HCQ extraction and analysis:

HCQ extraction from whole blood was based on previously reported methods [1]. HPLC analysis of HCQ was conducted on a Shimadzu HPLC system consisting of pump (LC-20AD), autosampler (SIL-20A) and DAD (SPD-20A) (Shimadzu Corp., Kyoto, Japan). Chromatographic separation was performed using a Gemini NX-C18 column (150 x 4.6 mm, 5 µm) coupled with a guard cartridge AJO-8368 (4 x 3 mm) (Phenomenex Inc., Torrance, California, USA) and mobile phase consisted of acetonitrile-ammonium formate (pH 4.0 adjusted with formic acid, 10:90, v/v). The flow rate was set at 1 ml/min and injection volume was 20 µL; detection wavelength was set at 329 nm during the data acquisition. The method was fully validated prior to patient sample analysis and the lower limit of detection was 8.5 ng and the intra-batch and inter-batch precisions were within 13% of RSD; the accuracy values of both intra-batch and inter-batch were < 8% deviation from the nominal values.

IM plasma levels:

IM plasma levels were conducted as previously described [2]. In brief, HPLC analysis was conducted using a Dionex UltiMate TM 3000 series. Patient plasma (200ul) was thawed at room temperature and spiked with clozapine, as an internal control, at a final concentration of 2500 ng/ml. Samples were run in duplicate. Samples were prepared as previously described and 50ul was introduced to a Gemini C6-Phenyl column fitted with a guard column. All TKI compounds were detected at an optimum wavelength of 260nm. Chromatograms were analysed using Chromeleon software version 6.8.

In vitro analysis:

In vitro analysis was performed as previously described, with 10uM HCQ used as an *in vitro* treatment [3]. In brief, CD34+ cells were isolated using the CliniMACs system, and cells cultured in physiological growth factor. For immunofluorescence analysis, cells were plated on 0.01% poly-l-lysine (Sigma, St Louis, Missouri, USA) pre-coated multispot microscope slides and, after 90min, fixed in PBS/3.7% formaldehyde

for 20min at room temperature. Cells were permeabilised in PBS/0.5% Triton-X-100 for 15min at room temperature. Slides were then washed with PBS and incubated with blocking solution (PBS/5% BSA) for 1h at room temperature followed by overnight incubation with LC3BII antibody (Cell signaling, Danvers, Massachusetts, USA) at 4°C. Slides were then washed with PBS and incubated with either Alexa Fluor 488 donkey anti-rabbit (Invitrogen, Waltham, Massachusetts, USA) or the isotype control (Rabbit IgG, Abcam, Cambridge, UK) for 1h at room temperature. Mounting media with DAPI (Vectashield) were used for nuclei staining and slides were analysed using a Zeiss LSM 780 confocal microscope. Analysis of the data was performed using the Imaging Software ZEN 2.1. For Colony Forming Cell (CFC) assays, 5×10^3 primary cells from each condition were added into 3mL of methylcellulose-based medium (Methocult H4034 Optimum, StemCell Technologies, Vancouver, Canada). 1.5 mL was transferred to a 35 mm tissue culture dish in duplicate and the number of colonies was counted after 10-14 days. For Long-term culture-initiating cell (LTC-IC) assays [4], cells were cultured on irradiated stromal feeder layers (M2-10B4 and S1/S1) and kept in culture with MyeloCult (StemCell Technologies, Vancouver, Canada) for 5 weeks. Cells were then transferred to CFC assays in duplicate and viable colonies were counted after 10-14 days.

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