



Clinical trial results:

Randomized Multicentre Phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in primary high risk rectal cancer compared to standard chemoradiotherapy and surgery

Summary

EudraCT number	2010-023957-12
Trial protocol	SE NL ES SI DK
Global end of trial date	08 September 2026

Results information

Result version number	v1 (current)
This version publication date	30 October 2026
First version publication date	30 October 2026

Trial information

Trial identification

Sponsor protocol code	RAPIDO
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01558921
WHO universal trial number (UTN)	-
Other trial identifiers	OMON: NL-OMON47895

Notes:

Sponsors

Sponsor organisation name	Universitair Medisch Centrum Groningen
Sponsor organisation address	Hanzeplein 1, Groningen, Netherlands, 9713 GZ
Public contact	Professor Geke Hospers, Universitair Medisch Centrum Groningen, g.a.p.hospers@umcg.nl
Scientific contact	Professor Geke Hospers, Universitair Medisch Centrum Groningen, g.a.p.hospers@umcg.nl

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	08 September 2026
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 September 2026
Global end of trial reached?	Yes
Global end of trial date	08 September 2026
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To decrease disease related treatment failure (DrTF)

Protection of trial subjects:

TO BE ANSWERED

Background therapy:

TO BE ANSWERED

Evidence for comparator:

standard therapy

Actual start date of recruitment	21 June 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	10 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 361
Country: Number of subjects enrolled	Norway: 23
Country: Number of subjects enrolled	Slovenia: 36
Country: Number of subjects enrolled	Spain: 119
Country: Number of subjects enrolled	Sweden: 332
Country: Number of subjects enrolled	Denmark: 29
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	920
EEA total number of subjects	900

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	556
From 65 to 84 years	364
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was between 18-06-2011 (first informed consent) and 02-06-2016 (last randomization).

Pre-assignment

Screening details:

- Medical history, concomitant medication and medical complaints
- Physical examination
- Rectoscopy and / or colonoscopy. A biopsy of the tumour might be taken
- If significant for the study an X-ray of the colon will be taken
- CT of lungs, abdomen and pelvis and a MRI of the pelvis will be performed to examine size and spread of the tumour.

Period 1

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

Blinding implementation details:

NA

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard of care

Arm description:

Long-course radiotherapy (1.8-2 Gy x 25-28) with concomitant capecitabine. After a "waiting period" of 8 weeks (± 2 weeks) during which response is evaluated, surgery according to TME/PME principles will be performed. In this arm it is allowed according to the local protocol of the participating institute to admit after recovery, optimally within 6-8 weeks, post-operative adjuvant chemotherapy consisting of 8 cycles oxaliplatin/capecitabine (or alternatively 24 weeks of FOLFOX4).

Arm type	Active comparator
Investigational medicinal product name	capecitabine
Investigational medicinal product code	L01BC06
Other name	Xeloda
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

825 mg/m² (twice daily) day 1-33-38 pre-surgery and optional 1000 mg/m² (twice daily) day 1-14 every 3 weeks post-surgery

Investigational medicinal product name	oxaliplatin
Investigational medicinal product code	L01XA03
Other name	
Pharmaceutical forms	Concentrate for solution for infusion, Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

130 mg/m² day 1 every 3 weeks

Arm title	Experimental
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Arm description:

Short-course radiotherapy (5 Gy x 5). Within 11-18 days after the last day of radiotherapy pre-operative systemic chemotherapy with oxaliplatin/capecitabine will commence and is delivered in 6 cycles. Alternatively 18 weeks cycles of FOLFOX4 is an option. Response is evaluated after the systemic chemotherapy. Within 2-4 weeks after the final chemotherapy cycle surgery according to TME/PME principles will be performed. No postoperative therapy.

