTER FEASIBILITY STUDY. Topic: 08. Chronic myeloid leukemia – Clinical Asuncion Borrero1, Adrian Segura1, Santiago Sanchez1, Ruth Stuckey1, Juan Francisco López1, Cristina Bilbao1, ***Maria Teresa Gomez casares1 1 HOSPITAL UNIVERSITARIO DE GRAN CANARIA DOCTOR NEGRIN, LAS PALMAS DE GRAN CANARIA, Spain.***

Background: Discontinuation has become a common practice in patients with CML treated with TKI who have maintained a deep molecular response. 50-60% of patients successfully discontinue treatment without relapsing (treatment-free remission, TFR), which implies that 40-50% will have to remain with TKI treatment for life. Many studies have been carried out on TKI treatment with reduced doses, often used to manage adverse events and TKI intolerance. Such studies have shown that most patients maintain MMR and many even achieve it when reduced doses are administered from diagnosis. There are fewer cases reported of patients who receive subtherapeutic doses, i.e. doses lower than those considered in the TKI data sheet. Reasons why subtherapeutic doses may be employed in clinical practice include the patient`s refusal to discontinue or a failed discontinuation attempt (loss of TFR), as a maintenance strategy, or in those patients with intolerance. Although its use is likely, information on patient outcome is scarce.

Aims: We investigated the feasibility of the use of subtherapeutic doses in CML patients. We studied the reason for the dose reduction and the impact of the dose reduction on molecular response.

Methods: In this observational, retrospective, single-center study, we searched the medical records of all patients diagnosed with CML in chronic phase at our hospital between 2003 and 2020. Patients were identified who were treated with TKIs at subtherapeutic doses. Subtherapeutic doses were defined as doses lower than those considered in the TKI data sheet: dasatinib 20 mg, imatinib 100 mg or 200 mg, nilotinib 150 mg, bosutinib 100 mg.

Results: Medical records were searched and 13 CML patients who received infratherapeutic TKI doses were identified, 7 men (53.9%) and 6 women (46.2%) with a mean age of 75.5 years. Of these patients, 7 (53.8%) received imatinib (6 with 200 mg doses and 1 with 100 mg), 1 (7.7%) received bosutinib 100 mg and 5 (38.5%) received dasatinib 20 mg. The mean follow-up time from the start of the dose reduction was 60.5 months and 40.7 months from the last reduction. None of the patients presented TKI resistance or progression during the follow-up period. 3 patients reduced the dose as a practical alternative for fear of discontinuation; 2 patients discontinued, but after relapse they remained with the minimum dose to maintain MMR; the rest of the patient reduced doses because of intolerance. All patients presented MMR at last follow-up and 92.3% deep MMR (≥MR4).

Summary/Conclusion: Our results show that TKI doses can be optimized on an individual basis to infratherapeutic levels and MMR or better can be maintained. Although only a small series of patients was studied, no patients developed TKI resistance or progression while receiving infratherapeutic doses during an average period of 5 years. For intolerant patients who received infratherapeutic doses, adverse events were resolved and quality of life improved. The administration of infratherapeutic TKI doses could also be a good option for patients who

relapse after a discontinuation attempt or for those who do not want to discontinue, as a form of "maintenance" therapy. The use of infratherapeutic doses, rather than a full TKI discontinuation, would still provide economic savings. Moreover, it would be interesting to evaluate if long-term use of infratherapeutic doses can prevent the development of serious off-target TKI toxicities, such as vascular events. Studies with larger patient cohorts are needed to validate the feasibility of this clinical practice.