

June 09, 2024

**Re: Scientific Advisor Review**

My comments regard the dissertation of Khaidarov Saken "Study of the antiviral activity of drugs against the SARS-CoV-2 virus in vitro" submitted to the defense for the degree Doctor of Philosophy (PhD) in specialty 8D05110 -Virology.

The SARS-CoV2 virus causes dangerous COVID19 (Corona virus disease 2019) and caused in 2020 the global pandemic and in worst clinical cases causes **the severe acute respiratory syndrome or atypical pneumonia** in human population. The SARS-CoV2 virus is highly contagious pathogen that is spread human to human, airborne and via infected surfaces.

The infectious nature of this virus disease in humans poses challenges in its control and treatment. Nowadays after several years after outbreak, we have learnt how to fight with COVID19 infection and various vaccines worldwide helped us to take the situation under relative control, nevertheless, during first year of pandemic, doctors around the world could do few things to mitigate the viral load and COVID19 progression inside the infected patients. Many lives could have been saved if the effective and potent antiviral drugs had been applied.

The antiviral drugs that are discussed in this thesis have not only broad-spectrum implementation strategies, but also the on-time, effective and potent viral infection treatment method inpatients ward as well as at home.

The main results of the work of S. Zh. Khaidarov are as follows:

-His work established the first time a purine analog treatment strategy in Kazakhstan: Tenvir (Tenofovir), Ribavirin and Fabiflu (Favipiravir) are effective against **SARS-CoV-2/human/KAZ/B1.1/2021** and highly likely against any strain of concern of SARS-COV2 virus, and therefore are recommended for clinical treatment against COVID19 in mild and moderate stages of progression. All four studied drugs could be used not only to treat COVID19 infected patients but also other pandemic sound outbreaks or seasonal Influenza A and B like infections within proper time line or antiviral effective time window.

- He identified the true potential of antiviral drugs in balanced equilibrium of drug cytotoxicity drug range, the optimal viral titer dilution, the non-structural protein (nsps) biological nature and its inhibition (replication interference). The peculiarity of SARS-CoV2 genome of Kazakh strain in comparison with Wuhan strain.

- No clinical recommendations should be made in this study. Perhaps a 'discussion' of possible usage could be made, but any hint of an actual clinical recommendation should be removed. This is not a clinical study and recommendations based on this work could be dangerous.

In general, the "Study of the antiviral activity of drugs against the SARS-CoV-2 virus in vitro" meets the requirements for a dissertation and is recommended for the degree Doctor of Philosophy (PhD) in specialty "8D05110 -Virology".

Sincerely,



Edan Tulman, Professor.

Pathology and Veterinary Science, and Center of Excellence for Vaccine Research