LETTER TO EDITOR
Precision Medicine Research 2021;3(4):18. https://doi.org/10.53388/PMR20210018

Targeting SARS-CoV-2 with therapeutic monoclonal antibodies

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Background

COVID-19 was initially found in Wuhan, China, in December 2019, and was later designated a pandemic by the World Health Organization (WHO) [1]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) quickly spread over the planet due to its great potential for human-to-human infection, causing significant harm to global health and worldwide trade. It is the 7th member of the Coronaviridae family known to infect humans, transmitted by direct contact COVID-19 patients, and results in breathing problems, cough, chest tightness, disorientation, fever, respiratory distress, or dyspnea, as well as myalgia and asthenia [2]. It is mostly a respiratory illness that also affects other organ systems such as the cardiovascular (CV), gastrointestinal (GI), kidneys, and neurological system [3]. SARS, Middle East Respiratory Syndrome (MERS), and the newly revealed SARS-CoV-2 are the well-known CoV strains [4–5].

MAbs treatment has recently acquired a lot of attention. MAbs recognize particular epitopes in the target antigen and bind to them. MAbs were originally primarily utilized to develop diagnosis; medicinal implications were constrained by the immunogenic capabilities and low efficacy linked with murine antibodies due to the lack of effector activity. Following that, modified antibodies containing a murine variable domain and a human constant domain were developed and demonstrated to have fewer side effects while maintaining binding ability, leading to the approval of chimeric MAbs for a variety of indications, including infectious diseases, genetic diseases, tumor, allergic conditions, and so on [6]. Therapeutic MAbs for COVID-19 therapy have been created at a breakneck speed that has never been seen before in any illness. Since the discovery of MAbs, the licenses were acquired in a record time of just 10 months, involving 3 to 4 months of clinical-grade MAbs manufacturing [7].

Celltrion, AstraZeneca, and Regeneron are among the pharmaceutical firms that support the development of MAbs as a therapy for COVID-19. The very first human study to cure COVID-19 is now ongoing, with the medication company "Lilly" using LY-CoV555 neutralizing MAbs against the spike protein. The neutralizing antibody LY-CoV555, at a dosage of 2800 mg, appeared to hasten the normal fall in viral load, but the two doses (700 mg and 7000 mg) did not. Bamlanivimab and Casirivimab-Imdevimab are new virus-neutralizing MAbs that have just been approved for the management of mild to moderate nCoV infected outpatients who are at an increased risk of getting to a serious infection. Early therapy may also be effective in halting the development of infection in highly infected patients. However, FDA granted an emergency use authorization (EUA) for Imdevimab and Casirivimab to be used jointly in adults and children with mild to moderate COVID-19 [8–11]. New SARS-CoV-2 viral variants have just been discovered. Mutations in the virus's DNA give rise to these variations. MAbs are still effective against the B.1.1.7 form of SARS-CoV-2. Certain mutations, though, may produce alterations in the spike protein, which might impair the efficacy of presently offered MAbs [12–13]. Bamlanivimab, which targets SARS-CoV-2 spike protein, has been suggested for use in patients 10 days after the beginning of symptoms, however, it is ideally suited to be used in individuals soon after confirmed SARS-CoV-2 virological identification. Tocilizumab, an anti-IL-6-MAbs, is approved for the treatment of COVID-19 infected individuals who require ventilator support. On a broad level, when it comes to infectious diseases, there are three distinct indications for their use: treatment of infected individuals, prophylaxis for high-risk individuals for patient-level outcomes, and prophylaxis to interrupt transmission in the average-risk population for population-level outcomes [14]. The large percentage of MAbs discovered so far address the spike protein's receptor-binding region, which permits SARS-CoV-2 to interact with the ACE 2 receptor. Neutralizing antibodies are expected to target additional areas of the spike protein as well, based on the current understanding of SARS-CoV and MERS-CoV. The efficacy of neutralizing MAbs in vitro in several cell culture tests is a crucial property utilized to assist identify MAbs with therapeutic application potential [15].

Even though MAbs are amongst the most rapidly increasing medication categories in the contemporary age, the exact mechanism through which they acquire their medicinal impact remains unknown. With therapeutic MAbs, any physiological reaction or result is dependent on many factors. Antigen cell surface density, tissue distribution, as well as the specificity, avidity, and isotype of any particular MAb, all play a significant influence. Attempts are being undertaken to address restrictions and increase therapeutic potential, and bioengineered human antibodies are showing new potential following chimeric and humanized MAbs [16].

Conclusion

As a consequence of the COVID-19 outbreak, clinical development and data review have been hastened, leading to speedy regulatory assessment and approval. Genomic characterization of developing variations of nCoVs has permitted the fast production of efficient post-exposure prophylactic neutralizing MAbs in tandem with vaccine development and therapeutic MAbs. The results of real-world research in high-risk groups will determine how these SARS neutralizing antibodies will be employed in clinical practice.

The first human trial to treat COVID-19 is currently underway, with the pharmaceutical company "Lilly" using LY-CoV555 neutralising MAbs against the spike protein. Bamlanivimab and Casirivimab-Imdevimab are two novel virus-neutralizing MAbs that were recently licenced for the treatment of mild to moderate nCoV-infected outpatients who are at risk of developing a severe illness. Early treatment may also be useful in preventing infection in those who are already infected.

Competing interests

The authors declare no conflicts of interest.

Abbreviations

WHO: World Health Organization; SARS-CoV-2: syndrome coronavirus 2; CV: cardiovascular; GI: gastrointestinal; MERS: Middle East Respiratory Syndrome.

Citation

Hussain S. Targeting SARS-CoV-2 with therapeutic monoclonal antibodies. *Precis Med Res* 2021;3(4):18. https://doi.org/10.53388/PMR20210018.

Executive editor: Nuo-Xi Pi.

Received: 15 November 2021**; Accepted:** 02 December 2021; **Available online:** 07 Decemberr 2021.

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Table 1 Phase 2, 3, and 4 trials of monoclonal antibodies are underway [17–19].

Sponsor	Trial ID	Study	Product	Clinical Phase
I-Mab Biopharma Co. Ltd.	NCT04341116	384 severe infected COVID-19 individuals under supportive care	TJ003234	2-3
Alexion Pharmaceuticals	NCT04369469	270 COVID-19 patients admitted to the hospital with severe pneumonia and acute lung damage	Ravulizumab	3
Assistance Publique - Hôpitaux de Paris	NCT04324073	239 COVID-19 patients included in CORIMUNO-19 cohort	Sarilumab	2-3
AstraZeneca/QuintilesIMS	NCT04625972	1,125 participants with exposure history within preceding 8 days	AZD7442	3
Brigham and Women's Hospital	NCT04570397	32 SARS-CoV-2 positive patients with thrombotic microangiopathy	Ravulizumab	3
Cambridge University Hospitals NHS Foundation Trust	NCT04390464	1,167 SARS-CoV-2 positive hospitalized pre-ICU patients	Ravulizumab + Baricitinib	4
CSL Behring	NCT04409509	124 COVID-19 positive severe patients with interstitial pneumonia	Garadacimab	2
CytoDyn, Inc.	NCT04347239	390 hospitalized severe or critically ill COVID-19 patients	Leronlimab	2
Eli Lilly and Company/AbCellera Biologics Inc./ Shanghai Junshi Bioscience Co., Ltd.	NCT04634409	500 non-hospitalized mild to moderate COVID-19 patients	LY3819253 + LY3832479	2
Fibrogen	NCT04432298	130 acute COVID-19 hospitalized patients	Pamrevlumab	2
Hadassah Medical Organization/ Sheba Medical Center/ Wolfson Medical Center	NCT04377750	500 participants with severe COVID-19 disease and suspected hyper-inflammation	Tocilizumab	4
Hospices Civils de Lyon	NCT04413838	120 SARS-CoV-2 positive hospitalized obese individual with risk of severe infection	Nivolumab	2
Implicit Bioscience/University of Washington	NCT04391309	300 adult Hospitalized COVID-19 patients	IC14	2
Johns Hopkins University/ Novartis/ Socar Research SA/ Brigham and Women's Hospital	NCT04435184	40 SARS-CoV-2 positive hospitalized acute COVID-19 patients	Crizanlizumab	2
Kinevant Sciences GmbH/Roivant Sciences, Inc.	NCT04351243	227 with lung injury or ARDS secondary to COVID-19	Gimsilumab	2
National Institute of Allergy and Infectious Diseases (NIAID)	NCT04583956	200 SARS-CoV-2 positive hospitalized adult patient	Risankizumab	2
Ospedale San Raffaele	NCT04397497	50 participants hospitalized with COVID-19 induced pneumonia	Mavrilimumab	2
Rapa Therapeutics LLC/ Hackensack Meridian Health	NCT04482699	88 hospitalized, severe, post-intubation COVID-19 patients	RAPA-501-Allo	2
Regeneron Pharmaceuticals	NCT04426695	2,970 adult Hospitalized COVID-19 patients	REGN10933 + REGN10987	1/2
Swedish Orphan Biovitrum	NCT04324021	54 hospitalized COVID-19 patients with respiratory distress and hyper inflammation	Emapalumab	2
Sorrento Therapeutics, Inc.	NCT04584697	50 SARS-CoV-2 RNA positive asymptomatic/mild symptomatic participants	COVI-AMG	1/2

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To summarise, MAbs are and will likely remain key treatment alternatives in the 21st century, not only for SARS-CoV-2 but also for other infectious diseases. MAbs that are extremely effective, can be created at a fraction of the present cost, and have a defined benefit group should be the focus of research.

References

1. Hussain MS, Mohit, Pamma P, Kumari B. Treatment modalities of the covid-19 pandemic through repurposed drugs and status of vaccines. Int J Appl Pharm 2021, 13: 48–58.
2. Kombe AJ, Zahid A, Mohammed A, Shi R, Jin T. Potent Molecular Feature-based Neutralizing Monoclonal Antibodies as Promising Therapeutics Against SARS-CoV-2 Infection. Front Mol Biosci 2021, 8: 670815.
3. Mohit, Hussain MS. Potential role of Curcumin as a treatment option for Covid-19: A Review. Plant Arch 2021, 21: 296–305.
4. Hussain A, Hasan A, Nejadi Babadaei MM, Bloukh SH, Chowdhury MEH, Sharifi M, et al. Targeting SARS-CoV2 Spike Protein Receptor Binding Domain by Therapeutic Antibodies. Biomed Pharmacother 2020, 130: 110559.
5. Kumari R, Kaur J, Hussain MS. Management of diabetes with Covid-19: A Review. Int J Pharm Pharm Sci. 12(12): 1–6.
6. Kumar D, Gauthami S, Bayry J, Kaveri SV, Hegde NR. Antibody Therapy: From Diphtheria to Cancer, COVID-19, and beyond. Monoclonal Antibodies in Immunodiagnosis and Immunotherapy 2021, 40: 36–49.
7. Kumar S, Chandele A, Sharma A. Current status of therapeutic monoclonal antibodies against SARS-CoV-2. PLoS Pathog 2021, 17: e1009885.
8. Bariola JK, McCreary EK, Wadas RJ, Kip KE, Marroquin OC, Minnier T, et al. Impact of Bamlanivimab Monoclonal Antibody Treatment on Hospitalization and Mortality Among Nonhospitalized Adults with Severe Acute Respiratory Syndrome Coronavirus 2 Infection. Open Forum Infect Di 2021, 8(7): ofab254.
9. Gottlieb RL, Nirula A, Chen P, Boscia J, Heller B, Morris J, et al. Effect of Bamlanivimab as Monotherapy or in Combination with Etesevimab on Viral Load in Patients With Mild to Moderate COVID-19A Randomized Clinical Trial. JAMA 2021, 325(7): 632–644.
10. Cohen MS. Monoclonal Antibodies to Disrupt Progression of Early Covid-19 Infection. New Engl J Med 2021, 384: 3.
11. Tabll AA, Shahein YE, Omran MM, Elnakib MM, Ragheb AA, Amer KE. A review of monoclonal antibodies in COVID-19: Role in immunotherapy, vaccine development and viral detection. Hum Antibodies 2021, 29: 179–191.
12. Goldin L, Elders T, Werhane L, Korwek K, Poland R, Guy J. Reactions and COVID-19 disease progression following SARS-CoV-2 monoclonal antibody infusion. Int J Infect Di 2021, 112: 73–75.
13. Kim PS, Read SW, Fauci AS. Therapy for early COVID-19: a critical need. JAMA 2020, 324: 2149–2150.
14. Deb P, Molla MMA, Saif-Ur-Rahman KM. An update to monoclonal antibody as therapeutic option against COVID-19. Biosaf Health 2021, 3: 87–91.
15. Marovich M, Mascola JR, Cohen MS. Monoclonal Antibodies for Prevention and Treatment of COVID-19. JAMA 2020, 324(2): 131–132.
16. Chames P, Regenmortel MV, Weiss E, Baty D. Therapeutic antibodies: successes, limitations and hopes for the future. Br J Pharmacol 2009, 157: 220–233.
17. Taylor PC, Adams AC, Hufford MM, Torre IDL, Winthrop K, Gottlieb RL. Neutralizing monoclonal antibodies for treatment of COVID-19. Nat Rev Immunol 2021, 21: 382–393.
18. López AT, Hermosilla J, Navas N, Rodríguez LC, Cabeza J, García AS. The Relevance of Monoclonal Antibodies in the Treatment of COVID-19.Vaccines (Basel) 2021, 9: 557.
19. Deb P, Molla MMA, Rahman KMS. An update to monoclonal antibody as therapeutic option against COVID-19. Biosaf Health 2021, 3(2): 87–91.