



Clinical trial results:

Multicenter, randomized, double-blind, placebo-controlled, phase III clinical trial to investigate the efficacy and safety of Dronabinol in the Improvement of ChemOthErapy-induced and tumor-Related symptoms in patients with locally advanced or metastatic pancreatic cancer during first-line chemotherapy (DIsCOvER)

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2019-000616-28 |
| Trial protocol | AT DE |
| Global end of trial date | 25 September 2024 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 |
| This version publication date | 23 October 2025 |
| First version publication date | 23 October 2025 |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | AGMT_DISCOVER |
|-----------------------|---------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03984214 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | AGMT |
| Sponsor organisation address | Gentzgasse 60/21, Vienna, Austria, 1180 |
| Public contact | Daniela Wolkersdorfer, AGMT gGmbH, +43 6626404411, d.wolkersdorfer@agmt.at |
| Scientific contact | Daniela Wolkersdorfer, AGMT gGmbH, +43 6626404411, d.wolkersdorfer@agmt.at |

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 | 21 July 2025 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 September 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary endpoint variable is the standardized area under the curve of the EORTC QLQ-C30 symptom summary score over the on-treatment period (scores at visits 1-9).

Protection of trial subjects:

All patients were closely monitored to be able to react immediately to any side effects. Rather mild to moderate side effects were expected from dronabinol therapy and a slow dose increase and a final tapering phase was chosen to allow a safe and manageable treatment. In case of the occurrence of intolerable side effects (e.g. intense fatigue, dizziness, vertigo etc.) the increase of doses could have been interrupted, delayed or the dose may have been decreased in steps until the side effects were on an acceptable level. The patient were advised to continue with the last well tolerated number of droplets of the substance after the recovery.

Supportive therapy for oncological patients was prescribed according to current version of national treatment guidelines.

Dronabinol is not recommended for use in pregnant women and women of child-bearing potential (WOCBP) not using contraception. The inclusion of women of childbearing potential had to follow specific recommendations for contraception and pregnancy testing. Women were advised not to become pregnant during and at least 4 weeks after end of the treatment with dronabinol. Male participants were not required to use birth control during exposure to dronabinol.

Background therapy:

Firstline chemotherapy with FOLFIRINOX or gemcitabine + Abraxane(R) according to investigator's decision.

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 16 December 2019 |
| 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 | Austria: 95 |
| Country: Number of subjects enrolled | Germany: 14 |
| Worldwide total number of subjects | 109 |
| EEA total number of subjects | 109 |

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) | 44 |
| From 65 to 84 years | 65 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Between 16-Dec-2019 and 31-Mar-2024, 109 patients were enrolled in 11 sites in Austria and Germany. 104 patients were exposed to the IMP dronabinol/placebo.

Pre-assignment

Screening details:

Due to slow recruitment initially planned sample size of 140 patients was downsized to 104 patients and the primary endpoint was adopted accordingly. In total 841 patients were screened, while 732 patients did not meet the criteria for inclusion.

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, Monitor |

Blinding implementation details:

After successful screening the site team registers the patient in the online "Randomizer". The patient was automatically assigned to either Dronabinol or Placebo arm by the allocation of the blinded treatment code. Only the treatment code was visible for site team, monitor or sponsor in the "Randomizer". Each IMP vial (dronabinol or placebo) was labeled with a unique number and could be unblinded with a unblinding list via the sponsor of the study.

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Dronabinol |

Arm description:

Titration period 4 weeks; maintenance 12 weeks; tapering period 2 weeks

| | |
|--|----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dronabinol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |

Dosage and administration details:

Dronabinol 2.5% oral solution, individual daily dose according to tolerability from 2.5 mg up to 30 mg THC per day

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Titration period 4 weeks; maintenance 12 weeks; tapering period 2 weeks

| | |
|--|----------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo oral solution, individual daily dose according to tolerability from 2.5 mg up to 30 mg THC placebo per day

