Antiviral evaluation of compounds against SARS-CoV-2

Molecule tested: olmesartan

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Introduction

In response to the recent emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, the Unité des Virus Émergents performed preclinical evaluation of drug candidates against SARS-COV-2. **This interim report has not been peer-reviewed.** The data of this report are available upon request.

The molecule tested here is the olmesartan, an antagonist of angiotensin II type 1 receptors marketed for the treatment of hypertension.

In vitro evaluation of efficacy of olmesartan

Olmesartan was identified as a potential hit by an antiviral screen based on the SARS-CoV-2 cytopathic effect inhibition (Touret et al., 2020). Its antiviral activity was further characterized from 40 µM to 0.6 µM in Vero-E6 cells using a viral RNA yield reduction assay as previously described (Touret et al., 2019, Touret et al., 2020). In these conditions, we did not measured any inhibition at 40µM. But despite this lack of activity, Olmesartan remains an interesting hit, because it interferes with the angiotensin pathways which play a key role in SARS-CoV-2 entry. Thus, we decided to go further and evaluated it *in vivo*.

In vivo evaluation of efficacy of olmesartan

Experiments were approved by the local ethical committee (C2EA—14) and French authorities (APAFIS#23975). Four-week-old female Syrian hamsters were intranasally infected with 10^4 TCID50 of the BavPat1 SARS-CoV2 strain as described previously (Driouich et al., 2020). To assess the efficacy of olmesartan, a group of 6 hamsters received the drug, orally, two times a day (BID). We used one dose of 8 mg/day (around 150 mg/kg/day). Treatment was initiated at day of infection, ended at 2 day post infection (dpi) and animals were sacrificed at 3 dpi. A control group of 6 infected/untreated animals received, orally, 0.9% Sodium Chloride solution. Viral replication was measured in lungs (infectious titres and viral RNA yields) and in plasma (viral RNA yields).

Results showed no significant reduction of viral replication in lungs and plasma compared to control group (**Figure 1**).

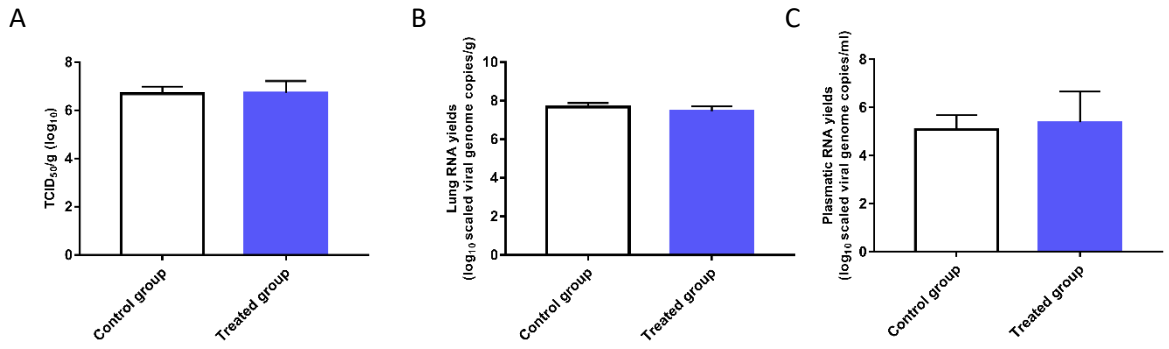

Figure 1: Viral replication in lungs (A-B) and in plasma (C). Lung infectious titers were measured using a $TCID_{50}$ assay and viral RNA yields were using an RT-qPCR assay as previously described (Driouich et al., 2020).

Conclusion

Olmesartan was found as a primary hit during the screen but then show poor efficiency *in vitro* with our RNA yield reduction assay. Moreover, results obtained using a hamster model suggest that this molecule is a poor inhibitor of SARS-CoV-2 replication *in vivo.*

References

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