Pre-exposure Prophylactic Treatment with Ensitrelvir Inhibited SARS-CoV-2 Infection in Hamster Aerosol Transmission Model

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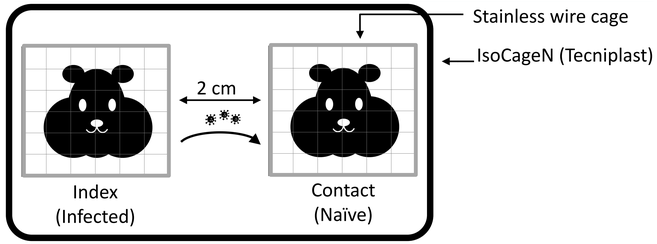
Background and Purpose

Although aerosol virus transmission is the major transmission route for SARS-CoV-2 and there remains a need to control SARS-CoV-2 spread with antivirals, prophylactic effect of pre-exposure antiviral treatments to prevent SARS-CoV-2 aerosol transmission remains to be clarified. Here, we administered ensitrelvir to naïve hamsters (contact) prior to exposure of virus aerosol shed by virus-infected hamsters (index) and evaluated the efficacy of the ensitrelvir on SARS-CoV-2 aerosol infection to elucidate the prophylactic effect of ensitrelvir on SARS-CoV-2 aerosol transmission.

Methods

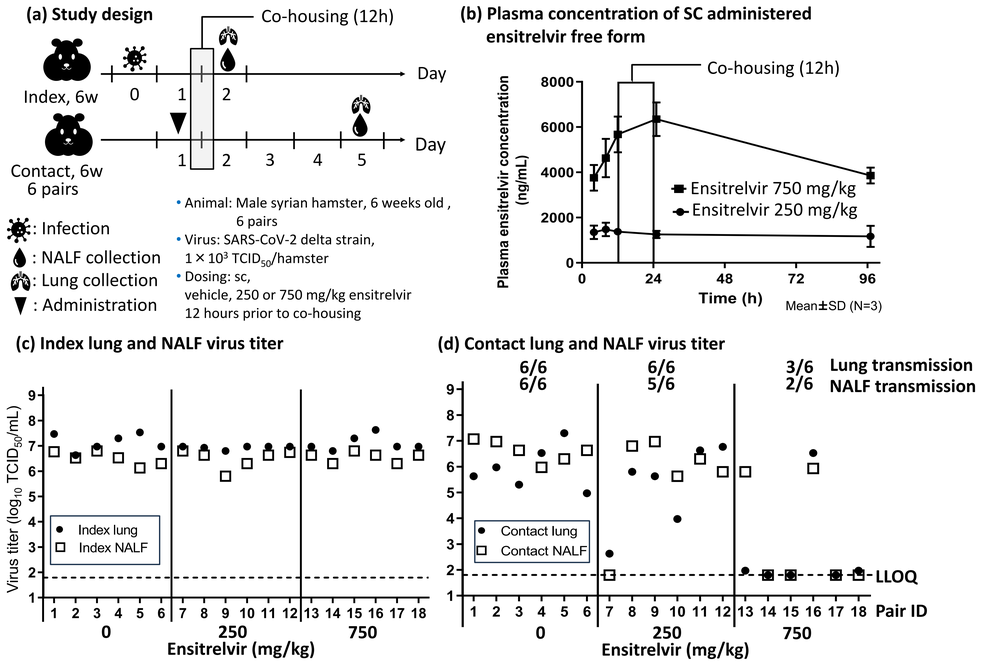
Six Syrian hamsters were intranasally inoculated with hCoV-19/Japan/TY11-927/2021 (delta strain) (index). Six naïve Syrian hamsters (contact) were subcutaneously administered ensitrelvir free form 250 or 750 mg/kg twelve hours before the cohousing based on ensitrelvir exposure in human. Index and contact hamsters were co-housed in separated two stainless wire cages to prevent direct viral transmission, and in same container allowing aerosol transmission of SARS-CoV-2 for twelve hours on one day post infection. To evaluate viral titers in lung and nasal lavage fluid (NALF), both samples were collected from index hamsters two days post infection and from contact hamsters four days after cohousing, respectively. To evaluate pathogenesis, body weight changes were monitored until ten days post infection and lung weights were measured ten days post infection.

Figure 1 Hamster SARS-CoV-2 aerosol transmission system [1]



Result

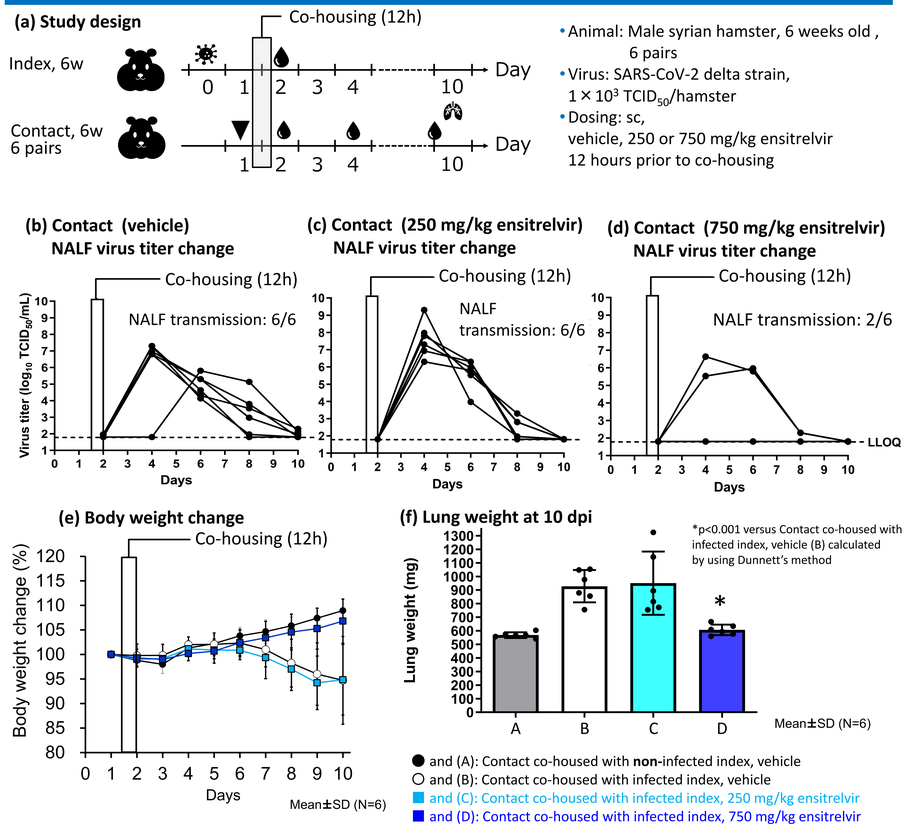
Figure 2 Effect of pre-exposure treatment with ensitrelvir on transmission



Conclusion

Pre-exposure treatment with 750 mg/kg ensitrelvir prevented hamsters from aerosol virus infection and suppressed body weight losses and lung weight increases of contact hamsters infected with SARS-CoV-2 via aerosol transmission route. Plasma concentration of ensitrelvir during co-housing was comparable to that of human ten days after initiation of dosing (orally once daily 375 mg on Day 0, 125 mg on Days 1 to 4) [2]. Therefore, the prophylactic effect against SARS-CoV-2 infection could be expected until ten days post first administration in human. These data suggest that prophylactic use of ensitrelvir may help protect at-risk individuals who live or work with SARS-CoV-2-infected patients.

Figure 3 Effect of pre-exposure treatment with ensitrelvir on pathogenesis



Acknowledgement

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Reference

[1] Sia SF et al. *Nature.* 2020 Jul;583(7818):834-838.
[2] Shimizu R et al. *Antimicrob Agents Chemother.* 2022 Oct 18;66(10):e0063222.