Clinical trial results:
A randomised controlled trial of eicosapentaenoic acid (EPA) and/or aspirin for colorectal adenoma (or polyp) prevention during colonoscopic surveillance in the NHS Bowel Cancer Screening Programme: The seAFOod (Systematic Evaluation of Aspirin and Fish Oil) polyp prevention trial.

Summary

EudraCT number	2010-020943-10
Trial protocol	GB
Global end of trial date	12 June 2017

Results information

Result version number	v1 (current)
This version publication date	22 January 2020
First version publication date	22 January 2020
Summary attachment (see zip file)	primary trial publication - The Lancet 2018 (seAFOod Trial paper final.pdf) primary publication - supplementary material (seAFOod Trial paper web appendix.pdf) seAFOod Trial - NIHR Journals article (seAFOod Trial NIHR Journals report.pdf)

Trial information

Trial identification

Sponsor protocol code	GA10/9312

Additional study identifiers

ISRCTN number	ISRCTN05926847
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Leeds
Sponsor organisation address	Worsley Building, Leeds, United Kingdom, LS2 9JT
Public contact	Professor Mark Hull, Professor of Molecular Gastroenterology, Leeds Institute of Medical Research, University of Leeds, 0113 3438650, M.A.Hull@leeds.ac.uk
Scientific contact	Professor Mark Hull, Professor of Molecular Gastroenterology, Leeds Institute of Medical Research, University of Leeds, 0113 3438650, M.A.Hull@leeds.ac.uk

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	12 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 June 2017
Global end of trial reached?	Yes
Global end of trial date	12 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether the naturally-occurring omega (ω)-3 polyunsaturated fatty acid eicosapentaenoic acid (EPA) prevents colorectal adenomas, either alone or in combination with aspirin.

Protection of trial subjects:

This clinical trial, which involved the use investigational medicinal products (IMPs) was designed and was be run in accordance with the Principles of GCP and the current regulatory requirements, as detailed in the Medicines for Human Use (Clinical Trials) Regulations 2004 (UK Statutory Instrument (S.I.) 2004 / 1031) and any subsequent amendments of the Clinical Trial Regulations. The seAFOod trial was monitored by the Sponsor to assess this. The trial used both a TSC and DMC. The eligibility criteria were robust and were approved by both the MHRA & a Research Ethics Committee.

Background therapy:

Trial participants all underwent a screening and surveillance colonoscopy as part of the English Bowel cancer Screening Programme.

Evidence for comparator:

The comparator for EPA and aspirin was a placebo, justified on the basis that there is no strong evidence for use of either agent for colorectal cancer (CRC) prevention and neither agent is used in best clinical practice. The intervention lasted for only 12 months, which is much shorter than the natural history of CRC development, as was followed by a colonoscopy. Therefore, there was deemed to be little if any harm associated with takingplacebo rather than active IMPs.

Actual start date of recruitment	14 October 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 707
Worldwide total number of subjects	707
EEA total number of subjects	707

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)	348
From 65 to 84 years	359
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients aged 55-73 who had undergone a screening colonoscopy in the English Bowel Cancer Screening Programme (BCSP) were recruited between November 2011 and June 2016 from 53 english NHS hospital endoscopy units.

Pre-assignment

Screening details:

3911 individuals, who were classified as 'high risk' (greater than/equal to 3 colorectal adenomas if one was greater than/equal to 10 mm in size; or 5 colorectal adenomas of any size) on the basis of the BCSP screening colonoscopy, were screened for eligibility. 3202 (82%) were not randomised (2179 ineligible and 1023 unwilling to take part)

Period 1

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

Blinding implementation details:

There were identical placebos for the capsule and tablet IMPs.
The sequence of treatment allocations was concealed until recruitment, data collection, and database lock were completed. Investigational Medicinal Product (IMP) allocation was not divulged to any research staff or participant.

Arms

Are arms mutually exclusive?	Yes
Arm title	Eicosapentaenoic acid (EPA)

Arm description:

EPA alone

Arm type	Experimental
Investigational medicinal product name	eicosapentaenoic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

99% EPA-FFA 2 g daily (as two 500 mg gastro-resistant capsules twice daily with food) or an equivalent FFA dose as 90% EPA-triglyceride (TG) 2780 mg daily (as five soft-gelatin capsules per day split over two meals

