Clinical trial results:
A Collagen-Fibrin Patch (Tachosil®) for the Prevention of Symptomatic Lymphoceles after Pelvic Lymphadenectomy in Women with Gynecologic Malignancies: a Randomized Clinical Trial

Summary

EudraCT number	2011-003115-34
Trial protocol	AT
Global end of trial date	31 December 2016

Results information

Result version number	v1 (current)
This version publication date	22 February 2021
First version publication date	22 February 2021

Trial information

Trial identification

Sponsor protocol code	V1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01470677
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Währinger Gürtel 18-20, Vienn, Austria, 1090
Public contact	Abtlg f. Gyn. und gyn. Onkologie, Medizinische Universität Wien, 0043 01404002915, alexander.reinthaller@meduniwien.ac.at
Scientific contact	Abtlg f. Gyn. und gyn. Onkologie, Medizinische Universität Wien, 0043 01404002915, alexander.reinthaller@meduniwien.ac.at

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	17 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 April 2015
Global end of trial reached?	Yes
Global end of trial date	31 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary outcome variable was defined as follows: to evaluate the incidence of symptomatic pelvic lymphoceles defined by CTCAE 4.03 grade ≥2 within 4 weeks after surgery in women undergoing open or laparoscopic pelvic lymphadenectomy for cervical, endometrial, or ovarian cancer with and without the application of fibrin-collagen patches during surgery.

Protection of trial subjects:

In order to ensure adequate application of the patches by laparoscopy, all surgeons must have had performed at least two prior laparoscopic operations during which they rolled the patch around a laparoscopic instrument, moved it through a 10 mm trocar into the abdomen, and flattened it out on the pelvic side wall.

All women underwent a gynecologic examination and a transvaginal and/or transabdominal ultrasound examination at the time of discharge of the hospital. All women were scheduled for a follow-up visit 4 weeks after surgery including a gynecologic examination and a transvaginal and transabdominal ultrasound examination, performed by a physician experienced in transvaginal and transabdominal ultrasound examinations, who had not participated in the original surgical procedure and was blinded to the treatment allocation.

Background therapy:

All women underwent pelvic lymphadenectomy by open or laparoscopic surgery. The procedures were performed as follows: the peritoneum was incised parallel to the iliac vessels. Then, the iliac vessels were screened for the presence of bulky lymph nodes. If a lymph node debulking was performed, no fibrin-collagen patches were applied. In women with routine pelvic lymphadenectomy, lymph node tissue was removed from the external iliac vessels, the obturator fossa, the interiliac region, and the common iliac region after identification and appropriate preparation of the surgical landmarks, ie iliac vessels, femoral canal, chorda, and obturator nerve. At the end of the procedure, hemostasis was checked and a fibrin-collagen patch of 4.8x4.8 cm was attached to the obturator fossa and another patch of 4.8x4.8 cm to the femoral canal of each side of the pelvic side wall in the intervention group. In the control group, no fibrin-collagen patches were used. No specific drainage of the retroperitoneum was performed.

Evidence for comparator: -

Actual start date of recruitment	01 October 2011
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	Austria: 46
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Czechia: 98

Worldwide total number of subjects	164
EEA total number of subjects	164

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)	116
From 65 to 84 years	47
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Inclusion criteria were as follows: open or laparoscopic surgery for cervical, endometrial, or ovarian cancer including bilateral systematic pelvic lymphadenectomy, age between 18 and 70 years, and provision of written informed consent. Exclusion criteria were as follows: a history of previously diagnosed lymph edema.

Pre-assignment

Screening details:

173 patients were screened, 9 patients were not eligible due to not meeting inclusion criterias.
164 patients were randomized, 11 patients were lost to follow-up.

Period 1

Period 1 title	baseline period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

Women were centrally randomized by one of the investigators (CT). Using the central randomization list, allocation numbers were assigned and sealed in opaque envelopes with consecutive numbers for each center. The envelopes were sent to respective study centers and were opened during surgery after completion of pelvic lymphadenectomy. Outcome assessment was not performed by the surgeon, who had performed the lymphadenectomy and outcome assessors were not aware of the treatment allocation.

Arms

Are arms mutually exclusive?	Yes
Arm title	Tachosil

Arm description:

At the end of the procedure, hemostasis was checked and a fibrin-collagen patch of 4.8x4.8 cm was attached to the obturator fossa and another patch of 4.8x4.8 cm to the femoral canal of each side of the pelvic side wall in the intervention group

Arm type	Experimental
Investigational medicinal product name	tachosil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicated sponge
Routes of administration	Intraabdominal use

Dosage and administration details:

two fibrin-collagen patch of 4.8x4.8 cm were attached to each pelvic sidewalls, i.e. four patches in total.

Arm title	Control

Arm description:

In the control group, no fibrin-collagen patches were used. No specific drainage of the retroperitoneum was performed.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: the trial is single blinded, as the patients were aware whether Tachosil was applied during surgery or not; the ultrasound assessor, which assessed the presence of lymphoceleand if yes the extent of a lymphocele were blinded to the intervention

Number of subjects in period 1	Tachosil	Control
Started	75	89
Completed	75	89

Baseline characteristics

Reporting groups	
Reporting group title	Tachosil
Reporting group description:	
At the end of the procedure, hemostasis was checked and a fibrin-collagen patch of 4.8x4.8 cm was attached to the obturator fossa and another patch of 4.8x4.8 cm to the femoral canal of each side of the pelvic side wall in the intervention group	
Reporting group title	Control
Reporting group description:	
In the control group, no fibrin-collagen patches were used. No specific drainage of the retroperitoneum was performed.	

Reporting group values	Tachosil	Control	Total
Number of subjects	75	89	164
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)	54	62	116
From 65-84 years	21	26	47
85 years and over	0	1	1
Age continuous			
Units: years			
arithmetic mean	57.1	55.4	
standard deviation	± 12.8	± 13.4	-
Gender categorical			
Units: Subjects			
Female	75	89	164

End points

End points reporting groups

Reporting group title	Tachosil
Reporting group description:	
At the end of the procedure, hemostasis was checked and a fibrin-collagen patch of 4.8x4.8 cm was attached to the obturator fossa and another patch of 4.8x4.8 cm to the femoral canal of each side of the pelvic side wall in the intervention group	
Reporting group title	Control
Reporting group description:	
In the control group, no fibrin-collagen patches were used. No specific drainage of the retroperitoneum was performed.	

Primary: primary endpoint: symptomatic lymphocele

End point title	primary endpoint: symptomatic lymphocele
End point description:	
End point type	Primary
End point timeframe:	
reduction of the incidence of symptomatic lymphoceles within 4 weeks after surgery	

End point values	Tachosil	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	89		
Units: patients	68	85		

Statistical analyses

Statistical analysis title	primary analysis
Statistical analysis description:	
presence of symptomatic lymphocele	
Comparison groups	Tachosil v Control
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.47
Method	Chi-squared

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

12 weeks after surgery

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	tachosil
Reporting group description: -	
Reporting group title	control group
Reporting group description: -	

Serious adverse events	tachosil	control group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 75 (0.00%)	0 / 89 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	tachosil	control group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 75 (0.00%)	0 / 89 (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: no non-serious adverse events or serious adverse events were observed

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 October 2012	change of the primary endpoint due to a recent publication presenting reliable data on the very important clinical endpoint "symptomatic lymphocele"

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported