Peptides in COVID-19 Clinical Trials

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Since the beginning of the COVID-19 pandemic, there has been a strong drive and desire to find effective treatments for and protection against the disease. On the webpage ClinicalTrials.gov, a total of 6505 clinical trials currently (September 2021) investigating various aspects of COVID-19 are registered. Of these, 124 studies involving peptides were identified. These 124 were further evaluated, and 88 trials that used peptides only for routine diagnostics were excluded. The remaining 36 trials were classified into 5 different classes according to their function: immunomodulatory (5 trials), regain homeostasis (10 trials), diagnostics/biomarkers (8 trials), vaccination (9 trials), and antiviral activity (4 trials, all overlap with immunomodulatory activities). In the current review, these 36 trials are briefly described and tabularly summarised. According to the estimated finish date, 14 trials have not yet finished. All of the finished trials are yet to report their results. Seven trials were based in the USA, and Egypt, France, the UK, Turkey, and the Russian Federation conducted three trials each. This review aims to present a snapshot of the current situation of peptides in COVID-19 clinical trials and provides a template to follow up on trials of interest; it does not claim to be a complete overview.

Keywords: COVID-19 ; SARS-CoV-2 ; peptide ; clinical trial

1. Introduction

According to the world health organization (WHO, September 2021), more than 200 million people have been infected with SARS-CoV-2 (confirmed cases), claiming more than 4.5 million deaths. A worldwide race to understand this new virus and develop novel and effective treatment regimens and vaccinations has begun. Based on the rising success of peptides as drugs, many were investigated in the context of COVID-19, and some are already in clinical trials. The review presents a snapshot of the current situation in which peptides are being used in clinical trials based on the information provided on the webpage ClinicalTrials.gov.

2. Clinical Trials

2.1. Immunomodulatory

Peptides that are synthesised in the thymus are a heterogeneous family of peptide hormones demonstrating effects within the immune and neuroendocrine systems [1]. Purified or crude extracts are used, for example, in the treatment of cancer to stimulate the immune system [2]. A single-arm, open-label, phase II clinical study in Honduras enrolled 22 patients to evaluate the safety and efficacy of thymic peptides as an adjunctive treatment of COVID-19 [3]. In addition to standard treatment, these patients received orally lyophilised thymic peptides for up to 20 days or until medical discharge. The composition and ratio of these thymic peptides were not declared. While the study was completed (May 2021), no results have yet been published.

One particular peptide from the thymus, thymosin-alpha 1 (Ac-SDAAVDTSSEITTKDLKEKKEVVEEAEN), is a potent immunomodulator, and it can enhance the Thl response and has shown to have efficacy in animal models against hepatitis, influenza, and various cancers [4]. In a phase II study performed in the US, thymosin-alpha 1 was used to determine whether this peptide can reduce the occurrence of COVID-19 in patients needing dialysis [5]. Thymosin-alpha 1 will be administered at 1.6 mg/mL subcutaneously by injection twice weekly after dialysis for 8 weeks. The study will enrol 240 participants, and it is estimated to finish in May 2022. In a second interventional phase II clinical trial in the US, thymosin-alpha 1 will be investigated as adjuvant treatment in COVID-19 patients with lymphocytopenia [6]. The peptide will be administered subcutaneously at 1.6 mg/mL daily for a total of 1 week. The estimated enrolment is 80 participants, and it was estimated to finish in June 2021, but no results have yet been published.

The exaggerated immune response that can lead to a cytokine storm is driving disease severity and mortality in COVID-19 patients. A novel peptide called LSALT (LSALTPSPSWLKYKAL) was discovered by Arch Biopartners (Toronto, ON, Canada) and has been shown to inhibit dipeptidase 1, which is important in the recruitment of leucocytes in the lungs and liver [7]. A randomised, double-blind, phase II proof of concept study of the LSALT peptide, performed in the US, Canada, and Turkey, will investigate the prevention of acute respiratory distress syndrome (ARDS) and acute kidney injury in patients infected with SARS-CoV-2 [8]. The study plans to enrol 60 patients in which the treatment group will receive 100 mL of the 5 mg LSALT peptide by intravenous infusion over 2 hours daily. The study was estimated to finish in June 2021, but no updates have yet been posted.

Peptide fragments of the COVID-19 proteome were used to stimulate donor-originated COVID-19 specific T-cells (CSTC) to produce exosomes that contain immunomodulatory compounds, including INF γ [9]. These exosomes were inhaled daily five times for five days to reduce the number of virus particles in the lung. This strategy was only applied at the beginning of pulmonary symptoms. This interventional phase I study in Turkey planned to enrol 60 participants and was estimated to finish in May 2021, but no results have yet been posted.

2.2. Regain Homeostasis

SARS-CoV-2 uses the transmembrane angiotensin converting enzyme 2 (ACE2) as a receptor to enter cells and, therefore, influences the renin–angiotensin system (RAS) in the host. Reduction in ACE2 leads to reduction in ANG(1-7) (DRVYIHP) and an increase in ANG II. Simplified, whereas ANG(1-7) lowers blood pressure and has cardioprotective effects, ANG II increases blood pressure by causing vasoconstriction and sodium retention [10]. The RAS also plays a role in coagulopathy and inflammation, which is increased in COVID-19. A study in Turkey with an estimated enrolment of 20 patients planned to investigate the effect of ANG(1-7) as a supplement treatment of COVID-19 patients [11]. The peptide was sourced from plasma. The primary outcome measure was the mortality rate. The study started 25 April 2020, but no results have yet been reported. In a similar study in Belgium, ANG(1-7) is currently being evaluated in a phase II/phase III trial to test its safety and efficacy in COVID-19 patients with respiratory failure requiring mechanical ventilation [12]. ANG(1-7) is administered intravenously at 0.2 µg/Kg/h for 48 h. The estimated enrolment is 60 participants, and it is estimated to finish in June 2023. A similar interventional phase I/II study in Brazil uses ANG(1-7) (intravenously) for the adjuvant treatment of severe COVID-19 cases, enrolling 130 participants [13]. It is estimated to finish in December 2021.

Another study uses a modified ANG(1-7) molecule, TRV027, which is a more potent agonist at the angiotensin II type I receptor (AT1R), in the hope of counteracting ANG II accumulation and regaining homeostasis [14]. This UK-based study enrolled 30 COVID-19 patients, where the treatment group received TRV027 intravenously for 7 days 12 mg/h, and the placebo was saline infusion. The primary outcome measure was coagulopathy associated with COVID-19. The study finished in May 2021, but no results have yet been published. A second study, based at multiple centres in the USA, investigates TRV027 and TXA127 (a pharmaceutical formulation of e ANG(1-7)) as modulators for host tissue, monitoring the recovery rate and mortality of 1600 participants; it is estimated to finish in December 2022 [15]. The results are expected to be interesting, especially in comparison to the treatment of recombinant ACE2, which unfortunately showed a higher mortality rate in the treatment group. This clinical trial using recombinant ACE2 examined COVID-19 patients, where the treatment group received recombinant human angiotensin-converting enzyme 2 (hrACE2) intravenously twice daily and the control group received physiological saline solution. It showed very minor positive effects related to all cause-death or invasive mechanical ventilation, 10.12% vs. 13.3%; however, mortality alone showed a slight detrimental effect, 10.2% vs. 7.8% [16].

The vasoactive intestinal peptide (VIP, HSDAVFTDNYTRLRKQMAKKYLNSILNG) is an important neurotransmitter/neuromodulator in the central and peripheral nervous systems and plays a vital role in maintaining homeostasis in the gastrointestinal tract, as well as being important for oxygen transfer, surfactant production, and maintenance of alveolar type 1 cells in the lungs [17]. A multicentre phase III study is evaluating the safety and efficacy of different drugs to treat COVID-19 patients adjunctive to the current standard of care [18]. One drug under investigation is VIP. An estimated 640 patients will be recruited, and VIP will be administered intravenously over 12 hours per day for three days. This study is estimated to be completed i April 2023 [19]. A phase II interventional trial in Turkey is evaluating an inhalable VIP analogue called Aviptadil in 80 participants, and this trial is estimated to finish in December 2022. Furthermore, intravenously administered Aviptadil was evaluated in a phase II/III multicentre trial in the USA, where patients were administered Aviptadil in escalating doses of 50l, 100, and 150 pmol/kg/h [20]. In total 196, patients have been enrolled; the study finished in February 2021, no results have yet been published.

A phase II interventional trial performed in France is investigating the novel drug FX06, a fibrin-derived peptide beta15-42 that is able to stabilise cell–cell interactions, in the context of treating acute respiratory distress syndrome (ARDS) [21]. The hypothesis is that the drug can reduce vascular leakage in the lung and therefore reduce ARDS. The study was completed (June 2021), 50 participants were enrolled, and no results have yet been posted.

According to Bhutta et al. the peptide RLS-0071 with the sequence IALILEPICCQERAA-dPEG24 is an inhibitor of the complement pathway and modulates neutrophil activation [22]. This peptide was recently developed for the treatment of acute lung injury in COVID-19 patients and was evaluated in a phase I clinical trial (USA) with 42 participants; it was estimated to finish in July 2021 [23].

2.3. Diagnostics/Biomarkers

A study in Egypt aimed to evaluate the N-terminal pro B-type natriuretic peptide (NTproBNP, MDPQTAPSRALLLLLFLHLAFLG-GRSHPLGSPGSASDLETSGLQEQRN-HLQGKLSELQVEQTSLEPLQESPRPTGV) as a marker for COVID-19 illness progression and correlation with mortality and cardiac injury [24]. In addition, D-dimer and serum tropinin I were evaluated. A second observatory study from Egypt investigated both NTproBNP and vitamin D levels in 100 COVID-19 patients and monitored disease progression [25]. Reduced vitamin D levels have been linked to disease severity [26][27][28]. High-dose vitamin D has shown to be antiviral, and, amongst other effects, it seems to stimulate the production of antimicrobial peptides in hosts; therefore, high-dose vitamin D is being studied in another

clinical trial in Egypt [29]. A similar observational study performed in France evaluated NTproBNP and the high-sensitive cardiac troponin T (hs-cTnT) as potential markers for disease prognosis [30]. In total, 111 patients were enrolled and the study finished in June 2020, but no results have yet been published. Another clinical trial based in the UK is using NTproBNP together with other markers to develop biomarkers for disease progression in paediatric inflammatory multisystem syndrome associated with SARS-Cov-2 (PIMS-TS) [31]. This observational study plans to enrol 100 participants and is estimated to finish in December 2021.

In an observational study in Israel, peptides were used to explore the T-cell response in convalescing and healthy individuals [32]. In addition, the T-cell response was compared to the antibody response. The estimated enrolment was 400 participants, and the study was estimated to finish in October 2021.

The integrin $\alpha_v\beta_6$ is usually undetectable in healthy adults but is expressed in various cancers [33]. Consequently, the $\alpha_v\beta_6$ binding peptide can be used for the detection of various cancers. A radioactively labelled variant is used for PET/CT scans ([18F]-$\alpha_v\beta_6$ binding peptide). A study in the US is using this peptide to perform PET/CT scans on COVID-19 patients to determine whether lung damage can be detected with this method [34]. Ten patients will be enrolled, and the study is estimated to be finished in May 2022. In a similar study, the expression of the integrin $\alpha_v\beta_3$ was evaluated to determine whether lung damage can be monitored in COVID-19 patients [35]. For this purpose, the already established peptide [68Ga]Ga-DOTA-(RGD)2 was used in PET/CT scans. This observational study planned to enrol 10 participants, and it was estimated to finish in March 2021. No results have yet been posted.

An observational trial in France intends to study pulmonary fibrosis in 200 COVID-19 patients [36]. The current standard of diagnostic is lung biopsy and pathological changes in samples. This trial will investigate biomarkers and CT scans to establish a non-evasive diagnostic method. Among other markers, amino-terminal type I (PINP) and type III (PIIINP) peptides of procollagen will be investigated. The enrolment is complete, and the study is estimated to finish in December 2021.

2.4. Vaccination

Peptides are also used for vaccination against COVID-19. In an open-labelled phase I trial, a novel multi-peptide vaccine is being tested for safety and immunogenicity on 36 non-COVID-19 volunteers [37]. The peptides represent T-cell epitopes shown to be effective against COVID-19 and are combined with the novel TLR1/2 ligand XS15 emulsified in Montanide ISA 51 VG as an adjuvant. The estimated completion date is December 2021. The same vaccine will be used in a phase I/II study to evaluate its safety and immunogenicity in patients (adults) with B-cell/antibody deficiency [38]. The study will enrol 68 patients, and it is estimated to finish in March 2022. A further vaccine that represents peptides from 11 different SARS-CoV-2 proteins aiming to achieve a T-cell response is called the CoVepiT vaccine (OSE-13E). This vaccine is being studied in a phase I interventional trial in Belgium, 48 participants are estimated to be enrolled, and the study is estimated to finish in March 2022 [39]. In a phase I clinical trial based in Taiwan, the vaccine UB-612, which contains Th/CTL epitope peptide pool, was studied with an anticipated enrolment of 60 participants [40]. The estimated finish date was May 2021, but no results or updates have yet been posted. The same vaccine (UB-612) is also being used in a phase II trial that enrolled 3850 participants, and it is estimated to finish in June 2022 [41]. An observational trial performed in the UK is studying T-cell epitopes by screening overlapping peptides from the SARS-CoV-2 proteome [42]. Identifying immunodominant T-cell epitopes might improve further vaccine development. The estimated enrolment is 200 participants, and the study is estimated to finish in December 2023.

A Russian phase I/II study will investigate the safety and immunogenicity of a peptide-based vaccine (EpiVacCorona) against COVID-19 [43]. The chemically synthesised peptides are antigens of SARS-CoV-2 proteins, conjugated to a carrier protein and adsorbed on an aluminium-containing adjuvant (aluminium hydroxide). Vaccination will be performed twice, with a break of 21 days in between. The same vaccine (EpiVacCorona) with the same protocol was used in a phase III study with 150 volunteers aged above 60, and this trial finished in January 2021 [44]. In addition, a phase III clinical trial to study the tolerability, safety, immunogenicity, and preventive efficacy of the EpiVacCorona vaccine has recruited 3000 volunteers [45]. The same protocol was used, and this trial was estimated to finish in September 2021. For these three studies, no results have yet been published.

2.5. Antiviral Activity

It was shown that the human ezrin peptide 324-337, HEP1 (TEKKRRETVEREKE), was very effective in the treatment of hepatitis C virus (HCV), accelerated and facilitated wound and ulcer healing in clinical applications, and was well tolerated [46][47]. This peptide was used in a randomised, double-blind phase I study to investigate the efficacy and safety of the peptides in COVID-19 patients [48]. An estimated 20 patients were recruited, and the treatment group received an induction dose of 2 mg HEP1 every 12 hours subcutaneously until their symptoms disappeared, followed by a maintenance supply of 0.2 mg/day, for 10 days.

Lactoferrin and its related peptides have been shown to possess antimicrobial, antiviral, and immunomodulatory activity [49]. An interventional phase II/III study based in Egypt is evaluating the effect of lactoferrin as adjuvant therapy; two concentrations are being tested, 400 and 600 mg daily (orally) [50]. The study's estimated enrolment was 150 participants, and it was estimated to finish in November 2020, but no results have yet been published. In another interventional phase

II/III trial located in Egypt, 200 mg of lactoferrin (orally) was used to study its prophylactic effect on healthcare workers [51]. A total of 200 participants were estimated to be enrolled, and the study was estimated to finish in November 2020, but no results have yet been posted.

Similar to lactoferrin, ovotransferrin and its derived peptides are antimicrobial, antiviral, and immunomodulatory [52][53]. In an interventional clinical trial in Italy, 200 mg ovotransferrin was orally administered for 10 days as adjunctive therapy for mild and moderate COVID-19 cases [54]. The targeted enrolment was 100 participants, and the study was estimated to finish in March 2021, but no results have yet been posted published.

The above-discussed clinical trials are summarised in **Table 1**. The selected peptides used in clinical trials are presented in **Figure 1**.

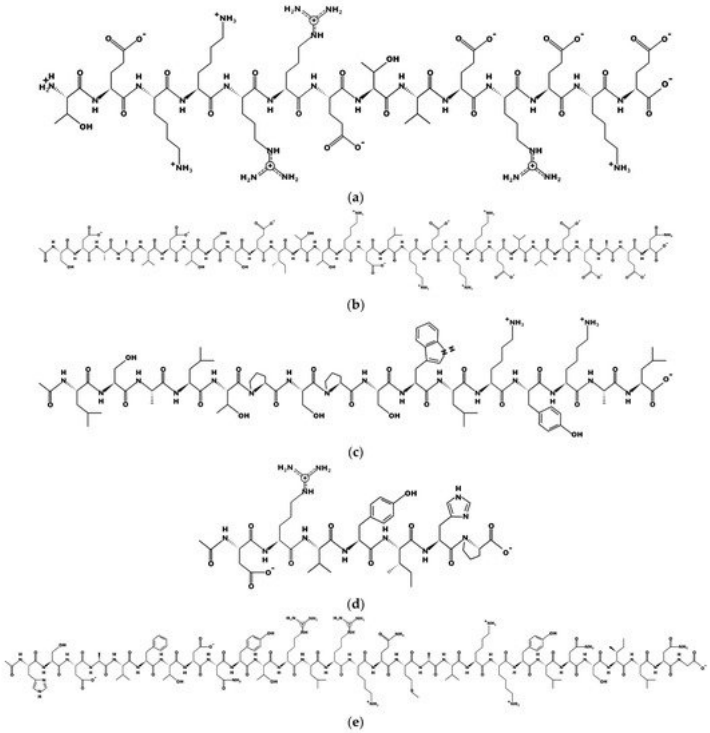

Figure 1. Schematic representation of selected peptides used in clinical trials. (**a**) Human ezrin peptide 324-337, HEP1; (**b**) thymosin-alpha; 1 (**c**) LSALT peptide; (**d**) angiotensin peptide (1-7); (**e**) vasoactive intestinal peptide (VIP) using the program PEPDRAW (http://pepdraw.com/) (accessed on 7 October 2021).

Table 1. Overview of 36 clinical trials according to information obtained from ClinicalTrials.gov. Bold indicates trials that are not yet finished according to the estimated finish date.

Title	Peptide	Function
Efficacy and Safety of Lactoferrin as an Adjunct Therapeutic Agent for COVID-19	**Peptides derived by proteolytic cleavage of lactoferrin**	**Antivira immunomo**
Efficacy of Lactoferrin as a Preventive Agent for Healthcare Workers Exposed to COVID-19	**Peptides derived by proteolytic cleavage of lactoferrin**	**Antivira immunomo**
The Clinical Trial of Application of Ezrin Peptide (HEP-1) for Treatment of Coronavirus Disease (COVID-19) Infection	**Human ezrin peptide 324-337, HEP1 (TEKKRRETVEREKE)**	**Antivira immunomo**
Efficacy and Safety of Ovotransferrin in COVID-19 Patients With Mild-to-Moderate Disease	**Peptides derived by proteolytic cleavage of ovotransferrin**	**Antivira immunomo**

Title	Peptide	Function
B-natriuretic Peptide (BNP), Serum Troponin-I, and D-dimer as Risk Factors for In-hospital Death in Patients With COVID-19	N-terminal pro B type natriuretic peptide (NTproBNP, MDPQTAPSRALLLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQEQRNHLQGKLSELQVEQTSLEPLQESPRPTGV)	Diagnostic/b
N-terminal Pro B-type Natriuretic Peptide and Vitamin D Levels as Prognostic Markers in COVID-19 Pneumonia	N-terminal pro B type natriuretic peptide (NTproBNP, MDPQTAPSRALLLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQEQRNHLQGKLSELQVEQTSLEPLQESPRPTGV)	Diagnostic/b
Cardiac Biomarkers and Mortality in Critically Ill Patients With SARS-CoV-2 (COVID-19): COROBIOCHIC	N-terminal pro B type natriuretic peptide (NTproBNP, MDPQTAPSRALLLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQEQRNHLQGKLSELQVEQTSLEPLQESPRPTGV)	Diagnostics/I
Incidence, Risk Factors and Prognosis of Pulmonary Fibrosis During Severe COVID-19 Pneumonia	amino-terminal type I (PINP) and type III (PIIINP) peptides of procollagen	Diagnostics/I
Prospective, One Center, Four Groups, Open, Comparative, Controlled Study to Explore T Cells Response to SARS COV 2 Peptides by Metabolic Activity Method in Convalesce and Healthy Individuals Versus Antibody Response	undefined SARS-CoV-2 peptides	Diagnostics/I
[68Ga]Ga-DOTA-(RGD)2 PET/CT Imaging of Activated Endothelium in Lung Parenchyma of COVID-19 Patients	[68Ga]Ga-DOTA-(RGD)2	Diagnostics/I
Investigating Cytokine Storm Biomarkers in Children Presenting to Acute Paediatric Services (Non-intensive Care) With Paediatric Inflammatory Multisystem Syndrome During the Covid-19 Pandemic. An Observation Study	N-terminal pro B type natriuretic peptide (NTproBNP, MDPQTAPSRALLLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQEQRNHLQGKLSELQVEQTSLEPLQESPRPTGV)	Diagnostics/I
18F-$\alpha_v\beta_6$-binding-peptide PET/CT in Patients Post SARS CoV2 Infection	[18F]-$\alpha_v\beta_6$ binding peptide	Diagnostics/I

Title	Peptide	Function
A Single-arm, Open-Label, Phase II Clinical Study to Evaluate the Safety and Efficacy of Thymic Peptides in the Treatment of Hospitalized COVID-19 Patients in Honduras	thymic peptides, composition and source unknown	Immunomo
Aerosol Inhalation of the Exosomes Derived From Allogenic COVID-19 T Cell in the Treatment of Early Stage Novel Coronavirus Pneumonia	peptide fragments of the COVID-19 proteome	Immunomo
A Pilot Trial of Thymalfasin (Ta1) to Prevent COVID-19 Infection in Renal Dialysis Patients)	thymosin-alpha 1 (Ac-SDAAVDTSSEITTKDLKEKKEVVEEAEN)	Immunomo
A Pilot Trial of Thymalfasin (Ta1) to Treat COVID-19 Infection in Patients With Lymphocytopenia	thymosin-alpha 1 (Ac-SDAAVDTSSEITTKDLKEKKEVVEEAEN)	Immunomo
Multicenter, Randomized, Double-Blind, Placebo-Controlled, Proof of Concept Study of LSALT Peptide as Prevention of Acute Respiratory Distress Syndrome (ARDS) and Acute Kidney Injury in Patients Infected With SARS-CoV-2 (COVID-19)	LSALT (LSALTPSPSWLKYKAL)	Immunomo
Angiotensin-(1,7) Treatment in COVID-19: the ATCO Trial	angiotensin peptide (1-7) (DRVYIHP)	Restor homeos
Randomized Clinical Trial Phase I/II for the Use of Angiotensin-(1-7) in the Treatment of Severe Infection by Sars-CoV-2	angiotensin peptide (1-7) (DRVYIHP)	Restor homeos
FX06 to Rescue Acute Respiratory Distress Syndrome During Covid-19 Pneumonia	fibrin-derived peptide beta15-42	Restor homeos
Evaluation of the Possible Role of Angiotensin Peptide (1-7) on Treatment of COVID-19	angiotensin peptide (1-7) (DRVYIHP)	Restor homeos

Title	Peptide	Function
A Comparative, Multicenter, Placebo-Controlled, Double-Blind Phase II Clinical Trial Evaluating the Efficacy, Safety and Tolerability of Inhaled Aviptadil in Patients 18 Years and Older With COVID-19 Pulmonary Involvement - HOPE	Aviptadil, a vasoactive intestinal peptide (VIP), analogue, inhalable	Restor homeos
Investigating the Relationship Between the Renin Angiotensin System and the Coagulopathy Associated With COVID-19	TRV027, a modified angiotensin peptide (1-7) (XRVYIHPA; X stands for sarcosine (Sar), and the C-terminal alanine residue has a hydroxy group)	Restor homeos
CONNECTS Master Protocol for Clinical Trials Targeting Macro-, Micro-immuno-thrombosis, Vascular Hyperinflammation, and Hypercoagulability and Renin-angiotensin-aldosterone System (RAAS) in Hospitalized Patients With COVID-19 (ACTIV-4 Host Tissue)	TRV027 and TXA127, (TRV027:XRVYIHPA; X stands for sarcosine (Sar), and the C-terminal alanine residue has a hydroxy group), TXA127: pharmaceutical formulation of the natural angiotensin peptide (1-7) DRVYIHP)	Restor homeos
ZYESAMI (Aviptadil) for the Treatment of Critical COVID-19 With Respiratory Failure	Aviptadil (HSDAVFTDNYTRLRKQMAVKKYLNSILN), a vasoactive intestinal peptide (VIP), analogue, intravenously administered	Restor homeos
A Randomized, Double-Blind, Placebo-Controlled, Two-Part Study to Evaluate the Safety, Tolerability, Preliminary Efficacy, PK, & PD of RLS-0071 in Patients With Acute Lung Injury Due to COVID-19 Pneumonia in Early Respiratory Failure	RLS-0071 (IALILEPICCQERAA-dPEG24)	Restor homeos
A Multicenter, Adaptive, Randomized, Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for Hospitalized Patients With Acute Respiratory Distress Syndrome Associated With COVID-19	vasoactive intestinal peptide (VIP: HSDAVFTDNYTRLRKQMAVKKYLNSILNG and other drugs)	Restor homeos

Title	Peptide	Function
A Randomized, Open Label, Phase 1 Study to Evaluate the Safety, Reactogenicity and Immunogenicity of OSE-13E, a Multiepitope-based Vaccine Candidate Against COVID-19, in Healthy Adults (COVEPIT-3)	T-cell epitopes from 11 different proteins of SARS-CoV-2	Vaccina
P-pVAC-SARS-CoV-2: Phase I Single-center Safety and Immunogenicity Trial of Multi-peptide Vaccination to Prevent COVID-19 Infection in Adults	a mixture of undefined peptides	Vaccina
B-pVAC-SARS-CoV-2: Phase I/II Multicenter Safety and Immunogenicity Trial of Multi-peptide Vaccination to Prevent COVID-19 Infection in Adults With Bcell/ Antibody Deficiency	a mixture of undefined peptides	Vaccina
Simple, Blind, Placebo-controlled, Randomized Study of the Safety, Reactogenicity and Immunogenicity of Vaccine Based on Peptide Antigens for the Prevention of COVID-19 (EpiVacCorona), in Volunteers Aged 18-60 Years (I-II Phase)	chemically synthesised peptides are antigens of SARS-CoV-2 proteins, undefined	Vaccina
An Open Study of the Safety, Reactogenicity and Immunogenicity of the Vaccine Based on Peptide Antigens for the Prevention of COVID-19 (EpiVacCorona), With the Involvement of Volunteers Aged 60 Years and Above (Phase III-IV)	chemically synthesised peptides are antigens of SARS-CoV-2 proteins, undefined	Vaccina

Title	Peptide	Function
Multicenter Double-blind Placebo-controlled Comparative Randomized Study of the Tolerability, Safety, Immunogenicity and Prophylactic Efficacy of the EpiVacCorona Peptide Antigen-based Vaccine for the Prevention of COVID-19, With the Participation of 3000 Volunteers Aged 18 Years and Above (Phase III-IV)	**chemically synthesised peptides are antigens of SARS-CoV-2 proteins, undefined**	**Vaccina**
A Phase I, Open-label Study to Evaluate the Safety, Tolerability, and Immunogenicity of UB-612 Vaccine in Healthy Adult Volunteers	**Th/CTL epitope peptide pool**	**Vaccina**
A Phase II, Placebo-controlled, Randomized, Observer-blind Study to Evaluate the Immunogenicity, Safety, and Tolerability of UB-612 Vaccine Against COVID-19 in Adolescent, Younger and Elderly Adult Volunteers	**Th/CTL epitope peptide pool**	**Vaccina**
Characterisation of the Immune Response to SARS-CoV-2 Infection	**overlapping peptides from the SARS-CoV-2 proteome**	**Vaccina**

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