



## Clinical trial results:

**Randomized, comparative and prospective clinical trial evaluating efficacy and safety of a dose of seasonal flu vaccine compared to two doses of vaccine for prevention of influenza in solid organ transplant recipients**

### Summary

EudraCT number	2011-003243-21
Trial protocol	ES
Global end of trial date	28 July 2016

### Results information

Result version number	v1 (current)
This version publication date	03 April 2021
First version publication date	03 April 2021
Summary attachment (see zip file)	final report of results (INFORME FINAL Transgripe def 8-8-2016.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	TRANSGRIPE 1-2
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	NA: NA

Notes:

#### Sponsors

Sponsor organisation name	Fundación Pública Andaluza Progreso y Salud
Sponsor organisation address	Parque Científico y Tecnológico Cartuja, Avda. Américo Vespucio, 15. Edificio S-2. 41092 Sevilla, Seville, Spain, 41092
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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	28 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 July 2016
Global end of trial reached?	Yes
Global end of trial date	28 July 2016
Was the trial ended prematurely?	No

Notes:

### General information about the trial

Main objective of the trial:

to study whether two doses of flu vaccine work better than single dose in transplant recipients

Protection of trial subjects:

The trial will be carried out in accordance with the principles of the Declaration of Helsinki (Annex 7), and according to the legal regulations in force (Royal Decree 223/2004), and will not start until the approval of the CEIC of reference, the conformity of the Directors of the Institutions, and the authorisation of the Spanish Agency of Medicines and Health Products have been obtained.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2012
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	Spain: 499
Worldwide total number of subjects	499
EEA total number of subjects	499

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)	499
From 65 to 84 years	0



## Subject disposition

### Recruitment

Recruitment details:

The patient must meet all of the following criteria:

1. solid organ transplant recipient (hepatic, renal, cardiac, or pulmonary).
2. Age greater than or equal to 16 years.
3. More than 30 days post-transplant.
4. Negative pregnancy test in the case of women of childbearing age.
5. Patient must give written consent

### Pre-assignment

Screening details:

The patient must meet all of the following criteria:

1. solid organ transplant recipient (hepatic, renal, cardiac, or pulmonary).
2. Age greater than or equal to 16 years.
3. More than 30 days post-transplant.
4. Negative pregnancy test in the case of women of childbearing age.
5. Patient must give written consent

### Period 1

Period 1 title	Recruitment and follow-up
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Control

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Standard seasonal influenza vaccination
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0,5 ml Standard seasonal influenza vaccination. Immunisation should be carried out by intramuscular or deep subcutaneous injection.

<b>Arm title</b>	Experimental
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Seasonal influenza vaccination
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0,5 ml Seasonal influenza vaccination boosted by a second dose of vaccine 5 weeks after first dose. Immunisation should be carried out by intramuscular or deep subcutaneous injection.

<b>Number of subjects in period 1</b>	Control	Experimental
Started	251	248
Completed	251	248

## Period 2

Period 2 title	Data analysis
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Control

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Standard seasonal influenza vaccination
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0,5 ml Standard seasonal influenza vaccination. Immunisation should be carried out by intramuscular or deep subcutaneous injection.

<b>Arm title</b>	Experimental
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Seasonal influenza vaccination
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0,5 ml Seasonal influenza vaccination boosted by a second dose of vaccine 5 weeks after first dose. Immunisation should be carried out by intramuscular or deep subcutaneous injection.

<b>Number of subjects in period 2</b>	Control	Experimental
Started	251	248
Completed	251	248

## Baseline characteristics

### Reporting groups

Reporting group title	Recruitment and follow-up
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Reporting group description: -

Reporting group values	Recruitment and follow-up	Total	
Number of subjects	499	499	
Age categorical Units: Subjects			
Adults (18-64 years)	499	499	
Age continuous Units: years			
median	56		
full range (min-max)	46 to 63	-	
Gender categorical Units: Subjects			
Female	145	145	
Male	354	354	
Type of transplantation Units: Subjects			
Renal	185	185	
Hepatic	156	156	
Cardiac	60	60	
Pulmonary	95	95	
Hepatorenal	3	3	
Time since transplantation Units: Subjects			
31-180 days	58	58	
181-365 days	107	107	
> 365 days	334	334	
Time from transplantation to vaccination Units: years			
median	1.8		
inter-quartile range (Q1-Q3)	0.8 to 4.3	-	

## End points

### End points reporting groups

Reporting group title	Control
Reporting group description: -	
Reporting group title	Experimental
Reporting group description: -	
Reporting group title	Control
Reporting group description: -	
Reporting group title	Experimental
Reporting group description: -	

### Primary: Seroprotection rate at 10 weeks

End point title	Seroprotection rate at 10 weeks <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe:	
At 10 weeks	

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: Not all the data required in the section are available. However, the final results report is attached, where the statistical analysis carried out is detailed.

End point values	Control	Experimental		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	211		
Units: Percentage				
number (not applicable)				
A/H1N1	43.2	54		
A/H3N2	45.5	56.9		
Influenza B	71.8	83.4		

### Statistical analyses

No statistical analyses for this end point

### Primary: Seroconversion rate

End point title	Seroconversion rate <sup>[2]</sup>
End point description:	
End point type	Primary
End point timeframe:	
During the study	

Notes:

[2] - 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: Not all the data required in the section are available. However, the final results report is attached, where the statistical analysis carried out is detailed.

