



Clinical trial results:

Targeted drug intervention to inhibit cancer progression in men on active surveillance for prostate cancer. Therapeutics in Active Prostate cancer Surveillance (TAPS01)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-001700-29 |
| Trial protocol | GB |
| Global end of trial date | 25 July 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 31 July 2020 |
| First version publication date | 31 July 2020 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | TAPS01 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03365297 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge |
| Sponsor organisation address | Box 277, Addenbrooke's Hospital, Hills Road, Cambridge, United Kingdom, CB2 0QQ |
| Public contact | Carrie Bayliss, CCTU, +44 1223 596474, cctu@addenbrookes.nhs.uk |
| Scientific contact | Carrie Bayliss, CCTU, +44 1223 596474, cctu@addenbrookes.nhs.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 | 26 March 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 25 July 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 July 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to test if short-term use of apalutamide can reduce image defined tumour volumes in men with prostate cancer and a detectable lesion on multi-parametric MRI (mpMRI) who are being managed by Active Surveillance (AS).

Protection of trial subjects:

Drug compliance monitoring throughout treatment (self-administered therapy).

Permitted dose reductions and omissions based on presence of drug-related toxicities.

safety review every 15 days throughout treatment, using CTCAE v4.03.

Laboratory investigations to detect adverse blood results at baseline, every 30 days through treatment, and at follow up.

Trial Steering Committee safety review of trial subjects.

Quality of life assessments at baseline, every 30 days through treatment, and at follow up.

Background therapy:

N/A

Evidence for comparator:

N/A

| | |
|---|--------------|
| Actual start date of recruitment | 05 June 2018 |
| 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 | United Kingdom: 11 |
| Worldwide total number of subjects | 11 |
| EEA total number of subjects | 11 |

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) | 2 |
| From 65 to 84 years | 9 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

First patient first visit: 15 Jun 2018; Last Patient last visit: 25 Jul 2019. 11 patients were enrolled in total in the UK (England), of which 9 were evaluable (target: at least 8 evaluable patients and up to 10) and 2 were non-evaluable. Evaluability was as per defined in the protocol. 1 patient did not complete treatment and 1 did not start.

Pre-assignment

Screening details:

A total of 31 patients were screened according to the eligibility criteria defined in the protocol, of which 11 were enrolled into the trial. Out of the 20 patients not enrolled, 4 patients were deemed non-eligible and 16 did not enrol into the study due to a variety of reasons (personal, health, IMP concerns, no reason given and lost contact)

Period 1

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

Arms

| | |
|--|--------------|
| Arm title | Apalutamide |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Apalutamide |
| Investigational medicinal product code | ARN509 |
| Other name | Erleada |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Patients were administered 240 mg (four 60 mg tablets) of apalutamide orally, once daily, for 90 consecutive days. Tablets to be swallowed whole with or without food.

Protocol allowed for one dose reduction per subject to 120 mg daily. The dose was not permitted to be re-escalated back to 240 mg daily.

A temporary break in apalutamide was acceptable in the event of a non-drug related AE. Patients were allowed to re-start apalutamide, at the previous dose, if the reason for the break had resolved within 30 days and patients did not meet the withdrawal criteria, as per defined in the study protocol. Dose modifications were also allowed for patients presenting drug-related adverse reactions, as per defined in the trial protocol (including but not limited to rash and pruritus with no rash).

| Number of subjects in period 1 ^[1] | Apalutamide |
|---|-------------|
| Started | 10 |
| Completed | 9 |
| Not completed | 1 |
| Adverse event, non-fatal | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The baseline period accounts for extra participants that were consented but did not meet the eligibility criteria to be formally enrolled in the trial.

