Sick of Covid-19? Listen in for THE source on the latest research, drug development and treatments
How AdisInsight keeps up with COVID-19 research

Global research on vaccines and treatments for Covid-19 has created an unprecedented amount of information.

- 5.8 billion results on Google
- 53 thousand articles on PubMed
- 6 thousand clinical trials

AdisInsight is an integrated database of profiles authored by our staff of expert medical editors from information that is publicly available through journals (all publishers), conferences, media releases, company websites, internet trial registries, SEC filings, and investor pages to give users quick and accurate insights into drugs in development, clinical trials, drug safety, deals, and patents to help them make more informed research decisions.
Answers to the Big Questions...

• **What is the status of pharmaceutical research for Covid-19?**
• What are the trends in pharmaceutical research for Covid-19?
• What are the PK/PD characteristics of novel treatments for Covid-19?
• What trial results are being reported for leading treatments for Covid-19?
• What are the adverse events associated with treatments for Covid-19?
What is the status of research for Covid-19?

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Mechanism of Action</th>
<th>Active Indication and Highest Phases</th>
<th>Originator</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRV 431</td>
<td>Cyclophilin inhibitors; Sodium-bile acid cotransporter inhibitors</td>
<td>Phase III: Non-alcoholic steatohepatitis. Phase III: Hepatitis B. Preclinical: Adult respiratory distress syndrome; COVID 2019 infections; Hepatitis D; Liver cancer; Non-alcoholic fatty liver disease</td>
<td>Isotechnika</td>
</tr>
</tbody>
</table>
What is the status of research for Covid-19?
What is the status of research for Covid-19?

Progress of Covid-19 Research Programs

- Marketed: 2
- Registered: 0
- Pre-registration: 0
- Phase III: 30
- Phase II/III: 25
- Phase II: 92
- Phase I/II: 18
- Phase I: 42
- Phase 0: 9
- Clinical Phase Unknown: 29
- Preclinical: 216
- Research: 106
- Phase Unknown: 2
- Discontinued: 5
What is the status of research for Covid-19?
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What are the class trends in research for Covid-19?

**Top Covid-19 Vaccine Research Classes**

- Vaccines: 169
- Viral vaccines: 164
- Recombinant proteins: 105
- Synthetic vaccines: 98
- Subunit vaccines: 73
- Peptide vaccines: 35
- Virus-like particle vaccines: 28
- RNA vaccines: 21
- DNA vaccines: 20
- Anti-infectives: 19
- Protein vaccines: 19
- Adjuvants: 19
- Attenuated vaccines: 19
- Cancer vaccines: 19
- Antibodies: 19
- Conjugate vaccines: 19
- Dendritic cell vaccines: 19
- Influenza virus vaccines: 19
- Antineoplastics: 19
- Antivirals: 19
- Bacterial vaccines: 19
- Gene therapies: 19
- Hepatitis C vaccines: 19
- Immunotherapies: 19
- Monoclonal antibodies: 19

**Top Covid-19 Drug Research Classes**

- Anti-infectives: 304
- Antivirals: 294
- Small molecules: 154
- Blood proteins: 120
- Immunoproteins: 118
- Serum globulins: 118
- Immunoglobulins: 117
- Antibodies: 109
- Antineoplastics: 109
- Monoclonal antibodies: 70
- Anti-inflammatories: 66
- Cardiovascular therapeutics: 66
- Skin disorder therapies: 66
- Carbohydrates: 66
- Antirheumatics: 28
- Azoles: 28
- Amides: 27
- Carboxylic acids: 23
- Immunotherapies: 23
- Peptides: 23
- Antibacterials: 21
- Cell therapies: 20
- Macrocyclic compounds: 20
- Antifibrotics: 19
- Recombinant proteins: 19
What are the MOA trends in research for Covid-19?
What are the biomarker trends in research for Covid-19?

**Top Covid 19 Drug Research Biomarkers**

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>32</td>
</tr>
<tr>
<td>IL6</td>
<td>26</td>
</tr>
<tr>
<td>TNF-alpha</td>
<td>17</td>
</tr>
<tr>
<td>IL8</td>
<td>15</td>
</tr>
<tr>
<td>CD4</td>
<td>15</td>
</tr>
<tr>
<td>IL10</td>
<td>14</td>
</tr>
<tr>
<td>IFN-gamma</td>
<td>14</td>
</tr>
<tr>
<td>IL1</td>
<td>12</td>
</tr>
<tr>
<td>A1C</td>
<td>11</td>
</tr>
<tr>
<td>BNP</td>
<td>11</td>
</tr>
<tr>
<td>CD8a</td>
<td>11</td>
</tr>
<tr>
<td>Creatinine</td>
<td>10</td>
</tr>
<tr>
<td>IL2</td>
<td>10</td>
</tr>
<tr>
<td>Nitric Oxide</td>
<td>10</td>
</tr>
<tr>
<td>VEGF-A</td>
<td>10</td>
</tr>
<tr>
<td>troponin I, cardiac</td>
<td>9</td>
</tr>
<tr>
<td>CKB</td>
<td>9</td>
</tr>
<tr>
<td>CKM</td>
<td>9</td>
</tr>
<tr>
<td>IL1 beta</td>
<td>9</td>
</tr>
<tr>
<td>MCP1</td>
<td>9</td>
</tr>
<tr>
<td>C-peptide</td>
<td>8</td>
</tr>
<tr>
<td>Insulin</td>
<td>8</td>
</tr>
<tr>
<td>MPO</td>
<td>8</td>
</tr>
<tr>
<td>BNP</td>
<td>7</td>
</tr>
<tr>
<td>PSA</td>
<td>7</td>
</tr>
<tr>
<td>CD3d</td>
<td>6</td>
</tr>
</tbody>
</table>

[Graph showing the top Covid 19 drug research biomarkers]
Answers to the Big Questions...

- What is the status of pharmaceutical research for Covid-19?
- What are the trends in pharmaceutical research for Covid-19?
- **What are the PK/PD characteristics of novel treatments for Covid-19?**
- What trial results are being reported for leading treatments for Covid-19?
- What are the adverse events associated with treatments for Covid-19?
What are the PK/PD characteristics of CRV-431?

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Mechanism of Action</th>
<th>Active Indication and Highest Phases</th>
</tr>
</thead>
</table>
| CRV-431   | Cyclophilin inhibitors; Sodium-biuret pump inhibitor | Phase II: Non-alcoholic steatohepatitis  
            |                                   | Phase III: Hepatitis B  
            |                                   | Preclinical: Adult respiratory distress syndrome; COVID-19 infections; Hepatitis B; Liver cancer; Non-alcoholic fatty liver disease |

**Refine Your Search**
- Indication
  - COVID 2019 infections
  - Inflammation
  - Liver disorders
  - Neurological disorders
  - Renal disorders
- Phase
  - Preclinical
- Development Location
  - phase I
- Rationale
  - see all
- Mechanism Of Action
  - see all
- Drug Class
  - see all
- Patient Segment
  - see all
- Route Of
  - see all
What are the PK/PD characteristics of CRV-431?

CRV 431

Alternative Names: CRV-431, Cyclosporine A analogue- Hepion Pharmaceuticals

Latest Information Update: 23 Sep 2020

At a glance

- **Originator**: Isotechnika
- **Developer**: Hepion Pharmaceuticals
- **Class**: Antineoplastic, Antimetabolites, Antiviral; Ciclosporins; Hepatoprotectants
- **Mechanism of Action**: Cytostatic, anti-inflammatory, anti-tumor effects
- **Orphan Drug Status**: No
- **New Molecular Entity**: Yes - Adult respiratory distress syndrome; COVID 19 infections; Hepatitis B

**High-level Development Phases**

- **Phase II**: Non-alcoholic steatohepatitis
- **Phase III**: Hepatitis B
- **Preclinical**: Adult respiratory distress syndrome; COVID 19 infections; Hepatitis D; Liver cancer; Non-alcoholic fatty liver disease
- **Discontinued**: Coronavirus infections; Hepatitis C; HIV-1 infections; Human papillomavirus infections

**Most Recent Events**

- **17 Sep 2020**: Pharmacodynamics data from preclinical trials in COVID-19 infections released by Hepion Pharmaceuticals
- **07 Jul 2020**: CRV 431 is available for licensing as of 07 Jul 2020. https://hepionpharma.com/
- **07 Jul 2020**: Preclinical trials in Adult respiratory distress syndrome in USA (unspecified route) before July 2020
What are the PK/PD characteristics of CRV-431?
What are the PK/PD characteristics of CRV-431?
Answers to the Big Questions...

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- **What trial results are being reported for leading treatments for Covid-19?**
- What are the adverse events associated with treatments for Covid-19?
What trial results are being reported for Remdesivir?

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Trial Status</th>
<th>Primary Drug</th>
<th>Number of patients</th>
<th>Indication</th>
<th>Trial design</th>
</tr>
</thead>
<tbody>
<tr>
<td>A multicentre, adaptive, randomized blinded controlled trial of the safety and efficacy of investigational therapeutics for the treatment of COVID-19 in hospitalized adults – version for European Union/United Kingdom sites</td>
<td>Completed</td>
<td>Baricitinib; Remdesivir</td>
<td>1062</td>
<td>COVID-19 infections; Respiratory tract infections</td>
<td>double-blind; multicentre; open; parallel; prospective; randomised</td>
</tr>
<tr>
<td>A Multicenter, Adaptive, Randomized Blind Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults (ACTT-2)</td>
<td>Active, No Longer Recruiting</td>
<td>Baricitinib; Remdesivir</td>
<td>1034</td>
<td>COVID-19 infections</td>
<td>double-blind; multicentre; parallel; prospective; randomised</td>
</tr>
<tr>
<td>A Phase 3 Randomized Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-573) in Participants With Moderate COVID-19 Compared to Standard of Care Treatment</td>
<td>Completed</td>
<td>Remdesivir</td>
<td>500</td>
<td>COVID-19 infections; Pneumonia</td>
<td>multicentre; open; parallel; prospective; randomised</td>
</tr>
<tr>
<td>An prospective (compassionate), open-label study assessing remdesivir in treatment of severe COVID-19 pneumonia in intensive care unit (ICU) and Non-ICU patients</td>
<td>Completed</td>
<td>Remdesivir</td>
<td>35</td>
<td>COVID-19 infections; Pneumonia</td>
<td>open; prospective</td>
</tr>
<tr>
<td>A Phase 3 Randomized Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-573) in Participants With Severe COVID-19</td>
<td>Completed</td>
<td>Remdesivir</td>
<td>4591</td>
<td>COVID-19 infections; Respiratory tract infections</td>
<td>multicentre; open; parallel; prospective; randomised</td>
</tr>
<tr>
<td>Compassionate Use Program For the Treating Severely Ill Patients of COVID-19 With Remdesivir</td>
<td>Recruiting</td>
<td>Remdesivir</td>
<td></td>
<td>COVID-19 infections; Severe acute respiratory syndrome</td>
<td>multicentre; open; prospective</td>
</tr>
</tbody>
</table>
What trial results are being reported for Remdesivir?

**Trial Profile**
A Phase 3 Randomized Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-573) in Participants With Moderate COVID-19 Compared to Standard of Care Treatment

**Trial Overview**

**Outcome**
Primary endpoint met: positive

**Purpose**
The primary objective of this study is to evaluate the efficacy of 2 remdesivir (RDV) regimens compared to standard of care (SOC), with respect to clinical status assessed by a 7-point ordinal scale on Day 11.

**Comments**
According to a Gilead Sciences media release, based on the NCT04407654 and ACTT-1 studies, the US Food and Drug Administration (FDA) has expanded the Emergency Use Authorization (EUA) use of the investigational antiviral Veklury (remdesivir) to treat all hospitalized patients with COVID-19, in addition to the previous authorization for patients hospitalized with severe COVID-19.

**Primary Endpoints**
The Odds of Ratio for Improvement on a 7-point Ordinal Scale on Day 11 (8 days randomized) [Met on 12 Aug 2020]

*On day 11, patients randomized to the 5-day remdesivir group on the 7-point ordinal scale compared with those randomized to standard care [1]*

The Odds of Ratio for Improvement on a 7-point Ordinal Scale on Day 11 (10 days randomized) [Not met; 12 Aug 2020]

The difference in clinical status distribution on day 11 between the 10-day remdesivir and standard care groups [1]

The Odds of Ratio for Improvement on a 7-point Ordinal Scale on Day 11 [Time Frame: Day 11]

[The odds ratio represents the odds of improvement in the ordinal scale between the treatment groups. The ordinal scale is an assessment of the clinical status at a given day. Each day, the worst score from the previous day will be recorded. The scale is as follows: 1. Death; 2. Hospitalized, requiring high level of supplemental oxygen; 3. Hospitalized, requiring low level of supplemental oxygen; 4. Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (coronavirus (COVID-19) related or otherwise); 5. Hospitalized, not requiring supplemental oxygen - no longer requiring ongoing medical care (other than per protocol Remdesivir administration). Not hospitalized.]

**Other Endpoints**

**Trial Details**

**Organisations**

**Sponsors**
Gilead Sciences

**Affiliations**
Gilead Sciences

**Trial Dates**

**Initiation Dates**
Planned: 01 Mar 2020
Actual: 15 Mar 2020

**Primary Completion Dates**
Planned: 01 Jun 2020
Actual: 20 Apr 2020

**End Dates**
Planned: 01 Jun 2020
Actual: 20 Jun 2020

**Substudies/Extensions**
An expansion phase of the study was added to enroll up to 1,000 additional patients with moderate disease.
What trial results are being reported for Remdesivir?

A Phase 3 Randomized Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-573) in Participants With Moderate COVID-19 Compared to Standard of Care Treatment

**Interventions**

**Drugs**   **Route**   **Formulation**
---   ---   ---
Remdesivir   Intravenous   Infusion, Lyophilised

**Part A: Remdesivir (RDV), 5 Days**
Participants will receive continued standard of care therapy together with RDV 200 mg on Day 1 followed by RDV 100 mg on Days 2, 3, 4, and 5. Drug: Remdesivir (Administered as an intravenous infusion) Other Name: GS-8734™, Veklury® Drug: Standard of Care (Standard of Care Treatment for COVID-19 infection)

**Part A: Remdesivir, 10 Days**
Participants will receive continued standard of care therapy together with RDV 200 mg on Day 1 followed by RDV 100 mg on Days 2, 3, 4, 5, 6, 7, 8, 9, and 10. Drug: Remdesivir (Administered as an intravenous infusion) Other Name: GS-8734™, Veklury® Drug: Standard of Care (Standard of Care Treatment for COVID-19 infection)

**Part B: Extension Treatment, Remdesivir 5 or 10 days**
Participants will receive continued standard of care therapy together with RDV 200 mg on Day 1 followed by RDV 100 mg on Days 2, 3, 4, 5, 6, 7, 8, 9, and 10. Drug: Remdesivir (Administered as an intravenous infusion) Other Name: GS-8734™, Veklury® Drug: Standard of Care (Standard of Care Treatment for COVID-19 infection)

**Part A: Continuous SOC Therapy**
Participants will receive continued standard of care therapy, Drug: Standard of Care (Standard of Care Treatment for COVID-19 infection)
What trial results are being reported for Remdesivir?

<table>
<thead>
<tr>
<th>Adis CI Record</th>
<th>Official Study Title</th>
<th>Study Results</th>
<th>Study Results - Efficacy</th>
<th>Study Results - Tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>700318955</td>
<td>A multicentre, adaptive, randomized blinded controlled trial of the safety and efficacy of investigational therapeutics for the treatment of COVID-19 in hospitalized adults 48 version for European Union/United Kingdom sites</td>
<td>Phase II</td>
<td>Therapeutic efficacy: Updated results from the phase III ACTT-1 trial demonstrated that administration of remdesivir statistically and significantly improved clinical odds at day 15 as compared to placebo group. The time for recovery as well as odds of improvement at day 15 were favourable for remdesivir group and consistent with overall study results - REF id: 809301633.</td>
<td>Updated results from the phase III ACTT-1 trial demonstrated that administration of remdesivir statistically and significantly improved clinical odds at day 15 as compared to placebo group. The time for recovery as well as odds of improvement at day 15 were favourable for remdesivir group and consistent with overall study results - REF id: 809301633.</td>
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<tr>
<td>700321638</td>
<td>A multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults (ACTT-2)</td>
<td>Phase II</td>
<td>Therapeutic efficacy: In the phase III ACTT-2 trial, treatment with baricitinib plus remdesivir showed statistically significant reduction in the time to recovery for patients in comparison with remdesivir alone. An approximately one-day reduction in median recovery time for the overall patient population treated with baricitinib in combination with remdesivir versus those treated with remdesivir.</td>
<td>In the phase III ACTT-2 trial, treatment with baricitinib plus remdesivir showed statistically significant reduction in the time to recovery for patients in comparison with remdesivir alone. An approximately one-day reduction in median recovery time for the overall patient population treated with baricitinib in combination with remdesivir versus those treated with remdesivir.</td>
</tr>
<tr>
<td>700319231</td>
<td>A Phase 3 Randomized Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-573) in Participants With Moderate COVID-19 Compared to Standard of Care Treatment</td>
<td>Phase II</td>
<td>Adverse events: In the phase III SIMPLE trial (SIMPLE moderate), conducted in patients with moderate manifestations of COVID-19, remdesivir in combination with standard of care was generally well-tolerated in both the 5-day and 10-day treatment groups and did not show any new safety signal. Adverse events were reported in 51% (97/191) patients in 5-day course, in 55% (105/193) patients in 10-day course and 45% (90/200) patients in standard-of-care group.</td>
<td>Updated results from phase III SIMPLE trial demonstrated that treatment with remdesivir improved COVID-19 symptoms statistically and significantly at day 5 compared to day 11 as compared to standard of care. The odds of improvement with the day 10 treatment group compared to those receiving only standard of care were numerically favourable, but not</td>
</tr>
</tbody>
</table>
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What are the risks of off-label use of Hydroxychloroquine?
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What are the risks of off-label use of Hydroxychloroquine?

Drug Safety: ADR Case Report

Hydroxychloroquine

Restrictive cardiomyopathy: case report

Serious

Release Date: 17 Sep 2020

Print Report Download Citation

Narrative Summary

A 70-year-old woman developed restrictive cardiomyopathy during treatment with hydroxychloroquine for rheumatoid arthritis (RA). The woman had a history of longstanding RA and recently diagnosed complete heart block requiring dual chamber pacemaker implantation. She had been receiving treatment with hydroxychloroquine [dosage and route not stated] for RA. She presented to the hospital with lower extremity swelling and worsening dyspnea for several weeks. Physical examination revealed intravascular and extravascular fluid accumulation with lower extremity edema and elevated jugular venous pressure. ECG showed normal pacemaker function and atrial-sensed, ventricular-paced rhythm. Echocardiography demonstrated moderate-severe increased wall thickness and moderate decrease in left ventricular ejection fraction (LVEF). Diastolic parameters were suggestive of low mitral annular tissue velocity, grade III abnormal filling pattern and global longitudinal strain (GLS) of 9.4% with relative apical sparing (ratio of apical/basal segments of 1 ± 2). Due to the concern of an infiltrative cardiomyopathy, she underwent 99m-technetium pyrophosphate scintigraphy, which revealed semi-quantitative visual grade III and diffused uptake (Perugini grade 3) on single-photon emission CT. Biopsy of the right ventricular was negative on Congo red staining. Electron microscopy showed abundant vacuoles, disorganised myofibrils, curvilinear cytoplasmic bodies and multiple lamellar inclusion bodies. These findings were suggestive of hydroxychloroquine-induced restrictive cardiomyopathy [duration of treatment to reaction onset not stated].

Hydroxychloroquine treatment was stopped, and the woman was treated with heart failure therapy. After several months, repeat echocardiography showed modest improvement in LVEF.

Author Comment

"Electron microscopy revealed disorganized myofibrils, abundant vacuoles, multiple lamellar inclusion bodies, and curvilinear cytoplasmic bodies, findings that are pathognomonic for hydroxychloroquine-induced restrictive cardiomyopathy."
AdisInsight helps you keep up with COVID-19 research

Our expert team identifies, reads, and assesses global biomedical information on your behalf then they provide you with comprehensive and accurate summaries to get you up to date quickly and easily.
Thank you

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Director, AdisInsight Product Management
Database Group

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