

Ebola and vaccine emergency access in Belgium and Europe

Federal Agency for Medicines and Health Products

BRUSSELS

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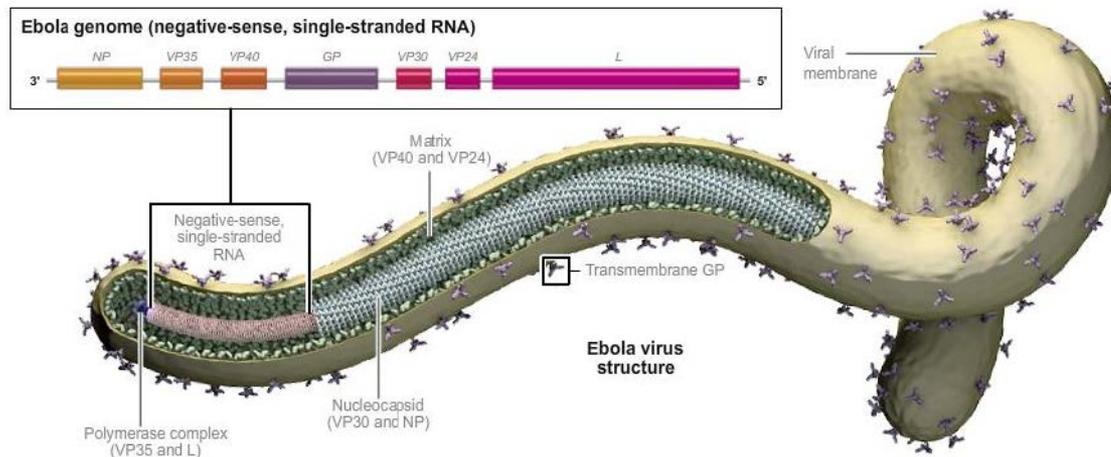
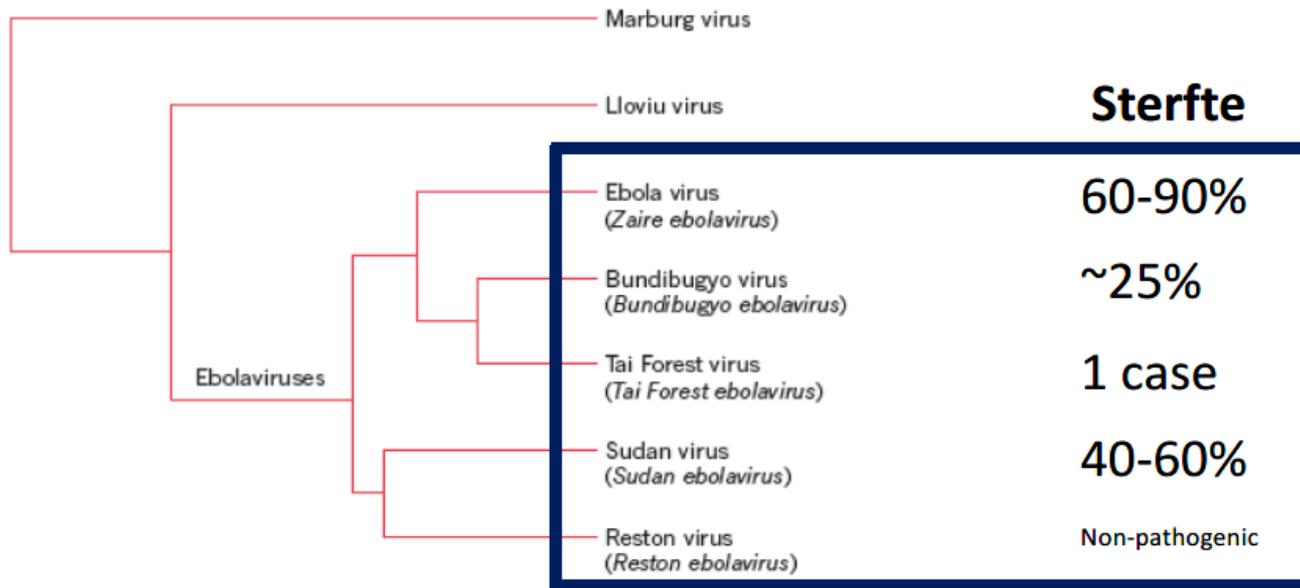
Nele BERTHELS

This presentation

1. Ebola virus disease and epidemiology
2. Possible Ebola treatments and vaccines
3. FAMHP preparedness activities



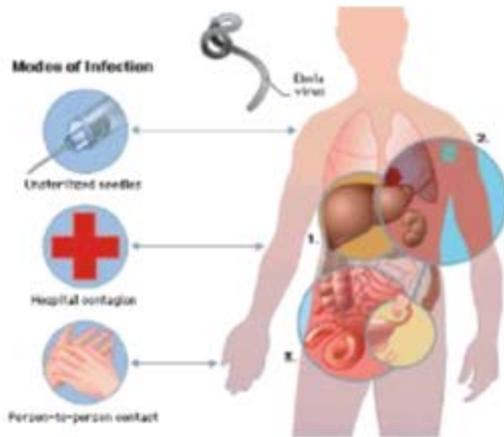
Ebola viruses



GP denotes glycoprotein, NP nucleoprotein, and VP viral protein.

Source: Patrick van Griensven (ITM Antwerp)

Ebola Virus Disease (EVD)



systemic disease with multi-organ involvement and ultimately failure



- **Fever**
- **Diarrhea and vomiting, fluid loss**
- **Hypotension**
- **Vascular permeability increased**
- **Renal failure, hepatitis**
- **Cerebral dysfunction**
- **Bleeding**
- **Circulatory collapse (shock)**

Higher mortality if:

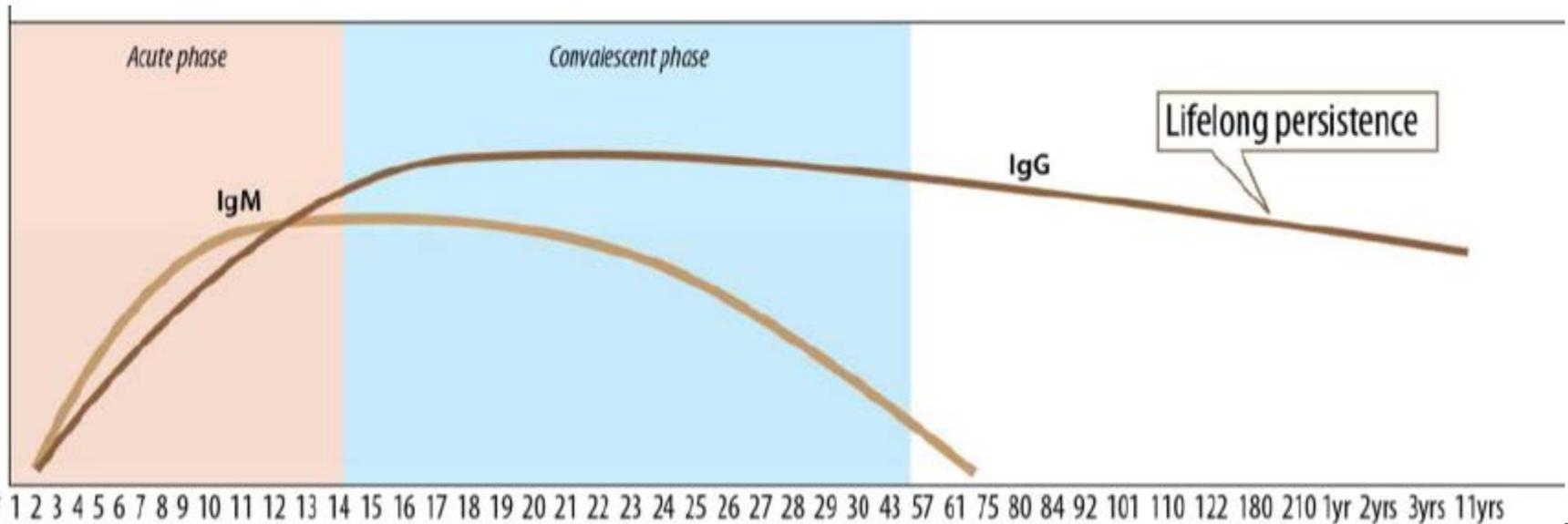
- **Age < 5 y or > 40 y**
- **Pregnant women**
- **High viraemia**

Hemorrhage only in 5-20% of cases!

EVD survivors



Ebola survivors develop neutralizing antibodies



Sequelae of Ebola virus disease in survivors

Common sequelae

- Neurological problems
- Persistent arthralgia, arthritis, vision-threatening uveitis
- Mental health problems

Virus latency and potential for reactivation

- Ebola virus might persist for weeks or months in selected immunologically privileged body sites of survivors, suggesting delayed viral clearance and an increased risk of renewed transmission in locations where the original outbreak has been controlled
- Virus can persist in the eye, brain, and epididymis (sanctuary sites)
- Virus can persist in semen (sexual transmission by Ebola survivors)
- Also in breastmilk?



EBOLA VIRUS DISEASE



Democratic Republic of the Congo External Situation Report 69

Date of issue: 26 November 2019
Data as reported by: 24 November 2019

1. Situation update



In the week of 18 to 24 November 2019, seven new confirmed EVD cases were reported from four health zones in two affected provinces in Democratic Republic of the Congo. The majority of the confirmed cases in this week came from Mabalako Health Zone (57%; $n=4$).

 **Violence and civil unrest** in the week have led to the  **suspension of Ebola response activities in some areas** of Beni, Butembo, and Oicha health zones. On 26 November 2019, some response personnel were temporarily relocated from Beni, though most remain in place to continue responding. The immediate focus will be on maintaining the safety and welfare of response personnel while preserving essential response activities in these places.

The disruptions to the response and lack of access to Ebola-affected communities is threatening to reverse recent progress. As seen previously during this outbreak, such disruptions limit contact tracing, surveillance, and vaccination efforts, and they often **result in increased transmission.**

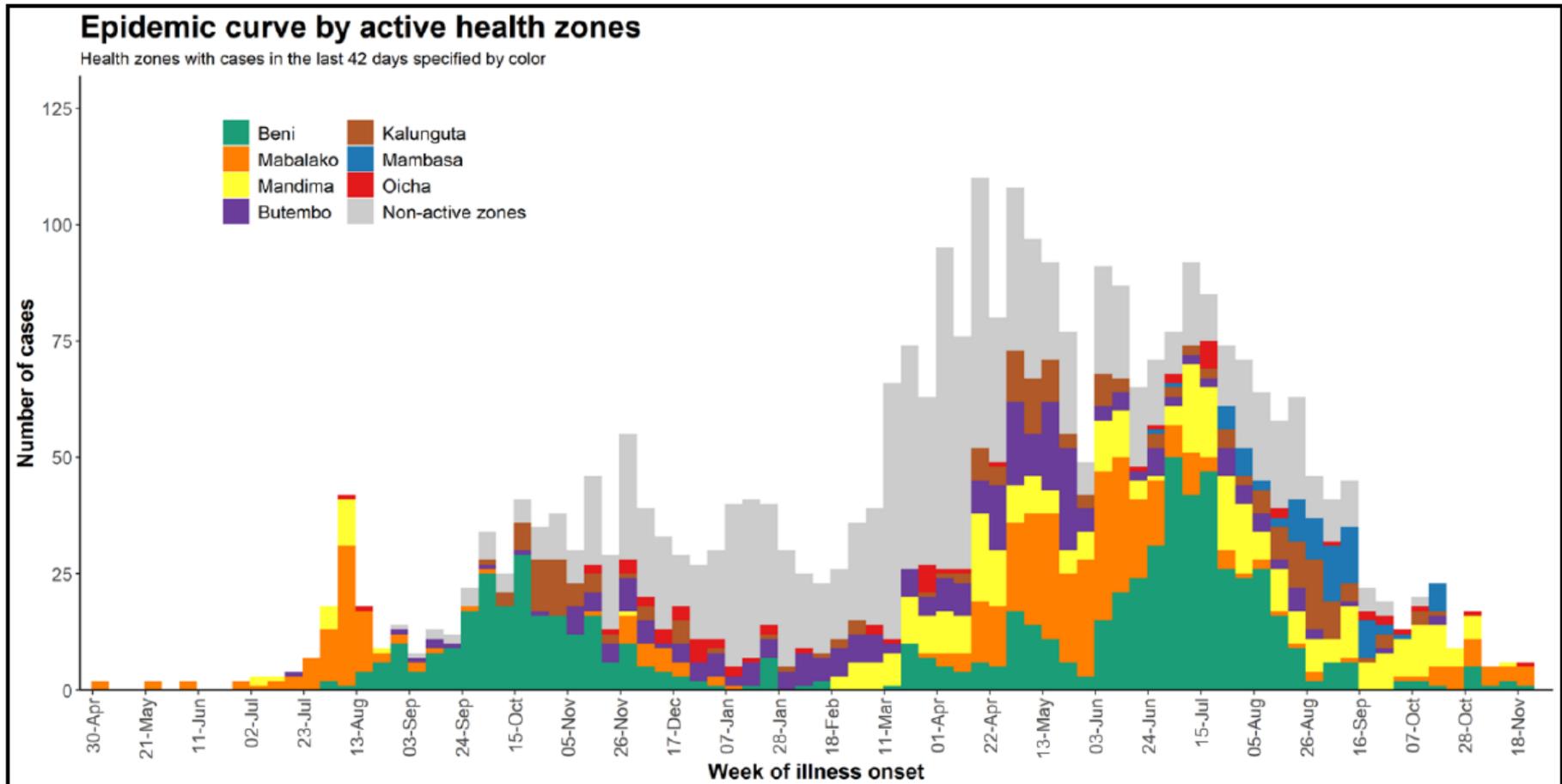
In the past 21 days (from 4 to 24 November 2019), 12 health areas and four health zones have reported cases (Table 1, Figure 2). During this period, a total of 28 confirmed cases were reported, with the majority reported from Mabalako (54%; $n=15$ cases) and Beni (32%; $n=9$). There have been no new confirmed cases in Nyakunde Health Zone for 42 days.

As of 24 November 2019, a total of 3303  EVD cases, including 3185 confirmed and 118 probable cases have been reported, of which 2199 cases died (**overall case fatality ratio 67%**). Of the total confirmed and probable cases, 56% (1862) were female, 28% (935) were children aged less than 18 years, and 5% (163) were healthcare workers.



Ebola epidemiology today

- Cases have been declining in the past few weeks, with more recent cases restricted to **rural, hard-to-reach communities** instead of the urban areas where hotspots were previously located.



Source: ECDC and WHO External Situation Report

Ebola epidemiology today

- The 10th outbreak of Ebola virus disease in the Democratic Republic of the Congo (DRC) has been ongoing since August 2018
- This is the largest ever outbreak reported in the country and the second largest in world history
- It has been declared a PHEIC (Public Health Emergency of International Concern) on 17 July 2019



Duration of Ebola outbreaks (weeks)

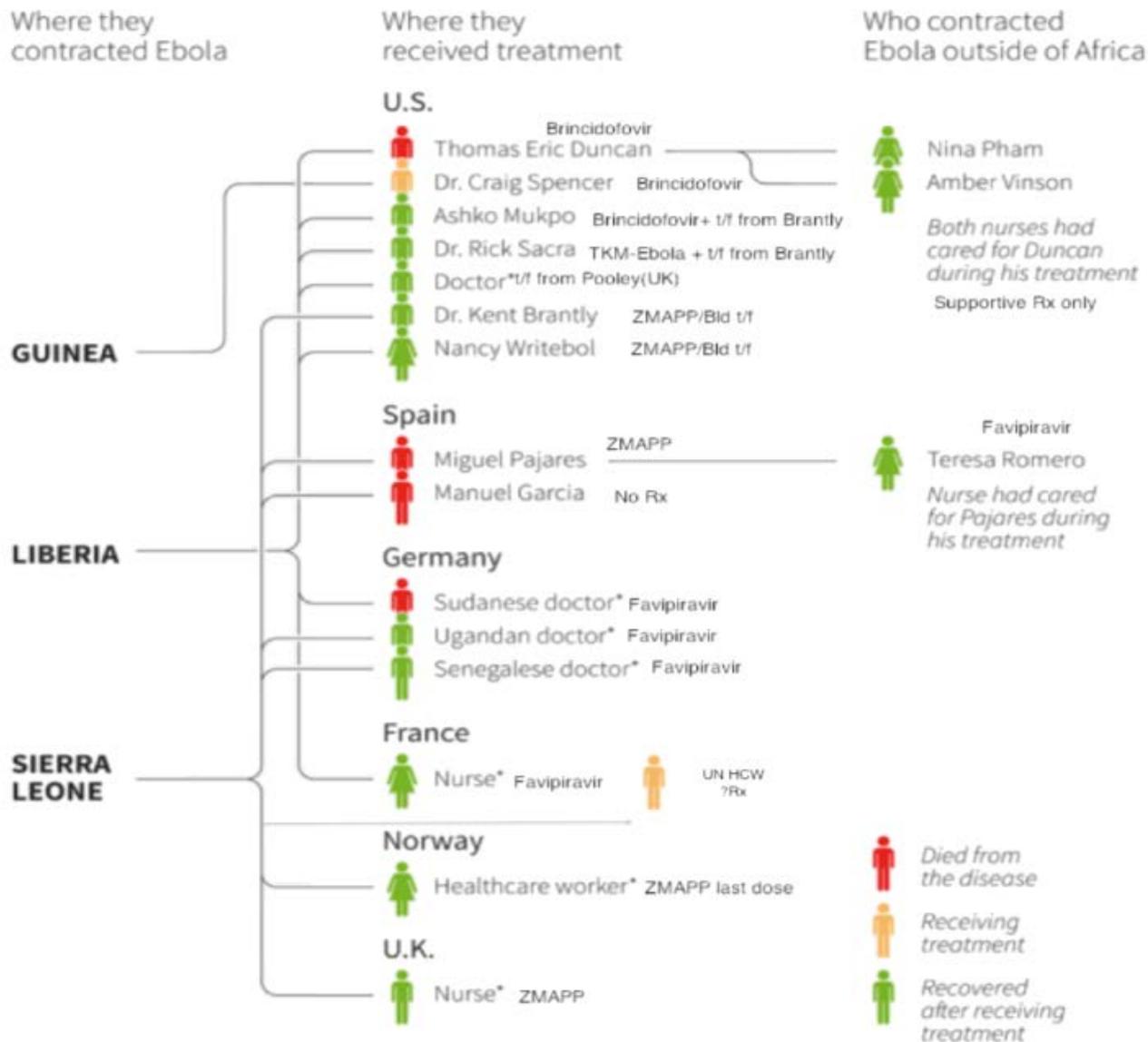


Weeks

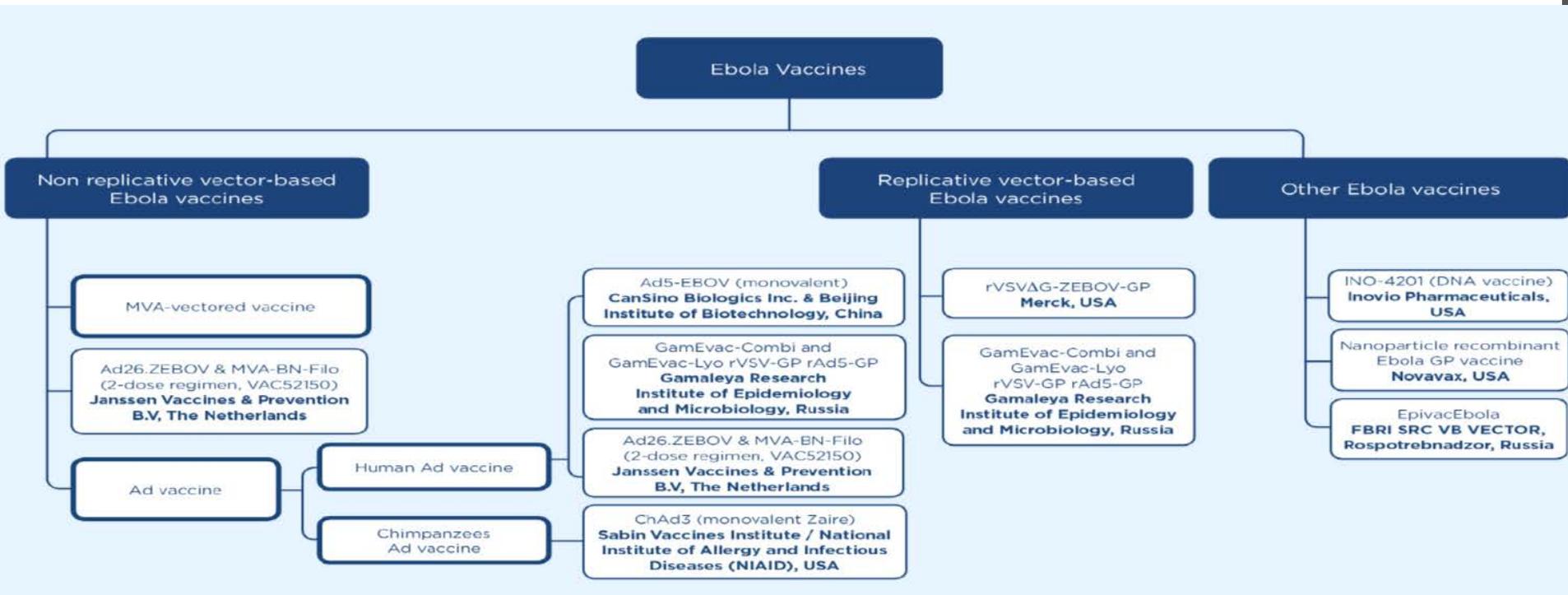
Source: WHO



Ebola epidemiology in EU (2014-2016)



Possible Ebola vaccines



Possible Ebola treatments

- Through close contact with developers of investigational treatments and with national regulators in EU member states, EMA has identified four treatments that could potentially be made available to patients, if required:
 - **REGN-EB3**, a co-formulated cocktail of three human monoclonal antibodies against the Ebola virus glycoprotein
 - **Mab114**, a recombinant human IgG1 antibody against the Ebola virus glycoprotein
 - **remdesivir**, a prodrug of a modified adenine nucleoside analogue (called GS-441524)
 - **ZMAPP**, an equimolar mixture of three mouse/human chimeric IgG1, kappa mAbs



Regulatory preparedness

Role of FAMHP in EMA activities

Outbreaks

The first Ebola disease outbreaks were reported back in 1976. Since then more than 30 outbreaks have occurred in Africa (mostly in Sudan, Uganda, the Democratic Republic of Congo, and Gabon).

Currently, the Democratic Republic of Congo (DRC) is grappling with the world's second largest Ebola epidemic on record.

August — WHO declared Ebola outbreak in West Africa a public health emergency

First vaccine

Ervebo is a genetically engineered, replication-competent, viral vectored vaccine. Data from clinical trials and compassionate use programs have shown that Ervebo protects against Ebola virus disease in humans, following a single dose.

Our role

Ebola virus disease is a rare but severe illness caused by the Ebola virus. Death rates in infected patients have ranged from 25% to 90% in past outbreaks.

Since 2014, EMA has provided advice on the development, evaluation and approval of medicines to fight Ebola virus disease.

2014

- EMA ad-hoc expert group established
- Review of experimental Ebola treatments started
- Interim report on experimental treatments review

2015

- Clinical trials of **1st investigational vaccine** started



June — Ebola outbreak in West Africa ended

2016

- Final report on experimental treatments review
- Application for accelerated assessment of **1st investigational vaccine**
- PRIME eligibility for **1st investigational vaccine**

May — DRC Ebola outbreak started
July — DRC Ebola outbreak ended

2017

May — DRC Ebola outbreak started
July — DRC Ebola outbreak ended
August — A second Ebola outbreak started in DRC

2018

- EMA contributed to WHO consultations on monitored emergency use of unregistered and investigational interventions for Ebola virus disease
- EMA contributed to a WHO ad-hoc expert consultation on clinical trials for Ebola therapeutics

July — WHO declared Ebola outbreak in DRC a public health emergency

2019

- EMA contributed to WHO Ebola vaccine evaluation and therapeutics consultations
- Marketing authorisation application for **1st vaccine against Ebola**
- Approval for accelerated assessment of **2nd investigational vaccine**
- EMA supported the EC's Health Security Committee to promote availability of investigational therapeutics and vaccines in Member States
- Positive opinion for granting a conditional marketing authorisation for **1st vaccine against Ebola**
- **Marketing authorisation** for 1st vaccine against Ebola **granted** by the European Commission

Vaccine approval

In October 2019, EMA's committee for human medicines adopted a positive opinion for granting a conditional marketing authorisation for Ervebo.

In November 2019, the European Commission (EC) adopted a decision on the EU-wide marketing authorisation of the vaccine—an important step on its path to patient access.

Access to possible Ebola medicines

- Depending on the member state, different ways are in place to use the unauthorised vaccine (emergency use, compassionate use, etc.)
- “Emergency use” provision in EU Medicines Directive 2001/83

2001L0083 — EN — 05.10.2009 — 008.001 — 14

▼ M6

the national legislation concerned to the Commission. The Commission shall make this information publicly available in a register.

▼ M4

Article 5

1. A Member State may, in accordance with legislation in force and to fulfil special needs, exclude from the provisions of this Directive medicinal products supplied in response to a bona fide unsolicited order, formulated in accordance with the specifications of an authorised health-care professional and for use by an individual patient under his direct personal responsibility.

2. Member States may temporarily authorise the distribution of an unauthorised medicinal product in response to the suspected or confirmed spread of pathogenic agents, toxins, chemical agents or nuclear radiation any of which could cause harm.



Access to possible Ebola medicines in Belgium

7th November 2014 – Decision to authorise the importation and use of medicines that are not authorised in the event of illness from the Ebola virus spreading

- Temporary measure to be used **to prevent or to treat EBV** in case of emergency in imported cases or travellers/HCW during the **West Africa outbreak (2014-2016)**
- 2 vaccines: rVSV-ZEBOV (Merck) and ChAd3-EBOV (GSK)
- 8 treatments:
 - Equine F(ab)2 (Hyper immune horse sera) from Fabentech (France)
 - ZMapp from Mapp Biopharmaceutical (USA)
 - ZmaB from Defyrus (Canada)
 - TKM-100802 from Tekmira Pharmaceuticals (Canada)
 - AVI-7537 from Sarepta (USA)
 - BCX-4430 from BioCryst (USA)
 - CMX001 (Brincidofovir) from Chimerix (USA)
 - Favipiravir from Toyama Chemicals, Fujifilm Group (Japan)
- Only imported by hospital pharmacies in **authorised hospitals**
- These products must be administered under medical supervision of a doctor working for one of the authorised hospitals
- The authorised hospitals must make a **report** monitoring the treatment, containing particularly any adverse effects, for each patient to whom one of these products has been administered; these reports should be sent to FAMHP



Access to Ebola medicines in BE



Update 10 October 2018 – Decision to authorise the importation and use of medicines that are not authorised in the event of illness from the Ebola virus spreading

- Valid until 31-12-2019
- In order to prevent or to treat: for imported cases and people departing to **current outbreak** region in DRC
- List of products reviewed
 - 2 vaccines: rVSV-ZEBOV (Merck) and Ad26/MVA (Janssen, J&J)
 - 6 treatments: Zmapp, Mab114, REGN-EB3, BCX-4430, remdesivir, favipiravir
- Request from MSF/AZG: potential vaccination with rVSV-ZEBOV vaccine in the EU for personnel to be deployed in Africa
- Raised questions regarding contained use or deliberate release of a GMO product
 - triggered the **GMO procedure**
- **Lessons learned** from first experience with this emergency procedure
 - Ministerial decree



DG SANCO (Health and Food Safety)

- Ongoing discussion through the Global Health Security Initiative focusing on the response to Ebola outbreak and potential best approaches to maintain **availability of Ebola vaccine and developed therapeutics** for the current outbreak in DRC and **for possible needs in EU citizens** deployed to DRC or other African country or in case an imported case of Ebola in to the EU will occur
- Ongoing discussions with EMA and Member States on the possible routes for use of unauthorised products including **possible harmonisation of emergency use/compassionate use**, for interested Member States

DG ECHO (European Civil Protection and Humanitarian Aid Operations)

- EU humanitarian aid has been supporting different aspects of the response, such as access to health care, **prevention and control of infections**, epidemiological surveillance, contact tracing, community engagement, food and psychosocial support to survivals and families of Ebola patients, and coordination





Thank you for your attention!
Any questions?



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A large, stylized graphic of a human eye, rendered in light blue and grey tones, serves as the background for the central text. The eye is composed of a large outer arc, a smaller inner arc, and a central circular pupil area.

Your medicines and health products,
our concern

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