IMPACT ASSESSMENT REPORT

Covid Care Relief Programme (CCRP)

October 2023

EXECUTIVE SUMMARY

The novel severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) emerged as a major pandemic coronavirus disease in 2019 (COVID-19). The World Health Organization (WHO) on March 11, 2020, declared the novel coronavirus (COVID-19) outbreak as a global pandemic. As a part of emergency response towards saving lives, Intas Pharmaceuticals conceived the COVID Care Relief Programme and initiated Convalescent Plasma (CP) project in April 2020 to collect plasma from voluntary donors who recovered from COVID-19 infection and had adequate antibody titers. Such plasma was then processed to prepare hyperimmune globulin (HIG) solution that was to be distributed on compassionate basis, free of cost, to patients who were being treated for COVID-19 across the country. Such product was also subjected to clinical trials for establishing its safety and efficacy.

Further, during the second surge, COVID-19 was found to be more virulent and lethal. The situation was alarming with respect to confirmed COVID-19 cases and the deaths. It was very likely that the trend of positivity and death might increase. Considering the scenario, Intas Foundation had taken up initiative (iCare) to establish a COVID Care isolation centre in Ahmedabad equipped with necessary emergency support systems, distribution of COVID-19 medications to people living in cities, villages and towns where Intas has its sites or is operating from (in Gujarat, Sikkim, Uttarakhand), and home care to patients and their caretakes through teleconsultations for specialist physicians.

Intas Foundation has adopted a philanthropic approach towards their CSR activity to support these research and community service initiatives aimed to deliver care and treatment for COVID-19 patients. The impact assessment of these initiatives has been undertaken as per the CSR Mandate.

The review showed that an efficient process was developed for manufacturing HIG, which was further found to be safe and efficacious through the clinical trial while iCare program passed on the tremendous benefits of the COVID Care centre, medications and home care to the patients in such a critical pandemic situation.

PART A:

Development, Efficacy and Safety evaluation of SARS-CoV-2 Hyper Immunoglobulin:

Introduction

It was believed that passive antibody therapy can be used to limit the scope of epidemics by providing patients with antibodies that lessen the severity of viral disease. Antibodies for passive immunotherapy can be manufactured from the plasma of recovered patients. Intas has a well-established platform for purification of immunoglobulin from plasma. As a part of intention to carry out covid care relief program and there by develop and provide developed medication on compassionate basis to the pandemic affected individuals, Intas team developed a purification process

capable of consistently producing hyperimmune IgG (COVID-19 HIG) from convalescent plasma and also established the safety and efficacy of COVID-19 HIG through clinical studies.

A. Objective

To develop a safe and effective therapeutic COVID-19 HIG treatment option against the COVID-19 infection. This included the development of a HIG product from convalescent plasma and clinical trials to generate the safety and efficacy data on COVID-19 HIG. The project was initiated as a corporate social responsibility of Intas Pharmaceuticals Ltd; to serve the nation by providing free of cost treatment to save lives of COVID-19 infected patients and to safeguard the human race through passive immunization against COVID-19.

B. Project implementation process: the project was categorized into following milestones,

1. Development of the process for manufacture of therapeutic COVID-19 HIG against COVID-19

I. Development of purification process and analytical tools

A two-step purification process was developed in short duration of approximately 3 months from April 2020 to June 2020 along with the characterization tools to estimate the quantities of specific antibodies in the purified preparations. Live virus challenge assays were performed at Translational Health Science and Technology Institute (THSTI), Haryana, for determination of the efficacy of the product which was showing neutralization of COVID-19 virus.

II. Process Scale-up and stability studies

Due to the scarcity of convalescent plasma the process development studies were executed at a small scale of 240 ml and the process was scaled up to 60 L and then to 300 L plasma with yield of approximately 55% of COVID-19 HIG. The quality attributes of drug product made at different scales was found to be similar. The product made was evaluated for stability at 2-8℃ (real-time conditions) for 12 months and 23-27℃ (accelerated conditions) for 6 months and was observed to be stable and complying with the predefined specifications.

2. Evaluation of Clinical safety and efficacy

The primary objective of the clinical trial was to compare the efficacy of treatment with COVID-19 HIG plus standard of care versus only standard of care as defined in the guidelines for clinical management of COVID-19 issued by the Ministry of Health and Family Welfare, Government of India, in participants with active COVID-19.

Secondary objectives comprised of various efficacy parameters, neutralizing antibodies, and safety with COVID-19 HIG plus standard of care versus only standard of care in participants with active COVID-19.

Various hospitals and medical institutes pan India were involved in the treatment of COVID-19 patients. This was a prospective, open-label, two-arm, randomized and controlled, multi-centric trial for evaluation of efficacy and safety of COVID-19 HIG solution. The trial was conducted between Oct 2020 to Dec 2020 in accordance with the applicable ethical standards and Good Clinical Practices guidance at seven sites after obtaining ethics committee approval and registration on the clinical trial registry of India (CTRI/2020/09/027903). Thirty patients in the test arm received COVID-19 HIG (350 AU/ mL) given as a 30 mL intravenous infusion on Day 1

and 2 (at the same time preferably) plus standard of care. 30 Patients in the control arm received only standard of care. By the end of the trial 26 patients in the test arm and 27 patients in the controlled arm completed the trial.

COVID-19 HIG was found to be safe and well-tolerated. Early viral clearance and high neutralizing antibodies were achieved in COVID-19 HIG recipients qualifying the product as a suitable treatment option, particularly in patients with comorbidities and an immunocompromised state where natural antibodies are not developed. It was noted that COVID-19 HIG should be given early in infection to mitigate progression to severe disease.

3. **Distribution of COVID-19 HIG product to hospitals on compassionate basis.**

At the end of phase II study, Intas team intended to carry out large scale distribution of COVID-19 HIG with simultaneous data generation for safety and efficacy among high risk COVID-19 patients in India but during this period the intensity of pandemic went down, and it was difficult to find enough beneficiaries and hence it could not be executed.

C. Project Outcome

- An efficient process was successfully developed and scaled-up for purification of COVID-19 HIG from convalescent plasma.
- Analytical methods were developed to estimate the amount of specific antibodies to make consistent doses.
- In-vitro efficacy of the product was established using surrogate virus titer assay and live virus challenge assays at THSTI.
- Product safety was established by pyrogen assay and abnormal toxicity at GLP certified third party lab.
- In-vivo efficacy of the product was proved during the Phase II clinical study in 60 patients (53 completed the study).
- The work was published in the form of following three publications (one review article and two research papers from the outcome of the process development work and clinical study):

1. Chavda VP, Bezbaruah R, Dolia S, Shah N, Verma S, Savale S, Ray S. Convalescent plasma (hyperimmune immunoglobulin) for COVID-19 management: An update. Process Biochem. 2023 Apr;127;66-81.
2. Verma S, Dolia S, Pawar A, Ray S. SARS-CoV-2 Hyper- Immunoglobulin: Purification and Characterization from Human Convalescent Plasma. BioProcess Int. 2021;19(4);30-45.
3. Parikh D, Chaturvedi A, Shah N, Patel P, Patel R, Ray S, Safety and Efficacy of COVID-19 Hyperimmune Globulin (HIG) Solution in the Treatment of Active COVID-19 infection-Findings from a Prospective, Randomized, Controlled, Multi-Centric Trial: The Indian Practitioner, 2021 Nov, 74(11);15-22.

PART B:

Covid Care Initiative

The emergence of the COVID-19 pandemic presented numerous complex challenges to the healthcare delivery organization. These challenges encompassed issues such as limited intake capacity of patients, shortages in essential supplies, the imperative process for care and financial setbacks.

In response to the escalating cases of COVID-19, the Intas Foundation facilitated proactive measures to address the situation. A detailed description of the outcomes achieved under the initiative are as follows:

1. **iCARE COVID CENTRE**

   A dedicated facility that functioned as a 30-bed COVID-19 First Care Response Centre was established for 1 month in May 2021 in Ahmedabad and managed to help COVID-19 patients. The center operated around the clock, offering continuous medical care, oxygen support, medicines, food, and experienced physicians. Moreover, specialized experts conducted regular visits to enhance the overall quality of service.

   The iCARE COVID CENTRE was equipped with comprehensive amenities to ensure optimal care delivery. This encompassed the presence of an on-site Laboratory and Diagnostic Centre to facilitate prompt medical testing and assessments. In-house pharmacy was established to ensure convenient access to essential medicine. Recognizing the significance of timely intervention, a 24*7 emergency ambulance was also made available to cater to unforeseen medical exigencies thereby enhancing the safety and well-being of the patients. Additionally, oxygen cylinders were kept at/ on stand-by for critical patients at the Covid Care Centre.

