



Clinical trial results:

Open-label Phase IV Study to Investigate Broad-and Cross-neutralizing Antibodies after Primary Vaccination with Two Different TBE Vaccines Summary

EudraCT number	2018-004674-94
Trial protocol	LV
Global end of trial date	14 June 2024

Results information

Result version number	v1 (current)
This version publication date	16 July 2025
First version publication date	16 July 2025

Trial information

Trial identification

Sponsor protocol code	WI237607
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Riga Stradiņš University
Sponsor organisation address	Dzirčiema 16, Rīga, Latvia, LV-1007
Public contact	Clinical Trial Information Desk, Riga Stradiņš University, +371 26494938, dace.zavadska@rsu.lv
Scientific contact	Clinical Trial Information Desk, Riga Stradiņš University, +371 26494938, dace.zavadska@rsu.lv

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 June 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 June 2024
Global end of trial reached?	Yes
Global end of trial date	14 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the immune response induced by FSME-IMMUN/TicoVac or Encepur against two virus strains Neudorfl (Nd) used to manufacture FSME/IMMUN/TicoVac and mutated Karlsruhe (mk23) (one homologous strain and one heterologous strain to each vaccine), as measured by NT using an established hybrid virus assay platform.

Protection of trial subjects:

The study was conducted in full compliance with the protocol, any applicable legal and regulatory requirements, as well as with scientific purpose, value, rigor, and followed the generally accepted research practices described in the ICH Good Clinical Practice guidelines. The study was performed in full compliance with the legal regulations according to the applicable law(s) in Latvia. The protocol, protocol amendments, ICD, and other relevant documents (e.g., advertisements) were submitted to an IEC by the investigator and reviewed and approved by the IEC before the study was initiated. Any amendments to the protocol required IEC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants. Informed consent was obtained from all participants or their legally authorized representative prior to enrollment. Based on the very well-defined safety profile of both vaccines, only SAEs occurring from administration of the first vaccination through 28 calendar days after the second vaccination and from administration of the third vaccination through 28 calendar days thereafter were collected. If the Investigator became aware of an SAE after the 28-day period and suspected a causal relationship between the vaccine and the SAE, this was also to be reported. Protocol deviations were identified and managed throughout the study by monitoring of informed consent documentation, source documents, and other clinical trial-related documents. In addition, protocol deviations were identified by CRF review and programmatically from the clinical trial database

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 April 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Latvia: 438
Worldwide total number of subjects	438
EEA total number of subjects	438

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	19
Children (2-11 years)	90
Adolescents (12-17 years)	108
Adults (18-64 years)	147
From 65 to 84 years	74
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participant recruitment was conducted at three locations in Latvia - Children's Clinical University Hospital, RSU Ambulance, and GK Neuroclinic. Recruitment period was from April 11, 2019 till June 3, 2020.

Pre-assignment

Screening details:

Participants were screened based on strict criteria. Inclusion required healthy individuals aged ≥ 1 year, with informed consent/assent and protocol compliance. Exclusion included prior TBE vaccination, flavivirus exposure, contraindications to TBE vaccine, pregnancy, immunosuppression and other conditions according to protocol.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

No blinding was implemented. Both investigators and participants were aware of the assigned vaccine—either FSME-IMMUN/TicoVac or Encepur—administered according to age-appropriate dosing schedules. Blinding was not considered necessary due to the study's primary focus on immunogenicity

Arms

Are arms mutually exclusive?	Yes
Arm title	FSME-IMMUN Group

Arm description:

Arm 1 of the study involved participants receiving three age-appropriate doses of the FSME-IMMUN (TicoVac) vaccine, an inactivated whole-virus tick-borne encephalitis (TBE) vaccine based on the Neudörfl (Nd) strain.

Arm type	Active treatment
Investigational medicinal product name	FSME-IMMUN vaccine
Investigational medicinal product code	
Other name	TicoVac
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were vaccinated on Day 0, at 1 month, and then 9-10 months later, following the standard FSME-IMMUN schedule. The vaccine was administered via intramuscular (IM) injection, with a dose volume of 0.25 mL for children aged 1–15 years (pediatric formulation) and 0.5 mL for individuals aged 16 years and older (adult formulation).

Arm title	ENCEPUR group
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Arm description:

Arm 2 of the study involved participants receiving three age-appropriate doses of the Encepur vaccine, an inactivated whole-virus tick-borne encephalitis (TBE) vaccine based on the Karlsruhe (mK23) strain.

Arm type	Active treatment
Investigational medicinal product name	Encepur vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were vaccinated on Day 0, at 1 month, and then 9–12 months later, following the standard Encepur schedule. The vaccine was administered via intramuscular (IM) injection, with a dose volume of

0.25 mL for children aged 1–11 years (pediatric formulation) and 0.5 mL for individuals aged 12 years and older (adult formulation).

Number of subjects in period 1	FSME-IMMUN Group	ENCEPUR group
Started	219	219
Randomized	219	219
Vaccinated - Dose 1	218	218
Vaccinated - Dose 2	214	212
Vaccinated - Dose 3	210	202
Vaccination phase (Completed Visits 1-5)	208	195
Seropersistence phase (Visits 6-8)	165	155
Completed	165	155
Not completed	54	64
Consent withdrawn by subject	40	36
Physician decision	6	8
Lost to follow-up	8	20

Baseline characteristics

Reporting groups

Reporting group title	FSME-IMMUN Group
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Reporting group description:

Arm 1 of the study involved participants receiving three age-appropriate doses of the FSME-IMMUN (TicoVac) vaccine, an inactivated whole-virus tick-borne encephalitis (TBE) vaccine based on the Neudörfl (Nd) strain.

Reporting group title	ENCEPUR group
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Reporting group description:

Arm 2 of the study involved participants receiving three age-appropriate doses of the Encepur vaccine, an inactivated whole-virus tick-borne encephalitis (TBE) vaccine based on the Karlsruhe (mK23) strain.

Reporting group values	FSME-IMMUN Group	ENCEPUR group	Total
Number of subjects	219	219	438
Age categorical			
Subjects were stratified evenly across four age groups: 1–11 years, 12–15 years, 16–59 years, and 60 years and older.			
Units: Subjects			
1–11 years	54	55	109
12–15 years	52	53	105
16–59 years	53	53	106
60 years and older	60	58	118
Gender categorical			
Units: Subjects			
Female	129	131	260
Male	90	88	178

End points

End points reporting groups

Reporting group title	FSME-IMMUN Group
Reporting group description: Arm 1 of the study involved participants receiving three age-appropriate doses of the FSME-IMMUN (TicoVac) vaccine, an inactivated whole-virus tick-borne encephalitis (TBE) vaccine based on the Neudörfl (Nd) strain.	
Reporting group title	ENCEPUR group
Reporting group description: Arm 2 of the study involved participants receiving three age-appropriate doses of the Encepur vaccine, an inactivated whole-virus tick-borne encephalitis (TBE) vaccine based on the Karlsruhe (mK23) strain.	
Subject analysis set title	Randomized (ITT Population)
Subject analysis set type	Intention-to-treat
Subject analysis set description: The randomized ITT population refers to all 438 participants who were randomized into the study, regardless of whether they actually received the vaccine or completed the study as per protocol.	
Subject analysis set title	Modified ITT population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The Modified Intent-to-Treat (mITT) population included 436 subjects. mITT is a refined subset of the randomized participants used for more targeted immunogenicity analyses, it includes all participants who received at least one dose of the study vaccine and had at least one postvaccination blood sample with a valid and determinate assay result.	
Subject analysis set title	Postdose 2 Per-Protocol Immunogenicity Population
Subject analysis set type	Per protocol
Subject analysis set description: Postdose 2 Per-Protocol Immunogenicity Population included 362 subjects. Of them, 187 subjects enrolled in Schedule A Dose 2 (6-Day Postdose 2 Per-Protocol Immunogenicity Population), which consisted of FSME-IMMUN group N=100 and ENCEPUR group N=87. And 175 subjects enrolled in Schedule B Dose 2 (1-Month Postdose 2 Per-Protocol Immunogenicity Population), which consisted of FSME-IMMUN group N=88 and ENCEPUR group N=87.	
Subject analysis set title	Predose 3 Per-Protocol Immunogenicity Population
Subject analysis set type	Per protocol
Subject analysis set description: Predose 3 Per-Protocol Immunogenicity Population included 362 subjects. Of them, FSME-IMMUN group N=190, ENCEPUR group N=172.	
Subject analysis set title	Postdose 3 Per-Protocol Immunogenicity Population
Subject analysis set type	Per protocol
Subject analysis set description: Postdose 3 Per-Protocol Immunogenicity Population included 343 subjects. Of them, 164 subjects enrolled in Schedule A Dose 3 (6-Day Postdose 3 Per-Protocol Immunogenicity Population), which consisted of FSME-IMMUN group N=88 and ENCEPUR group N=76. And 179 subjects enrolled in Schedule B Dose 3 (1-Month Postdose 3 Per-Protocol Immunogenicity Population), which consisted of FSME-IMMUN group N=94 and ENCEPUR group N=85.	
Subject analysis set title	1-Year Seropersistence Postdose 3 Per Protocol Immunogenicity
Subject analysis set type	Per protocol
Subject analysis set description: 1-Year Seropersistence Postdose 3 Per Protocol Immunogenicity included 334 subjects, of them FSME-IMMUN group N=179; ENCEPUR group N=155.	
Subject analysis set title	2-Year Seropersistence Postdose 3 Per Protocol Immunogenicity
Subject analysis set type	Per protocol
Subject analysis set description: 2-Year Seropersistence Postdose 3 Per Protocol Immunogenicity Population included 301 subject, of	

them FSME-IMMUN group N=157, ENCEPUR group N=144.

Subject analysis set title	3-Year Seropersistence Postdose 3 Per Protocol Immunogenicity
Subject analysis set type	Per protocol
Subject analysis set description:	
3-Year Seropersistence Postdose 3 Per Protocol Immunogenicity Population included 278 subjects, of them FSME-IMMUN group N=147, ENCEPUR group N=131.	

Primary: Subjects Achieving NT \geq 7.7 and Composite Response – FSME-IMMUN Per-Protocol Immunogenicity Populations

End point title	Subjects Achieving NT \geq 7.7 and Composite Response – FSME-IMMUN Per-Protocol Immunogenicity Populations ^{[1][2]}
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End point description:

The proportion of composite response of neutralizing titers against both homologous and heterologous antigens to the vaccines (FSME-IMMUN) at each blood draw visit. The composite response is defined as a subject with NT \geq 7.7 for both Nd and mK23.

End point type	Primary
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End point timeframe:

Blood draws for the investigation of the humoral immune response were performed prior to the first vaccination (FSME-IMMUN); after Dose 2; prior and after Dose 3; and for the 1-year, 2-year and 3-year post-Dose 3.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This was a descriptive study not powered to show superiority/ non-inferiority of any product. No formal hypothesis testing or statistical comparisons were pre-specified or conducted for the primary endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This was a descriptive study not powered to show superiority/ non-inferiority of any product. Encepur group results are reported as separate primary endpoint.

End point values	FSME-IMMUN Group			
Subject group type	Reporting group			
Number of subjects analysed	218 ^[3]			
Units: %				
6-Day Postdose 2 Per-Protocol (N=100)	87			
1-Month Postdose 2 Per-Protocol (N=88)	89			
Predose 3 Per-Protocol (N=190)	37			
6-Day Postdose 3 Per-Protocol (N=88)	75			
1-Month Postdose 3 Per-Protocol (N=94)	96			
1-Year Postdose 3 Per-Protocol (N=179)	82			
2-Year Postdose 3 Per-Protocol (N=157)	87			
3-Year Postdose 3 Per-Protocol (N=147)	80			

Notes:

[3] - Total number of subjects vaccinated with FSME-IMMUN.

Statistical analyses

No statistical analyses for this end point

Primary: Subjects Achieving NT \geq 7.7 and Composite Response – Encepur Per-Protocol Immunogenicity Populations

End point title	Subjects Achieving NT \geq 7.7 and Composite Response –
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End point description:

The proportion of composite response of neutralizing titers against both homologous and heterologous antigens to the vaccines (Encepur) at each blood draw visit. The composite response is defined as a subject with NT \geq 7.7 for both Nd and mK23.

End point type

Primary

End point timeframe:

Blood draws for the investigation of the humoral immune response were performed prior to the first vaccination (Encepur); after Dose 2; prior and after Dose 3; and for the 1-year, 2-year and 3-year post-Dose 3.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This was a descriptive study not powered to show superiority/ non-inferiority of any product. No formal hypothesis testing or statistical comparisons were pre-specified or conducted for the primary endpoint.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This was a descriptive study not powered to show superiority/ non-inferiority of any product. FSME-IMMUN group results are reported as separate primary endpoint.

End point values	ENCEPUR group			
Subject group type	Reporting group			
Number of subjects analysed	218 ^[6]			
Units: %				
6-Day Postdose 2 Per-Protocol (N=87)	93			
1-Month Postdose 2 Per-Protocol (N=87)	92			
Predose 3 Per-Protocol (N=172)	73			
6-Day Postdose 3 Per-Protocol (N=76)	91			
1-Month Postdose 3 Per-Protocol (N=85)	99			
1-Year Postdose 3 Per-Protocol (N=155)	95			
2-Year Postdose 3 Per-Protocol (N=144)	96			
3-Year Postdose 3 Per-Protocol (N=131)	90			

Notes:

[6] - Total number of subjects vaccinated with Encepur.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Information on SAEs were only to be collected from first vaccination through 28 calendar days after administration of the second vaccination and from the administration of the third vaccination through 28 calendar days thereafter.

Adverse event reporting additional description:

SAEs that occurred during the active collection period and any time after the active collection period were reportable if the Investigator suspected a causal relationship between the study vaccination and the SAE.

There was 1 SAE collected in the study that was unrelated to study vaccine; a participant was hospitalized for a hemorrhoidectomy.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	FSME-IMMUN Group
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Reporting group description:

No vaccine-related SAEs were reported in the study.

Reporting group title	ENCEPUR Group
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Reporting group description:

No vaccine-related SAEs were reported in the study.

There was 1 SAE collected in the study that was unrelated to study vaccine (Encepur). A participant was hospitalized for a hemorrhoidectomy.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There are no non-serious adverse events recorded in this study.

Serious adverse events	FSME-IMMUN Group	ENCEPUR Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 218 (0.00%)	1 / 218 (0.46%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events		0	
Gastrointestinal disorders			
Hemorrhoidectomy	Additional description: There was 1 SAE collected in the study that was unrelated to study vaccine; a participant was hospitalized for a hemorrhoidectomy.		
subjects affected / exposed	0 / 218 (0.00%)	1 / 218 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	FSME-IMMUN Group	ENCEPUR Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 218 (0.00%)	0 / 218 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This was a descriptive study not powered to show superiority/non-inferiority of any product.
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Notes: