Vaccine development Strategies in Korea; from R&D to Production

Manki Song, Ph.D.
Deputy Director General of Science
Nov. 01 2023
Background of Vaccine Self sufficiency

Importance of stable vaccine supply due to increased threat of emerging diseases

- SARS-CoV (2002, 775/8273 global, total damage 30 billion USD)
- Avian Influenza (2003, damage 1.5 billion USD Korea, recurrence in 2013)
- Pandemic influenza (2009, 270/750,000 Korea, estimated 5 to 30 billion USD in damage in Korea)
- FMDV (2011-2015, damage 4 billion USD Korea)
- MERS-CoV, (2015, 38/186 Korea, 10 billion USD in damage in Korea)

Vaccine self sufficiency; allows stable and low-cost supply of vaccines when you need it
Korea Experience: Influenza vaccine

MoTIE
Egg-based flu vaccine facilities (2005):
- Domestic flu vaccine production of 2009
- influenza pandemic outbreak; Failed to import vaccines on time
  ➡️ Supply of pandemic influenza vaccine; GC Biopharma, 26 million dose, 2010.01.05

MoHW
TEPIK established (Transgovernmental Enterprise of Pandemic Influenza in Korea):
- R&D (65M US$/6 yrs) (2010~2016)
  ➡️ Development of cell-based influenza vaccine; SK bioscience, First cell-based vaccine for WHO PQ certification

MoHW: Ministry of Health & Welfare
MoTIE: Ministry of Trade, Industry and Energy
Vaccine R&D and manufacturing capacity plan by Korean Government

2016

“Vaccine 3.0” Infrastructure building project for vaccine self sufficiency 2016-2020

• Funded by ROK government, BMGF, Korean manufacturers
• Focuses on global health R&D
• E.g. Cholera Conjugate Vaccine (CCV)

2018

“Right Fund” Research Investment for Global Health Technology Foundation

• Partner with Vaccine Innovative Technology Alliance (VITAL) Korea to promote R&D for global health
• Promote vaccine sovereignty of Korea and preparedness against EID

2020

“K-Vaccine Hub” Center of Excellence, providing essential support required in establishing K-Bio Hub

• Vaccine research: platform technology (mRNA, viral vector), adjuvant
• Innovation center: vaccine evaluation system through standard assays and reagents
• Translational hub: clinical development, regulatory affairs, and quality assurance
• Globalization: provide networking to industry to move to the next level

2021

Research Investment for Global Health Technology Foundation

Vaccine product development partnerships with Korean manufacturers & agencies

OCV, TCV, HEP B, HEP A, MERS Vaccine

• Sk bioscience
  - VI-D TCV
  - iNTS
• Euvichol® & Euvichol-Plus® OCV
• Hep A
• MERS

Eubiotics

• QuadMedicine
• Hep B microneedle patch

COVID-19 Vaccine

1. Additional partners include Hanmi Pharmaceuticals, NeoImmuneTech, Bioapp, GI Cell, GI Innovation, POSVAX, GeneMatrix and Korea Mouse Phenotyping Center (KMPC)

2011: 20%

2022: 40%

2030: 80%
SKYCovione

SK bioscience co-developed SKYCovione™;

- A recombinant protein vaccine, the Institute for Protein Design (IPD) at the University of Washington

- ASO3 adjuvant from GSK

- The Bill & Melinda Gates Foundation funded for early development

- CEPI Fund for clinical trials, variants research, and manufacturing process development.

- IVI supported the global clinical trial, sample analysis (with KDCA), and the regulatory process for the vaccine’s licensure
Phase 3 clinical study design of SKY Covione

SKY Covione conducted global clinical trials using ChAdOX1-S (AstraZeneca Covid-19 vaccine) as a reference vaccine for the purpose of evaluating humoral/cellular immunogenicity and safety in adults over 18 years of age.

**Title**
Multicenter, parallel comparison, observer-blind, active-controlled, randomized, phase 2, phase 3 clinical trial to evaluate the immunogenicity and safety of SARS-CoV-2 recombinant protein nanoparticle vaccine (GBP510) in adults 18 years of age or older.

**Purpose**
Humoral/Cellular Immunogenicity and safety evaluation of SARS-CoV-2 recombinant protein nanoparticle vaccine (GBP510) in adults 18 Years or older.