| Number of subjects in period 1 | Dronabinol | Placebo |
|--|------------|---------|
| Started | 54 | 55 |
| Study treatment started | 51 | 53 |
| Primary endpoint | 32 | 38 |
| Completed | 20 | 30 |
| Not completed | 34 | 25 |
| Adverse reaction IMP | 3 | 3 |
| Screening failure | 2 | 2 |
| Physician decision | 2 | 2 |
| Patient decision | 21 | 15 |
| Patient not compliant | 1 | - |
| Death due to underlying disease | - | 1 |
| Worsening general condition | - | 1 |
| Serious adverse event | 3 | - |
| Death due to panc. cancer prior to treatment start | 1 | - |
| Exclusion criterion revealed after randomization | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|---|------------|
| Reporting group title | Dronabinol |
| Reporting group description: | |
| Titration period 4 weeks; maintenance 12 weeks; tapering period 2 weeks | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Titration period 4 weeks; maintenance 12 weeks; tapering period 2 weeks | |

| Reporting group values | Dronabinol | Placebo | Total |
|--|------------|----------|-------|
| Number of subjects | 54 | 55 | 109 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: years | | | |
| median | 67 | 68 | |
| full range (min-max) | 49 to 83 | 46 to 82 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 29 | 28 | 57 |
| Male | 25 | 27 | 52 |
| Therapy | | | |
| Background therapy | | | |
| Units: Subjects | | | |
| FOLFIRINOX | 12 | 14 | 26 |
| Gemcitabine+Abraxane | 42 | 41 | 83 |
| Tumor stage | | | |
| Units: Subjects | | | |
| Locally advanced | 8 | 6 | 14 |
| Metastatic | 46 | 49 | 95 |

End points

End points reporting groups

| | |
|--|----------------|
| Reporting group title | Dronabinol |
| Reporting group description: | |
| Titration period 4 weeks; maintenance 12 weeks; tapering period 2 weeks | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Titration period 4 weeks; maintenance 12 weeks; tapering period 2 weeks | |
| Subject analysis set title | Dronabinol PRO |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| The patient-reported outcome (PRO) population includes all randomized patients who received at least one dose of IMP/placebo and additionally had to complete at least 3 EORTC questionnaires including visit 1. Patients are analyzed according to the treatment group to which they were randomized. | |
| Subject analysis set title | Placebo PRO |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| The patient-reported outcome (PRO) population includes all randomized patients who received at least one dose of IMP/placebo and additionally had to complete at least 3 EORTC questionnaires including visit 1. Patients are analyzed according to the treatment group to which they were randomized. | |

Primary: Standardized area under the curve (sAUC)

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|--|--|
| End point title | Standardized area under the curve (sAUC) |
| End point description: | |
| The primary endpoint is the standardized area under the curve (sAUC) of the EORTC QLQ-C30 Summary Score over the ontreatment period (visit 1-9). | |
| End point type | Primary |
| End point timeframe: | |
| Visit 1 to visit 9 (max. 18 weeks) | |

| End point values | Dronabinol PRO | Placebo PRO | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 32 | 38 | | |
| Units: none | | | | |
| arithmetic mean (standard deviation) | | | | |
| sAUC(V1-V9) | 69.1 (± 15.5) | 73.6 (± 13.5) | | |

Statistical analyses

| | |
|--|------------------------------|
| Statistical analysis title | Primary endpoint |
| Statistical analysis description: | |
| Linear regression (least square mean difference) | |
| Comparison groups | Dronabinol PRO v Placebo PRO |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 70 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1963 |
| Method | Regression, Linear |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -4.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.4 |
| upper limit | 2.4 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.465 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All patients having received at least one dose of the study medication were followed for adverse events for at least 28 days after discontinuing study treatment or completion of study treatment.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 27.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Dronabinol exposed |
|-----------------------|--------------------|

Reporting group description:

Safety analysis set - the safety analysis population is used for all safety analyses and is defined to include all randomized patients with at least one intake/administration of study treatment.

| | |
|-----------------------|-----------------|
| Reporting group title | Placebo exposed |
|-----------------------|-----------------|

Reporting group description:

Safety analysis set - the safety analysis population will be used for all safety analyses and is defined to include all randomized patients with at least one intake/administration of study treatment.

| Serious adverse events | Dronabinol exposed | Placebo exposed | |
|--|--------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 30 / 51 (58.82%) | 25 / 53 (47.17%) | |
| number of deaths (all causes) | 34 | 43 | |
| number of deaths resulting from adverse events | 4 | 0 | |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 5 / 53 (9.43%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Drug eruption | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood glucose decreased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 3 / 53 (5.66%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Overdose | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wrong product administered | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 3 / 51 (5.88%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Dementia Alzheimer's type | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |

| | | | |
|---|----------------|----------------|--|
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ascites | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Flatulence | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 3 / 51 (5.88%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obstruction gastric | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subileus | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholestasis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chromoblastomycosis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 5 / 53 (9.43%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis bacterial | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 53 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 53 (3.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 53 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 3.5 %

| Non-serious adverse events | Dronabinol exposed | Placebo exposed | |
|---|--------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 49 / 51 (96.08%) | 50 / 53 (94.34%) | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 1 / 53 (1.89%) | |
| occurrences (all) | 3 | 1 | |
| Hypotension | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 4 / 53 (7.55%) | |
| occurrences (all) | 5 | 4 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 2 / 53 (3.77%) | |
| occurrences (all) | 3 | 2 | |
| Chills | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 4 / 53 (7.55%) | |
| occurrences (all) | 0 | 4 | |
| Fatigue | | | |
| subjects affected / exposed | 26 / 51 (50.98%) | 22 / 53 (41.51%) | |
| occurrences (all) | 45 | 29 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 3 / 53 (5.66%) | |
| occurrences (all) | 2 | 4 | |
| Mucosal inflammation | | | |

| | | | |
|---|-----------------------------------|-----------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 51 (5.88%)</p> <p>3</p> | <p>2 / 53 (3.77%)</p> <p>4</p> | |
| <p>Oedema</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 51 (3.92%)</p> <p>2</p> | <p>2 / 53 (3.77%)</p> <p>2</p> | |
| <p>Oedema peripheral</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 51 (7.84%)</p> <p>4</p> | <p>21 / 53 (39.62%)</p> <p>25</p> | |
| <p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>12 / 51 (23.53%)</p> <p>13</p> | <p>7 / 53 (13.21%)</p> <p>11</p> | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>6 / 51 (11.76%)</p> <p>6</p> | <p>4 / 53 (7.55%)</p> <p>5</p> | |
| <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>7 / 51 (13.73%)</p> <p>7</p> | <p>5 / 53 (9.43%)</p> <p>5</p> | |
| <p>Epistaxis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 51 (5.88%)</p> <p>3</p> | <p>5 / 53 (9.43%)</p> <p>6</p> | |
| <p>Psychiatric disorders</p> <p>Aversion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 51 (3.92%)</p> <p>2</p> | <p>1 / 53 (1.89%)</p> <p>1</p> | |
| <p>Depression</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 51 (1.96%)</p> <p>1</p> | <p>3 / 53 (5.66%)</p> <p>3</p> | |
| <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 51 (3.92%)</p> <p>2</p> | <p>3 / 53 (5.66%)</p> <p>4</p> | |
| <p>Sleep disorder</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 51 (3.92%)</p> <p>2</p> | <p>4 / 53 (7.55%)</p> <p>4</p> | |
| Investigations | | | |

| | | | |
|---|---------------------|----------------------|--|
| Blood glucose abnormal subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 1 / 53 (1.89%) 1 | |
| Body temperature increased subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 1 / 53 (1.89%) 1 | |
| C-reactive protein increased subjects affected / exposed occurrences (all) | 5 / 51 (9.80%) 6 | 3 / 53 (5.66%) 4 | |
| Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 3 / 53 (5.66%) 3 | |
| Weight decreased subjects affected / exposed occurrences (all) | 4 / 51 (7.84%) 5 | 8 / 53 (15.09%) 9 | |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 2 | 3 / 53 (5.66%) 3 | |
| Blood glucose decreased subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 2 / 53 (3.77%) 2 | |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 4 / 51 (7.84%) 8 | 4 / 53 (7.55%) 5 | |
| Dysgeusia subjects affected / exposed occurrences (all) | 3 / 51 (5.88%) 3 | 4 / 53 (7.55%) 4 | |
| Headache subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 2 / 53 (3.77%) 3 | |
| Neuropathy peripheral subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 3 / 53 (5.66%) 5 | |
| Paraesthesia | | | |

| | | | |
|--------------------------------------|------------------|------------------|--|
| subjects affected / exposed | 2 / 51 (3.92%) | 7 / 53 (13.21%) | |
| occurrences (all) | 4 | 7 | |
| Polyneuropathy | | | |
| subjects affected / exposed | 19 / 51 (37.25%) | 20 / 53 (37.74%) | |
| occurrences (all) | 25 | 25 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 14 / 53 (26.42%) | |
| occurrences (all) | 7 | 20 | |
| Neutropenia | | | |
| subjects affected / exposed | 12 / 51 (23.53%) | 9 / 53 (16.98%) | |
| occurrences (all) | 15 | 10 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 12 / 51 (23.53%) | 5 / 53 (9.43%) | |
| occurrences (all) | 15 | 6 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 9 / 51 (17.65%) | 9 / 53 (16.98%) | |
| occurrences (all) | 9 | 9 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 3 / 53 (5.66%) | |
| occurrences (all) | 0 | 3 | |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 53 (3.77%) | |
| occurrences (all) | 2 | 2 | |
| Abdominal pain | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 11 / 53 (20.75%) | |
| occurrences (all) | 5 | 12 | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 3 / 53 (5.66%) | |
| occurrences (all) | 0 | 3 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 3 / 53 (5.66%) | |
| occurrences (all) | 3 | 3 | |
| Abnormal faeces | | | |

| | | | |
|--|------------------|------------------|--|
| subjects affected / exposed | 0 / 51 (0.00%) | 3 / 53 (5.66%) | |
| occurrences (all) | 0 | 3 | |
| Ascites | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 4 / 53 (7.55%) | |
| occurrences (all) | 5 | 7 | |
| Constipation | | | |
| subjects affected / exposed | 16 / 51 (31.37%) | 8 / 53 (15.09%) | |
| occurrences (all) | 18 | 10 | |
| Diarrhoea | | | |
| subjects affected / exposed | 20 / 51 (39.22%) | 25 / 53 (47.17%) | |
| occurrences (all) | 22 | 35 | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 53 (3.77%) | |
| occurrences (all) | 1 | 2 | |
| Nausea | | | |
| subjects affected / exposed | 23 / 51 (45.10%) | 33 / 53 (62.26%) | |
| occurrences (all) | 31 | 40 | |
| Vomiting | | | |
| subjects affected / exposed | 6 / 51 (11.76%) | 12 / 53 (22.64%) | |
| occurrences (all) | 9 | 18 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 6 / 53 (11.32%) | |
| occurrences (all) | 5 | 6 | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 53 (3.77%) | |
| occurrences (all) | 1 | 2 | |
| Erythema | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 2 / 53 (3.77%) | |
| occurrences (all) | 3 | 2 | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 2 / 53 (3.77%) | |
| occurrences (all) | 3 | 4 | |
| Night sweats | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 4 / 53 (7.55%) | |
| occurrences (all) | 2 | 6 | |

| | | | |
|---|-----------------|----------------|--|
| Pruritus | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 3 / 53 (5.66%) | |
| occurrences (all) | 0 | 3 | |
| Rash | | | |
| subjects affected / exposed | 6 / 51 (11.76%) | 4 / 53 (7.55%) | |
| occurrences (all) | 8 | 4 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 4 / 53 (7.55%) | |
| occurrences (all) | 2 | 4 | |
| Back pain | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 2 / 53 (3.77%) | |
| occurrences (all) | 5 | 2 | |
| Bone pain | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 1 / 53 (1.89%) | |
| occurrences (all) | 3 | 1 | |
| Muscular weakness | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 4 / 53 (7.55%) | |
| occurrences (all) | 3 | 4 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 3 / 53 (5.66%) | |
| occurrences (all) | 1 | 4 | |
| Spinal pain | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 3 / 53 (5.66%) | |
| occurrences (all) | 1 | 4 | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 5 / 53 (9.43%) | |
| occurrences (all) | 2 | 5 | |
| Erysipelas | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 53 (1.89%) | |
| occurrences (all) | 2 | 1 | |
| Infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 53 (3.77%) | |
| occurrences (all) | 5 | 2 | |
| Nasopharyngitis | | | |

| | | | |
|---|-----------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 2 / 53 (3.77%) 2 | |
| Pneumonia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 2 / 53 (3.77%) 2 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 5 / 53 (9.43%) 6 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 9 / 51 (17.65%) 10 | 12 / 53 (22.64%) 17 | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 8 / 51 (15.69%) 9 | 7 / 53 (13.21%) 11 | |
| Hyponatraemia subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 1 / 53 (1.89%) 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 14 February 2021 | Due to slow recruitment and higher drop-out rate, sample size was downsized. According to guidelines for assessing quality of life in EORTC clinical trials a difference of 10-20% is regarded a moderate change. Thus, it was decided that a sample size of 104 patients instead of 140 patients is large enough to show a difference in the summary score of 20% between the treatment groups with a power of 80%. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported