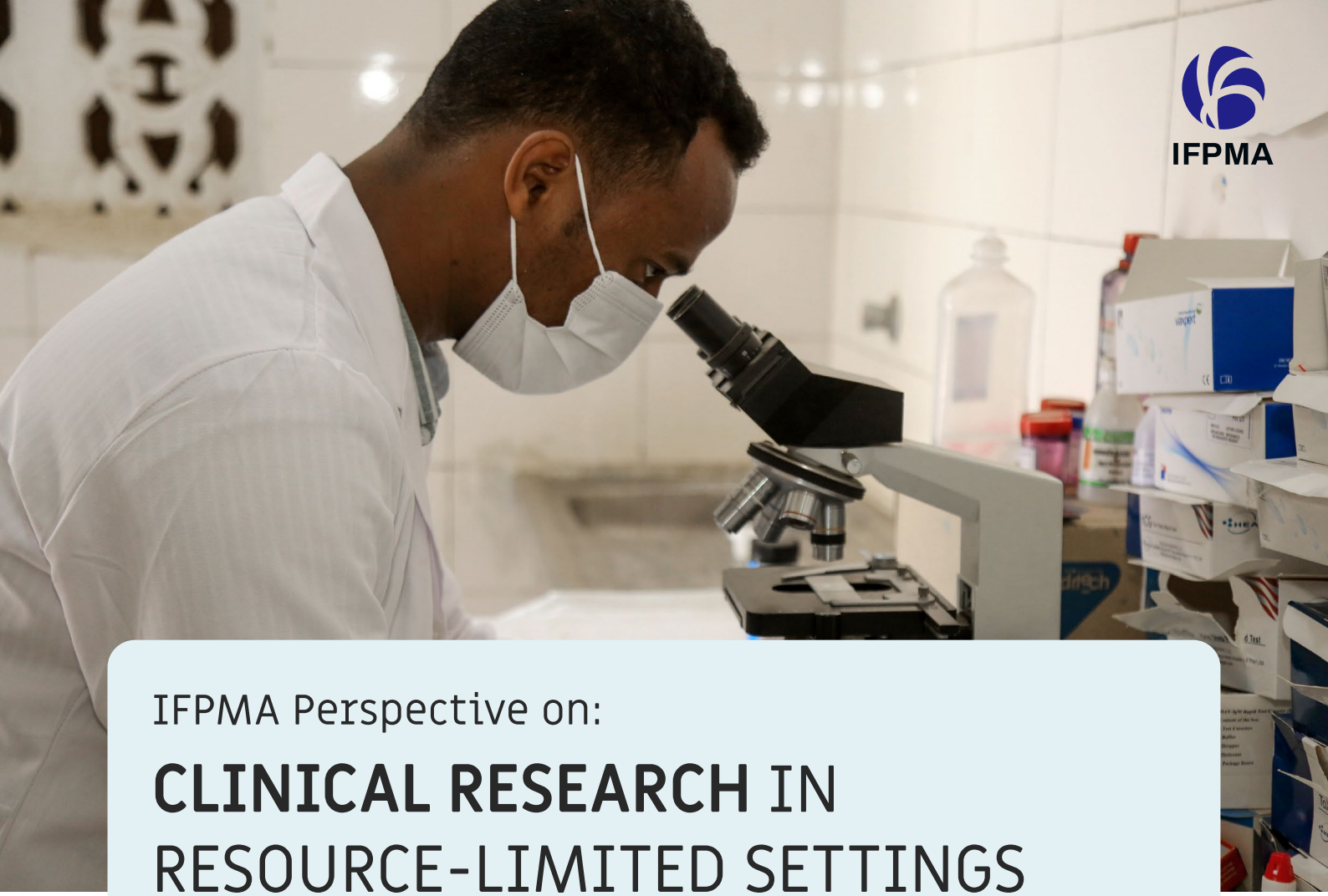

IFPMA Perspective on:

CLINICAL RESEARCH IN RESOURCE-LIMITED SETTINGS

The International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) congratulates the Council for International Organizations of Medical Sciences (CIOMS) and the work of its technical working group for the very comprehensive report on clinical research in resource-limited settings[1]. The biopharmaceutical industry is already actively engaged and contributes to the evolving clinical research ecosystem.

