



## 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
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#### 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
<b>Arm title</b>	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.

<b>Arm title</b>	Tamoxifen 20 mg BID
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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.

<b>Number of subjects in period 1</b>	<b>INCB024360 600 mg BID</b>	<b>Tamoxifen 20 mg BID</b>
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
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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
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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 <sup>[1]</sup>	20 <sup>[2]</sup>		
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
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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
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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 <sup>[3]</sup>	19 <sup>[4]</sup>		
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
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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 <sup>[5]</sup>	20 <sup>[6]</sup>		
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
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

### Reporting groups

Reporting group title	INCB024360 600 mg BID
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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
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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 %

<b>Non-serious adverse events</b>	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"><li>• The definition of CA 125 elevation was revised to require screening CA 125 values of <math>\geq 2 \times \text{ULN}</math> on 2 occasions at least 1 week apart.</li><li>• The protocol was revised to include the current CA 125 definitions agreed by GCIG in November 2005.</li></ul>
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: