Clinical trial results:
An Open-label phase III study to investigate the safety, tolerability and immunogenicity of a nine-valent human papillomavirus (HPV) vaccine (Gardasil®9) in solid organ transplant recipients and HIV-infected patients

Summary

EudraCT number	2017-004322-15
Trial protocol	BE
Global end of trial date	24 June 2020

Results information

Result version number	v1 (current)
This version publication date	05 April 2022
First version publication date	05 April 2022
Summary attachment (see zip file)	Publication HPV vaccination in immunocompromized patients (Boey_Immunogenicity and safety of Gardasil9 in immunocompromised_2020.pdf)

Trial information

Trial identification

Sponsor protocol code	V503-044-IC

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03525210
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UZ Leuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Leuven University Vaccinology Cente, KU Leuven, 32 16342020, lise.boey@kuleuven.be
Scientific contact	Leuven University Vaccinology Cente, KU Leuven, 32 16342020, lise.boey@kuleuven.be

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	11 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 December 2019
Global end of trial reached?	Yes
Global end of trial date	24 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the immunogenicity of Gardasil®9 with respect to HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 in adult HIV (age: 18-45 years) and transplant patients (age: 18-55 years).

Protection of trial subjects:

Patients with immunodeficiencies are at increased risk of developing persistent HPV infection and as such HPV-related disease (genital warts and cancer).

In this study HIV-patients and SOT-patients received 3 doses of Gardasil®9. Safety, tolerability and immunogenicity will be evaluated up to one month following the 3rd and last dose of Gardasil®9. Studies with other HPV vaccines (quadrivalent HPV vaccine Gardasil and bivalent HPV vaccine Cervarix) were already administered without safety issues in this specific patients population.

Background therapy:

Immunosuppressive medication in case of patients with transplant and retroviral therapy in case of patients living with HIV.

Evidence for comparator: -

Actual start date of recruitment	08 January 2018
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	Belgium: 271
Worldwide total number of subjects	271
EEA total number of subjects	271

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)	271
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

One hundred HIV-infected persons (age 18–45 years) and 171 SOT (kidney, heart, lung transplant) recipients (age 18–55 years) were enrolled between April 2018 and January 2019 in the outpatient clinic of the University Hospitals Leuven, Belgium.

Pre-assignment

Screening details:

Independent Ethics Committee (IEC)-approved written informed consent form (ICF) must be obtained from the subject prior to any study-related procedures Subject (man or woman) is between the age of 18 years and <46 years for HIV patients (have CD4+ T cell count of >200 cells/mm²), between 18 years and <56 years for transplant patients (>12 months)

Pre-assignment period milestones

Number of subjects started	271
Number of subjects completed	271

Period 1

Period 1 title	Vaccination period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Blinding was not necessary as all patients received the HPV vaccine and control group was historical healthy subjects

Arms

Are arms mutually exclusive?	Yes
Arm title	Patients living with HIV

Arm description:

HIV patients: have CD4+ T cell count of >200 cells/mm² at the last control (less than 12 months ago).

Arm type	Experimental
Investigational medicinal product name	Gardasil9
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Humaan papillomavirus1 type 6-L1-eiwit2,3 - 30 microgram
Humaan papillomavirus1 type 11-L1-eiwit2,3 - 40 microgram
Humaan papillomavirus1 type 16-L1-eiwit2,3 - 60 microgram
Humaan papillomavirus1 type 18-L1-eiwit2,3 - 40 microgram
Humaan papillomavirus1 type 31-L1-eiwit2,3 - 20 microgram
Humaan papillomavirus1 type 33-L1-eiwit2,3 - 20 microgram
Humaan papillomavirus1 type 45-L1-eiwit2,3 - 20 microgram
Humaan papillomavirus1 type 52-L1-eiwit2,3 - 20 microgram
Humaan papillomavirus1 type 58-L1-eiwit2,3 - 20 microgram

Administration through intramuscular injection in the deltoid muscle

Arm title	Patients after SOT-transplantation (heart, lung or kidney)

Arm description:

Solid-Organ-Transplant patients received their organ transplantation ≥12 months prior to vaccination and has been stable in the past 6 months (i.e. no acute rejection or other immunological reactions).

