Medior, Inc.
Offering Website File

About Medior

Medior is a biotech co company seeking to repurpose existing antiviral medications to treat SARS CoV 2 (Covid-19) We are working on modifications in delivery format to use a known therapy to combat a newer virus

Reasons to Invest

New drug development takes years and substantial capital investment
Repurposing existing therapies is faster and a fraction of the cost
Exciting opportunity to treat novel viruses means expanding markets and the potential for growth.
Extraordinary possibility for market development

Covid-19 Pandemic

Since the 4Q2019 a novel virus causing severe acute respiratory syndrome spread globally. For nearly a year now we have been witnessing an uncontrolled spread of a pandemic caused by the coronavirus known as SARS CoV 2 (Covid 19)

Globally there are 50mm infected and 1 2mm dead

- Death rate of over 2% from those infected
- Potential of killing >100mm globally

Economically, Covid-19 has led to extreme results:

- 2020 global economic output is expected to shrink -5.2%.
- Increased unemployment throughout all developed economies
- Millions of workers on government supported job retention schemes – 19% of total workforce furloughed in United Kingdom, 23% in Germany, 29% in Italy and 41% in France Continuing social unrest.
- In the US, real GDP in 2Q2020 contracted 31.7%, expected to continue through 2020
- Over 20mm jobs lost during
- After initially lifting restrictions most have paused or reversed reopening plans

Vaccine	Drug
Goal is to develop a vaccine targeting a specific strain of the virus	Goal is to target inhibit growth/multiplication of the virus at any stage of its development via specific chemical substances
Covid-19 fortunately has not as yet shown a strong tendency to mutate	Potential drugs include "high-molecular" forms containing peptide or antibody units and so "called small molecule chemicals, characterized by the ability to interact with any of the key enzymes implicated in the development of this pathogen
Evidence suggests Covid 19 may be challenging to combat via vaccine owing to virus's ability to effect immune memory	According to multiple studies, one promising route targets structural modifications of selected chemical compounds to obtain a product with the greatest potential for application against Covid-19
Clinical analysis shows unexplained neurological effects associated with virus	This is referred to as "Repurposing" which is further discussed in these materials
Several vaccine trials were suspended due to unexplained illnesses in trial participants	A completely new drug would take very significant amount of time to develop
Not all viruses are candidates for vaccine for example, no HIV vaccine has ever been developed due to certain challenges	

Situation Overview

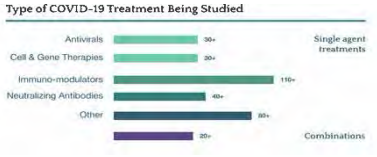
Development of Covid-19 Drugs

Globally governments have pledged billions of dollars for Covid 19 vaccine and treatment options.

Many pharmaceutical firms are racing to develop and test potential drugs that could help nations get back to "normal"

According to the IMF: Until such medical interventions become available in a country is safe

Hospitals and research labs are testing different therapies on coronavirus-positive patients in an effort to find a potential COVID-19 treatment



550+ Drug develop[illegible] planning

350+ Trials reviewed [illegible] Administration

5 COVID [illegible] authorized for emergency [illegible]

0 Treatments approved by FDA [illegible]

Role of Computational Chemistry

Repurposing antiviral drugs is a key for us to address the Covid 19 threat

Existing antiviral medications could effectively target Covid 19, yet are not effective in their existing form. Repurposing uses actionable and effective agents of existing antiviral medications via structural modifications of existing molecules with antiviral activity into potential active complex molecules.

Today, we can use computational chemistry to identify promising modifications and to create effective formulations. Computer models can predict outcomes, by using various drug properties as well as properties of other catalyst compounds to point us in the right direction for further research and development.

This approach is correlated with finding an effective drug combination to combat Covid-19 virus.

How do you normally develop drugs?

Drug development is a long and involved process. It often takes in the region of 15 years for a drug to be approved and prescribed to patients.

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1. This phase can include the early science done to understand a condition, and identify druggable targets. This is followed by identifying, or creating a compound to work on this target. Tens of thousands of compounds may be assessed with their potential to be therapeutic

2. This will include tests of your selected compound in chemical models, cell models, and eventually animal models of your disease. These tests will look for efficacy but also safety and toxicity of the drug.

3. This is the first stage at which a drug is tested in humans. Phase I trails are entirely geared towards tolerability and safety. As you move through Phase II there is a growing focus on efficacy, and a growing size of trial, with Phase III trails large and efficacy focused.

4. If trials are successful the drug then needs to be assessed by regulators before reaching patients.

Repurposing antiviral drugs is a key focus to address the Covid-19 threat.

- No NEW drugs
- Screen for drugs based on known behaviour
- Safety profile known
- Human use approved
- Fast track safety trials streamlined or skipped

- Repurposing offers a quicker, cheaper, and collaborative route to the development of effective treatments.
- It is an ideal route to rapidly address conditions with a high unmet need
- There are surprising commonalities between rare diseases and emerging infectious diseases that mean both can benefit from a repurposing approach to more rapidly deliver patient impact.
- Repurposing projects have a real chance on delivering a meaningful intervention to patients in a timely manner

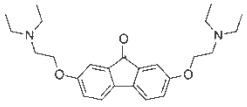
Zooming-In on Tilorone

Tilorone is the first recognized synthetic, small molecular weight compound that is an orally active interferon inducer. Tilorone induces the formation of interferons (alpha, beta, gamma) by intestinal epithelial cells, hepatocytes, T-lymphocytes, and granulocytes. After ingestion, the maximum production of interferon is determined in the sequence of the intestine – liver – blood after 4–24 hours.

The drug may work by activating specific innate immune system pathways that suppress viral replication.

Tilorone was originally synthesized and developed at the pharmaceutical company Merrell Dow which is now part of Sanofi. It is used in form of dihydrochloride salt.

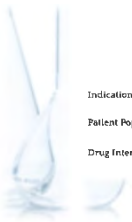
Tilorone is currently used clinically as an antiviral outside the USA and is sold under the trade names Amixin® or Lavomax®.



Tilorone has a track record of safe use in children and adults as both a prophylaxis and treatment for viral diseases.

Tilorone as a Broad-Spectrum Antiviral Therapeutic

Indications and Usage	- Treatment of EBOV - Post-exposure Prophylaxis of EBOV - Treatment of acute infections from ZIKV, CHIK, SARS-CoV, MERS-CoV, and/or influenza
Indications and Usage	Human Pharmacology: After oral administration, it is rapidly absorbed from the digestive tract. **Bioavailability is 40–60%.** Binding to plasma proteins is ~80%. It is not subject to biotransformation. **T1/2 = 48 h**, and is excreted unchanged in feces (70%) and urine (9%). It does not accumulate. According to Wacker et al. (1972) 16 h after intraperitoneal injection in mice high concentrations of ^{14}C-Tilorone were found in liver, followed by spleen, kidney, and lung. **Concentration in lungs was 16 times higher than in blood.** **Not a PGP substrate.**
Indications and Usage	No serious adverse effects. Acceptable therapeutic index to support treatment for life threatening.
Patient Populations	All age groups and populations
Drug Interactions	Compatible with antibiotics and other drugs for the treatment of viral and bacterial diseases



Tilorone – modes of antiviral action

Interferon induction

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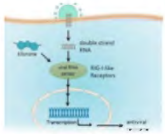
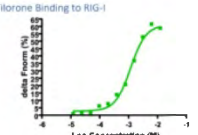


Tilorone Binding to RIG-I



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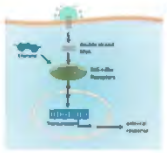
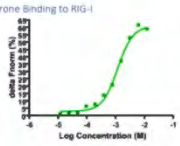




The Hypothesized Mechanism of Action for Tilorone is Activation of Innate Immunity Pathways such as the RIG-I-Like Receptor Pathway that Induces IFN and Activates a Cellular Antiviral Response. Binding Data of Tilorone to the Human Viral RNA Sensor RIG-I Shows a Low-Affinity (EC50 = 0.5 mM) in this Cell-Free in vitro Model (Ekins et al., 2020).

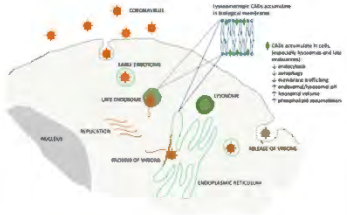
Tilorone – modes of antiviral action. Direct antiviral effect

Lysomorphotropic mechanism of action

Lysosomotropic compounds can diffuse freely and rapidly across the membranes of acidic cytoplasmic organelles in their unprotonated form, then when they enter the acidic environment they become protonated.

Tilorone, is an amphiphilic cationic compound.
The lysosomotropic mechanism may also have an important role as **Tilorone blocks viral entry**. Cationic amphiphilic drugs have been proposed recently as a useful starting point for broad spectrum antivirals.

Tilorone highly accumulates in lysosomes/endosomes and their membranes, reaching about 100-fold higher intracellular than their extracellular concentration (Ulf Norinder et all, 2020)

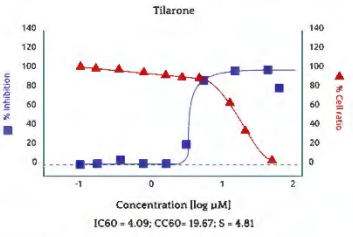


Interaction of lysosomotropic cationic amphiphilic drugs (CADs) and coronavirus with membrane trafficking in the cell (Ulf Norinder et all, 2020)

Tilorone anti-Sars-Cov-2 in-vitro efficacy

There are some preliminary signs that Tilorone, which was originally developed as an influenza treatment, may also work against other coronaviruses, including the ones that cause M E R S and S A R S. At least in vitro, it seems to have pan-coronavirus activity, it could be used against not just this coronavirus but others.

Tilorone as Potential COVID-19 Drug



IC60 = 4.09; CC60= 19.67; S = 4.81

Tilorone anti-Sars-Cov-2 in-vitro efficacy (Seungtaek Kim et all, 2020)

Dose- response anti-Sars-Cov-2 for Tilorone.

- Blue squares represent inhibition of virus infection (%)
- Red triangles represent cell viability (%)

Tilorone anti-Sars-Cov-2 in-vitro efficacy (own data)

In our own in vitro screening using visual detection of the cytopathic effect of infected Vero cells the direct ativiral effect has been determined with an EC50 of about 30 µM.

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Some key events in COVID-19 pathogenesis could be targeted by Tilorone:

- Cytokine storm. In severe SARS-CoV-2 infections, ARDS is the ultimate result of a cytokine storm. In this scenario, the release by immune effector cells of large amounts of pro-inflammatory cytokines (IFNα, IFNγ, IL-1β, IL-6, IL-12, IL-18, IL-33, TNFα, TGFβ) and chemokines (CXCL10, CXCL8, CXCL9, CCL2, CCL3, CCL5) precipitates and sustain s the aberrant systemic inflammatory response. The cytokine storm is readily followed by the immune system "attacking" the body, which in turn will cause ARDS and multiple organ failure, the final result being death, at least in the most severe cases of SARS-CoV-2 infection.
- Interferone type I deficiency. A distinct phenotype was observed in severe and critical patients, consisting of a highly impaired interferon (IFN) type I response (characterized by no IFN-b and low IFN-a production and activity), which was associated with a persistent blood viral load and an exacerbated inflammatory response. Inflammation was partially driven by the transcriptional factor nuclear factor-kB and characterized by increased tumor necrosis factor-a and interleukin-6 production and signaling. Type I IFN deficiency in the blood could be a hallmark of severe COVID-19 and provide a rationale for combined therapeutic approaches. (Jérôme Hadjadj et all, 2020)
- Auto-antibodies against type I IFNs. At least 10% of patients with life- threatening COVID-19 pneumonia have neutralizing auto- Abs against type I IFNs. The

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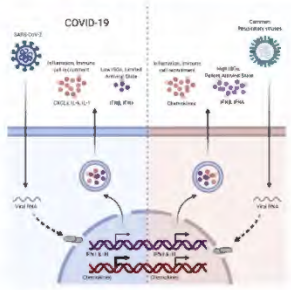
- Auto-antibodies against type I IFNs. At least 10% of patients with life- threatening COVID-19 pneumonia have neutralizing auto- Abs against type I IFNs. The crucial role of type I IFNs in protective immunity against SARS-CoV-2 confirmed for patients with inborn errors of type I IFNs and life- threatening COVID-19. These auto-Abs against type I IFNs were clinically silent until the patients were infected with SARS-CoV-2, which is a poor inducer of type I IFNs. The neutralizing auto-Abs against type I IFNs, like inborn errors of type I IFN production, tip the balance in favor of the virus with insufficient innate and adaptive immune responses (Paul Bastard et all, 2020).