IFPMA members conduct high quality, science-driven studies to develop innovative medicines and vaccines for unmet patient needs. These studies are conducted consistently according to international ethical and regulatory standards, such as the Declaration of Helsinki and ICH standards to ensure patient safety and data integrity. We also conduct our research in compliance with local regulations and ethical requirements. In addition, we are committed to support local policy makers to align on global and local standards as part of capacity building and a sustainable ecosystem.

The private sector is a crucial contributor to this ecosystem due to its vast experience in designing, initiating, and running global clinical trials according to the highest regulatory and ethical standards to deliver robust data for the development of innovative medicines and vaccines for patients worldwide.

The speed and mutual success of our development efforts depends on close collaboration with other partners. The availability of an ethical and scientific clinical research ecosystem ensures participant safety and can deliver high quality results that meet regulators' expectations. The creation of such a sustainable ecosystem requires open and transparent collaboration between all stakeholders to build trust, long term investment to develop sufficient capacity of trained clinical trial researchers, adequate healthcare infrastructure, quality assurance mechanisms and data collection tools.

IFPMA welcomes the opportunity to contribute our experience and knowledge to expand the clinical research infrastructure in LMICs, which will drive advancement of healthcare systems and address the needs of local and global patients' population. For example:

We are committed to conducting clinical trials globally according to the same high ethical and regulatory standards and respecting local laws and traditions, regardless of location. We apply ICH good clinical practice (ICH E6) implemented into regulatory frameworks in major markets around the world. We support and continue to advocate for adoption of these international standards across all countries participating in clinical research. Industry supports strengthening of clinical trial capability in LMICs to allow participation in global studies, and more broadly to ensure that all clinical studies can be conducted according to a single global standard.

We collaborate with academic researchers, clinicians, patient groups, and other healthcare participants to identify the unmet medical needs and ensure that our clinical trials are designed to meet them, while generating quality evidence even in resource-limited settings. To do this, we participate in patient community advisory boards, conduct expert advisory input forums and investigator trainings, and establish external data monitoring boards in specific cases.

We use innovative study designs, such as master protocols or quality by design, in a fit for purpose manner, as well as novel digital technologies where possible, to optimize the clinical trial conduct and patient experience. IFPMA is a standing observer to ICH and our experts are participating in the development of new international guidance on clinical trials[2]. In addition, some of our members are working in several initiatives[3] to improve the patient trial experience through involvement, shared decision making, and electronic tools.

We are currently actively working on increasing population diversity in our trials and consider this as a priority goal. Principles for design and conduct of multi-regional clinical trials (ICH E17) as well as consideration of ethnic differences in global clinical trials (ICH E5) are being implemented in our trial designs.

We are committed to scientific data integrity, transparency, and confidentiality of personal data according to national laws and regulations. We continue to support disclosure of clinical trial information via clinical trial registries and databases as well as the timely publication of clinical trial results in the scientific literature[4]. We are committed to responsible clinical trial data sharing with patients and researchers[5].

We recognize the increased number of countries adhering to international ethical and regulatory standards and call for all countries to move towards this direction to ensure patient safety regardless of the country in which the trial is conducted. This will facilitate the conduct of global and multi-regional trials and enable capacity building and inclusion of more clinical trial sites in LMICs.

The industry remains supportive towards this goal and will continue to contribute when necessary. We call on funders to coordinate initiatives and invest in building sustainable regional and international networks with sufficient capacity and scale that can speedily deliver high quality data for regulatory and other use.

IFPMA and its members stand ready to actively collaborate and contribute our scientific and professional experience in conducting clinical research in multiple regions around the globe.

The following case studies provide examples on how the biopharmaceutical industry supports clinical research in resource-limited settings, extracting lessons learned that can **inform policies** to further promote initiatives that **build capacity** for clinical trials and **strengthen the innovation ecosystem**.

EBOLA VACCINE DEVELOPMENT

Strong public-private partnership generating robust safety and efficacy data during an infectious disease outbreak to support development of a vaccine candidate

During the West African Ebola outbreak in 2014, researchers were able to rapidly build on promising vaccine candidates previously identified during R&D efforts[6]. Many vaccine candidates entered clinical development during the outbreak, resulting in the generation of safety and immunogenicity data for several of these novel vaccine candidates, and the demonstration of efficacy for one.

Extraordinary efforts were made to rapidly advance that one vaccine candidate, which was licensed to MSD through Phase 1, 2, and 3 clinical trials, and the data generated in the context of the West African Ebola outbreak has supported the vaccine's licensure by the US FDA, authorization by the EMA and several African countries, along with prequalification by the WHO. Thanks to a strong collaboration framework and public-private partnership efforts, the period of 5 years from the start of Phase 1 trials in Oct 2014 to the approval of this vaccine in Nov 2019, was much faster than the typical 10–15-year timeline for vaccine development and approval.

Sustainable ecosystem

In 2014, a diverse set of public-private partners joined forces to evaluate and develop a promising Ebola vaccine candidate. This global collaboration spanned a broad range of organizations, including national governments, various agencies, field response and non-governmental service organizations, global public health entities, and private sector companies[7]. Each of these entities played a specific role in the broad partnership, allowing them to employ their strengths and utilize preexisting expertise. These roles included conducting preclinical studies, Good Manufacturing Practices (GMP) trial materials, conducting clinical trials, assuring data quality, tailoring regulatory submissions and funding portions of the research and development.

One lesson learned from this experience is the importance of building clinical development and laboratory capacities and enhancing adverse event reporting infrastructure in outbreak-prone regions, so that these capabilities are ready for use in outbreak situations. MSD did not have prior experience with Ebola virus nor clinical development expertise in the African countries in which the Ebola outbreak was taking place. Therefore, MSD relied on the expertise of organizations that were already involved in the public health response efforts to implement and complete nearly all the clinical trials of the Ebola vaccine.

Innovative, science-driven studies of high quality

To match the urgency of the moment, clinical trials were launched within the space of a few months of the epidemic being declared a Public Health Emergency of International Concern. Developing vaccines during the challenging circumstances of epidemics requires an innovative approach to clinical trial design. In this case, the Ebola Ca Suffit trial conducted by the WHO in Guinea[8], for example, used a novel ring vaccination, cluster-randomized design that was modeled after smallpox eradication efforts to target populations at the highest risk of Ebola infection.

In addition, the outbreak necessitated the use of different study designs for the Phase 2/3 trials. MSD played a key role in analyzing all data according to appropriate international regulatory standards and presenting them for regulatory evaluation.

Strong ethics and regulatory requirements, and regulatory collaboration

Clinical data requirements for licensure need to be clearly defined. Placebo-controlled, randomized, double-blind studies are typically used to demonstrate the efficacy and safety for new vaccines, but are not always needed for licensure. In some circumstances, like the Ebola outbreak, it would be considered unethical to administer placebo to at-risk individuals. The design of the clinical trials must consider these regulatory and ethical requirements.

Regulatory agency collaboration is critical for success. Following the West African Ebola outbreak, as the data generated during the outbreak were being assembled and new outbreaks or flare ups were occurring, the US FDA, EMA, the WHO, and the African Vaccines Regulatory Forum (AVAREF) worked closely with each other and with the National Regulatory Authorities of at-risk African countries, sharing information about MSD's vaccine candidate, reviewing compassionate use clinical protocols, available data, and the benefit-risk profile. Frequent conversations with MSD helped the WHO, which spearheaded the response efforts to the new outbreaks, to expedite the start of the expanded access protocols in different countries.

Stakeholder engagement

Less developed parts of the world harbor concerns over the evaluation of any investigational product and these concerns may be further exacerbated during an outbreak. Therefore, clear and transparent communication with community leaders and the community at large, ethical review committees, local ministries of health, and other government agencies was critical to ensure that the purpose of the research was well understood by them and aligned with accepted local and international norms.

SUMMARY OF LESSONS LEARNED

A summary of the lessons learned from the Ebola vaccine development in an outbreak setting:

Clinical

- Existing preclinical data on the vaccine platform can accelerate the start of Phase I trials during outbreaks.
- Clear communication with community leaders and government agencies is critical to ensure the purpose of clinical research is well understood by them.
- Standardization of clinical trial protocols and data collection is needed, and late-stage clinical trial designs should be defined prior to outbreak.
- Build and maintain clinical development laboratory capacities, and adverse event reporting infrastructure in outbreak-prone regions.
- Deployment of investigational product requires careful consideration and thorough planning.

Regulatory

- Global and regional harmonization, specifically the clinical data requirements for authorization, are critical for efficient development and licensure of pandemic vaccines.
- Regulatory agency collaboration is critical for success and frequent discussions with regulatory agencies and expedited regulatory pathways can accelerate the approval process.
- WHO's leadership is helpful to facilitate innovative review processes and collaborative mechanisms to expedite global approvals.

General

- Public-private partnerships help accelerate product development by leveraging expertise from different organizations.

SCHISTOSOMIASIS TREATMENT FOR PRESCHOOL-AGED CHILDREN, MEETING AN UNMET NEED

Strengthening clinical research capacity through more sustainable infrastructure, upskilling and innovation

Finding a treatment solution to change the lives of over 240 million people suffering from diseases that are widespread in tropic and subtropical conditions, especially in low- and middle-income countries, is a complex challenge that no single innovative pharmaceutical company can undertake on its own. Successful clinical trials in low- and middle-income countries (LMICs), requires strong partnerships, cross-continental and cross-hemispherical knowledge-sharing and a strong foundation of trust backed by committed funders.

An example where international collaboration efforts have resulted in encouraging progress towards elimination of disease is Schistosomiasis, an acute and chronic disease caused by parasitic worms, affecting more than 240 million people worldwide, including at least 50 million preschool-aged children that are currently lacking adequate treatment[9].

Addressing an unmet need through close collaboration

Through the Pediatric Praziquantel Consortium[10] established in July 2012 and led by Merck KGaA, Darmstadt, Germany, partners aim to actively contribute to the elimination of Schistosomiasis. The benefit of the Consortium lies in the leveraging of global expertise, to develop new treatments, conduct clinical trials and create access channels to enable large scale access.

Enabling capacity-building for clinical research and valued community engagement

In some cases, capacity building is necessary, especially when clinical research into a tropical disease requires trial conduct in specific endemic countries, investigating solutions that make a tangible impact in specific communities. Merck enabled a local site with infrastructure capability, which at the end of the trial was handed to the district hospital as an additional ward for patient care and a facility useable for future clinical trials. In addition to infrastructure, the project invested in upskilling of staff, inclusive of study procedures, ICH Good Clinical Practice (ICH E6), and international and local clinical trial guidelines. In the long-term, this contributed to strengthening the clinical research infrastructure and provided employment to local unemployed healthcare workers for a 3-year period. In addition, strong emphasis was placed on community engagement (visits to villages, and local government officials), which has proven to be vitally important to a successful recruitment strategy. The phase III development program has benefited not only the subjects studied, but also the clinical, scientific and support staff and the service and academic institutions of the host countries.

Images: Provided by company during field visits

To reach its goal, collaborating with key players in endemic countries remains an integral element of the Consortium's strategy with the aim to build capacity, to exchange knowledge, both operational and tacit, and to facilitate the interaction with national health authorities.

Maintaining or creating sustainable networks with sufficient capacity

The conduct of clinical trials in LMICs undoubtedly requires innovative approaches and collaboration between clinical trial manager, sponsor company and all stakeholders as well as reflecting holistically about the environment in which the clinical research is conducted to seek solutions for maximizing the research program's success. Nevertheless, building and maintaining a dedicated, cohesive, and ever-learning trial team inclusive of the study sites, is the key to safely and successfully conducting a clinical trial in such settings. Acting on lessons learned, with urgency, facilitating open communication and respecting one another's expertise, within the borders of ICH E6, local and international law, has led to the successful conclusion of the project and expansion of clinical research infrastructure.

SUMMARY OF LESSONS LEARNED

- Community involvement is essential to ensure successful recruitment of participants in clinical research teams or patients for clinical trials, but also to solidify local ownership of research.
- Obtaining informed consent from participants can be a complex process, which needs to be carefully planned and executed with care.
- Dialogue with regulatory authorities in countries where clinical research is being scaled-up or strengthened ensures knowledge of the status of regulatory authorities, especially in research naïve countries.
- Investing in research capacity strengthening in LMICs is critical to effectively combating disease. This could also entail investing in the training and scientific capacity at local level, as well as building or upgrading physical infrastructure.
- Study procedures and assessments need to be well communicated, to optimize clinical trial conduct and patient experience. This also requires consideration of how to manage language constraints in case report forms.

IMPLEMENTATION OF A PREVENTIVE HIV VACCINE TRIAL IN SUB-SAHARAN AFRICA

Johnson & Johnson

A public-private partnership applying the IFPMA perspective on clinical research in resource-limited settings

Decades of concerted scientific research efforts have given way to new leads in the challenging field of developing HIV vaccines.

Of several clinical trials evaluating experimental HIV vaccines, the Imbokodo proof-of-concept trial (HVTN 705/HPX2008) evaluated a regimen in approximately 2600 young, cisgender women across 5 sub-Saharan African countries (Malawi, Mozambique, South Africa, Zambia, and Zimbabwe) between November 2017 and February 2022. The Imbokodo trial was supported by a public-private partnership led by Janssen Vaccines & Prevention B.V., part of the Janssen Pharmaceutical Companies of Johnson & Johnson (regulatory sponsor of the trial); the U.S. National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health; the Bill & Melinda Gates Foundation; and the HIV Vaccine Trials Network (HVTN)[11].

Sustainable ecosystem and stakeholder engagement

The trial was conducted in accordance with Good Participatory Practices (GPP), developed by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and AVAC. In line with GPP principles (such as identification of key stakeholders as one of the starting points in the implementation of biomedical HIV prevention trials), the Imbokodo Protocol Team (PT) identified a member of the Community Engagement staff from the HVTN Leadership Operations Center, two community advisory board (CAB) members, and two Community Educators/Recruiters (CERs) who served on the PT and represented communities during the development and implementation of the trial protocol and dissemination of trial results. The CER and CAB members were selected from sites that would participate in implementing the trial.

To facilitate community engagement, the PT consulted with community stakeholders to identify a name for the trial that would resonate with communities. They selected the Zulu name 'Imbokodo'.

During the protocol development process, the PT reviewed the protocol, including the informed consent form, the consent for other use of samples, the approved birth control methods information sheet, and all other participant-facing materials for the trial. A pictorial presentation of the study schema was also developed to help explain the trial to persons with low literacy. All sites that participated in the trial identified key stakeholders in their local communities and developed an Annual Plan for Community Engagement that was inclusive of education, participant recruitment and retention strategies that would be used by each site. The protocol and participant-facing materials were reviewed by each site's CAB and their suggestions were implemented locally, following local Ethics Committee (EC) approval.

Prior to trial start, two consultation meetings for CAB members and other stakeholders were organized. The Imbokodo Study Chairs and other PT members provided an overview of the trial and welcomed community feedback, including any concerns, about the trial. Based on feedback from these consultations, educational materials to support sites' community engagement efforts were developed, including a trial website that included information on volunteering

for the trial. Another consultation was held with civil society representatives, regulators, ethicists and scientists to discuss the inclusion of oral HIV-1 pre-exposure prophylaxis (PrEP) to the Standard of Care for study participants, which was ultimately implemented at each site.

During the conduct of the trial, CABs were updated on a regular basis with the latest developments, including results from the regular reviews conducted by the independent Data Safety Monitoring Board. A retention workshop was organized for site staff members in March 2019 by the HVTN's Community Engagement Unit and PT, and CAB members supported retention efforts made by sites locally.

At trial conclusion, the trial results were promptly communicated to participants, the site CABs, advocacy groups, regulatory and other stakeholders, and scientific and civil society stakeholders. Additional HIV risk reduction counselling was provided to participants at their exit visit.

Throughout the conduct of the Imbokodo trial, the PT and sites walked the GPP path to ensure a full circle of accountability and transparency. Engagement of communities and stakeholders occurred from the earliest initiation of protocol development until the trial closed and results were disseminated.

Trial conduct during the COVID-19 pandemic

Several steps were taken to minimize disruption of trial activities and to protect site staff and participants during the COVID-19 pandemic. High retention and completion of vaccinations were achieved despite a hard lockdown, due to innovation by the sites and protocol teams.

Strong ethics and regulatory requirements

As vaccine development is a complicated process, early interactions in the form of a scientific advice meeting including the ECs, National Regulatory Agencies, other governmental agencies, and local communities (sites, local affiliates, protocol chair) presented an opportunity for exchange of information between all stakeholders. This allowed the sponsor to provide the necessary scientific background and for the National Regulatory Authorities to build understanding of the clinical trial prior to initiating the review process, leading to more transparency, and increased mutual understanding. Three informal face-to-face regulatory interactions were performed in Mozambique, South Africa, and Zimbabwe. These interactions provided a platform to discuss various aspects of the trial with all concerned stakeholders in a transparent manner and facilitated the protocol review and approval process. There were a few lessons learned from these interactions, including the importance of involving local colleagues with an understanding of the local environment, and connecting with important stakeholders.

SUMMARY OF LESSONS LEARNED

- Community engagement is critical in conducting a successful clinical trial.
- Trial conduct should be in accordance with international ethical standards regardless of location.
- To encourage and sustain clinical research, particularly in resource-limited settings, training and capacity building is required.
- An understanding of local regulatory landscapes and early interactions with agencies can go a long way in establishing mutual trust and understanding.

REIMAGINING THE MANAGEMENT OF SICKLE CELL DISEASE IN AFRICA

NOVARTIS

Building a solid, sustainable foundation for the treatment of sickle cell disease

Sickle Cell Disease (SCD) is a life-threatening condition with chronic debilitating manifestations, including acute painful episodes, anemia, organ damage, chronic pain, and fatigue. It is regarded by the World Health Organization (WHO) as a public health priority and a neglected health problem in sub-Saharan Africa, where 80% of babies with SCD globally are born each year[12].

SCD is a global health problem, yet sub-Saharan Africa (SSA) bears the highest burden of disease. To help bridge disease management and outcome disparities between Africa and the rest of the world, Novartis established the Novartis Africa Sickle Cell Disease program. The program is implemented through public-private partnerships with local governments, as well as collaborations with universities, patient groups, professional societies and other organizations. A key element of the strategy is a comprehensive approach to disease management that encompasses early intervention strategies, such as screening and diagnosis; research to investigate new treatments; and education and advocacy to improve access to existing therapies.

Enabling access in Africa to next-generation therapies for SCD

Whilst one of the objectives of the program includes improving accessibility of current SCD treatments, there is also a great need to bring innovative therapies to sickle cell patients in sub-Saharan Africa.

Early diagnosis and education of the parents of a sickle cell baby is considered vital for treatment of this disease. Novartis is partnering with the government and the Sickle Cell Association of Ghana. This partnership aims to expand a newborn screening program, expand distribution of the drug hydroxyurea to treat sickle cell, and conduct clinical trials in Ghana for a new, sickle cell treatment.

Kumasi, Ghana: A sickle cell screening program for newborns at Kumasi General Hospital. (Photo: Brent Stirton/Getty Images for Novartis)

P3 ref. no: EE2211228925

High-quality science-driven studies

Novartis is conducting a phase III, multicenter, randomized, double-blind study to assess efficacy and safety of two doses of crizanlizumab versus placebo, with or without hydroxyurea/ hydroxycarbamide therapy, in adolescent and adult sickle cell disease patients with vaso-occlusive crises – The STAND Study[13].

This is a global trial being conducted in multiple countries, including Ghana at the Ghana Institute of Clinical Genetics, Korle Bu Teaching hospital, Accra. Crizanlizumab is a novel next-generation biologic therapy licensed for the prevention of recurrent vaso-occlusive crises (VOCs) in sickle cell patients aged 16 years and older.

Novartis protocols and data collection methods go through same scientific rigor regardless of geographical location where trial is being conducted.

Data and Safety Monitoring Boards (DSMBs) are essential for all the studies to ensure that quality evidence is generated, and data is robust. Novartis has data privacy principles which follow international standards and are uniformly implemented across all our studies irrespective of the geography.

Capacity-building

Novartis also focuses on capacity building within the region to increase the experience in clinical trials, such as:

- Partnering with external vendors to provide training to Health Care Professionals, nurses, pharmacists etc. on Good Clinical Practice (GCP) and conducting clinical trials. Trainees complete the training at their own pace and receive certification once they have passed the exam.
- Setting up local depots to facilitate smooth conduct of the trial in Ghana and enable prompt distribution of investigational products to sites.
- Setting up local laboratory to support blood sample storage and local safety assessments as needed. The site now has access to specialty assessments such as echography assessments.

SUMMARY OF LESSONS LEARNED

- Digital assessments, i.e., electronic Patient Related Outcome assessments (ePRO) are more difficult to implement where internet connections are weak. However, the Ghana site has implemented measures to ensure better internet stability and continued connections.
- Early engagement of the regulatory authority is key to allow for smooth clinical trial approval process.
- Proactive communication with investigators to assist in obtaining import licenses to enable seamless importation of study drug, laboratory supplies and equipment needed for the study.

FOSTERING DIVERSITY AND INCLUSIVENESS IN CLINICAL TRIAL PARTICIPATION IN AFRICA

Partnering to address barriers to clinical trial participation

Clinical trials are essential to determine whether new drugs or diagnostics are safe and effective when used to diagnose or treat people. Because disease outcomes and drug responses can vary across populations, research must include patients who are racially, ethnically, and gender representative of those who experience disease. As part of its commitment to inclusive research, Roche is working in partnership with others to address barriers to clinical trial participation, diversifying genetic data for scientific discovery, and increasing access to innovative diagnostic and therapeutic solutions.

More clinical research will increase local evidence generation which has a wider positive effect upon patients and healthcare systems. Positive effects Roche expects to see in turn include:

- Better health outcomes for African patients
- Unlocked access
- Enhanced political will to increase health care spend
- Increased capabilities for health care practitioners (HCPs) with early access to innovation and standard of care for HCP's and patients
- Creation of opportunities to translate genomic or biomarker findings to underrepresented populations.

By building trusted partnerships with patients, providers and across the healthcare ecosystem, scientific advances can be combined with new technologies and real-world data to drive scientific innovation and create new standards for inclusive research.

Increasing the footprint

Roche's clinical trial partnerships extend over several therapeutic areas, including oncology, malignant haematology, infectious disease, immunology, neuroscience and ophthalmology, fostering enhanced access to innovative diagnostic tools and treatments through clinical research across Africa. Roche is seeking to expand its clinical trial footprint in Africa, increasing the number of countries beyond the eight states where clinical trials are currently conducted. By engaging all relevant stakeholders to jointly build sustainable ecosystems for clinical research in Africa, the partnerships provide learnings for the company and also create lasting benefits for patients in those countries.

As per Roche operating procedures, all trials conducted by Roche in Africa respect the international standards (International Council for Harmonisation (ICH), Good Clinical Practice (GCP) and Good Pharmacovigilance Practice (GVP)), local regulations and laws and data privacy regulations in each of the countries. This also means that data information collected from clinical settings across Africa can contribute to global research and advance global medicine.

Realizing potential of Personalised Healthcare by increasing inclusion and building capacity

Personalised Healthcare (PHC) seeks to develop a precise clinical and genomic picture of a patient to support treatment options. To enable this PHC concept, Roche is partnering with patients, caregivers, health and technology companies, and governments to collectively deliver evidence-based, technology-enabled healthcare solutions tailored to the individual. To facilitate a better understanding of how drugs work in specific populations, Roche has also brought innovative trial designs to Africa, especially in oncology.

The WHO Science Council report[14] on Promotion, implementation, collaboration, and ethical, legal, and social issues recommends that "current uses and future applications of genomic technologies are critical for improving the health and livelihood of people in all parts of the world, regardless of economic status". One of the main pillars for PHC is the use of genomics in the management of patients. For this reason,

through the Roche African Genomics Program, the company aims to play a critical role in catalyzing and supporting research in Africa that will accelerate the engagement of African citizens, scientists and institutions in genomic and clinical research and provide tangible improvements in health care for people in Africa and people worldwide. The approach aims to catalyze the development of an African-led open federation of large-scale clinical, genomics and outcomes biobanks hosted in Africa.

At the same time, Roche continues its approach to diversity in clinical trials through Foundation Medicine (FMI) a genomic sequencing platform which is part of the Roche organization. The company is currently running two trials in Africa which include FMI. The trial design will give African patients the opportunity to benefit from the innovative and personalized treatments.

To make research more inclusive, the Roche approach is based on two pillars: creating sustainable partnership and building capacity and investing in the necessary infrastructure for site governance of trials.

Sustainable partnerships

As an organization, Roche is committed to make sure medical advances are not only available, but also meet local health technology assessment (HTA) requirements and are affordable. Therefore it is important to be more holistic in the evidence generation approach – and invest early in different types of data like Real World Data (RWD), Non-Interventional Studies (NIS) and Investigator Initiated Studies (IIS). For this, partnership with external stakeholders and international research centres has been key. Roche is building partnerships with national and international research institutions to generate local data that could help countries in their decision making according to local needs. For example, Roche is partnering with Fred Hutchinson Cancer Research Centre and the Uganda Cancer Institute for a trial in Paediatric Lymphoma.

Building capabilities and infrastructure

Building capacity and investing in the necessary infrastructure for site governance of trials is essential to create an environment conducive to research at international standards, as well as increasing confidence. To foster this, Roche is working towards the development of four Centres of Excellence in clinical research in four countries through investment in strengthening capacities of investigators, lab technicians and supporting the development of infrastructures that will help shape the conditions for clinical research. These Centres of Excellence will be ready to host all stages of clinical research from early phase to late phase. Early phase clinical trials provide early access to innovation, which could be critical to patients with terminal and/or rare diseases with limited treatment options. Early phase trials also provide educational opportunities to healthcare professionals to have hands-on experience with new therapies before they become more widely available.

SUMMARY OF LESSONS LEARNED

- Fostering an inclusive approach to clinical trials supports a better understanding of disease outcomes and drug responses across a varied population.
- Partnership and collaboration with health authorities has proven to be beneficial to enhancing clinical trials regulation and shortening timelines for approval. In turn, this has made African countries more competitive so that they can attract more clinical trials.
- Investing in strengthening skills and capacity will ensure trials in Africa are conducted according to international standards and performed with the highest quality.

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2 E.g., ICH E6(R3) on Good Clinical Practices; ICH E8(R1) on Revision of General Considerations for Clinical Trials; ICH E9 on Statistical Principles of Clinical Trials and ICH E20 on Adaptive Clinical Trials

3 Examples of initiatives are: CTTi, DiME, DTRA, EU-Pearl; TransCelerate, Principles on Conduct of Clinical Trials | PhRMA; Sharing clinical trial information (efpia.eu); EFPIA statement on EMA's "Accelerating Clinical Trials in the EU (ACT EU)" initiative

4 IFPMA Clinical trials position papers

5 Biopharmaceutical companies are committed to enhancing public health through responsible sharing of clinical trial data in a manner that is consistent with the following principles: Safeguarding the privacy of patients, respecting the integrity of national regulatory systems, maintaining incentives for investment in biomedical research. IFPMA Principles; EFPIA Principles.

6 Applying lessons from the Ebola vaccine experience for SARS-CoV-2 and other epidemic pathogens | npj Vaccines (nature.com)

7 Examples include: national governments (such as Canada, the United States, and African countries); various agencies (such as the Public Health Agency of Canada, US National Institutes of Health, US Centers for Disease Control and Protection, US Biomedical Advanced Research and Development Authority, US Defense Threat Reduction Agency); field response and non-governmental service organizations (such as Médecins Sans Frontières); global public health entities (such as the World Health Organization, Wellcome Trust, and Gavi); Universities (e.g., the University of Geneva, Dalhousie University) and private sector companies (such as NewLink Genetics, IDT Biologika, and MSD).

8 Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ca Suffit!) - ScienceDirect

9 Schistosomiasis factsheet, World Health Organization: https://www.who.int/news-room/fact-sheets/detail/schistosomiasis

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11 Additional partners who provided support included the US Army Medical Research and Development Command (USAMRDC) and the Ragon Institute of MGH, MIT and Harvard. The trial was conducted at clinical sites coordinated by the HVTN, with implementation facilitated by the South African Medical Research Council (SAMRC) in South Africa. Community engagement efforts were led by the HVTN.

12 Global distribution of the sickle cell gene and geographical confirmation of the malaria hypothesis | Nature Communications

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14 WHO Science Council report: https://www.who.int/publications/i/item/9789240052857