Arm type	Experimental
Investigational medicinal product name	Gardasil9
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Humaan papillomavirus1 type 6-L1-eiwit2,3 - 30 microgram
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Humaan papillomavirus1 type 18-L1-eiwit2,3 - 40 microgram
Humaan papillomavirus1 type 31-L1-eiwit2,3 - 20 microgram
Humaan papillomavirus1 type 33-L1-eiwit2,3 - 20 microgram
Humaan papillomavirus1 type 45-L1-eiwit2,3 - 20 microgram
Humaan papillomavirus1 type 52-L1-eiwit2,3 - 20 microgram
Humaan papillomavirus1 type 58-L1-eiwit2,3 - 20 microgram

Administration through intramuscular injection in the deltoid muscle

Number of subjects in period 1	Patients living with HIV	Patients after SOT-transplantation (heart, lung or kidney)
Started	100	171
Completed	96	169
Not completed	4	2
Consent withdrawn by subject	4	2

Baseline characteristics

Reporting groups	
Reporting group title	Patients living with HIV
Reporting group description:	
HIV patients: have CD4+ T cell count of >200 cells/mm² at the last control (less than 12 months ago).	
Reporting group title	Patients after SOT-transplantation (heart, lung or kidney)
Reporting group description:	
Solid-Organ-Transplant patients received their organ transplantation ≥12 months prior to vaccination and has been stable in the past 6 months (i.e. no acute rejection or other immunological reactions).	

Reporting group values	Patients living with HIV	Patients after SOT-transplantation (heart, lung or kidney)	Total
Number of subjects	100	171	271
Age categorical			
Subject (man or woman) is between the age of 18 years and 0 days and 45 years and 365 days for HIV patients, between 18 years and 0 days and 55 years and 365 days for transplant patients at time of signing the ICF			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	100	171	271
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	15	53	68
Male	85	118	203
Race			
Race (Caucasian or African Black) was collected as additional study specific baseline characteristics			
Units: Subjects			
Caucasian	68	168	236
African Black	23	2	25
Other	9	1	10

End points

End points reporting groups

Reporting group title	Patients living with HIV
Reporting group description:	
HIV patients: have CD4+ T cell count of >200 cells/mm² at the last control (less than 12 months ago).	
Reporting group title	Patients after SOT-transplantation (heart, lung or kidney)
Reporting group description:	
Solid-Organ-Transplant patients received their organ transplantation ≥12 months prior to vaccination and has been stable in the past 6 months (i.e. no acute rejection or other immunological reactions).	

Primary: Seroconversion Following 3 Doses of 9-valent HPV Vaccines

End point title	Seroconversion Following 3 Doses of 9-valent HPV Vaccines
End point description:	
Seroconversion rates of neutralizing antibodies against each HPV vaccine genotypes (6/11/16/18/31/33/45/52/58) one month after completion of a three doses schedule (0, 2 and 6 months) in patients seronegative at baseline for these antibodies: subjects who were seronegative to the appropriate HPV type at Day 1, had serology results based on acceptable day ranges and had no protocol deviations that could interfere with the subject's vaccine as judged by the principal investigator.	
End point type	Primary
End point timeframe:	
7 months	

End point values	Patients living with HIV	Patients after SOT-transplantation (heart, lung or kidney)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	155		
Units: number of subjects				
HPV type 6	91	100		
HPV type 11	91	110		
HPV type 16	91	107		
HPV type 18	91	80		
HPV type 31	91	87		
HPV type 33	91	104		
HPV type 45	91	71		
HPV type 52	91	101		
HPV type 58	91	112		

Statistical analyses

Statistical analysis title	Seroconversion rates
Statistical analysis description:	
The geometric mean titers (GMT) and seroconversion rates are only descriptive. The 95% CIs were	

calculated based on the exact binomial disribution (binomial test) for seroconversion rate, and parametric with T-distribution for the log transformed antibody titers (and afterward transformed again to the metric scale).

Comparison groups	Patients living with HIV v Patients after SOT-transplantation (heart, lung or kidney)
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	≤ 0.05
Method	Regression, Logistic
Parameter estimate	regression coefficient
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Notes:

[1] - This was a descriptive study in which we did not use a control group and only one vaccine was used. We did try to see whether factors would have an impact on the immune response

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 to 1 month post-dose 3 (or approximately one month following the third and last HPV vaccine dose

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Patients with HIV
Reporting group description: -	
Reporting group title	Patients after SOT

Reporting group description: -

Serious adverse events	Patients with HIV	Patients after SOT	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 99 (3.03%)	28 / 170 (16.47%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Relapse renal cell carcinoma			
subjects affected / exposed[1]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst in transplant kidney			
subjects affected / exposed[2]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemorrhage in adenohypophysis in macroadenoma			
subjects affected / exposed[3]	0 / 1 (0.00%)	1 / 170 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Ischaemic stroke			

subjects affected / exposed[4]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Acute rejection transplant organ			
subjects affected / exposed[5]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Burnout syndrome			
subjects affected / exposed[6]	1 / 1 (100.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory pathology			
subjects affected / exposed[7]	0 / 1 (0.00%)	5 / 5 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed[8]	1 / 1 (100.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fracture tibia plateau			
subjects affected / exposed[9]	1 / 1 (100.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial flutter			
subjects affected / exposed[10]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia paroxysmal			

subjects affected / exposed[11]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed[12]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
abdominal pain			
subjects affected / exposed[13]	0 / 1 (0.00%)	2 / 2 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed[14]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Pathology of the kidney			
subjects affected / exposed[15]	0 / 1 (0.00%)	2 / 2 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthrosis neck			
subjects affected / exposed[16]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Fever without focus			
subjects affected / exposed[17]	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastro-intestinal infections			

subjects affected / exposed[18]	0 / 1 (0.00%)	7 / 7 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory infections			
subjects affected / exposed[19]	0 / 1 (0.00%)	10 / 10 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infections			
subjects affected / exposed[20]	0 / 1 (0.00%)	2 / 2 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalized infections			
subjects affected / exposed[21]	0 / 1 (0.00%)	2 / 2 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urogenital infections			
subjects affected / exposed[22]	0 / 1 (0.00%)	3 / 3 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dysregulation glycemia			
subjects affected / exposed[23]	0 / 1 (0.00%)	3 / 3 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
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[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
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[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
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[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[16] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[17] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the

total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[18] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[19] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[20] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[21] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[22] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[23] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.

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

Non-serious adverse events	Patients with HIV	Patients after SOT	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 99 (80.81%)	127 / 170 (74.71%)	
Nervous system disorders			
Headache			
subjects affected / exposed[24]	9 / 9 (100.00%)	14 / 14 (100.00%)	
occurrences (all)	9	14	
General disorders and administration site conditions			
Injection site pain			
alternative assessment type: Non-systematic			
subjects affected / exposed[25]	67 / 67 (100.00%)	93 / 93 (100.00%)	
occurrences (all)	67	93	
Injection site swelling			
subjects affected / exposed[26]	7 / 7 (100.00%)	14 / 14 (100.00%)	
occurrences (all)	7	14	
Injection site erythema			
subjects affected / exposed[27]	10 / 10 (100.00%)	10 / 10 (100.00%)	
occurrences (all)	10	10	

Notes:

[24] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[25] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[26] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.
[27] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: It is not clear to me what is requested of me. The message is not clear. I have entered the total number of patients who received at least 1 study vaccine in the "number of subjects exposed". However, this does not seem to be correct. PLease advise on which number must be entered.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 April 2018	- Adjustment of time interval between visits to comply with other care programs of the different patient groups - Adjustment of inclusion criterium for patients living with HIV: an undetectable viral load in the past 16 months instead of 12 months to allow for inclusion of more HIV patients who have a yearly assessment, but in practice this is often around 12 months (taking broad intervals)
21 November 2018	- Adjustment of number of patients living with HIV to be included from 140 originally to 100 patients - Add additional evaluation criterium, namely GMT ratio (Pre- and post-vaccination) in patients who are already seropositive for one or more HPV types. - Adjustment in the framework of the new European privacy laws

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33373429