

## Non-hospitalized COVID-19-Adult Patients Treating with Oral Nirmatrelvir

Attapon Cheepsattayakorn<sup>1,2\*</sup>, Ruangrong Cheepsattayakorn<sup>3</sup> and Porntep Siriwanarangsun<sup>1</sup>

<sup>1</sup>Faculty of Medicine, Western University, Pathumtani Province, Thailand

<sup>2</sup>10<sup>th</sup> Zonal Tuberculosis and Chest Disease Center, Chiang Mai, Thailand

<sup>3</sup>Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

\*Corresponding Author: Attapon Cheepsattayakorn, 10<sup>th</sup> Zonal Tuberculosis and Chest Disease Center, Chiang Mai, Thailand.

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Nirmatrelvir (PF-07321332), an orally administered antiviral agent targeting on the SARS-CoV-2 3-chymotrysin-like cysteine protease enzyme (Mpro) with exhibition of inhibition of Mpro activity and coronavirus replication *in vitro* via metabolism mainly by CYP3A4 [1] were administered 300 mg plus 100 mg of ritonavir, as a pharmacokinetic enhancer [1,2] every 12 hours for 5 days in 1,120 symptomatic, unvaccinated, non-hospitalized COVID-19 patients, compared to 1,126 controls in a recent phase 2-3 double-blind, randomized, controlled trial [3]. *In vitro*, 90% effective concentration of nirmatrelvir on inhibition of SARS-CoV-2 viral replication was identified [3]. At day 5, nirmatrelvir plus ritonavir decreased viral load by an additional 0.689 +/- 0.082 log<sub>10</sub> copies/mL (95% CI: -0.849 to -0.529 relative to control group), whereas the preliminary analysis of 731 matched patients' specimens from day 1 and day 5 indicated no significantly statistical associations between treatment failure and Mpro mutations without evidence-based safety concerns [3].

In conclusion, in comparison to placebo, oral nirmatrelvir plus ritonavir revealed lowering the risk of severe COVID-19 progression.

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