Clinical trial results:
Thromboprophylaxis in Oesophageal Cancer Patients – A Randomized, Controlled Trial

Summary

EudraCT number	2021-001335-24
Trial protocol	DK
Global end of trial date	01 August 2024

Results information

Result version number	v1 (current)
This version publication date	31 May 2025
First version publication date	31 May 2025

Trial information

Trial identification

Sponsor protocol code	141190

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 99, Aarhus N, Denmark, 8200
Public contact	Department of Clinical Biochemistry, Aarhus University Hospital, 0045 78455252, biokemi@auh.rm.dk
Scientific contact	Department of Clinical Biochemistry, Aarhus University Hospital, 0045 78455252, biokemi@auh.rm.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	01 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 August 2024
Global end of trial reached?	Yes
Global end of trial date	01 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the study is to examine the efficacy and safety of prolonged thromboprophylactic treatment with Fragmin® in oesophageal cancer patients undergoing intended curative surgery.

Protection of trial subjects:

Monitoring of side effects to study drug

Background therapy:

All patients underwent intended curative surgery for oesophageal cancer.

Evidence for comparator: -

Actual start date of recruitment	01 May 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 94
Worldwide total number of subjects	94
EEA total number of subjects	94

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)	35
From 65 to 84 years	59
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were included between September 2021 and April 2024.
Adult patients with esophageal adenocarcinomas or squamous cell carcinomas referred for intended curative esophagectomy at Aarhus University Hospital, Denmark, were included.

Pre-assignment

Screening details:

152 patients screened and of this 58 were not eligible due to:
Cancelled surgery (n=6), logistics (n=12), ongoing anticoagulant treatment (n=28), declined to participate (n=9), not oesophageal cancer (n=2), inherited bleeding disorder (n=1)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard treatment

Arm description:

The standard group received prophylaxis with 5000
IU Fragmin (dalteparin, Pfizer ApS) for the duration of admittance to
the hospital after esophagectomy, usually 10 days according to the local standard of care.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Intervention arm

Arm description:

The intervention group received prophylaxis with 5000
IU Fragmin (dalteparin, Pfizer ApS) for 30 days.

Arm type	Experimental
Investigational medicinal product name	Fragmin®
Investigational medicinal product code	00069-0196-01
Other name	Dalteparin
Pharmaceutical forms	Anticoagulant and preservative solution for blood
Routes of administration	Solution for injection

Dosage and administration details:

5,000 IU solution for injection in prefilled syringes

Number of subjects in period 1	Standard treatment	Intervention arm
Started	48	46
Completed	39	40
Not completed	9	6
Physician decision	4	3
Protocol deviation	5	3

Baseline characteristics

Reporting groups	
Reporting group title	Standard treatment
Reporting group description:	
The standard group received prophylaxis with 5000 IU Fragmin (dalteparin, Pfizer ApS) for the duration of admittance to the hospital after esophagectomy, usually 10 days according to the local standard of care.	
Reporting group title	Intervention arm
Reporting group description:	
The intervention group received prophylaxis with 5000 IU Fragmin (dalteparin, Pfizer ApS) for 30 days.	

Reporting group values	Standard treatment	Intervention arm	Total
Number of subjects	48	46	94
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	66	68	
inter-quartile range (Q1-Q3)	56 to 77	53 to 76	-
Gender categorical			
Units: Subjects			
Female	13	12	25
Male	35	34	69

End points

End points reporting groups

Reporting group title	Standard treatment
Reporting group description:	
The standard group received prophylaxis with 5000 IU Fragmin (dalteparin, Pfizer ApS) for the duration of admittance to the hospital after esophagectomy, usually 10 days according to the local standard of care.	
Reporting group title	Intervention arm
Reporting group description:	
The intervention group received prophylaxis with 5000 IU Fragmin (dalteparin, Pfizer ApS) for 30 days.	

Primary: Levels of prothrombin fragment 1+2

End point title	Levels of prothrombin fragment 1+2
End point description:	
End point type	Primary
End point timeframe:	
Measured one month after surgery	

End point values	Standard treatment	Intervention arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: pmol/L				
median (inter-quartile range (Q1-Q3))	246 (182 to 262)	232 (173 to 356)		

Statistical analyses

Statistical analysis title	Primary endpoint analysis
Statistical analysis description:	
Difference in prothrombin fragment 1 + 2 levels in the 2 groups 1 month after surgery as an intention-to-treat analysis	
Comparison groups	Standard treatment v Intervention arm
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.41
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From inclusion to one month after surgery.

Assessment type	Systematic

Dictionary used

Dictionary name	SNOMED CT
Dictionary version	2025-03-31

Reporting groups

Reporting group title	Standard treatment

Reporting group description:

The standard group received prophylaxis with 5000
IU Fragmin (dalteparin, Pfizer ApS) for the duration of admittance to
the hospital after esophagectomy, usually 10 days according to the local standard of care.

Reporting group title	Intervention arm

Reporting group description:

The intervention group received prophylaxis with 5000
IU Fragmin (dalteparin, Pfizer ApS) for 30 days.

Serious adverse events	Standard treatment	Intervention arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 39 (23.08%)	7 / 40 (17.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Anastomosis leakage or fistula			
subjects affected / exposed	4 / 39 (10.26%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Displaced intestine	Additional description: Requiring reoperation		
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial flutter	Additional description: Following discharge requiring readmission		
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest	Additional description: Cardiac arrest with non-fatal outcome		

subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting and nausea	Additional description: Vomiting, nausea and problems eating following discharge, of a degree requiring readmission		
subjects affected / exposed	3 / 39 (7.69%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia	Additional description: Postoperative pneumonia		
subjects affected / exposed	2 / 39 (5.13%)	2 / 40 (5.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Standard treatment	Intervention arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 39 (10.26%)	2 / 40 (5.00%)	
Surgical and medical procedures			
Broken nasogastric tube	Additional description: Requiring gastrocopy		
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Reoperation	Additional description: Due to displaced intestine		
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Vasopressor requirement	Additional description: Requiring readmission to ICU		
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	
occurrences (all)	0	1	
Nervous system disorders			
Generalized seizure			
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

Pneumonia subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	1 / 40 (2.50%) 1	

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.

Risk of type II error due to low accrual

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/39242497

http://www.ncbi.nlm.nih.gov/pubmed/39842514

http://www.ncbi.nlm.nih.gov/pubmed/40095681