Efficacy and Safety of Nelfinavir in Asymptomatic and Mild COVID-19 Patients: A Multicenter, Randomized Controlled Trial

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Background

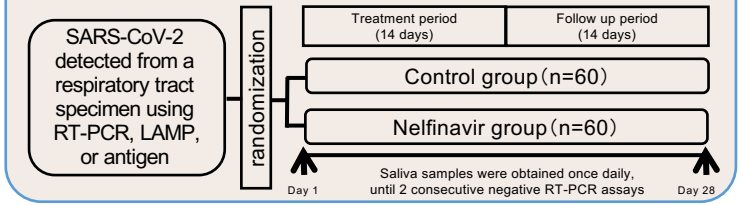
Nelfinavir, an orally administered inhibitor of HIV protease, inhibited the replication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) *in vitro*. The simulation of nelfinavir treatment for SARS-CoV-2 infection using a mathematical model suggested that the approved dosage for HIV was sufficient to reduce viral load [1]. To evaluate clinical efficacy and safety of nelfinavir, we conducted a randomized controlled trial.

Methods [2]

- Study design : a multicenter, open-label, blinded outcome assessment, parallel group, investigator-initiated, exploratory, randomized (1:1 ratio) controlled clinical trial.
- Patients : Asymptomatic and mild coronavirus disease 2019 (COVID-19)
- Settings : 11 university and teaching hospitals in Japan.
- Sample size : 120 patients (60 patients in each group)
- Investigational drug : nelfinavir (control group : standard-of-care alone)
- Dosage regimen : 750 mg orally 3 times daily for 14 days

(the treatment could be discontinued by the decision of investigator, if patients had 2 consecutive negative test results by qRT-PCR.)

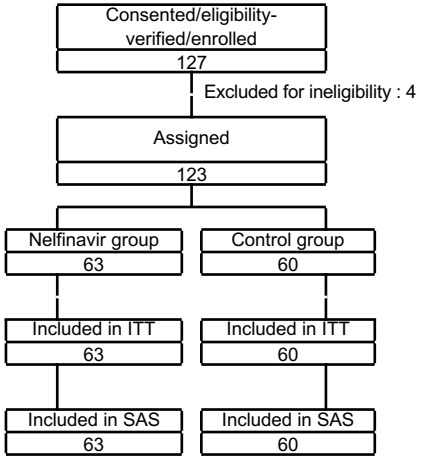
- Primary endpoint : time to clearance of SARS-CoV-2
- Secondary endpoints : viral dynamics, resolution of COVID-19 symptoms, and adverse events.
- Key inclusion criteria : adult patients testing positive for SARS-CoV-2 infection within 3 days
- Key exclusion criteria : onset of symptoms ≥ 8 days before enrollment, oxygen saturation of 95% or less on room air, and vaccinated patients.
- Adjustment factors for dynamic allocation : severity, age (<60 years)



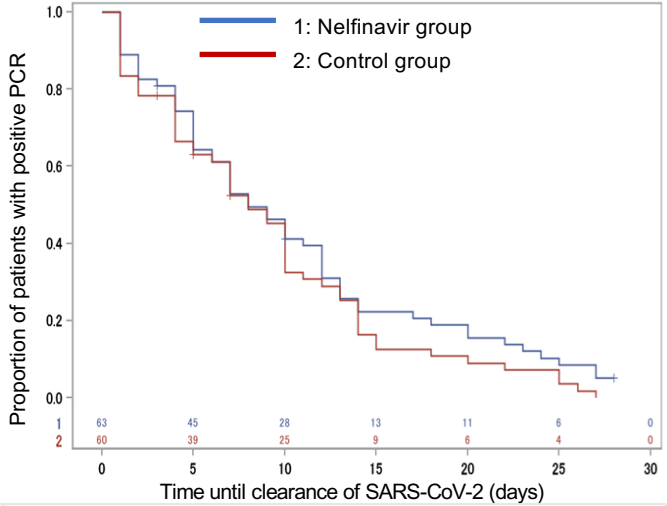
Results and Conclusion

- 123 participants (63 in the nelfinavir group and 60 in the control group) between July 2020 and October 2021
- Primary endpoint ; Median time to viral clearance
  nelfinavir group : 8.0 days (95% confidence interval [CI] 7.0 to 12.0), the control group : 8.0 days (95% CI 7.0 to 10.0)
  → statistically no significant difference (hazard ratio 0.815, 95% CI 0.563 to 1.182; $P = 0.1870$).
- Secondary endpoints : Nelfinavir were not associated with reduction in viral load or COVID-19 related symptoms.
- Adverse events were reported in 47 (74.6%) patients in the nelfinavir group and 20 (33.3%) in the control group.
  The most common adverse events in the nelfinavir group were diarrhea (49.2%).

Nelfinavir did not reduce the time to viral clearance in this setting.



ITT : intention to treat, SAS : safety analysis set



References; [1] Ohashi H, et al. iScience 2021; 24:102367.
[2] Hosogaya N, et al. Trials 2021; 22:309.

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