Clinical Trials in DRCongo: Challenges and opportunities

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Plan

1. • General information
2. • Economics and Culture
3. • Health system and Health problems
4. • Clinical research Process
5. • Challenges and Opportunities
1. General Information

Democratic Republic of the Congo (DRC)

**LOCATION**

- **World map**
- **CLIMATE** tropical wet (with difference in the rain period length within the country) Rain+++)
- 8 natural parks
- 2nd highest mount in Africa
- 2nd rain forest in the world (carbon)
- 2nd longest river in Africa (5th world)
- Volcanoes
- 13% world hydroelectric potential

**DEMOGRAPHY**

- Area: 2,345,408 Km²; 2nd largest Country in Africa (Japan X6)
- Population: 78 millions (density: 30 inhabitant per km²)
  - Age repartition ≥20y = 57%, 20 à 59y = 38,8%, ≥60y = 4,1%.
  - Life expectancy (2016): 60.4y for men; 62.7y for women
- Fertility rate: 5.9
- Educational attainment: 7.1y
- Urban site: 30.4%, Rural site 69.6%

**CLIMATE**

- Tropical wet (with difference in the rain period length within the country) Rain+++)
- 8 natural parks
- 2nd highest mount in Africa

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2. ECONOMICS and CULTURE

50% world’s reserve of Co, 10% of Cu, 30% of diamond and 70% of coltan. High rate of exportation (35%) with 41% to China.

Cultural diversity. 5 official languages. >400 tribes with very different dialects and practices. Mostly religious people, Popular music.

Agricultural: million ha arable lands, forest (woods).

Despite all these natural resources, the DRC remains a developing country. Many reasons???

→ Challenges
3. Health system and Health Problems

Health system

Procurement system

Health problems
3. Health system and Health Problems

HEALTH SYSTEM

Primary healthcare-based district health systems.

The country is strengthening his health system in collaboration with the world Bank, the USAID, WHO, JICA (NCGM) and others stakeholders mainly from Europe.

- Most healthcare services in DRC charge a fee
- Unregulated, fee-for-service payments → unpredictable cost of care for the patient.
- Direct payment for every single intervention.
- No public insurance
- Some private insurances but only for the rich and companies workers

Still Challenging!!!! But Promising!!!

401 hospitals (176 publics, 179 from churches, 49 from companies)
3. Health system and Health Problems

PROCUREMENT SYSTEM

SNAME (Public network + EU)

Operational actors

FEDECAME (BCAF)

Institutional actors

National Level
- MOH
- DPM
- PNAM
- DEP
- DSSP

Provinces level
- DPS
- CNPS

Public sector

Religious sector

Private sector (NPO and companies)

Patients


Private network
1. Some private pharmaceutical companies (Pakistan, India)
2. International NPO’s (Caritas, Red cross, Salvation army...)
3. Some religious orders.
3. Health system and Health problems

**HEALTH PROBLEMS**

**Ten most causes of deaths, all ages**
- Malaria
- Lower respiratory infection
- Tuberculosis
- Diarrheal diseases
- Cerebrovascular diseases
- Ischemic heart diseases
- Protein-energy malnutrition
- HIV/AIDS
- Preterm birth complications
- Birth asphyxia and trauma

**Ten most causes of deaths < 5**
- Malaria
- Lower respiratory infection
- Tuberculosis
- Diarrheal diseases
- Protein-energy malnutrition
- Neonatal preterm birth
- Neonatal encephalopathy
- HIV/AIDS
- Neonatal sepsis
- Congenital defects

**Equatorial Zone** 55%
**Mountain zone** 8%
**Tropical Zone** 27%

**High mortality of the under-5 (80.5/1000 live births) with 51.9 for under-1**

**MALARIA PROFILE**

[Map showing malaria distribution in different zones]

Some Epidemics: Yellow fever, Ebola, Cholera

Last Ebola outbreak: May 2018
53 cases, 38 Confirmed, 29 Deaths

Opportunities for clinical researches and trials
In both communicable and non-communicable diseases

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HIV/TUBERCULOSIS PROFILE: Top 10

Mortality rate
(Rate per 100,000 population per year)

Incidence rate
(Rate per 100,000 population per year)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Estimated Number of Cases</th>
<th>Rank in Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hookworm Infection</td>
<td>31 million</td>
<td>2nd</td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>15 million</td>
<td>3rd</td>
</tr>
<tr>
<td>Ascariasis</td>
<td>23 million</td>
<td>3rd</td>
</tr>
<tr>
<td>Trichuriasis</td>
<td>26 million</td>
<td>2nd</td>
</tr>
<tr>
<td>Lymphatic Filariasis</td>
<td>49 million at risk</td>
<td>2nd</td>
</tr>
<tr>
<td>Human African Trypanosomiasis</td>
<td>10,269-18,592</td>
<td>1st</td>
</tr>
<tr>
<td>Leprosy</td>
<td>3,621</td>
<td>1st</td>
</tr>
</tbody>
</table>

Incidence (MDR/RR-TB)**: 9.7 (4.9–15) per 100,000.

** MDR is TB resistant to rifampicin and isoniazid;
RR is TB resistant to rifampicin

Anne W. Rimoin, Peter J. Hotez NTDs in the Heart of Darkness: The Democratic Republic of Congo’s Unknown Burden of Neglected Tropical Diseases. Plos NTD’s 2013

Data: www.who.int/tb/data
4. Clinical Research Process

Clinical Trials Implementing process

1. National Ethics Committee and IRB.
2. CT Coordination Committee

Directorate of pharmacy and medicine DPM

IRB meeting: 1/month can be shorter if urgent
Fees: 1% of Budget

Documents
1. Protocol (10 copies)
2. Informed consent form
3. Essential documents
4. Data collection form
5. CV of the PI and collaborators
6. Budget of the study
7. Proof of financing
8. Protocol amendment (if any)
9. Insurance certificate
11. Approval from the counterpart IRB if multinational studies

Study initiation

Clinical Trial registration

Issuance of the import authorization for research drug and the authorization of temporary use
(Investigational Product)

Under the ICH regulations:
1. The investigator’s brochure
2. GMP certificate
3. Ethics committee documents and approval
4. Batch certificate of the drug (certificate of Product Registration WHO guidelines)
5. Pharmaceutical data, preclinical data
6. Certificate of Pharmaceutical Product (CPP)

All documents to be translated in French
Drug development process, Clinical Trials Status and Infrastructures

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Phase 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

INRB (JICA Centre) | UNIKIN | Universities Sponsor trials centers

Laboratories and research institutions
- Institut national de recherche biologique (INRB)
- Pronanut: (National program for nutrition)
- Institut de recherche sur les sciences de la santé (IRSS)
- Centre national de transfusion sanguine (CNTS)
- Centre de recherche en médecine tropicale de l’Ituri

53 studies registered in Clinicaltrials.gov

Research institutions (Universities)
- University of Kinshasa
- University of Lubumbashi
- University of Bukavu
- University of Goma
- Catholic University of Graben
- University of Kisangani
- Kongo University
- Others provincials and privates Universities

There is a lack of facilities for drug development and clinical trials
## Examples of some Clinical Trials

<table>
<thead>
<tr>
<th>Title</th>
<th>condition</th>
<th>Intervention</th>
<th>Location</th>
<th>Sponsor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic Tools for Human African Trypanosomiasis Elimination and Clinical Trials: Early Test-of-cure (DiTECT-WP4)</td>
<td>African Trypanosomiasis</td>
<td>Diagnostic Test: RNA and neopterin detection</td>
<td>Many sites in the country</td>
<td>Belgium Tropical Medicine Institute</td>
</tr>
<tr>
<td>Arresting Vertical Transmission of Hepatitis B Virus (AVERT-HBV)</td>
<td>Hepatitis B</td>
<td>Tenofovir Disoproxil Fumarate</td>
<td>Kinshasa</td>
<td>University of North Carolina</td>
</tr>
<tr>
<td>Community Access to Rectal Artesunate for Malaria</td>
<td>Malaria</td>
<td>Artesunate</td>
<td>Kinshasa School of Public Health, University of Kinshasa Kinshasa, The Democratic Republic of the Congo, Akena Associates Ltd. Abuja, Nigeria Makerere University School of Public Health Kampala, Uganda</td>
<td>Swiss Tropical &amp; Public Health Institute</td>
</tr>
<tr>
<td>Study Comparing Moxidectin And Ivermectin In Subjects With Onchocerca Volvulus Infection</td>
<td>Onchocerciasis</td>
<td>Moxidectin And Ivermectin</td>
<td>DRCongo, Ghana, Liberia</td>
<td>Medicines Development Limited</td>
</tr>
<tr>
<td>Efficacy and Safety of Feninidazole in Children at Least 6 Years Old and Weighing Over 20 kg With Human African Trypanosomiasis (HAT) Due to T.b. Gambiense: a Prospective, Multicentre, Open Study, plug-in to the Pivotal Study</td>
<td>Human African Trypanosomiasis</td>
<td>Feninidazole</td>
<td>Many locations in DRCongo</td>
<td>DNDi</td>
</tr>
</tbody>
</table>
Registration of Medicines and Medical devices

Candidate medicine or device

Directorate of pharmacy and medicine (DPM)
http://www.dpmrdc.org

Technical commission of drugs and medical devices (90 days)

Marketing authorisation application

Required documents
If known chemical component
1. Information on the manufacturers
2. Pharmacologic effects of the product
3. GMP inspection of manufacturing sites
4. Marketing authorization from the origin country
5. Certificate of local quality control
6. List of others country who registered the product
7. Pharmacovigilance data
8. Certificate of Pharmaceutical Product (CPP)
9. Reference data from a Stringent Regulatory Authority

If new chemical compound (to add)
1. Biochemistry data of the product
2. Data from animal studies
3. Toxicologic data

Special cases
Marketing authorisation granted in another country can be recognised in the DRC in the case of innovative medicines and also for specialist medicines from ICH regions
Provisions for waivers in the registration process in case of a disaster or epidemic
Revision of guidelines: 2 years

How about the PMDA???
Training program with regulatory authorities Nov/2018

SRA*
ICH regulations
The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme (PIC/S)
US Food and Drug Administration (FDA)
Medicines Control Council of South Africa (MCC),
European Medicines Agency (EMEA),
European Union and the French Agency for the Safety of Health Products (AFFSAPS)
WHO-PQ

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5. Challenges and Opportunities

**CHALLENGES**

1. No local insurance (sponsor private insurance) and low health expenditure.
2. Poor infrastructures in rural (roads), logistical challenges
3. Political instability
4. Lack of enough human resources for clinical trial
5. Language barrier
6. Tribes with very different dialects and practice
7. Low public awareness

**OPPORTUNITIES**

1. WIDE variety of diseases (non communicable and communicable)
2. COST-effectiveness (Reduced cost and in less time)
3. EMERGENT market (almost unexplored)
4. EASY approval process
5. WIDE Cultural diversity
6. NO long standing CRO’s

**Legend**

I. Prepaid private spending
II. Out-of-pocket spending
III. Government health spending
IV. Development assistance for health
PPP: Purchasing power parity

Source: Financing Global Health Database 2017
5. Challenges and Opportunities

OPPORTUNITIES

1. NOT only Congo but Africa still Unexplored despite his cultural and genetic diversity
2. Japan is the big absent in the African world despite his high renown in term of innovation
3. There are already some existing structures for clinical trials.
5. Challenges and Opportunities

Malaria Clinical Trials Alliance (MCTA)

1. Pr. Ogutu is an Association of the Clinical Research Professionals (ACRP) certified Physician Investigator (CPI) and is the founding president of the East African Chapter of the ACRP.

2. From Kenya Medical Research Institute (KEMRI), he is member of the Malaria Clinical Trials Alliance (MCTA).

MCTA’s key activities

- Networking and Training
  - Malaria diagnosis (training and EQA)
  - Good Clinical Practice
  - Data management
  - Training of finance managers
  - Short-term attachments to sites with more expertise in specific areas

- Long-term sustainability of research capacity at the sites
  - Site mentorship programme
  - Development of site’s strategic plan
  - Create a broad research agenda beyond malaria
  - Strong research team

Key Message

1. People in Africa would like to collaborate with Japanese manufacturers, same as they are doing with the US and Europe, but, some Japanese companies who tried to connect do not give neither any response nor any follow up.

2. There is need to conducting researches and business between Japan and Africa, because there are many diseases and structures are available NOT ONLY JAPANESE CARS, but also JAPANESE other business, such as Pharmaceutical one.
Tchegera Island

MERCI pour votre attention

ありがとうございました