**Subjects**
- Target subjects: 3,990 adults 18 years of age or older
- Countries participating in clinical trials: Korea, New Zealand, Ukraine, Philippines, Thailand, Vietnam

**Dose**
GBP510-AS03 (25μg), reference vaccine: ChAdOX1-S (AstraZeneca Covid-19 vaccine)
- 2-Primary doses 4 weeks apart (on Day 0 & 28 for each)

**Endpoints**
- Safety
  - Solicited AE, Unsolicited AE, AESI, SAE, COVID-19 cases
- Immunogenicity
  - GMT(Superiority)/GMFR(Non-inferiority)/seroconversion of IgG antibody and Neutralizing antibody, and Cell-mediated response

**Diagrams**
- Primary #1: 0 day
- Primary #2: 28 day
- Booster: At least 3 month (Planned)
- Safety Follow-up: 12 month
Phase 3 study results – Primary endpoint

The results of the phase 3 clinical trial of SKYCovione confirmed the superiority of immunogenicity compared to the reference vaccine, the same as the results of the phase 1/2

**FRNT¹ Neutralizing Ab – Superiority**

<table>
<thead>
<tr>
<th></th>
<th>SKYCovione</th>
<th>AZ vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before injection</td>
<td>8.18</td>
<td>8.13</td>
</tr>
<tr>
<td>After 2 dose</td>
<td>272.12</td>
<td>92.75</td>
</tr>
</tbody>
</table>

2.93-fold

**SCR² - Non-inferiority**

<table>
<thead>
<tr>
<th></th>
<th>SKYCovione</th>
<th>AZ vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>After 2 dose</td>
<td>98.06</td>
<td>87.3</td>
</tr>
</tbody>
</table>

10.76%↑

---

GBP510

<table>
<thead>
<tr>
<th></th>
<th>SKYCovione</th>
<th>AZ Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>877</td>
<td>441</td>
</tr>
<tr>
<td>Post- GMT</td>
<td>8.18(1.08)</td>
<td>8.13(1.06)</td>
</tr>
<tr>
<td>GMR (95% CI)</td>
<td>1.01 [1.00, 1.01]</td>
<td></td>
</tr>
</tbody>
</table>

2W after Dose 2

<table>
<thead>
<tr>
<th></th>
<th>SKYCovione</th>
<th>AZ Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>877</td>
<td>441</td>
</tr>
<tr>
<td>Adjusted GMT (SE)*</td>
<td>272.12(1.07)</td>
<td>92.75(1.07)</td>
</tr>
<tr>
<td>GMR (95% CI)</td>
<td>2.93 [2.63, 3.27]</td>
<td></td>
</tr>
</tbody>
</table>

SCR

<table>
<thead>
<tr>
<th></th>
<th>SKYCovione</th>
<th>AZ Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>877</td>
<td>441</td>
</tr>
<tr>
<td>SCR</td>
<td>98.06%</td>
<td>87.30%</td>
</tr>
<tr>
<td>Diff. (95% CI)</td>
<td>10.76% [7.68, 14.32]</td>
<td></td>
</tr>
</tbody>
</table>

---

1. FRNT (Focus Reduction Neutralization Test) : SARS-CoV-2 Wild type virus ND50 Titer converted to IU/mL
2. SCR (Seroconversion Rate) : Ratio of subjects whose neutralizing antibody titers increased 4 times or more compared to before administration

* GMTs adjusted with treatment group, age group (18~64, ≥65) as factors, and baseline antibody level as covariate

**P-value for baseline GMT : t-test / P-value for adjusted GMT : ANCOVA / P-value for SCR : Chi-square test
SKYCovione

- June 29, 2022, Skycovione was approved for use in South Korea
- May 26 2023 authorised by the Medicines and Healthcare products Regulatory Agency (MHRA), UK
- June 23, 2023, listed on the WHO Emergency Use Listing (EUL)
- South Korean government purchased 10 million doses of SKY Covione of which 600,000 doses released into hospitals

Lessons Learned; for successful vaccine development

- International Collaborations for public sector funding and development efforts: IPD at the University of Washington, GSK, The Bill & Melinda Gates Foundation, CEPI, IVI, AstraZeneca, Korea Government
- Good antigen and adjuvant
- Rigorous regulatory process for vaccine manufacturing and clinical evaluation
- Need Vaccine experts and trained staffs

Global Equity in Access and Development?
Established in 2000, one of the longest-running vaccinology courses in the Asia-Pacific region.

Trained nearly 5,000 vaccine professionals from LMIC worldwide.

Collaborators: Karolinska Institutet, Sweden

International Vaccinology Course by IVI
Launched in 2022, the trainings are supported by the Ministry of Health and Welfare of Republic of Korea and the WHO.

Aims to equip participants with the critical skills and knowledge needed for biomanufacturing.

400+ participants have taken part in the trainings.

The entire training course is free of charge to all participants. (exclusive travel and visa costs)
GTH-B: Introductory Course for Biologics Development and Manufacturing

- 2-week, in-person training on introduction to all aspects of biomanufacturing.
  - Includes didactic training and interactive activities (e.g., case studies, presentations, panel discussions, etc.)
- Participants start to build the skills and competencies needed to work along the entire cycle of vaccine development, production and licensing.
- Includes excursion to and networking sessions with Korea Biopharmaceutical companies and networking

- Two trainings held

<table>
<thead>
<tr>
<th>2022</th>
<th>2023</th>
</tr>
</thead>
<tbody>
<tr>
<td>July 18-29</td>
<td>June 19-30</td>
</tr>
<tr>
<td>138 participants: 106 participants from 24 LMICs</td>
<td>187 participants: 150 participants from 40 LMICs</td>
</tr>
<tr>
<td>Scholarships provided by: PAVM, IDB</td>
<td>Scholarships provided by: PAVM, IDB, EAC RCE-VIHSCM, PAHO</td>
</tr>
</tbody>
</table>
GTH-B: Introductory Course for Standard Practice (GxP)

- **3-week, in-person training**
  - Provide participants with a strong understanding of global standards for biomanufacturing (GMP, GCP, GLP, GCLP, and biosafety)
  - Includes didactic training and interactive activities (e.g., case studies, presentations, panel discussions, etc.)
  - Includes excursion to and networking sessions with Korea Biopharmaceutical companies and networking

- **First training held in Oct-Nov 2022**
  - 151 participants from 31 LMICs and 36 participants from South Korea

- **Next training is scheduled for Oct 30-Nov 17**
  - Participant confirmation ongoing: Expecting 180 participants
Development of training programs for WHO global bio-training hub (GTH-B) in Korea (Global Bio Campus program development and planning): Proposed training program

**Scope of GBC program**

**Scope of GBC Training**
Jobs throughout the entire cycle of biopharmaceutical and vaccine development, manufacturing, commercialization, and supply

- Manufacturing (Hands-on under GMP)
- GMP
- Pre-clinical (GLP)
- Regulatory Affairs (WHOPQ+RAPS)
- Clinical (GCP)
- Supply and Marketing

**Job diversity in GBC training programs**
Specialized training by career unit

<table>
<thead>
<tr>
<th>Entry Level / Junior specialist</th>
<th>Senior / Manager</th>
<th>Director/C-Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic/intermediate level overview program</td>
<td>Hands-on training session</td>
<td>Intensive / advanced program Trainer to Trainer Training (TTT)</td>
</tr>
</tbody>
</table>

**Major 6 modules of GBC Training Program**

<table>
<thead>
<tr>
<th>Module 1</th>
<th>Module 2</th>
<th>Module 3</th>
<th>Module 4</th>
<th>Module 5</th>
<th>Module 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introductory training course</td>
<td>Hands-on training</td>
<td>Intensive course</td>
<td>Company-linked training program</td>
<td>Biotech entrepreneur training</td>
<td>Master Degree</td>
</tr>
</tbody>
</table>

- Training to strengthen basic knowledge of biopharmaceutical and vaccine development
- Vaccine and biopharmaceutical hands-on training at GMP-like facility
- Trainer to Trainer level training, In-depth training for each job of vaccine/biopharmaceutical industry
- Training based on industry needs and on-site training programs
- Biopharmaceutical entrepreneur training to build a domestic biopharmaceutical ecosystem
- Master's degree program combining GBC training program and internship Master degree in biopharmaceutical science and Vaccinology
Development of training programs for WHO global bio-training hub (GTH-B) in Korea (Global Bio Campus program development and planning): Operation model

Propose the efficient 6 biomanufacturing training module programs and operation model contributing to global bio campus.

- **Introductory Training Course**
- **GMP hands-on training set-up**
- **Intensive course**
- **GMP hands-on training**
- **Master degree course/Biotech entrepreneur training**

**Module 1**: Biopharmaceutical (Introductory Course)
- Biopharmaceutical

**Module 2**: Biotechnological Hands-on Training (didactic)
- Vaccinology
- Hands-on training (didactic)

**Module 3**: Company linked training course
- Company-linked manpower training

**Module 4**: CMC/TPP (Intensive course)
- CMC/TPP
- Tech transfer

**Module 5**: GMP (Intensive course)
- GMP
- RA
- PM
- On-site Training
- Hands-On Training
- Biotech entrepreneur training

**G&I network lab**
Thank You!