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Overall Period |
|-----------------------|----------------|

Reporting group description: -

| Reporting group values | Overall Period | Total | |
|---------------------------|----------------|-------|--|
| Number of subjects | 10 | 10 | |
| Age categorical | | | |
| Units: Subjects | | | |
| 60-69 years | 4 | 4 | |
| 70-74 years | 5 | 5 | |
| 75 plus years | 1 | 1 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 70 | | |
| standard deviation | ± 5 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 10 | 10 | |
| ECOG | | | |
| Units: Subjects | | | |
| No | 0 | 0 | |
| Yes | 10 | 10 | |
| ECOG performance status | | | |
| Units: Subjects | | | |
| Zero | 10 | 10 | |
| One | 0 | 0 | |
| Two | 0 | 0 | |
| T stage | | | |
| Units: Subjects | | | |
| T1 | 0 | 0 | |
| T2 | 10 | 10 | |
| Prostate cancer histology | | | |
| Units: Subjects | | | |
| Adenocarcinoma | 10 | 10 | |
| Other | 0 | 0 | |
| Gleason Grade: Grade X: | | | |
| Units: Subjects | | | |
| Gleason sum 6 | 10 | 10 | |
| Gleason =7 | 0 | 0 | |
| Gleason >=8 | 0 | 0 | |
| Gleason Grade: Grade Y | | | |
| Units: Subjects | | | |
| Gleason sum 6 | 10 | 10 | |
| Gleason =7 | 0 | 0 | |
| Gleason >=8 | 0 | 0 | |

| | | | |
|--|---------------|---|--|
| Height (cm): Units: cm arithmetic mean standard deviation | 173 ± 6 | - | |
| Weight Units: Kg arithmetic mean standard deviation | 78.4 ± 8.6 | - | |
| Pulse Units: beats/min arithmetic mean standard deviation | 71 ± 15 | - | |
| Systolic blood pressure Units: mmHg arithmetic mean standard deviation | 139 ± 12 | - | |
| Diastolic blood pressure Units: mmHg arithmetic mean standard deviation | 80 ± 6 | - | |
| Temperature Units: Degrees celcius arithmetic mean standard deviation | 36.6 ± 0.3 | - | |

End points

End points reporting groups

| | |
|--------------------------------|-------------|
| Reporting group title | Apalutamide |
| Reporting group description: - | |

Primary: Percentage change in tumour size measured by mpMRI (tumour volume - cm³)

| | |
|-----------------|--|
| End point title | Percentage change in tumour size measured by mpMRI (tumour volume - cm ³) ^[1] |
|-----------------|--|

End point description:

Percentage change in tumour size measured by mpMRI (tumour volume³) or absence of a lesion between baseline and day 90. The percentage of patients achieving tumour downsizing with their 95% confidence interval was estimated using the primary lesion (i.e. the largest lesion if a patient had more than one lesion).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Tumour volume (cm³) change from baseline at day 90.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: It's a single arm study.

| | | | | |
|---|-----------------|--|--|--|
| End point values | Apalutamide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 | | | |
| Units: tumour volume (cm ³) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Percentage change | 51.86 (± 17.1) | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in total tumour volume

| | |
|-----------------|-------------------------------|
| End point title | Change in total tumour volume |
|-----------------|-------------------------------|

End point description:

Percentage change in total tumour size measured by mpMRI (tumour volume³) or absence of a lesion between baseline and day 90.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Percentage change from baseline at day 90

| | | | | |
|--|-----------------|--|--|--|
| End point values | Apalutamide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 | | | |
| Units: total tumour volume - cm ³ | | | | |
| arithmetic mean (standard deviation) | 52.4 (± 17.4) | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in gland volume

| | |
|-----------------|------------------------|
| End point title | Change in gland volume |
|-----------------|------------------------|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Gland volume (cm³) change from baseline at day 90

| | | | | |
|--|-----------------|--|--|--|
| End point values | Apalutamide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 | | | |
| Units: Gland volume in cm ³ | | | | |
| arithmetic mean (standard deviation) | 36.2 (± 8.7) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

AE additional description

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Treatment |
|-----------------------|-----------|

Reporting group description: -

| Serious adverse events | Treatment | | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Investigations | | | |
| Neutrophil Count Decreased | Additional description: Neutrophil Count Decreased | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Treatment | | |
|---|--------------------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 10 (100.00%) | | |
| Vascular disorders | | | |
| Hot flashes | Additional description: Hot flashes | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Hypertension | Additional description: Hypertension | | |
| subjects affected / exposed | 3 / 10 (30.00%) | | |
| occurrences (all) | 4 | | |

| | | | |
|--|--|--|--|
| General disorders and administration site conditions | | | |
| Fatigue | Additional description: Fatigue | | |
| subjects affected / exposed | 4 / 10 (40.00%) | | |
| occurrences (all) | 6 | | |
| Flu like symptoms | Additional description: Flu like symptoms | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Nipple tenderness | Additional description: Nipple tenderness | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Non-cardiac chest pain | Additional description: Non-cardiac chest pain | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Pain | Additional description: Pain | | |
| subjects affected / exposed | 2 / 10 (20.00%) | | |
| occurrences (all) | 2 | | |
| Reproductive system and breast disorders | | | |
| Breast pain | Additional description: Breast pain | | |
| subjects affected / exposed | 4 / 10 (40.00%) | | |
| occurrences (all) | 4 | | |
| Erectile Dysfunction | Additional description: Erectile Dysfunction | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Laryngeal inflammation | Additional description: Laryngeal inflammation | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Anxiety | Additional description: Anxiety | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Libido decreased | Additional description: Libido decreased | | |
| subjects affected / exposed | 2 / 10 (20.00%) | | |
| occurrences (all) | 2 | | |
| Investigations | | | |

| | | | |
|--|--|--|--|
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | Additional description: Alanine aminotransferase increased | | |
| | 6 / 10 (60.00%) 6 | | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | Additional description: Aspartate aminotransferase increased | | |
| | 3 / 10 (30.00%) 3 | | |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | Additional description: Lymphocyte count decreased | | |
| | 4 / 10 (40.00%) 8 | | |
| Serum amylase increased subjects affected / exposed occurrences (all) | Additional description: Serum amylase increased | | |
| | 1 / 10 (10.00%) 1 | | |
| White Blood Cell Decreased subjects affected / exposed occurrences (all) | Additional description: White Blood Cell Decreased | | |
| | 1 / 10 (10.00%) 1 | | |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | Additional description: Dizziness | | |
| | 1 / 10 (10.00%) 1 | | |
| Dysgeusia subjects affected / exposed occurrences (all) | Additional description: Dysgeusia | | |
| | 1 / 10 (10.00%) 1 | | |
| Headache subjects affected / exposed occurrences (all) | Additional description: Headache | | |
| | 1 / 10 (10.00%) 1 | | |
| Blood and lymphatic system disorders | | | |
| Anemia subjects affected / exposed occurrences (all) | Additional description: Anemia | | |
| | 2 / 10 (20.00%) 2 | | |
| Ear and labyrinth disorders | | | |
| Vertigo subjects affected / exposed occurrences (all) | Additional description: Vertigo | | |
| | 1 / 10 (10.00%) 2 | | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | Additional description: Abdominal Pain | | |
| | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Dyspepsia | Additional description: Dyspepsia | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Vomiting | Additional description: Vomiting | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | Additional description: Pruritus | | |
| subjects affected / exposed | 3 / 10 (30.00%) | | |
| occurrences (all) | 3 | | |
| Rash maculo-papular | Additional description: Rash maculo-papular | | |
| subjects affected / exposed | 2 / 10 (20.00%) | | |
| occurrences (all) | 5 | | |
| Renal and urinary disorders | | | |
| Cystitis Noninfective (Nocturia) | Additional description: Cystitis Noninfective (Nocturia) | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Cystitis noninfective (Dysuria) | Additional description: Cystitis noninfective (Dysuria) | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Proteinuria | Additional description: Proteinuria | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Renal and urinary disorders - Other, | Additional description: Renal and urinary disorders - Other, | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Urinary Frequency | Additional description: Urinary Frequency | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 2 | | |
| Urinary Tract Pain | Additional description: Urinary Tract Pain | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Endocrine disorders | | | |

| | | | |
|--|--|--|--|
| Hyperthyroidism subjects affected / exposed occurrences (all) | Additional description: Hyperthyroidism | | |
| | 1 / 10 (10.00%) 1 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | Additional description: Arthralgia | | |
| | 1 / 10 (10.00%) 1 | | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) | Additional description: Upper respiratory tract infection | | |
| | 1 / 10 (10.00%) 1 | | |
| Metabolism and nutrition disorders Hypertriglyceridemia subjects affected / exposed occurrences (all) | Additional description: Hypertriglyceridemia | | |
| | 8 / 10 (80.00%) 10 | | |
| Metabolism and nutrition disorders subjects affected / exposed occurrences (all) | Additional description: Metabolism and nutrition disorders | | |
| | 1 / 10 (10.00%) 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

None reported