



## IMMUNOGENICITY AND SAFETY OF TBE VACCINES REVIEWED

### Background

Tick-borne encephalitis (TBE) is one of the most important causes of viral encephalitis and is the most frequent cause of viral meningitis in Europe. Being endemic in 27 European countries with around 5'000–10'000 reported cases annually. It is trending towards both an expansion of risk areas and an increase in incidence. Switzerland has seen an increase in cases in the last years and risk areas have expanded from the eastern part to the western and southern part of the country. As there exists no therapeutical approach, vaccination is the only effective preventive measure. There are two European vaccines: Encepur© (Bavarian Nordic) and FSME-Immun© (Pfizer), both having an adult and children-dose vaccine. A systematic review published in September 2020 examines safety and immunogenicity of these vaccines.

### Results & Discussion

A In regard to the PRISMA guidelines, 49 publications (40 pieces of original articles, five research abstracts of poster/oral sessions, three case reports and one case series) were investigated for immunogenicity (n=37) and safety (n=17). Local reactions were found in 26% (4.3-54%), systemic reactions in 30% (0.6-45.9%), and in 4455 vaccinees no serious adverse event was recorded. There were three out of 17 studies describing serious adverse events. First, a follow up study showed in 5% of 278 vaccinees serious adverse events, which were interpreted by the authors of the study as life events not related to the vaccine during the 5 year follow up time (including two grade IV glioblastomas and one myocardial infarction). A second publication investigated a swiss passive adverse events reporting system and concluded an incidence of 2.3 serious adverse events in 100'000 administered vaccine doses. Thirdly, a

retrospective analysis of a German pediatric database revealed 2 cases of serious adverse events after TBE-vaccine administration, leading to a calculated 0.69 cases of serious adverse events per 1'000'000 vaccine doses. In summary, TBE vaccines presents itself to be a safe vaccination with rare serious adverse events.

For assessing Immunogenicity, seropositivity after primary vaccination schedule and after several booster doses were investigated. If possible, results were analyzed in different subpopulations. Seropositivity of vaccinees was presented to be highest after primary vaccination schedule with application of the same vaccine in the conventional schedule. Rapid or accelerated schedules should only be used in situations with need for fast application (for example for travelers). More research is needed for mixed vaccination approaches (i.e., application of both, Encepur© and FSME Immun©). Results lead to a better outcome after a same vaccine approach in primary vaccination schedule. The superiority in seropositivity compared to a mixed vaccine approach was reduced the more booster doses a vaccinee received.

In healthy individuals below 50 years of age a first booster dose after five years and a following booster doses after ten years lead to high immunogenicity. A reduced immune response to TBE-vaccination was highlighted in individuals aged above 60 years. A need was shown for a four-dose primary vaccination and/or a shorter time to booster vaccinations of around three years. Decreased seropositivity after vaccination was found even in people aged above 50 years.

Furthermore, publications presented that if vaccinees did not get the vaccine application within the regular time schedule, a postponed continuation of the schedule leads to adequate immunogenicity. So, for TBE-vaccination "every shot counts".



## Literature

JE Rampa, HH Askling, P Lang, KD Zens, N Gültekin, Z Stanga, P Schlagenhauf; Immunogenicity and safety of the tick-borne encephalitis vaccination (2009–2019): A systematic review; *Travel Med Infect Dis*, 37 (2020), p. 101876, [10.1016/j.tmaid.2020.101876](https://doi.org/10.1016/j.tmaid.2020.101876)

**Author:** Pract. med. John Ethan Rampa

**Compiled:** December 2020