#4 / RBDCOV: The project's origins and future endeavours

1. The RDBCOV Project

In the wake of the global COVID-19 pandemic at the end of 2019 and the release of the SARS-CoV-2 genome sequence in January 2020, a monumental effort was initiated to develop a vaccine against the coronavirus disease (COVID-19).

As part of these endeavours, HIPRA launched a vaccine development programme against SARS-CoV-2 that resulted in a recombinant spike (S) protein receptor binding domain (RBD) fusion heterodimer (B.1.351 and B.1.1.7 strains) vaccine, formulated with an oil-based adjuvant, which showed outstanding safety and efficacy levels, making it readily available for vaccination campaigns worldwide. The vaccine, commercially known as BIMERVAX®, is based on a dimeric recombinant protein vaccine platform, which was selected to facilitate the development of both, monovalent and bivalent vaccines as it provides the versatility of being adaptable as homodimer or heterodimer, aiming to enhance the immune response against emerging SARS-CoV-2 variants. It also seeks to induce a long-lasting response while maintaining a favourable reactogenicity profile compared to mRNA vaccines.

The RBDCOV project emerged in December 2021 as a collaboration between relevant scientific entities in response to the global emergency and the urgent need to provide a COVID-19 vaccine to populations who are at higher risk of severe COVID-19. Its objective was to assess the efficacy, tolerability, and safety of the BIMERVAX® vaccine in children, adolescents and in adults with pre-existing immunocompromising conditions.

The consortium partnership has catalysed collaboration between the biotech company HIPRA and different European clinical research and health centres (IDIBAPS, FLS, IrsiCaixa, VHIR) in order to enhance new vaccine development and manufacturing pathways. The collaboration of the consortium serves to control and minimise the impact of the pandemic.

In addition, the consortium includes a diverse array of key stakeholders, each contributing with different perspectives and expertise. This gives the project the opportunity to encompass the point of view of the general public and specifically focus on population target groups, such as people living with immunocompromising conditions or children and adolescents, who were not initially involved in the COVID-19 vaccine development plan. Other European organisations and companies like PENTA, EATG, Metpharm, VERISTAT, ZABALA and Vinces have been an integral part of this project as well.

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2. BIMERVAX® vaccine received the marketing authorisation in the European Union in March 2023

Two years after the launch of the RBDCOV project, the study with people living with immunocompromising conditions has been successfully completed with promising preliminary immunogenicity results. The scientific publication of this achievement is on-going.

The paediatric programme, involving three consecutive trials in adolescents, children, and infants (12-18 years, 5-12 years, and younger than 5 years), was scheduled to start in April 2023, once the EU marketing authorisation was issued. The clinical study with adolescents (12 to 18 years) started in May 2023 and is currently ongoing achieving significant recruitment rates despite the evolving epidemiological context.
A number of challenges still lie ahead for BIMERVAX®, including the assessment of the immune response against the emerging SARS-CoV-2 variants and the need to adapt RBDCOV developments and study objectives to vaccination recommendations issued by health and regulatory authorities based on available and limited real-data evidence. Despite this, the vaccine development plan for BIMERVAX® is ongoing to deal with all these challenges.

3. SARS-CoV-2 evolution and Agencies recommendations

Since the beginning of the pandemic, successive mutations of the SARS-CoV-2 virus have led to many circulating variants different from the ancestral virus. The virus variants have been identified and categorised as variants of concern (VOC), variants of interest (VOI), and variants under monitoring (VUM). These classifications consider different parameters, such as increase in transmissibility, increased hospitalisations or deaths, significant reduction in neutralisation by antibodies generated during previous infection or vaccination, and reduced effectiveness of treatments or vaccines, or diagnostic detection failures.

Currently, the WHO is tracking several SARS-CoV-2 variants, including four VOIs (XBB.1.5, XBB.1.16, BA.2.86 and EG.5) and five VUMs (DV.7, XBB, XBB.1.9.1, XBB.1.9.2 and XBB.2.3.).

In June 2023, the European Medicines Agency issued a joint statement with the ECDC, in line with international partners such as Members of the International Coalition of Medicines Regulatory Authorities (ICMRA) including WHO and the WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC), to take stock of the pandemic evolution and to define how to adapt authorised COVID-19 vaccines and their boosters in time for the autumn 2023 vaccination campaign so that the burden caused by COVID-19 could be further reduced. As a result, monovalent vaccines including a strain belonging to the XBB family of Omicron subvariants were recommended for use in the upcoming vaccination programmes alongside the flu vaccination campaign.

4. VACCINE adaptation

Following the recommendations of the competent health authorities, HIPRA's COVID-19 vaccine is going through an adaptation to be in line with the current requirements. The vaccine is developed on a stable RBD protein-based platform and allows rapid antigen adaptations while maintaining the safety profile and high-quality standards.

As part of this process, a monovalent homodimer XBB.1.16 variant strain was selected by HIPRA as the best option to face the current season considering the epidemiological situation and the outstanding results obtained *in vitro* and in non-clinical studies. In November 2023, a clinical trial began to test the efficacy and tolerability of HIPRA's COVID-19 adapted vaccine based on XBB.1.16.

After the completion of the RBDCOV project, HIPRA commits continue developing and adapting the COVID-19 vaccine based on the needs of the epidemiological context and official recommendations.

The RBDCOV's project results play a pivotal role in extending COVID-19 prevention to all population groups, especially those populations who are at higher risk of severe COVID-19, such as people with immunocompromising conditions, children and adolescents.

This specialized article has been created by the research team of HIPRA.

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