FAQ: What is the Role of Azithromycin in Treatment of Patients with COVID-19?

A recent open-label non-randomized study including 36 patients in France reported that hydroxychloroquine was associated with a higher rate of undetectable SARS-CoV-2 RNA in upper respiratory tract specimens at day 6 as compared with supportive care (70% vs 12.5%, p=0.001). In a subgroup of 6 patients that also received azithromycin to prevent bacterial superinfections, viral eradication rates at day 6 were higher as compared with hydroxychloroquine monotherapy (100% vs 57%, p<0.001). This study has received significant press, which has led to widespread prescribing of these agents for patients with possible or confirmed COVID-19 infection. This FAQ highlights several key limitations of this study:

- This study was an open-label, non-randomized trial that included few (n=36) patients
- No clinical outcomes or adverse events data were reported
- The study began with n=26 patients in the hydroxychloroquine group; however, results of the primary endpoint, virologic eradication at day 6, are only reported for n=20 patients. If these six patients were included as failures, the results of this study would be substantially different and perhaps less compelling. The six patients that were not included in the primary endpoint had the following outcomes:
  - three were transferred to the ICU (all PCR positive)
  - one died (PCR negative)
  - one left the hospital (PCR negative)
  - one withdrew due to nausea (PCR positive)
- Patients receiving hydroxychloroquine/azithromycin combination therapy generally had lower initial viral loads than patients in other groups, which suggests less anti-viral effect may have been required to achieve the endpoint of virologic eradication at day 6 among patients receiving combination therapy
- This study utilized nasopharyngeal swabs, which have been shown to be less sensitive than tests performed on bronchoalveolar lavage and sputum specimens

Given the limitations outlined above, we do not recommend routine prescribing of hydroxychloroquine/azithromycin therapy in patients with COVID-19 infection outside the setting of a clinical trial. In the event these agents must be co-administered, we agree with the CDC’s statement on this issue and recommend more frequent monitoring for cardiac events, such as QT prolongation: “Hydroxychloroquine and azithromycin are associated with QT prolongation and caution is advised when considering these drugs in patients with chronic medical conditions (e.g. renal failure, hepatic disease) or who are receiving medications that might interact to cause arrythmias”.

Reviewed on 3/24/20.

References:
Patients receiving combination therapy generally had lower initial viral loads vs patients receiving monotherapy or supportive care, which might have led to more rapid virologic eradication.

Despite n=26 patients initially included in the hydroxychloroquine monotherapy group, outcomes are only reported for n=20 patients. If the outstanding 6 patients were reported as failures, the results of this study would be arguably much less compelling.

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Take Home Points:

- Given the significant limitations of this study, we do not recommend routine use of the combination of hydroxychloroquine/azithromycin outside of a clinical trial setting.
- In the event these two agents must be co-administered, more frequent monitoring for cardiac events, such as QT prolongation, are warranted.