

## Important Information

### To whom it concerns

### COVID-19, D-dimer; anticoagulation, argatroban

In COVID-19 patients, increased D-dimer levels and disseminated intravascular coagulation (DIC) indicate thromboembolic processes

**Tang et al (2020)** compared the 28-day mortality of severely ill Covid-19 patients anticoagulated with heparin for more than 7 days and those without anticoagulation.

The 28-day mortality was lower in the heparin group in patients with a score of  $\geq 4$  for sepsis-induced coagulopathy or D-dimer  $> 3.0 \mu\text{g/ml}$ . Covid-19 patients anticoagulated with heparin seem to have a better prognosis.

DOI: <https://doi.org/10.1111/jth.14817>

**Lippi and Favaloro (2020)** published the results of a pooled analysis of previously published data. Although elevated D-dimer levels may be due to a variety of factors, published results suggest that D-dimer elevation and disseminated intravascular coagulation (DIC) are commonly found in Covid-19 patients with severe disease progression. This has also been described for other serious infectious diseases (HIV, Ebola, Zika and Chikungunya virus). The authors urge that clinical trials should be conducted to show whether adjuvant antithrombotic therapy (e.g. with anticoagulants) is helpful in Covid-19 patients.

DOI: <https://doi.org/10.1055/s-0040-1709650>

**Han et al (2020)** published the results of a study with SARS-CoV-2 infected patients. In addition to lowered antithrombin levels, D-dimer levels and fibrinogen were also significantly increased in these patients. The level of D-dimer levels correlated with the severity of the infection. The thrombin time was shorter in critically ill patients compared to the control.

DOI: <https://doi.org/10.1515/ccim-2020-0188>

**Effective anticoagulation with unfractionated heparin (UFH) can improve the prognosis in COVID-19 patients with severe disease progression. If heparin is suspected of causing HIT or the patient has a confirmed HIT, Argatroban (Argatra®, Arganova®, Novastan®, Exembol®) is an alternative anticoagulant:**

- Argatroban is approved as an alternative anticoagulant to heparin (suspected HIT; confirmed HIT)
- Argatroban is a low molecular weight direct thrombin inhibitor (DTI)
- No dependence from antithrombin (in contrast to heparin)
- Dosage body weight related
- Fast onset of action and good manageability through a continuous intravenous infusion
- Individual adjustment of the dose required for sufficient anticoagulation
- Therapy control aPTT (as alternative diluted TT or ECT)

- Low intra- and interindividual scattering of the effect
- Binds free and fibrin-bound thrombin
- No interaction with drugs currently being used experimentally in Covid-19 therapies (<https://www.covid19-druginteractions.org/>)
- Has anti-inflammatory properties (Hoppensteadt DA et al. Semin Thromb Hemost. 2008; 34 suppl 1: 97-102.)
- Preclinical studies have shown that thrombin inhibition with argatroban has a protective effect on pulmonary fibrosis and the mortality associated with it (Francois et al., 2018 - - <https://ashpublications.org/bloodadvances/article-lookup/doi/10.1182/bloodadvances.2018018283>).

For further questions we are at your disposal under [h.borbe@mt-pharma-de.com](mailto:h.borbe@mt-pharma-de.com) or [j.stange@mt-pharma-de.com](mailto:j.stange@mt-pharma-de.com) or mobile: +49 172 100 30 30 available at any time.



**Jan Stange**  
Deputy General Manager  
DACH Operation Department



**Dr. Harald Borbe**  
Medical Scientific Advisor  
DACH Operation Department