Arm title	aspirin

Arm description:

aspirin alone

Arm type	Experimental
Investigational medicinal product name	aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

enteric-coated aspirin 300 mg tablet daily with food

Arm title	EPA + aspirin

Arm description:	
Combined EPA and aspirin	
Arm type	Experimental
Investigational medicinal product name	EPA capsules and aspirin tablet combined as in active agent alone arms
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft, Tablet
Routes of administration	Oral use
Dosage and administration details:	
Identical dosage and administration of EPA capsules and aspirin tablet as single agent arms	
Arm title	placebo
Arm description:	
Double (capsule and tablet) placebo	
Arm type	Placebo
Investigational medicinal product name	capsule placebo (capric and capryllic acid) and tablet placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft, Tablet
Routes of administration	Oral use
Dosage and administration details:	
Identical administration to active capsule (EPA) and active tablet (aspirin) arm	

Number of subjects in period 1	Eicosapentaenoic acid (EPA)	aspirin	EPA + aspirin
Started	178	176	177
Completed	154	163	161
Not completed	24	13	16
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	12	5	7
Adverse event, non-fatal	1	1	2
various	4	-	2
required more than one rpt colonoscopy	-	4	-
Lost to follow-up	7	3	4
reason missing	-	-	1

Number of subjects in period 1	placebo
Started	176
Completed	163
Not completed	13
Adverse event, serious fatal	1
Consent withdrawn by subject	8
Adverse event, non-fatal	1
various	1

required more than one rpt colonoscopy	-
Lost to follow-up	2
reason missing	-

Baseline characteristics

Reporting groups	
Reporting group title	Eicosapentaenoic acid (EPA)
Reporting group description: EPA alone	
Reporting group title	aspirin
Reporting group description: aspirin alone	
Reporting group title	EPA + aspirin
Reporting group description: Combined EPA and aspirin	
Reporting group title	placebo
Reporting group description: Double (capsule and tablet) placebo	

Reporting group values	Eicosapentaenoic acid (EPA)	aspirin	EPA + aspirin
Number of subjects	178	176	177
Age categorical			
age categories by treatment arm			
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)	90	92	76
From 65-84 years	88	84	101
85 years and over	0	0	0
Age continuous			
age at enrolment			
Units: years			
arithmetic mean	65.2	65.3	65.6
standard deviation	± 4.5	± 4.5	± 4.7
Gender categorical			
sex of trial subjects			
Units: Subjects			
Female	40	36	31
Male	138	140	146

Reporting group values	placebo	Total	
Number of subjects	176	707	
Age categorical			
age categories by treatment arm			
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)	90	348	
From 65-84 years	86	359	
85 years and over	0	0	
Age continuous			
age at enrolment			
Units: years			
arithmetic mean	65.2		
standard deviation	± 4.6	-	
Gender categorical			
sex of trial subjects			
Units: Subjects			
Female	37	144	
Male	139	563	

End points

End points reporting groups	
Reporting group title	Eicosapentaenoic acid (EPA)
Reporting group description: EPA alone	
Reporting group title	aspirin
Reporting group description: aspirin alone	
Reporting group title	EPA + aspirin
Reporting group description: Combined EPA and aspirin	
Reporting group title	placebo
Reporting group description: Double (capsule and tablet) placebo	

Primary: Adenoma Detection Rate	
End point title	Adenoma Detection Rate
End point description: Adenoma Detection Rate = % number of individuals with one or more colorectal adenomas at surveillance colonoscopy at 12 months	
End point type	Primary
End point timeframe: at 12 month surveillance colonoscopy	

End point values	Eicosapentaenoic acid (EPA)	aspirin	EPA + aspirin	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	153[1]	163[2]	161[3]	163[4]
Units: 1-100	63	61	61	61

Notes:

[1] - participants with colorectal adenoma data at 12 months

[2] - participants with colorectal adenoma data at 12 months

[3] - participants with colorectal adenoma data at 12 months

[4] - participants with colorectal adenoma data at 12 months

Statistical analyses

Statistical analysis title	EPA users vs no EPA users
Statistical analysis description: EPAanalysis by factorial margins	
Comparison groups	Eicosapentaenoic acid (EPA) v aspirin v EPA + aspirin v placebo

Number of subjects included in analysis	640
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.81
Method	mixed-effects log-binomial regression
Parameter estimate	Risk difference (RD)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	6.9

Statistical analysis title	aspirin users vs no aspirin users
Statistical analysis description: aspirin analysis by factorial margins	
Comparison groups	Eicosapentaenoic acid (EPA) v aspirin v EPA + aspirin v placebo
Number of subjects included in analysis	640
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.88
Method	mixed-effects log-binomial regression
Parameter estimate	Risk difference (RD)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.5
upper limit	7.2

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected for all participants from first dose of trial treatment until the final trial visit (which coincides with the BSCP routine post-colonoscopy visit) scheduled for 2 weeks after the last dose of trial treatment.

Adverse event reporting additional description:

Information about AEs, whether volunteered by the participant, discovered by SSP/RN/Investigator questioning or detected through physical examination, laboratory test or other investigation were collected and recorded on the CRF.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	4.0

Reporting groups

Reporting group title	Eicosapentaenoic acid (EPA)
Reporting group description:	
EPA alone	
Reporting group title	aspirin
Reporting group description:	
aspirin alone	
Reporting group title	EPA + aspirin
Reporting group description:	
Combined EPA and aspirin	
Reporting group title	placebo
Reporting group description:	
Double (capsule and tablet) placebo	

Serious adverse events	Eicosapentaenoic acid (EPA)	aspirin	EPA + aspirin
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 177 (6.78%)	12 / 174 (6.90%)	5 / 170 (2.94%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder squamous cell carcinoma stage unspecified			
subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			

subjects affected / exposed	1 / 177 (0.56%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal carcinoma			
subjects affected / exposed	1 / 177 (0.56%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate Cancer			
subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

femoral artery occlusion			
subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 177 (0.56%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	5 / 177 (2.82%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 177 (0.56%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Transient ischaemic attack			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	1 / 177 (0.56%)	0 / 174 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faeces discoloured			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Oesophageal haemorrhage			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal perforation			
subjects affected / exposed	1 / 177 (0.56%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 177 (0.56%)	0 / 174 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 177 (0.56%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	1 / 177 (0.56%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			

subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 177 (0.56%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic Abscess			
subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Labyrinthitis			
subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	1 / 177 (0.56%)	0 / 174 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal abscess			
subjects affected / exposed	0 / 177 (0.00%)	0 / 174 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 177 (0.00%)	1 / 174 (0.57%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	placebo		

Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 176 (7.39%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder squamous cell carcinoma stage unspecified			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lung neoplasm malignant			
subjects affected / exposed	2 / 176 (1.14%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metastases to bone			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oesophageal carcinoma			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate Cancer			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal cancer			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
femoral artery occlusion			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arrhythmia			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			

subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Duodenitis			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Faeces discoloured			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastritis				
subjects affected / exposed	0 / 176 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 176 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hiatus hernia				
subjects affected / exposed	0 / 176 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal haemorrhage				
subjects affected / exposed	0 / 176 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal perforation				
subjects affected / exposed	0 / 176 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 176 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 176 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 176 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colonic Abscess			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Labyrinthitis			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	1 / 176 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection			

subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pharyngeal abscess			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural infection			
subjects affected / exposed	0 / 176 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Eicosapentaenoic acid (EPA)	aspirin	EPA + aspirin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	82 / 177 (46.33%)	68 / 174 (39.08%)	76 / 170 (44.71%)
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	38 / 177 (21.47%)	20 / 174 (11.49%)	11 / 170 (6.47%)
occurrences (all)	38	20	11
UGI Symptoms			
subjects affected / exposed	36 / 177 (20.34%)	26 / 174 (14.94%)	29 / 170 (17.06%)
occurrences (all)	36	26	29
Lower Abdominal pain			
subjects affected / exposed	37 / 177 (20.90%)	10 / 174 (5.75%)	9 / 170 (5.29%)
occurrences (all)	37	10	9
Eructation			
subjects affected / exposed	5 / 177 (2.82%)	1 / 174 (0.57%)	4 / 170 (2.35%)
occurrences (all)	5	1	4

Non-serious adverse events	placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 176 (44.32%)		
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	16 / 176 (9.09%)		
occurrences (all)	16		
UGI Symptoms			
subjects affected / exposed	28 / 176 (15.91%)		
occurrences (all)	28		
Lower Abdominal pain			
subjects affected / exposed	21 / 176 (11.93%)		
occurrences (all)	21		
Eructation			
subjects affected / exposed	5 / 176 (2.84%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 August 2011	SA02: seAFOod Trial Protocol, version 2.0, dated 08 August 2011. Changes to the protocol and PIL to ensure wording is clearer for study personnel and participants.
30 November 2011	SA04. seAFOod Trial Protocol, version 3.0, dated 28 November 2011. Inclusion criteria - age reduced to 73 to reflect BCSP surveillance guidelines. Exclusion criteria updated to exclude patients who are taking any non-aspirin anti-platelet therapy
25 May 2012	SA06:seAFOod trial Protocol, version 4.0, dated 04 May 2012. Change to exclusion criteria to now include patients who need a second repeat screening endoscopy, allowing inclusion of participants who have a second screening procedure.
19 June 2013	SA10: seAFOod trial Protocol, version 5.0, dated 17 June 2013. Change to inclusion criteria to include patients identified through the BowelScope FS screening programme
14 August 2014	SA14: seAFOod trial Protocol, version 6.0, dated 11 August 2014. Changes to the protocol in line with the introduction of the replacement capsule IMP. This includes additional information on the new EPA-TG formulation.

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/30466866