<b>End point values</b>	Control	Experimental		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	211		
Units: Percentage				
number (not applicable)				
A/H1N1	32.7	46.7		
A/H3N2	30.2	39.1		
Influenza B	63.9	75.9		

### Statistical analyses

No statistical analyses for this end point

### Primary: Seroprotection rate to at least one, two or all three vaccine antigens

End point title	Seroprotection rate to at least one, two or all three vaccine antigens <sup>[3]</sup>
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End point description:

End point type	Primary
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End point timeframe:

During the study

Notes:

[3] - 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: Not all the data required in the section are available. However, the final results report is attached, where the statistical analysis carried out is detailed.

<b>End point values</b>	Control	Experimental		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	211		
Units: Percentage				
number (not applicable)				
seroprotection rate at least one vaccine antigen	75.6	86.3		
seroprotection rate at least one vaccine antigens	53.5	70.6		

### Statistical analyses

No statistical analyses for this end point

### Primary: GMT tittle

End point title	GMT tittle <sup>[4]</sup>
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End point description:

End point type	Primary
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End point timeframe:

During the study

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: Not all the data required in the section are available. However, the final results report is attached, where the statistical analysis carried out is detailed.

<b>End point values</b>	Control	Experimental		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	211		
Units: GMT tittle				
median (confidence interval 95%)				
A/H1N1	33.3 (25.5 to 43.7)	41.61 (32.90 to 52.61)		
A/H3N2	27.2 (21.4 to 34.4)	44.7 (35.2 to 56.9)		
Influenza B	95.3 (71.9 to 126.3)	180.1 (139.5 to 232.6)		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

During the study

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.1
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### Reporting groups

Reporting group title	Control
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Reporting group description: -

Reporting group title	Experimental
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Reporting group description: -

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 were 184 mild and 95 moderate adverse events. Not all the required information is available, although it should be noted that these adverse events are all listed in the product data sheet of the investigational product.

<b>Serious adverse events</b>	Control	Experimental	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 251 (3.59%)	7 / 148 (4.73%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Fever			
subjects affected / exposed	1 / 251 (0.40%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	0 / 251 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Transplant rejection			
subjects affected / exposed	1 / 251 (0.40%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ascites			

subjects affected / exposed	1 / 251 (0.40%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hepatobiliary disorders</b>			
Cholangitis			
subjects affected / exposed	1 / 251 (0.40%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Respiratory, thoracic and mediastinal disorders</b>			
Pneumonitis			
subjects affected / exposed	0 / 251 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Renal and urinary disorders</b>			
Proteinuria			
subjects affected / exposed	1 / 251 (0.40%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 251 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
Pyelonephritis			
subjects affected / exposed	1 / 251 (0.40%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 251 (0.40%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	1 / 251 (0.40%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Urinary tract infection		
subjects affected / exposed	1 / 251 (0.40%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatobiliary infection		
subjects affected / exposed	0 / 251 (0.00%)	1 / 148 (0.68%)
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: 4 %

<b>Non-serious adverse events</b>	Control	Experimental
Total subjects affected by non-serious adverse events		
subjects affected / exposed	0 / 251 (0.00%)	0 / 148 (0.00%)

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2012	Summary of changes: <ul style="list-style-type: none"><li>- Extension of selection criteria to pulmonary patients.</li><li>- Modification of inclusion and follow-up schedules (from 2011 to 2012).</li><li>- Change of medicine: seasonal vaccine 2012-2013.</li><li>- Expansion of centres: Ramón y Cajal Hospital, Madrid; Gregorio Marañón Hospital, Madrid; Hospital 12 Marañón, Madrid; Hospital 12 de Octubre, Madrid; Hospital Clinic, Barcelona; Hospital Universitario Bellvitge, Barcelona; Hospital Vall d'Hebron, Barcelona; Hospital de Cruces, Bilbao; Hospital Universitario La Fe, Valencia.</li></ul>
04 May 2012	Summary of changes: <ul style="list-style-type: none"><li>- Inclusion of new secondary objectives associated with the performance of a genetic sub-study.</li><li>- New follow-up visit in arm B patients 15 weeks after the first vaccine dose (10 weeks after re-vaccination).</li><li>- Changes in the randomisation procedure (by blocks, stratified by centre, type of transplant and time since transplant).</li></ul>
01 July 2012	Summary of changes: <ul style="list-style-type: none"><li>- Inclusion of new secondary objectives associated with the performance of an immunological sub-study.</li><li>- Extension of centres: Virgen Macarena University Hospital, Seville; Marqués de Valdecilla University Hospital, Santander.</li></ul>
05 October 2012	Summary of changes: <ul style="list-style-type: none"><li>- New follow-up visit in patients in arm A at 15 weeks after the first vaccine dose.</li><li>- Extension of the recruitment period (until 14 December 2012).</li><li>- Removal of the requirement for quarterly telephone follow-up.</li></ul>
09 November 2013	Summary of changes: <ul style="list-style-type: none"><li>- Expansion of the sample size by 10% (from 462 to 508 patients) to make up for loss to follow-up.</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported