



Clinical trial results:

A randomized, open-label, phase 2 study of the IDO inhibitor INCB024360 versus tamoxifen for subjects with biochemical-recurrent-only epithelial ovarian cancer, primary peritoneal carcinoma, or fallopian tube cancer following complete remission with first-line chemotherapy

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2012-001472-10 |
| Trial protocol | GB |
| Global end of trial date | 23 October 2014 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 05 January 2017 |
| First version publication date | 05 January 2017 |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | INCB24360-210 |
|-----------------------|---------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01685255 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Incyte Corporation |
| Sponsor organisation address | 1801 Augustine Cut-Off, Wilmington, United States, 19803 |
| Public contact | Incyte Corporation Call Centre, Incyte Corporation, +44 (0)330 100 3677, globalmedinfo@incyte.com |
| Scientific contact | Incyte Corporation Call Centre, Incyte Corporation, +44 (0)330 100 3677, globalmedinfo@incyte.com |

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 | 23 October 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-----------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 23 October 2014 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To determine efficacy based on investigator-assessed progression-free survival (PFS) of INCB024360 versus tamoxifen among subjects with CA 125 elevation following complete remission with first-line chemotherapy for advanced disease.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Conference on Harmonisation Guidelines.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 07 March 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | United Kingdom: 7 |
| Country: Number of subjects enrolled | Australia: 2 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | Russian Federation: 16 |
| Country: Number of subjects enrolled | Ukraine: 3 |
| Country: Number of subjects enrolled | United States: 12 |
| Worldwide total number of subjects | 42 |
| EEA total number of subjects | 7 |

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) | 27 |
| From 65 to 84 years | 15 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 52 study centers, including 5 in Australia, 4 in Canada, 12 in Great Britain, 9 in Russia, 5 in Ukraine, and 17 in the United States.

Pre-assignment

Screening details:

Subjects were randomized (1:1) to 1 of 2 treatment groups, INCB024360 or tamoxifen, and stratified based on the number of months since prior first-line chemotherapy to the time of their first CA 125 elevation (3 to < 12 months or \geq 12 months).

Period 1

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

Arms

| | |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | INCB024360 600 mg BID |

Arm description:

Subjects randomized to Arm A (INCB024360) will take INCB024360 tablets at a dose of 600 mg BID, beginning on Day 1.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | INCB024360 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablets were taken approximately 12 hours apart, and at least 2 hours after a meal. Subjects were to abstain from food for 1 hour after administration.

| | |
|------------------|---------------------|
| Arm title | Tamoxifen 20 mg BID |
|------------------|---------------------|

Arm description:

Subjects randomized to Arm B (tamoxifen) will take tamoxifen tablets at a dose of 20 mg BID, beginning on Day 1.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | tamoxifen |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects randomized to Arm B (tamoxifen) will take tamoxifen tablets at a dose of 20 mg BID, beginning on Day 1.

| Number of subjects in period 1 | INCB024360 600 mg BID | Tamoxifen 20 mg BID |
|--|-----------------------|---------------------|
| Started | 22 | 20 |
| Completed | 0 | 0 |
| Not completed | 22 | 20 |
| Disease progression | 10 | 11 |
| Adverse event, non-fatal | 6 | - |
| Termination of the clinical study by the sponsor | 6 | 9 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | INCB024360 600 mg BID |
|-----------------------|-----------------------|

Reporting group description:

Subjects randomized to Arm A (INCB024360) will take INCB024360 tablets at a dose of 600 mg BID, beginning on Day 1.

| | |
|-----------------------|---------------------|
| Reporting group title | Tamoxifen 20 mg BID |
|-----------------------|---------------------|

Reporting group description:

Subjects randomized to Arm B (tamoxifen) will take tamoxifen tablets at a dose of 20 mg BID, beginning on Day 1.

| Reporting group values | INCB024360 600 mg BID | Tamoxifen 20 mg BID | Total |
|------------------------|-----------------------|---------------------|-------|
| Number of subjects | 22 | 20 | 42 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 14 | 13 | 27 |
| From 65-84 years | 8 | 7 | 15 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 60.8 | 60.4 | |
| standard deviation | ± 12.44 | ± 9.91 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 22 | 20 | 42 |
| Male | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|---|-----------------------|
| Reporting group title | INCB024360 600 mg BID |
| Reporting group description: Subjects randomized to Arm A (INCB024360) will take INCB024360 tablets at a dose of 600 mg BID, beginning on Day 1. | |
| Reporting group title | Tamoxifen 20 mg BID |
| Reporting group description: Subjects randomized to Arm B (tamoxifen) will take tamoxifen tablets at a dose of 20 mg BID, beginning on Day 1. | |

Primary: Progression free survival (PFS)

| | |
|---|---------------------------------|
| End point title | Progression free survival (PFS) |
| End point description: Progression-free survival, using RECIST criteria, was defined as the length of time between randomization and death or investigator-assessed progressive disease, whichever occurred earlier as determined by the investigator. | |
| End point type | Primary |
| End point timeframe: PFS is defined as the number of days from randomization to the earlier of death or disease progression for up to 36 months. | |

| End point values | INCB024360 600 mg BID | Tamoxifen 20 mg BID | | |
|----------------------------------|--------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 ^[1] | 20 ^[2] | | |
| Units: months | | | | |
| median (confidence interval 95%) | 3.75 (2.01 to 7.43) | 5.56 (1.68 to 9.24) | | |

Notes:

[1] - Modified Intent-to-Treat Subjects

[2] - Modified Intent-to-Treat Subjects

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Summary of Progression-Free Survival |
| Comparison groups | Tamoxifen 20 mg BID v INCB024360 600 mg BID |
| Number of subjects included in analysis | 42 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.544 |
| Method | Stratified Log-rank Test |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.344 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.576 |
| upper limit | 3.136 |

Secondary: Percentage of participants with at least a 50% reduction in Cancer Antigen (CA) 125 levels

| | |
|-----------------|--|
| End point title | Percentage of participants with at least a 50% reduction in Cancer Antigen (CA) 125 levels |
|-----------------|--|

End point description:

A CA 125 response was defined as at least a 50% reduction in CA 125 levels from a pretreatment sample and that was maintained for at least 28 days.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

CA 125 response rate defined as at least 50% reduction on study as compared to pretreatment sample; pre-treatment sample must be at least 2x ULN and response must be sustained for at least 28 days.

| End point values | INCB024360 600 mg BID | Tamoxifen 20 mg BID | | |
|-----------------------------------|--------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 ^[3] | 19 ^[4] | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Responders confirmed | 5 | 15.8 | | |
| Response but unconfirmed | 10 | 10.5 | | |
| Non-Responders | 85 | 73.7 | | |

Notes:

[3] - mITT Subjects

[4] - mITT Subjects

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Cancer Antigen (CA) 125 response rate |
| Comparison groups | INCB024360 600 mg BID v Tamoxifen 20 mg BID |
| Number of subjects included in analysis | 41 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.3416 |
| Method | Fisher exact |

Secondary: Overall survival

| | |
|-----------------|------------------|
| End point title | Overall survival |
|-----------------|------------------|

End point description:

Overall survival is reported here as the number of deaths from randomization until the data cut-off.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Overall survival followed every 12 weeks until last date known to be alive, until subjects withdraw consent or up to 36 months, whichever is longest. | |

| End point values | INCB024360 600 mg BID | Tamoxifen 20 mg BID | | |
|-----------------------------|--------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 ^[5] | 20 ^[6] | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Death events | 1 | 0 | | |
| Censored events | 21 | 20 | | |

Notes:

[5] - Modified Intent-to-Treat

[6] - Modified Intent-to-Treat

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected during study drug treatment period and within 60 days of the last dose of study drug.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 15.0 |

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | INCB024360 600 mg BID |
|-----------------------|-----------------------|

Reporting group description:

Subjects randomized to Arm A (INCB024360) will take INCB024360 tablets at a dose of 600 mg BID, beginning on Day 1.

| | |
|-----------------------|---------------------|
| Reporting group title | Tamoxifen 20 mg BID |
|-----------------------|---------------------|

Reporting group description:

Subjects randomized to Arm B (tamoxifen) will take tamoxifen tablets at a dose of 20 mg BID, beginning on Day 1.

| Serious adverse events | INCB024360 600 mg BID | Tamoxifen 20 mg BID | |
|---|-----------------------|---------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 1 / 20 (5.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | 0 / 20 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ascites | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | 1 / 20 (5.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | INCB024360 600 mg BID | Tamoxifen 20 mg BID | |
|---|-----------------------|---------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 17 / 22 (77.27%) | 15 / 20 (75.00%) | |
| Cardiac disorders | | | |
| Dyspnea | | | |
| subjects affected / exposed | 2 / 22 (9.09%) | 3 / 20 (15.00%) | |
| occurrences (all) | 3 | 3 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 22 (13.64%) | 3 / 20 (15.00%) | |
| occurrences (all) | 3 | 3 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 8 / 22 (36.36%) | 8 / 20 (40.00%) | |
| occurrences (all) | 9 | 8 | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 22 (9.09%) | 0 / 20 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Influenza-like illness | | | |
| subjects affected / exposed | 2 / 22 (9.09%) | 1 / 20 (5.00%) | |
| occurrences (all) | 2 | 1 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 6 / 22 (27.27%) | 6 / 20 (30.00%) | |
| occurrences (all) | 7 | 8 | |
| Abdominal distension | | | |
| subjects affected / exposed | 4 / 22 (18.18%) | 3 / 20 (15.00%) | |
| occurrences (all) | 4 | 3 | |
| Constipation | | | |
| subjects affected / exposed | 4 / 22 (18.18%) | 2 / 20 (10.00%) | |
| occurrences (all) | 6 | 4 | |
| Vomiting | | | |
| subjects affected / exposed | 4 / 22 (18.18%) | 3 / 20 (15.00%) | |
| occurrences (all) | 4 | 3 | |
| Abdominal pain | | | |

| | | | |
|---|-----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 3 / 22 (13.64%) 4 | 0 / 20 (0.00%) 0 | |
| Dyspepsia subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 2 | 0 / 20 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 2 | 0 / 20 (0.00%) 0 | |
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 2 | 0 / 20 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 5 / 22 (22.73%) 11 | 0 / 20 (0.00%) 0 | |
| Pruritus subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 3 | 0 / 20 (0.00%) 0 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 3 / 22 (13.64%) 3 | 1 / 20 (5.00%) 2 | |
| Anxiety subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 3 | 0 / 20 (0.00%) 0 | |
| Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 3 | 0 / 20 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 3 / 22 (13.64%) 3 | 2 / 20 (10.00%) 2 | |
| Muscle spasms | | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 2 | 1 / 20 (5.00%) 1 | |
| Muscle twitching subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 2 | 0 / 20 (0.00%) 0 | |
| Myalgia subjects affected / exposed occurrences (all) | 2 / 22 (9.09%) 2 | 1 / 20 (5.00%) 1 | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 3 / 22 (13.64%) 3 | 4 / 20 (20.00%) 5 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 18 June 2012 | Amendment 1 was issued in the UK before any subjects were enrolled in the study. The purpose of this amendment was to address revisions requested by the Medicines and Healthcare products Regulatory Agency regarding inclusion of assessments for serotonin syndrome. |
| 24 July 2012 | Amendment 1 version 1.1 was issued to all study sites, except those in the UK, before any subjects were enrolled in the study. The primary purpose of Amendment 1 version 1.1 was to revise the dose of INCB024360 from 400 mg to 600 mg BID, provide an updated summary of the ongoing clinical experience to justify the change in dose, and provide clarifications regarding eligibility, dose interruption and duration, PK sampling, and the survival follow-up schedule. |
| 07 September 2012 | The primary purpose of Amendment 1 version 1.2 was the same as Amendment 1 version 1.1 (to bring the sites in the UK up to date with the change in the dose of INCB024360 from 400 mg BID to 600 mg BID). All of the clinically important changes noted for Amendment 1 version 1.1 were noted for Amendment 1 version 1.2. Additional changes that were UK-specific to Amendment 1 version 1.2 included: <ul style="list-style-type: none">• The definition of CA 125 elevation was revised to require screening CA 125 values of $\geq 2 \times \text{ULN}$ on 2 occasions at least 1 week apart.• The protocol was revised to include the current CA 125 definitions agreed by GCIG in November 2005. |
| 04 February 2013 | Amendment 2 The primary purpose of this amendment is to revise eligibility criteria, add guidance for missed dosing, allow subjects more than one opportunity for screening, update regions for pharmacodynamic sample collection, and incorporate UK-specific Protocol requirements into the Protocol for all participating sites. |
| 31 October 2013 | Amendment 3 The primary purpose of this amendment is to allow subjects with Stage IC and II ovarian cancer to participate in this study and to include the option for subjects to have prescreening CA 125 monitoring. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|-----------------|---|--------------|
| 23 October 2014 | Study was terminated by the sponsor for lack of evidence of superiority and slow study accrual. | - |

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No significant safety issues were identified during the Phase 1 or Phase 2 monotherapy programs. Development for this indication was terminated by the sponsor for lack of evidence of superiority and slow study accrual.

Notes: