Abstract: P675

Title: IMATINIB THERAPY IN PREVIOUSLY UNTREATED CHRONIC MYELOID LEUKAEMIA PATIENTS WHO ACHIEVE MMR AFTER 12 MONTHS THERAPY WITH DASATINIB: A STRATEGY TO AVOID LONG TERM OFF TARGET TOXICITY

Abstract Type: Poster Presentation

Session Title: Chronic myeloid leukemia - Clinical

Background:

Despite the impressive outcomes seen with tyrosine kinase inhibitor (TKI) therapy in chronic myeloid leukaemia (CML), the optimal upfront therapy remains unclear. Second generation TKI (2G TKI) trials have shown significantly more rapid and deeper levels of molecular response with a lower incidence of progression to advanced stage disease, but no improvement in overall survival. 2G TKIs are however associated with long term side effects, including increased vascular events in patients receiving nilotinib and pulmonary toxicity in patients on dasatinib. In contrast, the innovator TKI imatinib has now been used in New Zealand for over 20 years, with side effects that are mild and manageable, and no emergent long term toxicity, making it an attractive option for safe, long term therapy.

Aims:

The objective of the KISS study (Kinase Inhibition with Sprycel Startup) is to investigate the efficacy and safety of de-escalating upfront 2G TKI therapy with dasatinib to imatinib in patients with chronic myeloid leukaemia (CML) who have reached a “safe haven” as defined by achieving MR3.0 after 12 months of therapy.

Methods:

This is a phase II trial of newly diagnosed adult patients with chronic phase CML (CP-CML) recruited from 9 New Zealand haematology centres, and treated upfront with dasatinib 100mg once daily. Patients achieving a confirmed MR3.0 at 12 months were transitioned to imatinib 400mg once daily and followed for 24 months. The primary objective is the proportion of patients who remain in MR3.0 for 2 years following the change of therapy from dasatinib to imatinib.

Results:

96 patients with CP-CML were recruited between 17 July 2017 and 14 April 2022, with data cut off 31 December 2022. Currently 75 patients have at least 12 months of follow up and 10 patients continue on dasatinib but have not yet reached the 12 month assessment. During the first 12 months of the study, 19 patients have withdrawn (n=11, including 2 patients with variant transcripts not able to be monitored by quantitative PCR) or discontinued study treatment (n=8); toxicity was the cause of this in 11 out of 19 patients. To date, 44 of 67 patients have achieved a confirmed MR3.0 after 12 months of dasatinib treatment. Of the 44 patients with confirmed MR3.0 at 12 months, 38 have consented to transition to imatinib.

Summary/Conclusion: Preliminary analysis of the KISS study suggests this is a feasible and well tolerated strategy. Longer term follow up, and molecular data will confirm whether this strategy can be used to rapidly induce a molecular response with initial 2G TKI therapy, followed by ongoing therapy with imatinib, avoiding the potential for significant off target side effects.

Keywords: Molecular response, Tyrosine kinase inhibitor, Chronic myeloid leukemia, Toxicity