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CERTARA®
Accelerating Medicines, Together

CASE STUDY

LEVERAGING CLINICAL DATA FROM ONE RARE DISEASE TO SUPPORT DRUG APPROVAL FOR ANOTHER

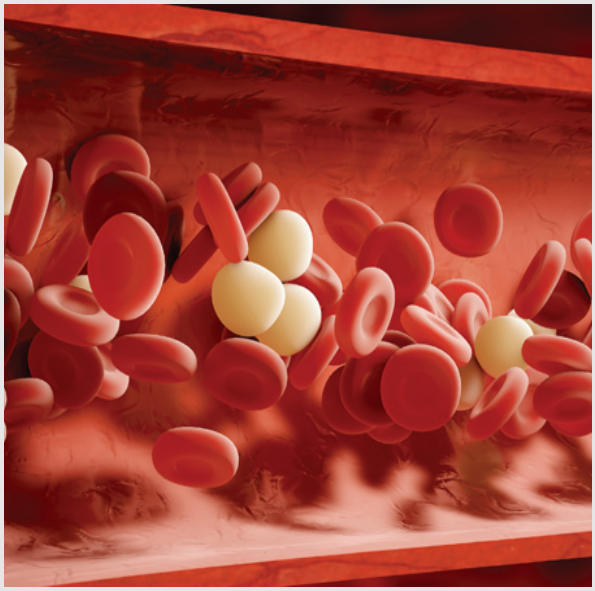
Atypical hemolytic uremic syndrome (aHUS) is an ultra-rare genetic disease that causes abnormal blood clot formation in small blood vessels throughout the body leading to kidney failure, other organ damage, and premature death. At the start of this project, there were no FDA-approved aHUS treatments. Furthermore, as only a few thousand aHUS patients are diagnosed each year, recruiting enough participants to conduct clinical trials was difficult.

However, the FDA had approved a humanized monoclonal antibody (mAb), eculizumab, to treat a related, rare, life-threatening disease – paroxysmal nocturnal hemoglobinuria (PNH), which is characterized by destruction of red blood cells and excessive blood clotting. Both aHUS and PNH symptoms result from chronic, uncontrolled complement system activation. Knowing eculizumab's mechanism of action for PNH suggested that it could confer clinical benefit in aHUS.

A population PK model for eculizumab, which had been previously constructed for adult PNH patients, was repurposed to determine dosing for aHUS patients. The mAb's PK/PD relationship in PNH was also leveraged to determine drug exposure and inform pediatric aHUS dosing.

Two small Phase II studies and a retrospective observational study were conducted, involving just 57 aHUS patients. PK/PD modeling of those data was used to determine the dose- response-effect relationships for two surrogate endpoints. Then, trial simulations based on that modeling were used to determine the best dosing for pediatric and adult patients with aHUS.

Patients with aHUS who were treated with eculizumab had improved platelet counts and other blood parameters and better kidney function with some patients no longer requiring plasmapheresis. The FDA approved eculizumab to treat both adult and pediatric aHUS patients.



Trial simulations were used to determine the best dosing for pediatric and adult aHUS patients.

Headquartered in the U.S., our client has been a leader in the discovery, development, and commercialization of medicines for rare diseases for nearly 30 years. Its research efforts focus on novel molecules and targets in the complement cascade, and it operates in more than 50 countries.

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