   The well-being of the patients remained a top priority. Recognizing the mental health challenges posed by the pandemic, the center further extended its support by providing access to professional counselling services by expert psychologists.

   To address the holistic needs of beneficiaries, the center also ensured provision for nutritious meal. Through the amalgamation of medical expertise through external resources, comprehensive services and a compassionate approach, the iCARE COVID CENTRE stood as a testament to effective pandemic-responsive healthcare delivery for 18 patients admitted at center and all of them recovered.

2. **Comprehensive Home-Care and Well-being:**

- Daily support and monitoring: The establishment of the COVID Taskforce team as a voluntary initiative, constituting departmental experts within Intas, ensured personalized care to each patient. Over 15,000 calls were made to patients, who had tested positive for COVID-19, ensuring that everyone received the necessary support, guidance, and reassurance throughout their recovery journey. This meticulous approach not only contributed to the physical recovery but also alleviated their anxieties during a challenging period.

- Food support: Recognizing the multifaceted impact of the pandemic, the organization extended its support beyond medical care. A total of 964 meals were provided to both COVID-positive patients and their family members.
- Efforts were also undertaken to strengthen efforts by communities through local administrations towards covid relief and care in various districts of Gujarat, Uttarakhand, and Sikkim, ensuring vital supplies like rations/food, along with essential COVID-19 items like masks and sanitizers.

3. **Accessibility and Availability of Critical Medicine and Equipment:**
   Critical medicines were distributed on need basis to strengthen availability and accessibility to needy patients for COVID-19 during the pandemic. Additionally, 22 oxygen cylinders were kept at/ on stand-by for critical patients.

4. **Tele-Health and Mental Well-being:**
   Keeping in view of the challenges of the pandemic, a tele-health facility was provided to patients. About 72 virtual doctor consultations were facilitated during the peak of the second wave.

5. **Vaccination Drive:**
   About 20+ vaccination drives were organized in Gujarat to raise awareness, reduce vaccination hesitancy and promote 100% vaccination.
   In the face of the formidable challenges brought about by the COVID-19 pandemic, the organization demonstrated exceptional resilience, commitment, and agility in its efforts to ensure the well-being of COVID-19 affected patients. Through meticulous care, medical attention, and comprehensive support, a total of 3,331 patients who had tested positive for COVID-19, recovered through the support provided under this initiative. The outcomes achieved stand as a testament to the organization's proactive approach and unwavering dedication to navigating the complexities of this global health crisis.

Conclusion

Through the CSR initiative - COVID Care Relief Programme - Intas Pharmaceuticals has successfully developed novel and efficient process for manufacturing of Hyperimmune globulin (COVID-19 HIG) from convalescent plasma (CP). The research work has significantly added to the scientific understanding of process, technology and has been published in scientific journal. This technology and the approach can be easily adapted by the industry and academic research community for a specific disease condition where HIG is used as the treatment strategy. Further, the safety and efficacy of the COVID-19 HIG in patients with minor to moderate COVID-19 infections as a prospective therapy has been established, thus, providing a potential therapeutic option to develop passive immunity especially in patients with comorbidities. The HIG therapy, as an advanced version of CP treatment, brings in many advantages over the conventional plasma therapy, such as lower administration volumes, consistent dosage amounts, negligible risk of virus transmission, and no requirement of blood-group subtyping.

On the other hand, the Intas Foundation launched a multifaceted initiative when the COVID-19 pandemic posed intricate challenges for healthcare organizations such as limited patient capacity, supply shortages, inadequate care processes, and financial constraints. The initiative involved establishment of the 30-bed iCare COVID Centre in Ahmedabad. The Centre catered to the patient needs and could mobilize all the necessary critical support equipment to the patients during the second surge of COVID-19. The round-the-clock medical care, oxygen support, medicines, and mental health services provided by the Centre resulted in recovery of the patients admitted at the Centre. The Foundation also offered comprehensive home-care support, making calls to COVID-positive patients, providing meals, and aiding local communities with essential supplies. Critical medicines and oxygen cylinders were distributed as-needed, tele-health consultations were made available, and vaccination drives were organized. Through meticulous care, medical attention, and comprehensive support provided under this initiative, a total of 3,331 patients who had tested positive for COVID-19, recovered. This illustrates Intas Foundation's proactive and resilient response to the challenges thrown by the COVID-19 pandemic.

Overall, CSR initiatives, which were aimed to provide therapeutic alternative for COIVD-19 treatment as well as medical care and home care for patients and their families to facilitate their recovery, have made a significant social impact.