Arm type	Experimental
Investigational medicinal product name	capecitabine
Investigational medicinal product code	L01BC06
Other name	Xeloda
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

1000 mg/m² (twice daily) day 1-14 every 3 weeks

Investigational medicinal product name	oxaliplatin
Investigational medicinal product code	L01XA03
Other name	
Pharmaceutical forms	Concentrate for solution for infusion, Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

130 mg/m² day 1 every 3 weeks

Investigational medicinal product name	leucovorin
Investigational medicinal product code	V03AF03
Other name	folonic acid, calcium folinate
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

leucovorin (200 mg/m²) administered as a 2-hour infusion on day 1 and day 2

Investigational medicinal product name	fluorouracil
Investigational medicinal product code	L01BC02
Other name	5-FU
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

a loading dose of 5-FU (400 mg/m²) IV bolus, then 5-FU (600 mg/m²) administered for a period of 22 hours on day 1 and day 2 every 2 weeks

Number of subjects in period 1	Standard of care	Experimental
Started	452	468
Completed	400	426
Not completed	52	42
Adverse event, serious fatal	3	1
Consent withdrawn by subject	2	3
personal event	2	1
refused surgery or watch & wait	16	-
progressive disease	25	10
refused surgery or not fit or watch & wait	-	22
switched arm	3	1
ineligible	1	3
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	920	920	
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			
Age at randomization			
Units: years			
median	62		
full range (min-max)	23 to 84	-	
Gender categorical			
Gender			
Units: Subjects			
Female	303	303	
Male	617	617	

End points

End points reporting groups

Reporting group title	Standard of care
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Reporting group description:

Long-course radiotherapy (1.8-2 Gy x 25-28) with concomitant capecitabine. After a "waiting period" of 8 weeks (± 2 weeks) during which response is evaluated, surgery according to TME/PME principles will be performed. In this arm it is allowed according to the local protocol of the participating institute to admit after recovery, optimally within 6-8 weeks, post-operative adjuvant chemotherapy consisting of 8 cycles oxaliplatin/capecitabine (or alternatively 24 weeks of FOLFOX4).

Reporting group title	Experimental
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Reporting group description:

Short-course radiotherapy (5 Gy x 5). Within 11-18 days after the last day of radiotherapy pre-operative systemic chemotherapy with oxaliplatin/capecitabine will commence and is delivered in 6 cycles. Alternatively 18 weeks cycles of FOLFOX4 is an option. Response is evaluated after the systemic chemotherapy. Within 2-4 weeks after the final chemotherapy cycle surgery according to TME/PME principles will be performed. No postoperative therapy.

Primary: DrTF at 3 years

End point title	DrTF at 3 years
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End point description:

Disease related Treatment Failure

End point type	Primary
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End point timeframe:

3 years

End point values	Standard of care	Experimental		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	450	462		
Units: percentage				
number (confidence interval 5%)	30.4 (26.1 to 34.6)	23.7 (19.8 to 27.6)		

Attachments (see zip file)	DrTF/Chart DrTF.png
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Statistical analyses

Statistical analysis title	Primary endpoint
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Statistical analysis description:

calculated HRs and 95% CIs using Cox regression.

Comparison groups	Standard of care v Experimental
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Number of subjects included in analysis	912
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During therapy

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	5
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Reporting groups

Reporting group title	Experimental
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Reporting group description:

During treatment

Reporting group title	Standard Care
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Reporting group description: -

Reporting group title	Standard Care - adjuvant chemotherapy
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Reporting group description: -

Serious adverse events	Experimental	Standard Care	Standard Care - adjuvant chemotherapy
Total subjects affected by serious adverse events			
subjects affected / exposed	177 / 460 (38.48%)	87 / 441 (19.73%)	64 / 187 (34.22%)
number of deaths (all causes)	4	4	0
number of deaths resulting from adverse events	4	4	0
Investigations			
Dehydration/laboratory deviation			
subjects affected / exposed	3 / 460 (0.65%)	5 / 441 (1.13%)	4 / 187 (2.14%)
occurrences causally related to treatment / all	3 / 3	5 / 5	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Thromboembolic			
subjects affected / exposed	13 / 460 (2.83%)	6 / 441 (1.36%)	2 / 187 (1.07%)
occurrences causally related to treatment / all	13 / 13	6 / 6	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiovascular disease			
subjects affected / exposed	8 / 460 (1.74%)	10 / 441 (2.27%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	8 / 8	10 / 10	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

General disorders and administration site conditions			
Weakness/Fatigue			
subjects affected / exposed	1 / 460 (0.22%)	3 / 441 (0.68%)	2 / 187 (1.07%)
occurrences causally related to treatment / all	1 / 1	3 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Other			
subjects affected / exposed	9 / 460 (1.96%)	3 / 441 (0.68%)	4 / 187 (2.14%)
occurrences causally related to treatment / all	9 / 9	3 / 3	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain/obstipation/obstruction			
subjects affected / exposed	27 / 460 (5.87%)	10 / 441 (2.27%)	3 / 187 (1.60%)
occurrences causally related to treatment / all	27 / 27	10 / 10	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood loss (oral, rectal, urine)			
subjects affected / exposed	6 / 460 (1.30%)	2 / 441 (0.45%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	6 / 6	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	45 / 460 (9.78%)	11 / 441 (2.49%)	5 / 187 (2.67%)
occurrences causally related to treatment / all	45 / 45	11 / 11	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea/vomiting/anorexia			
subjects affected / exposed	8 / 460 (1.74%)	1 / 441 (0.23%)	2 / 187 (1.07%)
occurrences causally related to treatment / all	8 / 8	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Other, abdominal			
subjects affected / exposed	16 / 460 (3.48%)	4 / 441 (0.91%)	6 / 187 (3.21%)
occurrences causally related to treatment / all	16 / 16	4 / 4	6 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary			

subjects affected / exposed	6 / 460 (1.30%)	2 / 441 (0.45%)	2 / 187 (1.07%)
occurrences causally related to treatment / all	6 / 6	2 / 2	2 / 2
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 0
Psychiatric disorders			
Psychological			
subjects affected / exposed	1 / 460 (0.22%)	2 / 441 (0.45%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Infections and infestations			
Infectious, abdominal			
subjects affected / exposed	11 / 460 (2.39%)	6 / 441 (1.36%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	11 / 11	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Infectious, other			
subjects affected / exposed	18 / 460 (3.91%)	8 / 441 (1.81%)	8 / 187 (4.28%)
occurrences causally related to treatment / all	18 / 18	8 / 8	8 / 8
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0

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

Non-serious adverse events	Experimental	Standard Care	Standard Care - adjuvant chemotherapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	382 / 460 (83.04%)	427 / 441 (96.83%)	135 / 187 (72.19%)
Nervous system disorders			
Neurological toxicity			
subjects affected / exposed	382 / 460 (83.04%)	31 / 441 (7.03%)	135 / 187 (72.19%)
occurrences (all)	1439	53	637
General disorders and administration site conditions			
Faecal incontinence			
subjects affected / exposed	32 / 460 (6.96%)	43 / 441 (9.75%)	2 / 187 (1.07%)
occurrences (all)	55	88	2
Fatigue/lethargy			
subjects affected / exposed	310 / 460 (67.39%)	258 / 441 (58.50%)	126 / 187 (67.38%)
occurrences (all)	934	702	464
Blood and lymphatic system disorders			

Febrile neutropenia subjects affected / exposed occurrences (all)	5 / 460 (1.09%) 6	1 / 441 (0.23%) 1	1 / 187 (0.53%) 1
Immune system disorders Allergic reaction subjects affected / exposed occurrences (all)	25 / 460 (5.43%) 41	3 / 441 (0.68%) 3	7 / 187 (3.74%) 9
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	213 / 460 (46.30%) 476	159 / 441 (36.05%) 360	39 / 187 (20.86%) 80
Diarrhoea subjects affected / exposed occurrences (all)	261 / 460 (56.74%) 670	250 / 441 (56.69%) 672	103 / 187 (55.08%) 262
Nausea subjects affected / exposed occurrences (all)	248 / 460 (53.91%) 589	142 / 441 (32.20%) 312	94 / 187 (50.27%) 246
Oral mucositis subjects affected / exposed occurrences (all)	52 / 460 (11.30%) 74	23 / 441 (5.22%) 35	21 / 187 (11.23%) 33
Proctitis subjects affected / exposed occurrences (all)	48 / 460 (10.43%) 65	54 / 441 (12.24%) 99	3 / 187 (1.60%) 4
Rectal bleeding subjects affected / exposed occurrences (all)	98 / 460 (21.30%) 150	94 / 441 (21.32%) 172	2 / 187 (1.07%) 6
Rectal mucositis subjects affected / exposed occurrences (all)	46 / 460 (10.00%) 74	56 / 441 (12.70%) 125	5 / 187 (2.67%) 5
Rectal pain subjects affected / exposed occurrences (all)	110 / 460 (23.91%) 178	140 / 441 (31.75%) 347	22 / 187 (11.76%) 45
Vomiting subjects affected / exposed occurrences (all)	100 / 460 (21.74%) 162	40 / 441 (9.07%) 55	39 / 187 (20.86%) 53
Skin and subcutaneous tissue disorders			

Alopecia subjects affected / exposed occurrences (all)	9 / 460 (1.96%) 30	6 / 441 (1.36%) 8	3 / 187 (1.60%) 3
Hand-foot syndrome subjects affected / exposed occurrences (all)	142 / 460 (30.87%) 299	82 / 441 (18.59%) 146	72 / 187 (38.50%) 200
Radiation dermatitis subjects affected / exposed occurrences (all)	26 / 460 (5.65%) 33	126 / 441 (28.57%) 277	1 / 187 (0.53%) 1
Rash maculopapular subjects affected / exposed occurrences (all)	18 / 460 (3.91%) 23	18 / 441 (4.08%) 27	5 / 187 (2.67%) 5
Renal and urinary disorders Cystitis subjects affected / exposed occurrences (all)	39 / 460 (8.48%) 56	97 / 441 (22.00%) 232	9 / 187 (4.81%) 13
Metabolism and nutrition disorders Weight loss subjects affected / exposed occurrences (all)	81 / 460 (17.61%) 142	49 / 441 (11.11%) 69	22 / 187 (11.76%) 31

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 March 2016	In protocol version 3.0, 3-year disease free survival (DFS) was the primary endpoint. But DFS is not a suitable outcome measure in a neo-adjuvant setting where all patients experience disease at time of randomisation. Some of the patients will never become free of disease. For this reason the protocol was amended. A new primary endpoint was formulated in protocol version 3.1: Time to Disease related Treatment Failure (tDrTF).
04 September 2019	<p>After a median follow-up of more than 3 years, the number of events is much lower than anticipated and the required number (n=452) would never be reached. Reasons for the lower number of events are: change of the endpoint in amendment 3.1 (e.g. death due to other reasons is no event, new primary other tumor is no event), maximum duration of follow-up of 5 year (statistical programs assume endless follow-up) and perhaps better overall outcome of patients. Therefore, the hypothesis is changed from 50% 40% Disease related Treatment Failures into 30 22.5% DrTF events. These numbers correspond to 280 required events.</p> <p>Additional data-collection for recurrence and survival at 7.5 and 10 years</p>

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/42556586>

<http://www.ncbi.nlm.nih.gov/pubmed/41020329>

<http://www.ncbi.nlm.nih.gov/pubmed/40354950>

<http://www.ncbi.nlm.nih.gov/pubmed/40183423>

<http://www.ncbi.nlm.nih.gov/pubmed/40276906>

<http://www.ncbi.nlm.nih.gov/pubmed/39522647>

<http://www.ncbi.nlm.nih.gov/pubmed/38636289>

<http://www.ncbi.nlm.nih.gov/pubmed/37889954>

<http://www.ncbi.nlm.nih.gov/pubmed/38192084>

<http://www.ncbi.nlm.nih.gov/pubmed/38001376>

<http://www.ncbi.nlm.nih.gov/pubmed/37713932>

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<http://www.ncbi.nlm.nih.gov/pubmed/33301740>
<http://www.ncbi.nlm.nih.gov/pubmed/32240909>
<http://www.ncbi.nlm.nih.gov/pubmed/23742033>
<http://www.ncbi.nlm.nih.gov/pubmed/42455037>