Clinical trial results:
Effect of vaccination in patients with recurrent respiratory papillomatosis– can we improve the quality of life of these patients?

Summary

EudraCT number	2011-002667-14
Trial protocol	CZ
Global end of trial date	31 December 2018

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022
Summary attachment (see zip file)	Outcomes After Human Papillomavirus Vaccination in Patients With Recurrent Respiratory Papillomatosis (jamaotolaryngology_smahelova_2022_oi_220027_1652724692.91036.pdf)

Trial information

Trial identification

Sponsor protocol code	UHKT-RLP/2011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01375868
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Institute of Hematology and Blood Transfusion
Sponsor organisation address	U Nemocnice 1, Prague, Czechia, 128 20
Public contact	Head of the Laboratory, Institute of Hematology and Blood Transfusion, 00420 325873922, tachezr@natur.cuni.cz
Scientific contact	Head of the Laboratory, Institute of Hematology and Blood Transfusion, 00420 325873922, tachezr@natur.cuni.cz

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	06 November 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2018
Global end of trial reached?	Yes
Global end of trial date	31 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Vaccines against human papillomaviruses are now commercially available. One of the commercial vaccine contains antigens of both LR HPV types which cause virtually all cases of RRP. Clinical trials have documented the safety and immunogenicity of this vaccine as well as its effectiveness in prevention of incident and persistent infection of the vaccinal types as well as a development of lesions caused by these types. After vaccination the antibodies level increases dramatically and the high levels of antibodies are present in the blood still after 6 years. Furthermore, the neutralization antibodies to the vaccinal antigens have been detected in the cervical mucus of vaccinated women. The preliminary data are now available showing the presence of HPV-specific antibodies in the oral cavity in women after vaccination. The level of antibodies has been dependent on time since vaccination.

Protection of trial subjects:

All subjects were enroled upon signature of the informed consent. The cinical trial was insured. All side effects were reported to the regulatory organ.

Background therapy:

No

Evidence for comparator:

No

Actual start date of recruitment	12 August 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czechia: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	46
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

ENROLMENT OF THE FIRST PATIENT OCTOBER 25, 2011
CZECHIA, PRAGUE

Pre-assignment

Screening details:

50 subjects screened

Pre-assignment period milestones

Number of subjects started	50
Number of subjects completed	50

Period 1

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

Arms

Arm title	didn´t RRP patients

Arm description:

Patients with RRP. All of the enroled subjects were vaccinated.

Arm type	Experimental
Investigational medicinal product name	HPV tetravalent vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

The first dose of the vaccine within 1 month after enrollment, the second dose followed within 2 months, and the third one within 6 months after the first dose.

Number of subjects in period 1	didn´t RRP patients
Started	50
Completed	42
Not completed	8
not fulfilled protocol	8

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description:

50 adults with active RRP were enrolled and followed up. For the final outcome, follow-up data for 42 patients were available. Eight patients who did not fulfill the protocol were excluded.

Reporting group values	overall trial	Total	
Number of subjects	50	50	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	46	46	
From 65-84 years	4	4	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	11	11	
Male	39	39	

Subject analysis sets	
Subject analysis set title	The number of recurrences
Subject analysis set type	Full analysis

Subject analysis set description:

We have evaluated if the HPV vaccination lowers the number of recurrences requiring surgical intervention in patients with new and recurrent RRP.

Subject analysis set title	Level of HPV-specific antibodies
Subject analysis set type	Full analysis

Subject analysis set description:

We compared the prevaccination and postvaccination positivity for HPV-specific antibodies.

Reporting group values	The number of recurrences	Level of HPV-specific antibodies	
Number of subjects	42	42	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	

Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	42	42	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	9	9	
Male	33	33	

End points

End points reporting groups

Reporting group title	didn´t RRP patients
Reporting group description:	
Patients with RRP. All of the enroled subjects were vaccinated.	
Subject analysis set title	The number of recurrences
Subject analysis set type	Full analysis
Subject analysis set description:	
We have evaluated if the HPV vaccination lowers the number of recurrences requiring surgical intervention in patients with new and recurrent RRP.	
Subject analysis set title	Level of HPV-specific antibodies
Subject analysis set type	Full analysis
Subject analysis set description:	
We compared the prevaccination and postvaccination positivity for HPV-specific antibodies.	

Primary: Number of recurrences

End point title	Number of recurrences
End point description:	
This study compared the prevaccination and postvaccination positivity for HPV-specific antibodies. The main outcome was the difference in the frequency of RRP recurrences in the prevaccination and postvaccination period.	
End point type	Primary
End point timeframe:	
The number of reccurences in the post-enrolment (postvaccination) period	

End point values	didn´t RRP patients	The number of recurrences		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	50	42		
Units: number of recurrences	50	42		

Statistical analyses

Statistical analysis title	The number of recurrences
Statistical analysis description:	
The prevaccination and postvaccination frequency of RRP recurrences were compared by the Wilcoxon signed-rank test. A 1-sided alternative of lower frequency after vaccination was considered.	
Comparison groups	didn´t RRP patients v The number of recurrences
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)

Confidence interval	
level	95 %
sides	2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The reporting starts immediately after the application of the first dose of the vaccine and continuous for up to 4 months after application of the third dose.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	RRP group

Reporting group description:

All enroled patients. All received at least one dose of the vaccine.

Serious adverse events	RRP group		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 50 (2.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Death			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	RRP group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 50 (50.00%)		
General disorders and administration site conditions			
Fatigue, Headache,Malaise,Vomiting, Pain			
subjects affected / exposed	25 / 50 (50.00%)		
occurrences (all)	25		

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.

The absence of a placebo group due to a very variable course of the disease we determined that comparison of the disease outcome before and after the vaccination for the same participant would be more informative.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35653138