HYPERIMMUNE GLOBULIN

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Introduction

Hyperimmune globulin is collected from convalescent plasma donors with higher titers of the antibody of interest as determined by a particular standard. High titers can be achieved by natural immunity, prophylactic immunization or target immunization. Based on the procedure for production of SARS-CoV hyperimmune globulin,[1] convalescent plasma samples from different individuals were pooled to undergo cold ethanol precipitation. The separated serum portion of the blood underwent ion-exchange chromatography followed by virus inactivation and removal procedures to ensure safety. Optimal titers of neutralizing antibodies were then achieved. For COVID-19, the levels suitable for active treatment and prevention have yet to determined.

Mechanism of Action

The effects of hyperimmune globulin is based on the same principle of action of neutralizing antibodies as mentioned in CP. With the higher titers of purified neutralizing antibodies, it is expected to be more efficient than CP in clearing the virus.

Clinical Studies

At present, not enough evidence on actual COVID-19 patients can be cited as to the efficacy and safety of using hyperimmune globulin. Piechotta et al. in a Cochrane systematic review[2] did not find completed studies on any of the ff: Convalescent plasma therapy versus hyperimmune immunoglobulin, hyperimmune immunoglobulin versus standard care or placebo or hyperimmune immunoglobulin versus control treatment, for example, drug treatments (including but not limited to hydroxychloroquine, remdesivir).

Among those in the pipeline is an RCT from Iran listed as IRCT20200310046736N1 on plasma derived immunoglobulin-enriched solution (PDIES), produced by an improved Cohn method.

Another study listed as ClinicalTrials.gov/show/NCT04383548 aims to study the efficacy and safety of anti-SARS-CoV-2 hyper-immunoglobulins prepared from COVID-19 convalescent plasma using VIPS Mini-Pool IVIG medical device. The system is describe to potentially reduce the cost of production.

Recommended Dose

No reference studies available.

Adverse Effects

Since the product is presently still unavailable, adverse reactions are largely unknown. They may, however, be very similar to the adverse reactions of convalescent plasma preparations if given intravenously.

Availability

Several pharmaceutical companies are eyeing its development:

Takeda Pharmaceutical Company Limited (TSE:4502/NYSE: TAK) announced early in March the company's plan to develop a plasma-derived therapy for anti-Severe acute respiratory syndrome coronavirus 2 (anti-SARS-CoV-2) polyclonal hyperimmune globulin (H-IG), TAK-888, to treat high-risk individuals with COVID-19.[3]

Emergent BioSolutions (NYSE:EBS) is also developing plasma-based treatments for COVID-19, including COVID-HIG, which will be derived from recovered patients, and COVID-EIG, made from plasma taken from horses that were given the virus.[4]

Giga Gen, Inc., based in California, USA, created recombinant hyperimmune globulin, that offers 100-fold higher potency than convalescent serum therapy. Hyperimmune globulins are derived from human donor B cells and are produced recombinantly at large scale in mammalian cells. The product called GIGA-2050 is a mix of 12,500 different antibody sequences selected from 16 exceptional responders to COVID-19. They are slated for the first human trials in early 2021[5]

Other companies joining the race to produce other hyperimmune globulin preparations include Regeneron, Astra Zeneca, Eli Lilly, and GSK.

Conclusion

Hyperimmune globulin has potential for a more efficient cost/benefit approach to preventive therapy for COVID-19. Its efficacy for prophylaxis as well as active treatment must be proven by better controlled trials once the product becomes available.

REFERENCES:

1. Zhang Z, Xie YW, Hong J, et al. Purification of severe acute respiratory syndrome hyperimmune globulins for intravenous injection from convalescent plasma. Transfusion. 2005; 45(7):1160-4.
2. Piechotta V, Chai KL, Valk SJ, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review. Cochrane Database of Systematic Reviews 2020, Issue 7. Art. No.: CD013600. DOI: 10.1002/14651858.CD013600.pub2.
3. Hopkins JS. Drugmaker Takeda is working on coronavirus drug. Wall Street Journal. Published March 4, 2020. Available from: https://www.wsj.com/articles/drugmaker-takeda-is-working-on-coronavirus-drug-11583301660. Accessed March 10, 2020.
4. Emergent BioSolutions. Emergent BioSolutions Partners with U.S. Government for Comprehensive Response to Expedite Development of Plasma-Derived Therapy for COVID-19. GlobeNewswire. Published April 02, 2020. Available from: https://www.globenewswire.com/news-release/2020/04/02/2011095/0/en/Emergent-BioSolutions-Partners-with-U-S-Government-for-Comprehensive-Response-to-Expedite-Development-of-Plasma-Derived-Therapy-for-COVID-19.html.
5. Keating SM, Mizrahi RA, Adams MS, et al. Capturing and Recreating Diverse Antibody Repertoires as Multivalent Recombinant Polyclonal Antibody Drugs. bioRxiv 2020. doi: 10.1101/2020.08.05.232975.