Some key events in COVID-19 pathogenesis could be targeted by Tilorone

Interferons deficiency as substantial difference between COVID-19 and Common respiratory viruses



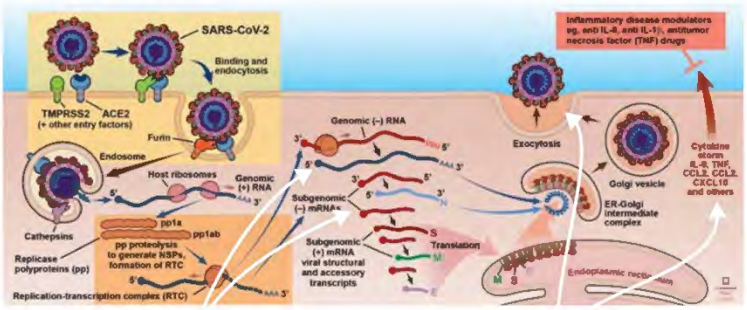
In comparison to other respiratory viruses, SARS-CoV-2 infection drives a lower antiviral transcriptional response that is marked by low IFN-I and IFN-III levels and elevated chemokine expression, which could explain the pro- inflammatory disease state associated with COVID-19.

- SARS-CoV-2 infection induces low IFN-I and -III levels with a moderate ISG response
- Strong chemokine expression is consistent across in vitro, ex vivo, and in vivo models
- Low innate antiviral defenses and high pro-inflammatory cues contribute to COVID-19

(Daniel Blanco-Melo et all, 2020)

Key Events

Key events of Sars-CoV-2 viral life-circle, targeted by Tilorone



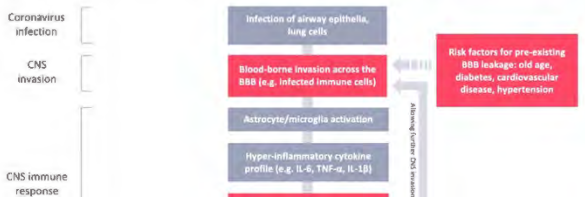
Intermolecular interactions of Tilorone with viral RNA and/or with RNA in the host cells could be considered as one of the molecular mechanism of antiviral activity of Tilorone

Interferon (IFN) response can be increased by Tilorone as IFN inducer. Tilorone can repress of viral IFN antagonists, and enhance of host antiviral IFN pathways. As a result the "cytokine storm" induced as a host response to rampant virus replication may be targeted by Tilorone.

Some other key events in COVID-19 pathogenesis could be targeted by Tilorone:

- SARS-CoV-2 Neuroinvasiveness in the brain
- SARS-CoV-2 persistence in testicles
- SARS-CoV-2 dependent ischemia
- Post-COVID-19 Lung fibrosis

SARS-CoV-2 neuroinvasiveness in the brain and pathogenesis neuropathological manifestations



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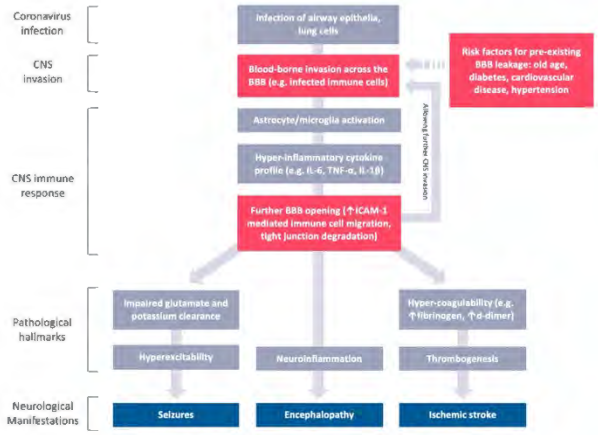

Tilorone as a potential anticovid drug

As evident from the above figures Tilorone can interact with Covid-19 at different levels of the disease:

- Via induction of INFs and an innate immune response
- Via direct antiviral effects
- Via immune privileged sites penetration (Brain, Testicles)
- Via its antifibrotic effect
- Via its antiischemic action

Proprietary Tilorone Research and Development

Financial Requirements for Next Steps