Single hospital retrospective review of patients in treatment-free remission (TFR) following therapy with tyrosine kinase inhibitors (TKIs) for chronic myeloid leukaemia

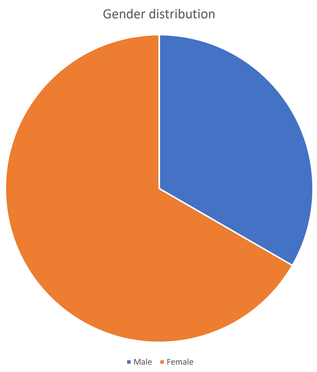
S. Kundu*, B. Lee, H. Grubb

Background:
Chronic phase CML (CML-CP) patients who obtain a durable major molecular response (MMR) or better on first and second generation TKIs can achieve long-term survival. TKI discontinuation is now being considered in patients with optimal molecular response and is a potential treatment goal for such patients. We did a retrospective review of patients who discontinued TKIs, if they had sustained molecular response (MR) of 4 (MR4) for at least 3 years on second generation TKIs and 5 years on first generation TKIs.

Objectives:
To retrospectively assess the duration of molecular response, relapse and withdrawal syndrome in evaluable TKI discontinued patients in a district general hospital (DGH) over a 2-year period.

Methods:
Data were collected from patient notes and health board laboratory portal from patients with CML-CP. Variable assessed included age, sex, lines of treatment, molecular response at time of TKI discontinuation, duration of continuing molecular response following TKI discontinuation, time of relapse and withdrawal syndrome.

Figure 1: Gender distribution of patients included in study



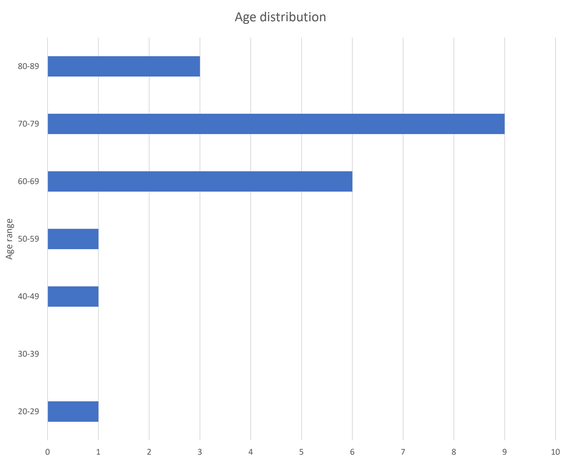


Figure 2: Age distribution of patients included in our study

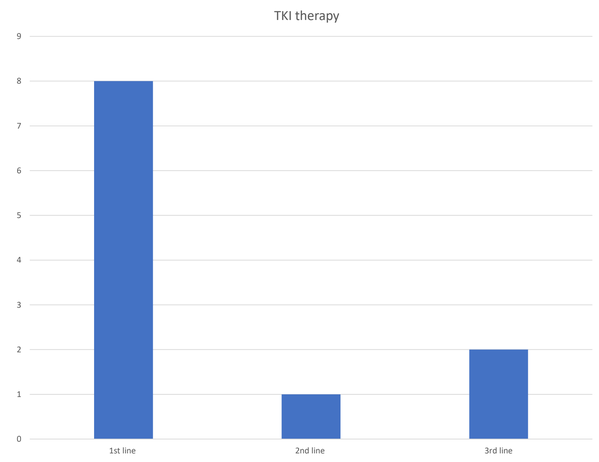


Figure 3: Line of therapy patients who were TFR eligible were receiving

Results:
We present an updated analysis of our results. There was a total of 21 CML-CP patients of whom 14 were female and 7 were male (Figure 1). Age range was 29 to 88 years with average age of patients being 69 years (Figure 2). Out of 21 patients, two patients with advanced age and associated co-morbidities received modified once daily dose of Nilotinib 300mg. Ten patients fulfilled the TFR eligibility and were included in our retrospective analysis. An additional patient who achieved MR4.5 followed by continuous MR of 24 months on first-line standard dose Nilotinib was also included in our review after discontinuing it for pancreatitis. Among these 11 patients, eight received first line, one patient received second line and two patients received third line TKIs (Figure 3). All patients receiving second- and third-line TKIs were primarily due to intolerance and not resistance. Of these, eight had discontinued TKIs while one patient on modified once daily Nilotinib refused to stop. One patient who had discontinued TKI subsequently died due to relapsed Hodgkin's lymphoma with her last response being MR4. Both elderly patients on once daily Nilotinib had deep MR though one has died, cause of which was unrelated to CML while the other was not keen on discontinuing. Average duration of MR was 15 months, ranging from 4 months to 30 months with two patients having molecular relapse at 5 months and 8 months respectively. Two of eight patients developed symptoms of withdrawal syndrome with both patients requiring re-institution of TKIs at 4 months and 8 months respectively.

Conclusion:
Our patient numbers are small as we are a small DGH. Majority of our patients maintained MMR or better off TKIs while two patients had molecular relapse. A proportion of our patients developed withdrawal syndrome and some of them required re-institution with TKIs. Elderly patients with co-morbidities receiving modified reduced doses could achieve and maintain optimal molecular response including deep MR. In our hospital, practice of TKI discontinuation in patients with optimal MR was adopted late in view of a single patient report we published in 2016. We had reported (BSH abstract number 520-2016) a rare occurrence in a patient with continuing MMR of over 5 years on TKIs who had sudden transformation to Philadelphia positive acute lymphoblastic leukaemia (ALL). A recent correspondence to British Journal of Haematology (BJH) also reported of a single patient developing sudden blastic lymphoid transformation in TFR CML (BJH 2019, 187, 543-545). Although in CML, TFR is a potential treatment goal in majority who achieve optimal MR, rare instances of blastic transformation in such patients is a concern and the trigger for this event remains unknown.