Clinical trial results:
Mesenchymal stem cells for radiation-induced xerostomia (MESRIX) in previous HPV-positive oropharyngeal head and neck cancer patients

Summary

EudraCT number	2014-004349-29
Trial protocol	DK
Global end of trial date	03 June 2017

Results information

Result version number	v1 (current)
This version publication date	20 August 2021
First version publication date	20 August 2021
Summary attachment (see zip file)	Paper (Grønhøj et al MESRIX 1.pdf)

Trial information

Trial identification

Sponsor protocol code	01-10-2014

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Rigshospitalet
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark,
Public contact	Rigshospitalet, Dept. of Otolaryngology, Head and Neck surgery, 0045 35452071, christian.von.buchwald@regionh.dk
Scientific contact	Rigshospitalet, Dept. of Otolaryngology, Head and Neck surgery, 0045 35452071, christian.von.buchwald@regionh.dk

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	02 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2017
Global end of trial reached?	Yes
Global end of trial date	03 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective is to examine whether enrichment of the submandibular gland with injection of autologous ASC will improve the result of salivary function in radiation-induced gland hypofunction.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Ethical reason, Regulatory reason, Scientific research
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 33
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	23
From 65 to 84 years	10

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligibility criteria included previous radio-
therapy, with or without concomitant chemotherapy, for a

human papilloma virus-positive, T1-T2, and N0, N1, or N2A
oropharyngeal squamous cell carcinoma; (12) two years of
follow-up without disease progression; an unstimulated
whole saliva flow rate in the range of 0.05 to 0.20 ml/min,
correspon

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	ASC arm

Arm description:

Intervention

Arm type	Experimental
Investigational medicinal product name	Mesenchymal stem cells
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

injection of 2.8 million ASCs/cm3 pr gland

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	saline with 1% human albumin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

2 ml in each submandibular gland

Number of subjects in period 1	ASC arm	Placebo
Started	17	16
Completed	15	15
Not completed	2	1
Consent withdrawn by subject	-	1
failed to expand ASCs	2	-

Baseline characteristics

Reporting groups	
Reporting group title	ASC arm
Reporting group description:	
Intervention	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	ASC arm	Placebo	Total
Number of subjects	17	16	33
Age categorical 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)	13	10	23
From 65-84 years	4	6	10
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	6	11	17
Male	11	5	16

Subject analysis sets	
Subject analysis set title	Experimental arm
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects randomized to experimental arm	
Subject analysis set title	Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects randomized to placebo arm	

Reporting group values	Experimental arm	Placebo	
Number of subjects	15	15	
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)	11	9	
From 65-84 years	4	6	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	6	5	
Male	9	10	

End points

End points reporting groups

Reporting group title	ASC arm
Reporting group description: Intervention	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	Experimental arm
Subject analysis set type	Per protocol
Subject analysis set description: Subjects randomized to experimental arm	
Subject analysis set title	Placebo
Subject analysis set type	Per protocol
Subject analysis set description: Subjects randomized to placebo arm	

Primary: Safety

End point title	Safety
End point description:	
End point type	Primary
End point timeframe: 4 months	

End point values	ASC arm	Placebo	Experimental arm	Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	15	15	15	15
Units: Adverse events	0	0	0	0

Statistical analyses

Statistical analysis title	Primary endpoints

Statistical analysis description:

For salivary flow rates, patient-reported outcome measures, and tissue type analysis we evaluated the changes from baseline to the one- and four-month follow-up visits.

Within-group comparisons were performed with the Wilcoxon signed-rank test, and between-group comparisons

were performed with the Mann-Whitney U test. We chose

to use non parametric statistics as the data were not normally distributed, evaluated by Shapiro-Wilks tests.

Comparison groups	ASC arm v Placebo

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Unstimulated whole saliva flow

End point title	Unstimulated whole saliva flow

End point description:

Unstimulated whole salivary flow rates significantly increased in the ASC-arm at one (33%; P Z .048) and four months (50%; P Z .003), but not in the placebo-arm (P Z .6 and P Z .8), compared to baseline.

End point type	Secondary

End point timeframe:

4 months

End point values	Experimental arm	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: ml/min				
number (not applicable)	50	33		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 4 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	All patients

Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		

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 no.

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

None reported