Global Health Cast 35
April 27th, 2023

Dr. Melvin Sanicas  
Prof. Dr. Joe Schmitt

Every Week
12.00 noon - CET
What we talk about today

- COVID-19 update
- RSVPreF OA: Efficacy and license
- COVID19: Past and future of vaccine platforms
- HPV vaccine – 1 dose sufficient?
- “Most Infectious Diseases”: Lassa Fever
Figure 1. COVID-19 cases reported by WHO Region, and global deaths by 28-day intervals, as of 16 April 2023**
Highest numbers of new 28-day cases
1. United States of America
2. Republic of Korea
3. Russian Federation
4. France
5. Brazil
Highest numbers of new 28-day deaths
1. United States of America
2. Brazil
3. Russian Federation
4. Germany
5. Islamic Republic of Iran

Percentage change in confirmed COVID-19 deaths
-50 to 0: Decreasing
-10 to 0: Limited change
0 to 10: Increasing
> 10: Increasing
No reported confirmed deaths
Table 2. Weekly prevalence of SARS-CoV-2 VOIs and VUMs, week 9 to week 13 of 2023

<table>
<thead>
<tr>
<th>Lineage</th>
<th>Countries</th>
<th>Sequences</th>
<th>2023-09</th>
<th>2023-10</th>
<th>2023-11</th>
<th>2023-12</th>
<th>2023-13</th>
</tr>
</thead>
<tbody>
<tr>
<td>XBB.1.5* (VOI)</td>
<td>96</td>
<td>163 056</td>
<td>46.24</td>
<td>47.30</td>
<td>47.45</td>
<td>48.94</td>
<td>50.81</td>
</tr>
<tr>
<td>XBB.1.16* (VOI)</td>
<td>31</td>
<td>3038</td>
<td>0.52</td>
<td>1.19</td>
<td>1.99</td>
<td>4.18</td>
<td>4.15</td>
</tr>
<tr>
<td>BA.2.75*</td>
<td>121</td>
<td>106 256</td>
<td>5.13</td>
<td>4.91</td>
<td>4.66</td>
<td>2.10</td>
<td>1.76</td>
</tr>
<tr>
<td>CH.1.1*</td>
<td>88</td>
<td>41 605</td>
<td>6.44</td>
<td>5.68</td>
<td>5.46</td>
<td>4.66</td>
<td>5.18</td>
</tr>
<tr>
<td>BQ.1*</td>
<td>144</td>
<td>413 059</td>
<td>11.12</td>
<td>9.19</td>
<td>7.45</td>
<td>5.04</td>
<td>3.99</td>
</tr>
<tr>
<td>XBB*</td>
<td>124</td>
<td>84 336</td>
<td>8.40</td>
<td>11.67</td>
<td>14.62</td>
<td>19.95</td>
<td>25.80</td>
</tr>
<tr>
<td>XBB.1.9.1*</td>
<td>64</td>
<td>11 530</td>
<td>4.41</td>
<td>5.34</td>
<td>6.22</td>
<td>6.96</td>
<td>7.91</td>
</tr>
<tr>
<td>XBF*</td>
<td>49</td>
<td>8 947</td>
<td>1.08</td>
<td>1.21</td>
<td>0.93</td>
<td>0.78</td>
<td>0.70</td>
</tr>
<tr>
<td>Unassigned</td>
<td>98</td>
<td>293 052</td>
<td>10.42</td>
<td>8.83</td>
<td>8.92</td>
<td>7.75</td>
<td>0.46</td>
</tr>
<tr>
<td>Other*</td>
<td>207</td>
<td>6 693 030</td>
<td>1.08</td>
<td>1.04</td>
<td>1.02</td>
<td>1.42</td>
<td>2.07</td>
</tr>
</tbody>
</table>

* Includes descendant lineages, except those individually specified elsewhere in the table. For example, XBB* does not include XBB.1.5, XBB.1.9.1, XBF and XBB.1.16.

$ The prevalence of XBB.1.16 was extracted from GISAID on 17 April 2023 using the nucleotide substitutions T12730A, T28297C, A28447G.

+ Others are other circulating lineages excluding the VOI, VUMs, BA.1*, BA.2*, BA.3*, BA.4*, BA.5*, BF.7*. 

Weekly epidemiological update on COVID-19 - 20 April 2023 (who.int)
RSVPreF3 OA Efficacy in Older Adults

BACKGROUND

RSV is an important cause of LRTI-ARI in older adults.

METHODS

Ongoing, international, placebo-controlled, phase 3 trial, random 1:1 assignment of adults ≥60 years: single dose of AS01E-adjuvanted RSV pre F protein (RSVPreF OA; 120 µg) or placebo before the RSV season. Primary objective: VE against RSV-related (PCR+, subtype A and B) LRTI / severe LRTI disease during one RSV season. (Lower limit of the CI around efficacy estimate > 20%. RSV subtype (A and B) were performed. Safety evaluation.

RESULTS

24,966 participants (12,467 RSVPreF3 OA; 12,499 placebo. Median follow-up 6.7 months,

- VE: LRTI 82.6% (96.95% CI, 57.9 to 94.1); 7 vaccine group versus 40 placebo-group cases.
- VE severe LRTI 94.1% (95% CI, 62.4 to 99.9) (assessment by investigator)
- VE RSV-ARI: 71.7% (95% CI, 56.2 to 82.3)
- VE RSV-A/B LRTI: 84.6% / 80.9%; ARI 71.9% and 70.6%,

High VE in those with underlying diseases; RSVPreF3 OA more reactogenic than placebo. SAE / potential immune-mediated diseases similar in both groups.

CONCLUSIONS

A single dose of the RSVPreF3 OA had acceptable safety profile and prevented RSV-related acute respiratory infection and lower respiratory tract disease and severe RSV-related lower respiratory tract disease in adults 60 years of age or older, regardless of RSV subtype and the presence of underlying coexisting conditions.
Cumulative Incidence, RSV-Related LRT-disease / RSV-Related ARI

A. RSV-Related Lower Respiratory Tract Disease

B. RSV-Related Acute Respiratory Infection

No. at Risk

Placebo 12,494 12,403 12,290 11,887 11,640 11,022 8,291 5,464 2,709 559 2 0

RSVPreF3 OA 12,466 12,392 12,286 11,892 11,655 11,046 8,320 5,495 2,727 571 2 0

No. at Risk

Placebo 12,494 12,390 12,268 11,853 11,597 10,973 8,355 5,441 2,697 554 2 0

RSVPreF3 OA 12,466 12,390 12,282 11,881 11,641 11,029 8,305 5,481 2,717 570 2 0

Efficacy of Bivalent RSVpreF, Adults ≥60 Years, (Interim)

Vaccine Efficacy (96.66% CI)
percent 66.7 (28.8–85.8)

Vaccine Efficacy (96.66% CI)
percent 85.7 (32.0–98.7)

Vaccine Efficacy (95% CI)
percent 62.1 (37.1–77.9)
First vaccine to protect older adults from respiratory syncytial virus (RSV) infection

News 26/04/2023

EMA has recommended a marketing authorisation in the European Union (EU) for Arexvy (recombinant, adjuvanted), the first vaccine for active immunisation to protect adults aged 60 years and older against lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV).

RSV is a common respiratory virus that usually causes mild, cold-like symptoms. Most people recover within one to two weeks, but RSV can be serious in vulnerable people, including older adults and those with lung or heart disease and diabetes. In Europe, RSV causes an estimated 250,000 hospitalisations and 17,000 in-hospital deaths every year in people aged 65 years and older.

Arexvy contains an engineered version of the RSV fusion surface glycoprotein. This protein is essential for RSV to infect the body and is also the main target of the antibodies generated to fight the infection. The vaccine also contains an 'adjuvant', a substance to help strengthen the immune response to the vaccine. When a person is given the vaccine, their immune system generates specific antibodies and T cells that help prevent RSV infection.
## Covid vaccines doses per company in 2023 worldwide

<table>
<thead>
<tr>
<th>Company</th>
<th>Number of Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer/BioNTech (mRNA)</td>
<td>153,027,497,763</td>
</tr>
<tr>
<td>Moderna (mRNA)</td>
<td>40,437,997,824</td>
</tr>
<tr>
<td>Oxford/AstraZeneca (AdV)</td>
<td>15,681,378,479</td>
</tr>
<tr>
<td>Sinopharm/Beijing (WV)</td>
<td>5,181,992,534</td>
</tr>
<tr>
<td>Johnson&amp;Johnson (AdV)</td>
<td>2,989,398,379</td>
</tr>
<tr>
<td>Sputnik V (AdV)</td>
<td>2,256,033,397</td>
</tr>
<tr>
<td>Sinovac (WV)</td>
<td>1,026,888,299</td>
</tr>
<tr>
<td>Novavax (SU adjuv)</td>
<td>110,670,879</td>
</tr>
<tr>
<td>CanSino (AdV)</td>
<td>97,695,715</td>
</tr>
<tr>
<td>Valneva (WV)</td>
<td>1,602,322</td>
</tr>
<tr>
<td>Sanofi/GSK (SU adjuv)</td>
<td>670,314</td>
</tr>
<tr>
<td>SKY Covione (SU-np-ASO3)</td>
<td>50,282</td>
</tr>
<tr>
<td>Covaxin (WV)</td>
<td>16,433</td>
</tr>
</tbody>
</table>

>20 million lives saved to date

Source: University of Oxford
## Future Covid Vaccine Pipeline

<table>
<thead>
<tr>
<th>Platform</th>
<th>Candidate vaccines (no. and %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein subunit</td>
<td>59 32%</td>
</tr>
<tr>
<td>Viral Vector (non-replicating)</td>
<td>25 14%</td>
</tr>
<tr>
<td>DNA</td>
<td>17 9%</td>
</tr>
<tr>
<td>Inactivated Virus</td>
<td>22 12%</td>
</tr>
<tr>
<td>RNA</td>
<td>43 24%</td>
</tr>
<tr>
<td>Viral Vector (replicating)</td>
<td>4 2%</td>
</tr>
<tr>
<td>Virus Like Particle</td>
<td>7 4%</td>
</tr>
<tr>
<td>VVr + Antigen Presenting Cell</td>
<td>2 1%</td>
</tr>
<tr>
<td>Live Attenuated Virus</td>
<td>2 1%</td>
</tr>
<tr>
<td>VVnr + Antigen Presenting Cell</td>
<td>1 1%</td>
</tr>
<tr>
<td>Bacterial antigen-spore expression vector</td>
<td>1 1%</td>
</tr>
</tbody>
</table>

Total candidate vaccines: 183
NEW Kenyan Study: 1-Dose HPV Vaccine Highly Efficacious over 3 years

- A randomized, multicenter, double-blind, controlled trial included 2,275 women between the ages of 15-20, who were randomly assigned to receive either a single dose of the bivalent or nonavalent HPV vaccine or the control vaccine.
- Participants were regularly tested for HPV DNA, with cervical and vaginal swabs collected at regular intervals.
- The results showed that the single dose of both the bivalent and nonavalent HPV vaccines were highly efficacious, with a vaccine efficacy of 98%. Additionally, the nonavalent vaccine had a vaccine efficacy of 96% for the nine types of HPV it targets.

The Kenya Medical Research Institute (KEMRI) is a State Corporation established in Kenya in 1979 and currently ranks as one of the leading Centres of excellence in health research both in Africa globally.
9 of the most infectious diseases the WHO has identified to date:

- Nipah virus **Check out GHC 33**
- Crimean-Congo hemorrhagic fever **Check out GHC 34**
  - Lassa fever
  - Rift Valley fever
  - Zika
  - Ebola and Marburg
  - Middle East respiratory syndrome (MERS)
  - Severe acute respiratory syndrome (SARS)
  - COVID-19

Disease X (any unknown pathogen that could cause a future outbreak)
9 of the most infectious diseases the WHO has identified to date:

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Disease X (any unknown pathogen that could cause a future outbreak)
Lassa fever is reported in Benin, Côte d’Ivoire, Ghana, Guinea, Liberia, Mali, Nigeria, Sierra Leone and Togo
Lassa fever Transmission

Reservoir *Mastomys* rats
- The virus maintains itself in *Mastomys* rat population
- Virus is present in urine and feces of infected rats

Primary human infections
- 80 to 90% of humans are infected through:
  - Food or household items contaminated by infected rats’ urine and faeces.
  - Direct contact while handling *Mastomys* rats (food source)

Secondary human infections
- Secondary human-to-human transmission occurs through direct contact with the blood, secretions, organs or other body fluids of infected persons.

https://www.who.int/health-topics/lassa-fever#tab=tab_1
Evolution of Lassa fever symptoms

Evolution of Lassa fever disease from symptom onset

- Fever
- Extreme fatigue
- General weakness

- Headache
- Severe sore throat
- Diarrhoea
- Vomiting

- Face swelling
- Low blood pressure
- Nose bleeding

Days

https://www.who.int/health-topics/lassa-fever#tab=tab_1
Lassa fever in pregnancy and infants

- Particularly severe in pregnant women and their fetuses (fetal death rate greater than 85%)
- Increased maternal mortality in third trimester (greater than 30%)

- Significant cause of pediatric hospitalizations in some areas of West Africa
- Infants (up to 2 years old) can present a ‘swollen baby syndrome’ and is associated with high case fatality rate

https://www.who.int/health-topics/lassa-fever#tab=tab_1
What we talked about today

- COVID-19 update
- RSVPref OA: Efficacy and license
- COVID19: Past and future of vaccine platforms
- HPV vaccine – 1 dose sufficient?
- "Most Infectious Diseases": Lassa Fever
Unlike the brain, the stomach alerts you when it is empty.

The big difference is the stomach alerts only that person, but the brain alerts everyone else when it's empty.