Clinical trial results:
Neoadjuvant degarelix +/- apalutamide (ARN-509) followed by radical prostatectomy for intermediate and high-risk prostate cancer: a randomized, placebo-controlled trial.

Summary

EudraCT number	2016-002854-19
Trial protocol	BE
Global end of trial date	22 July 2024

Results information

Result version number	v1 (current)
This version publication date	03 January 2025
First version publication date	03 January 2025

Trial information

Trial identification

Sponsor protocol code	S58827

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	ClinicalTrial.gov: NCT03080116

Notes:

Sponsors

Sponsor organisation name	UZ Leuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Clinical Trial Center (CTC), UZ Leuven, ctc@uzleuven.be
Scientific contact	Clinical Trial Center (CTC), UZ Leuven, ctc@uzleuven.be

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	06 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the difference in treatment antitumor effect between the treatment arms by measuring pathological tumor volume following radical prostatectomy.

Protection of trial subjects:

Patients were seen on regular visits for safety follow-up including adverse events.
No pain or distress was expected.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2017
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	Belgium: 89
Worldwide total number of subjects	89
EEA total number of subjects	89

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)	32
From 65 to 84 years	57
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible patients had unfavorable intermediate risk (defined as two or more of the following risk factors: bISUP 2-3, PSA 10–20 ng/ml and/or cT2b [MRI]) or high-risk PCa (bISUP 4-5, PSA >20 ng/ml, >= cT2c [MRI], and/or cN1) and were amenable to RP + ePLND.
Exclusion: cM1, ECOG >1, neuroendocrine differentiation, contra-indication for ADT or APA

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	Degarelix + Placebo

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Degarelix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

Degarelix is administered monthly via injections.
The first dose is 240 mg (2x 120 mg).
Afterwards, there are monthly injections of 80 mg. This was performed twice.
The total treatment period is 3 months.

Arm title	Degarelix + Apalutamide

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Degarelix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

Degarelix is administered monthly via injections.
The first dose is 240 mg (2x 120 mg).
Afterwards, there are monthly injections of 80 mg. This was performed twice.
The total treatment period is 3 months.

Investigational medicinal product name	Apalutamide
Investigational medicinal product code	
Other name	ARN-509, Erleada
Pharmaceutical forms	Buccal tablet
Routes of administration	Oral use

Dosage and administration details:

Daily oral intake of 240 mg of apalutamide. This is 4 tablets of 60 mg at the same time.

Number of subjects in period 1	Degarelix + Placebo	Degarelix + Apalutamide
Started	44	45
Completed	44	45

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	89	89	
Age categorical Units: Subjects			
Adults (18-64 years)	32	32	
From 65-84 years	57	57	
Age continuous Units: years			
median	66		
inter-quartile range (Q1-Q3)	61 to 70	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	89	89	

End points

End points reporting groups	
Reporting group title	Degarelix + Placebo
Reporting group description: -	
Reporting group title	Degarelix + Apalutamide
Reporting group description: -	

Primary: Minimal Residual Disease (MRD)	
End point title	Minimal Residual Disease (MRD)
End point description:	
End point type	Primary
End point timeframe:	
Pathology was assessed after surgery.	

End point values	Degarelix + Placebo	Degarelix + Apalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	45		
Units: 2				
No MRD	40	28		
MRD	4	17		

Statistical analyses

Statistical analysis title	Fisher's Exact test
Comparison groups	Degarelix + Placebo v Degarelix + Apalutamide
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Fisher exact

Secondary: pT-stage	
End point title	pT-stage
End point description:	
End point type	Secondary
End point timeframe:	
Assessed at pathology.	

End point values	Degarelix + Placebo	Degarelix + Apalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	45		
Units: 5				
ypT0	0	0		
ypT2	12	23		
ypT3a	17	12		
ypT3b	15	9		
ypT4	0	1		

Statistical analyses

Statistical analysis title	Fisher’s exact test
Comparison groups	Degarelix + Placebo v Degarelix + Apalutamide
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022
Method	Fisher exact

Secondary: PSA nadir of <0.3 ng/ml

End point title	PSA nadir of <0.3 ng/ml
End point description:	
End point type	Secondary
End point timeframe:	
Assessed at the time of surgery.	

End point values	Degarelix + Placebo	Degarelix + Apalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	45		
Units: 2				
PSA nadir <0.3 ng/ml	4	39		
PSA nadir >0.3 ng/ml	40	6		

Statistical analyses

Statistical analysis title	Fisher’s exact test
Comparison groups	Degarelix + Placebo v Degarelix + Apalutamide
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Fisher exact

Secondary: Surgical Margin	
End point title	Surgical Margin
End point description:	
End point type	Secondary
End point timeframe:	
Assessed at surgery.	

End point values	Degarelix + Placebo	Degarelix + Apalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	45		
Units: 2				
Negative	36	37		
Positive	8	8		

Statistical analyses

Statistical analysis title	Fisher’s exact test
Comparison groups	Degarelix + Placebo v Degarelix + Apalutamide
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Fisher exact

Secondary: Lymph node status	
End point title	Lymph node status
End point description:	
End point type	Secondary
End point timeframe:	
Assessed after surgery.	

End point values	Degarelix + Placebo	Degarelix + Apalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	45		
Units: 3				
pN0	37	35		
pN1	7	9		
pNx	0	1		

Statistical analyses

Statistical analysis title	Fisher’s exact test
Comparison groups	Degarelix + Placebo v Degarelix + Apalutamide
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Fisher exact

Secondary: BCR-free survival

End point title	BCR-free survival

End point description:

End point type	Secondary

End point timeframe:

Time between radical prostatectomy and BCR (or until last patients had a minimal follow-up of 3 years).

End point values	Degarelix + Placebo	Degarelix + Apalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	45		
Units: 100	41	31		

Statistical analyses

Statistical analysis title	Log-rank test
Comparison groups	Degarelix + Placebo v Degarelix + Apalutamide

Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3
Method	Logrank

Secondary: Testosterone recovery

End point title	Testosterone recovery

End point description:

End point type	Secondary

End point timeframe:

Radical prostatectomy until testosterone recovery

End point values	Degarelix + Placebo	Degarelix + Apalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	45		
Units: Months				
median (inter-quartile range (Q1-Q3))	6 (5 to 10)	7 (5 to 11.5)		

Statistical analyses

Statistical analysis title	Logrank
Comparison groups	Degarelix + Placebo v Degarelix + Apalutamide
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.15
Method	Logrank

Secondary: Urinary incontinence @3Y

End point title	Urinary incontinence @3Y

End point description:

End point type	Secondary

End point timeframe:

At 3-year post-surgery

End point values	Degarelix + Placebo	Degarelix + Apalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	45		
Units: Urinary Incontinence scale				
arithmetic mean (confidence interval 95%)	4.84 (3.54 to 6.15)	4.58 (3.31 to 5.85)		

Statistical analyses

Statistical analysis title	Mann-Whitney U test
Comparison groups	Degarelix + Placebo v Degarelix + Apalutamide
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.77
Method	Wilcoxon (Mann-Whitney)

Secondary: IIEF5 @3Y

End point title	IIEF5 @3Y
End point description:	
End point type	Secondary
End point timeframe:	
At 3Y post-surgery	

End point values	Degarelix + Placebo	Degarelix + Apalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	45		
Units: IIEF5 score				
arithmetic mean (confidence interval 95%)	6.22 (4.95 to 7.5)	6.31 (5.06 to 7.56)		

Statistical analyses

Statistical analysis title	Mann-Whitney U test
Comparison groups	Degarelix + Placebo v Degarelix + Apalutamide

Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.92
Method	Wilcoxon (Mann-Whitney)

Secondary: Global health QLQ @3Y

End point title	Global health QLQ @3Y

End point description:

End point type	Secondary

End point timeframe:

At 3Y post-surgery

End point values	Degarelix + Placebo	Degarelix + Apalutamide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	45		
Units: QLQ30 Global health score				
arithmetic mean (confidence interval 95%)	75.12 (69.52 to 80.72)	74.81 (69.37 to 80.24)		

Statistical analyses

Statistical analysis title	Mann-Whitney U test
Comparison groups	Degarelix + Placebo v Degarelix + Apalutamide
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.94
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 3-month period prior to RP	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.03
Reporting groups	
Reporting group title	ADT + PLB
Reporting group description: -	
Reporting group title	ADT + APA
Reporting group description: -	

Serious adverse events	ADT + PLB	ADT + APA	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 44 (2.27%)	6 / 45 (13.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Social circumstances			
Insomnia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed	0 / 44 (0.00%)	4 / 45 (8.89%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	ADT + PLB	ADT + APA	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 44 (100.00%)	45 / 45 (100.00%)	
Social circumstances			
Hot flush			
subjects affected / exposed	42 / 44 (95.45%)	43 / 45 (95.56%)	
occurrences (all)	42	43	
Fatigue			
subjects affected / exposed	17 / 44 (38.64%)	17 / 45 (37.78%)	
occurrences (all)	17	17	
Insomnia			
subjects affected / exposed	8 / 44 (18.18%)	9 / 45 (20.00%)	
occurrences (all)	8	9	
Headache			
subjects affected / exposed	4 / 44 (9.09%)	4 / 45 (8.89%)	
occurrences (all)	4	4	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	2 / 44 (4.55%)	5 / 45 (11.11%)	
occurrences (all)	2	5	
Ejaculation disorder			
subjects affected / exposed	2 / 44 (4.55%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Libido decreased			
subjects affected / exposed	1 / 44 (2.27%)	2 / 45 (4.44%)	
occurrences (all)	1	2	
Gynaecomastia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal			

disorders			
Dyspnoea			
subjects affected / exposed	0 / 44 (0.00%)	4 / 45 (8.89%)	
occurrences (all)	0	4	
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 44 (6.82%)	1 / 45 (2.22%)	
occurrences (all)	3	1	
Irritability			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Hypersomnia			
subjects affected / exposed	0 / 44 (0.00%)	2 / 45 (4.44%)	
occurrences (all)	0	2	
Memory impairment			
subjects affected / exposed	3 / 44 (6.82%)	5 / 45 (11.11%)	
occurrences (all)	3	5	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	17 / 44 (38.64%)	16 / 45 (35.56%)	
occurrences (all)	17	16	
Leukopenia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	0 / 44 (0.00%)	2 / 45 (4.44%)	
occurrences (all)	0	2	
Epistaxis			
subjects affected / exposed	0 / 44 (0.00%)	5 / 45 (11.11%)	
occurrences (all)	0	5	
Ear and labyrinth disorders			
Dizziness			

subjects affected / exposed	2 / 44 (4.55%)	3 / 45 (6.67%)	
occurrences (all)	2	3	
Eye disorders			
Blurred vision			
subjects affected / exposed	1 / 44 (2.27%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Conjunctivitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	8 / 44 (18.18%)	8 / 45 (17.78%)	
occurrences (all)	8	8	
Diarrhea			
subjects affected / exposed	3 / 44 (6.82%)	3 / 45 (6.67%)	
occurrences (all)	3	3	
Obstipation			
subjects affected / exposed	2 / 44 (4.55%)	2 / 45 (4.44%)	
occurrences (all)	2	2	
Flatulency			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	1 / 44 (2.27%)	6 / 45 (13.33%)	
occurrences (all)	1	6	
Nausea			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Loss of appetite			
subjects affected / exposed	1 / 44 (2.27%)	3 / 45 (6.67%)	
occurrences (all)	1	3	
Increased appetite			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Bloating			

subjects affected / exposed	1 / 44 (2.27%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Reflux			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
ALT increase			
subjects affected / exposed	8 / 44 (18.18%)	10 / 45 (22.22%)	
occurrences (all)	8	10	
AST increase			
subjects affected / exposed	6 / 44 (13.64%)	8 / 45 (17.78%)	
occurrences (all)	6	8	
Bilirubin increase			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	8 / 44 (18.18%)	8 / 45 (17.78%)	
occurrences (all)	8	8	
Rash			
subjects affected / exposed	6 / 44 (13.64%)	14 / 45 (31.11%)	
occurrences (all)	6	14	
Pruritus			
subjects affected / exposed	4 / 44 (9.09%)	8 / 45 (17.78%)	
occurrences (all)	4	8	
Nail discolouration			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Peri-orbital edema			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Edema hands			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Renal and urinary disorders			

Urinary frequency			
subjects affected / exposed	5 / 44 (11.36%)	2 / 45 (4.44%)	
occurrences (all)	5	2	
Urinary Urgency			
subjects affected / exposed	1 / 44 (2.27%)	3 / 45 (6.67%)	
occurrences (all)	1	3	
Urinary mictalgia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Urinary nycturia			
subjects affected / exposed	4 / 44 (9.09%)	8 / 45 (17.78%)	
occurrences (all)	4	8	
Musculoskeletal and connective tissue disorders			
Musculoskeletal disorder			
subjects affected / exposed	6 / 44 (13.64%)	5 / 45 (11.11%)	
occurrences (all)	6	5	
Chest pain			
subjects affected / exposed	1 / 44 (2.27%)	1 / 45 (2.22%)	
occurrences (all)	1	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.

See publication.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36167599

http://www.ncbi.nlm.nih.gov/pubmed/29606109