Clinical trial results:
Long term immunity and safety following vaccination with the Japanese Encephalitis vaccine IC51 (IXIARO®, JESPECT®) in a pediatric population in non-endemic countries. Uncontrolled, Phase 3 Follow-up study.

Summary

EudraCT number	2010-022266-27
Trial protocol	DE
Global end of trial date	15 September 2014

Results information

Result version number	v1 (current)
This version publication date	01 February 2016
First version publication date	03 July 2015

Trial information

Trial identification

Sponsor protocol code	IC51-324

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01246479
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Valneva Austria GmbH
Sponsor organisation address	Campus Vienna Biocenter 3, Vienna, Austria, 1030
Public contact	Clinical Operations, Valneva Austria GmbH, 0043 1206200, info@valneva.com
Scientific contact	Clinical Operations, Valneva Austria GmbH, 0043 1206200, info@valneva.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000559-PIP01-09
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 February 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess long-term immunity following vaccination with purified inactivated Japanese Encephalitis (JE) vaccine IC51 in terms of Geometric Mean Titers (GMTs) and rate of subjects with a PRNT50 ≥ 1:10 in a pediatric population from regions where JE is not endemic.

Protection of trial subjects:

To avoid unreasonable visits and blood samplings, subjects were to be withdrawn from the study as soon as the result of the PRNT analysis of Visit 1, 2 or 3 was known to be negative (PRNT50 titer < 1:10).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 October 2010
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	Germany: 7
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	23
EEA total number of subjects	7

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)	0
Children (2-11 years)	4

Adolescents (12-17 years)	19
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited in 6 study centers located in Australia, Germany and the United States. Recruitment started on 20-Oct-2010 and was completed on 20-Aug-2012. Study visits occurred 7, 12, 24 and 36 months after the first IC51 vaccination in parent study IC51-322.

Pre-assignment

Screening details:

Uncontrolled, open-label Phase 3 follow-up study in subjects who received 2 injections of IC51 and participated in the immunogenicity subgroup of the parent study IC51-322.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Safety and Immunogenicity follow-up M7 - M36

Arm description: -

Arm type	Experimental
Investigational medicinal product name	IC51
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IC51 was only administered in parent study IC51-322 where subjects received 2 vaccinations of either 0.25 ml or 0.5 ml IC51 (depending on their age) at an interval of 4 weeks. IC51-324 is a follow-up study to examine long-term immunity.

Number of subjects in period 1	Safety and Immunogenicity follow-up M7 - M36
Started	23
Completed	18
Not completed	5
Subjects abroad	3
Negative PRNT	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	23	23	
Age categorical Units: Subjects			
Children (2-11 years)	4	4	
Children (12-17 years)	19	19	
Age continuous			
Age in years as given by the investigator at Visit 1 (Month 7)			
Units: years			
arithmetic mean	14.3		
full range (min-max)	3 to 18	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	12	12	

End points

End points reporting groups

Reporting group title	Safety and Immunogenicity follow-up M7 - M36

Reporting group description: -

Primary: Rate of subjects with PRNT50 titers of ≥ 1:10 at Month 12 after the first IC51 vaccination (in study IC51-322).

End point title	Rate of subjects with PRNT50 titers of ≥ 1:10 at Month 12 after the first IC51 vaccination (in study IC51-322).[1]

End point description:

End point type	Primary

End point timeframe:

12 Months after the first IC51 vaccination.

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: Analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Safety and Immunogenicity follow-up M7 - M36			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: % of subjects				
number (confidence interval 95%)	89.5 (68.6 to 97.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: GMT for JEV neutralizing antibodies measured using the PRNT at Month 12 after the first IC51 vaccination (in study IC51-322).

End point title	GMT for JEV neutralizing antibodies measured using the PRNT at Month 12 after the first IC51 vaccination (in study IC51-322).

End point description:

End point type	Secondary

End point timeframe:

12 Months after the first IC51 vaccination.

End point values	Safety and Immunogenicity follow-up M7 - M36			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: GMT				
geometric mean (confidence interval 95%)	47.8 (28.7 to 79.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were recorded at Visits 1-4. Any AE reported as "not recovered/not resolved" at Visit 4 in study IC51-322 and all new abnormalities occurring after Visit 4 in IC51-322 were documented as AEs in study IC51-324.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Safety Population

Reporting group description:

All subjects who were enrolled in the study.

Serious adverse events	Safety Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 23 (8.70%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Tonsillitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection	Additional description: Methicillin resistant infection		
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Safety Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 23 (34.78%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Skin papilloma subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 4		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2		
Infections and infestations Otitis media acute subjects affected / exposed occurrences (all) Pharyngitis streptococcal subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2 2 / 23 (8.70%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 January 2012	Due to change of primary objective in parent study IC51-322 from immunogenicity to safety (Clinical Study Protocol V10.0), limitation of follow-up on long-term immunogenicity in IC51-324 to those subjects that participated in the immunogenicity subgroup in IC51-322. Revision of incl./excl. criteria, estimated sample size and planned analyses. Updates on background information, number of participating study centers and immunogenicity assay.
11 June 2013	Name change of Sponsor. Interim Analysis after Month 12 was removed (only Interim Analysis after M24 was performed).

Notes:

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.

As the number of subjects in individual age groups was low a meaningful comparison between age/dose groups is not possible.

Notes: