Metodevarsel LM nr 105 2019
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folkehelseinstituttet
MedNytt

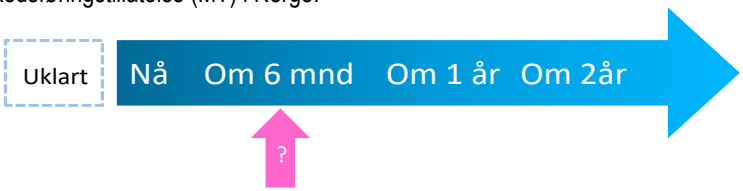
Statens legemiddelverk
Norwegian Medicines Agency

Live attenuated recombinant viral vaccine for the prevention of Ebola virus disease (EVD)

Type metode: Legemiddel; Vaksine
Område: Vaksiner
Virkestoffnavn:Recombinant vesicular stomatitis virus - zaire ebola virus vaccine (live)
Handelsnavn:
ATC-kode: J07BX
MT søker/innehaver:: Merck Sharp & Dohme B.V. [1]
Finansieringsansvar:

Status for bruk og godkjenning

Tidsperspektiv markedsføringstillatelse (MT) i Norge:



Metoden omfatter et nytt virkestoff. Metoden har foreløpig ikke MT i Norge, EU eller i USA, men er under vurdering hos det Europeiske Legemiddelbyrået (EMA) og US Food and Drug Administration (FDA) [2].

Beskrivelse av den nye metoden

This intervention is a live attenuated recombinant viral vaccine for the prevention of Ebola virus disease (EVD) caused by the Zaire species of Ebola (see below). This recombinant viral vaccine, rVSV-ZEBOV-GP (also known as V920), is chimeric. It is composed of recombinant vesicular stomatitis virus (rVSV) where the surface G-glycoprotein of VSV has been completely replaced by the glycoprotein (GP) of the Zaire Ebola virus. This substitution eliminates the neurovirulence associated with wild type VSV and attenuates the virus. The Zaire Ebola virus GP is displayed on the surface of VSV in its native conformation whilst maintaining the natural bullet-like shape of VSV. Since rVSV-ZEBOV-GP carries the Zaire Ebola virus glycoprotein (GP) on its surface, rVSV-ZEBOV-GP thereby acquires the tropism and host range of the Zaire Ebola virus. rVSV-ZEBOV-GP is replication competent [3] and can therefore stimulate the broad range of immune responses associated with natural infection. rVSV-ZEBOV-GP is administered intramuscularly as a single injection [4].

Sykdomsbeskrivelse og pasientgrunnlag

Ebola virus is classified in the virus family Filoviridae and genus Ebolavirus. Within the genus Ebolavirus, six species have been identified: Zaire, Bundibugyo, Sudan, Taï Forest, Reston and Bombali. The virus causing the current outbreak in the Democratic Republic of Congo (DRC) and the 2014–2016 West African outbreak belongs to the Zaire ebolavirus species [5]. The Ebola virus causes an acute, serious illness. Case fatality rates have varied from 25% to 90% in past outbreaks. Ebola is introduced into the human population through close contact with blood, secretions, other body fluids or organs of infected animals such as fruit bats, chimpanzees, gorillas, monkeys, forest antelope or porcupines found ill or dead in the rainforest. Human-to-human transmission occurs through direct contact (through broken skin or mucous membranes) via body fluids (such as blood, faeces, vomit) from a person who is sick with or has died from Ebola, or objects that have been contaminated with such bodily fluids. The symptoms of EVD can be sudden and include fever, fatigue, muscle pain, headache and sore throat. This is followed by vomiting, diarrhoea, rash, impaired kidney and liver function, in some cases both internal and external bleeding can occur (for example, oozing from the gums, or blood in the stools). Transmission does not occur during the initial incubation period (2-21 days), but will occur as long as virus is detectable. In an outbreak, family members of infected individuals and healthcare professionals are at particular risk. In survivors, Ebola virus may persist in some body fluids, including semen for several months. A number of medical complications have been reported in people who recovered from Ebola, including mental health issues. Ebola survivors require comprehensive support for the medical and psychosocial challenges they face and also to minimize the risk of continued Ebola virus transmission [5].

The 2014–2016 Ebola epidemic resulted in more than 28,000 cases and more than 11,000 deaths and presented a critical public health emergency. The outbreak primarily affected Guinea, Liberia, and Sierra Leone in West Africa, although cases were also identified and treated in Italy, Mali, Nigeria, Senegal, Spain, the United Kingdom, United States and Norway [4]

Dagens behandling

Treatment options for patients infected with Ebola virus are limited. There is no licensed treatment proven to neutralize the virus. However, a range of potential treatments including blood products, immune therapies and drug therapies are currently being evaluated [5]. Supportive therapy is centred on fluid resuscitation, electrolyte imbalance correction, treating complicating infections, and preventing complications of shock. In addition, convalescent whole blood or plasma collected from patients who have recovered from EVD may be used for transfusion as an empirical treatment during outbreaks [6].

Status for dokumentasjon

Metodevurderinger eller systematiske oversikter –norske

- Ingen relevante identifisert

Metodevurdering eller systematiske oversikter -internasjonale

Det foreligger minst en relevant internasjonal metodevurdering eller systematisk oversikt [7]

Metodevarsler

- Ingen relevante identifisert i Norge

Det foreligger minst ett internasjonalt metodevarsel [1,8]

Klinisk forskning

De antatt viktigste studiene for vurdering av metoden er vist i tabellen under:

Populasjon (N =antall deltagere)	**Intervensjon**	**Kontrollgruppe**	**Utfallsmål**	**Studienavn og nummer* (fase)**	**Tidsperspektiv resultater**
Healthy volunteers 18-64 years of age. Enrolled n=1197	rVSV-ZEBOV-GP (V920 Ebola vaccine) Consistency Lot: A (n = 266) B (n = 265) C (n = 266) High dose Lot (n = 264)	Placebo (saline) (n = 133)	Safety and Immunogenicity	NCT02503202 EudraCT2015-001658-14 Phase 3	Completed. Has results [9]
Participants 18 years or older who are at high risk of exposure to EVD through their daily work. Enrolled n=8651	rVSV-ZEBOV-GP (V920 Ebola vaccine)	None. Two groups: Immediate and deferred vaccination	vaccine efficacy (VE) and safety with phased vaccine introduction in the target population	NCT02378753 CDC-NCIRD-6689 (STRIVE) Phase 2/3	Completed. Has results [10]
Healthy individuals 6 years or older. Participants from the age of 1 year may also be enrolled if they are a contact of a laboratory confirmed case. Enrolment: n=500	rVSV-ZEBOV-GP (V920 Ebola vaccine)	None.	Safety and effectiveness	NCT03161366 Phase 3	Completed. No results available.

*ClinicalTrials.gov Identifier www.clinicaltrials.gov

Relevante vurderingselementer for en metodevurdering

Klinisk effekt relativt til komparator	☐	Ny virkningsmekanisme
Sikkerhet relativt til komparator	☐	Ny bivirkningsprofil
Kostnader/ressursbruk	☐	
Kostnadseffektivitet	☐	
Organisatoriske konsekvenser	☐	
Etikk	☐	
Juridiske konsekvenser	☐	
Annet	☒	Bør gjøres en internasjonal vurdering

Hva slags metodevurdering kan være aktuell

Hurtig metodevurdering	☒
Fullstendig metodevurdering	☐
Tatt til orientering; ikke aktuelt for offentlig finansiering	☐

Hovedkilder til informasjon

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3. Monath TP et al. rVSVDG-ZEBOV-GP (also designated V920) recombinant vesicular stomatitis virus pseudotyped with Ebola Zaire Glycoprotein: Standardized template with key considerations for a risk/benefit assessment. Vaccine 2019. Open Access: https://doi.org/10.1016/j.jvacx.2019.100009
4. Coller B-A G et al. Clinical development of a recombinant Ebola vaccine in the midst of an unprecedented epidemic. Vaccine 2017; 35:4465–9
5. Ebola virus disease. WHO Factsheet. [oppdatert 30. mai 2019]. Tilgjengelig fra https://www.who.int/news-room/fact-sheets/detail/ebola-virus-disease
6. Ebola treatment and care. World Health Organisation. Tilgjengelig fra https://www.who.int/csr/disease/ebola/training/treatment/en/
7. Bishop BM, et al. Potential and emerging treatment options for Ebola virus disease. Ann Pharmacother, 2015; 49(2), 196-206.
8. rVSV-ZEBOV-GP vaccine. [nettdokument]. (16. januar 2019). Specialist Pharmacy Service, NHS. Tilgjengelig fra https://www.sps.nhs.uk/medicines/rvsv-zebov-vaccine/
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10. Samai M et al. The Sierra Leone Trial to Introduce a Vaccine against Ebola: An Evaluation of rVSVΔG-ZEBOV-GP vaccine tolerability and safety during the West Africa Ebola Outbreak. J Infect Dis Suppl. 2018; 217:s6–15.

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