

## Case Report

# Ramadan Fasting in a Patient with Chronic Myeloid Leukemia Receiving Nilotinib as Upfront

Husam N. Al-Dubai<sup>a</sup> Mohammed A. Yassin<sup>b</sup> Mohammed A. Abdulla<sup>b</sup>  
Mahmood S. Aldapt<sup>b</sup> Rola S. Ghassoub<sup>c</sup>

<sup>a</sup>Internal Medicine Department, Hamad General Hospital, HMC, Doha, Qatar;

<sup>b</sup>Department of Medical Oncology/National Centre for Cancer Care and Research, HMC, Doha, Qatar; <sup>c</sup>Department of Pharmacy, National Centre for Cancer Care and Research, HMC, Doha, Qatar

## Keywords

Fasting · Ramadan · Chronic myeloid leukemia · Nilotinib

## Abstract

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm classically described as triphasic disease: chronic, accelerated, and blast crisis. There are many unmet needs and unanswered questions about CML. Intermittent fasting in patients with CML on tyrosine kinase inhibitors is among these unmet needs. Here we report the effect of intermittent fasting on response to nilotinib as upfront in a 49-year-old female Muslim who fasted during Ramadan and took her medication once instead of twice daily and remained in major molecular response.

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## Introduction

Chronic myeloid leukemia (CML, also known as chronic myelocytic, chronic myelogenous, or chronic granulocytic leukemia) is a myeloproliferative neoplasm characterized by the dysregulated production and uncontrolled proliferation of mature and maturing granulocytes with fairly normal differentiation [1]. The clinical hallmark of CML is the uncontrolled production of mature and maturing granulocytes, predominantly neutrophils, but also basophils and eosinophils [2].

Dr. Husam N. Al-Dubai  
Internal Medicine Department, Hamad General Hospital  
Al Rayyan Road  
Doha (Qatar)  
HAlDubai@hamad.qa

Tyrosine kinase inhibitors (TKIs) are the initial treatment of choice for the majority of patients with CML. Adherence to daily administration of TKIs is critical to successful treatment of CML [2].

Ramadan fasting represents one of the five pillars of Islam and is considered as a mandatory religious duty. It includes absolute fasting from sunrise till sunset. Based on the geographical location, fasting hours vary and can reach up to 16 h, as here in Qatar [3].

Currently, imatinib, nilotinib, and dasatinib are approved for treatment of CML as upfront [4].

### Case Presentation

A 46-year-old female, previously healthy, was incidentally found to have leukocytosis. CBC showed WBC  $88.9 \times 10^3/\mu\text{L}$  (normal range:  $4\text{--}10 \times 10^3/\mu\text{L}$ ), Hb 12 g/dL (normal range: 12–15 g/dL), and platelet count  $397 \times 10^3/\mu\text{L}$  (normal range:  $150\text{--}400 \times 10^3/\mu\text{L}$ ). Peripheral smear showed marked leukocytosis with marked neutrophilia, marked shift to left and occasional circulating blast. Bone marrow aspiration and biopsy plus cytogenetic and FISH evaluations confirmed the diagnosis of CML in chronic phase. She was started on nilotinib 300 mg p.o. b.i.d. daily as upfront. She achieved complete hematological remission, complete cytogenetic remission, and major molecular response as per European Leukemia Net Recommendations 2013. The patient fasted during Ramadan and she admitted that she was taking nilotinib once instead of twice daily (since fasting hours were 16 h) and she inquired whether taking the medicine once instead of twice a day during Ramadan would affect her disease outcome or not. She was assessed objectively by looking at her CBC before, during, and after Ramadan as well as BCR/ABL quantification before, during, and after Ramadan and there was no change.

### Discussion

CML is a myeloproliferative disorder associated with the Philadelphia chromosome t(9;22)(q34;q11) resulting in the BCR-ABL1 fusion gene. This genetic abnormality results in the formation of a unique gene product (BCR-ABL1), a constitutively active tyrosine kinase that produces a continued proliferative signal resulting in the clinical manifestations of CML.

TKIs are the initial treatment of choice for the majority of patients with CML. They block the initiation of the BCR-ABL1 pathway. Adherence to daily administration of TKIs is critical to successful treatment of CML [2].

TKIs approved as upfront therapy are imatinib, nilotinib, and dasatinib. Imatinib and dasatinib are given as daily doses (400 mg/day and 100 mg/day, respectively apart from cases where smaller doses are enough to achieve MMR [5, 6]). Taking these medications during Ramadan fasting is feasible, as the patient can take them in the evening (i.e., after fast breaking). However, taking nilotinib is challenging for patients who intend to fast during Ramadan for 2 reasons. First, the dose of nilotinib is 300 mg twice daily (approximately 12 h apart). With fasting hours up to 16 h, the patients will have 8 h only during which they can take the two doses of nilotinib. Second, patients should avoid food  $\geq 2$  h before and  $\geq 1$  h after taking each dose of nilotinib [7]. Adherence to these considerations will be difficult and this will affect the drug absorption.

Our patient admitted that she took one dose of nilotinib daily instead of 2 doses. She was assessed before, during, and after Ramadan and she remained in disease remission.

It will be of importance in patients with CML to look for unmet needs and unanswered questions like ophthalmic manifestation [8], obesity [9], and obesity-related surgeries [10], AIHA [11–13] as well as fasting.

### Conclusion

In patients with CML who are on nilotinib, and in CHR, CCYR, MMR, nilotinib can be taken once instead of twice daily during Ramadan fasting. However, further studies are needed to confirm this result.

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### Statement of Ethics

This case report is approved by Hamad Medical Corporation Research Center and consent was taken from the patient for publication.

### Disclosure Statement

All authors declare no conflict of interest.

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Qatar National Library.

### Author Contributions

Husam N. Al-Dubai and Mohammed A. Yassin: writing and editing. Other authors: clinical care.

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