



## Clinical trial results:

**A follow-up study exploring number of cycles for weekly treatment with Paclical® in patients with metastatic breast cancer, previously treated in study OAS-11PAC-W**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2011-002456-14 |
| Trial protocol           | LV             |
| Global end of trial date | 25 April 2014  |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 14 May 2017  |
| First version publication date | 14 May 2017  |

### Trial information

#### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | OAS-11PAC-W-fu |
|-----------------------|----------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Oasmia Pharmaceutical AB   |
| Sponsor organisation address | Vallongatan 1, Uppsala, Sweden, SE-752 28  |
| Public contact               | Nina Heldring, Oasmia Pharmaceutical AB, +46 18 50 54 40, nina.heldring@oasmia.com |
| Scientific contact           | Nina Heldring, Oasmia Pharmaceutical AB, +46 18 50 54 40, nina.heldring@oasmia.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:

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**Results analysis stage**

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|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 20 November 2015 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 25 April 2014    |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 25 April 2014    |
| Was the trial ended prematurely?                     | Yes              |

Notes:

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**General information about the trial**

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Main objective of the trial:

To explore the number of cycles for weekly treatment with Paclical®

Protection of trial subjects:

Laboratory measurements were assessed to monitor safety of patients (haematology and clinical chemistry). Blood pressure, pulse rate and body temperature were measured prior and during the infusion of IMP. Patients were withdrawn if medically necessary according to investigator.

Background therapy: -

Evidence for comparator:

N.A.

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 28 January 2013 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Russian Federation: 22 |
| Country: Number of subjects enrolled | Latvia: 7              |
| Worldwide total number of subjects   | 29                     |
| EEA total number of subjects         | 7                      |

Notes:

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**Subjects enrolled per age group**

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|   |    |
|---|----|
| 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)                      | 22 |
| From 65 to 84 years                       | 7  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Female patients with histologically confirmed metastatic breast cancer completing the study OAS-11PAC-W were eligible. Patients with progressive disease or unacceptable toxicity at last visit of OAS-11PAC-W or with dose-reduction during OAS-11PAC-W were excluded. Out of 31 screened patients, 22 were included and 2 were screening failures.

### Period 1

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

### Arms

|  |                                  |
|--|----------------------------------|
| Are arms mutually exclusive?           | Yes                              |
| <b>Arm title</b>                       | Paclical 100 mg/m2               |
| Arm description: -                     |                                  |
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Paclical                         |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

|  |                                  |
|--|----------------------------------|
| <b>Arm title</b>                       | Paclical 110 mg/m2               |
| Arm description: -                     |                                  |
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Paclical                         |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

|  |                                  |
|--|----------------------------------|
| <b>Arm title</b>                       | Paclical 120 mg/m2               |
| Arm description: -                     |                                  |
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Paclical                         |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m<sup>2</sup>). The treatment was administered over approximately 30 minutes once weekly.

|  |                                  |
|--|----------------------------------|
| <b>Arm title</b>                       | Paclical 130 mg/m <sup>2</sup>   |
| Arm description: -                     |                                  |
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Paclical                         |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m<sup>2</sup>). The treatment was administered over approximately 30 minutes once weekly.

|  |                                  |
|--|----------------------------------|
| <b>Arm title</b>                       | Paclical 140 mg/m <sup>2</sup>   |
| Arm description: -                     |                                  |
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Paclical                         |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m<sup>2</sup>). The treatment was administered over approximately 30 minutes once weekly.

|  |                                  |
|--|----------------------------------|
| <b>Arm title</b>                       | Paclical 150 mg/m <sup>2</sup>   |
| Arm description: -                     |                                  |
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Paclical                         |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m<sup>2</sup>). The treatment was administered over approximately 30 minutes once weekly.

|  |                                  |
|--|----------------------------------|
| <b>Arm title</b>                       | Paclical 160 mg/m <sup>2</sup>   |
| Arm description: -                     |                                  |
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Paclical                         |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m<sup>2</sup>). The

treatment was administered over approximately 30 minutes once weekly.

|  |                                  |
|--|----------------------------------|
| <b>Arm title</b>   | Paclical 170 mg/m2               |
| Arm description: -   |                                  |
| Arm type   | Experimental                     |
| Investigational medicinal product name   | Paclical                         |
| Investigational medicinal product code   |                                  |
| Other name   |                                  |
| Pharmaceutical forms   | Powder for solution for infusion |
| Routes of administration   | Intravenous use                  |
| Dosage and administration details:   |                                  |
| Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly. |                                  |
| <b>Arm title</b>   | Paclical 180 mg/m2               |
| Arm description: -   |                                  |
| Arm type   | Experimental                     |
| Investigational medicinal product name   | Paclical                         |
| Investigational medicinal product code   |                                  |
| Other name   |                                  |
| Pharmaceutical forms   | Powder for solution for infusion |
| Routes of administration   | Intravenous use                  |
| Dosage and administration details:   |                                  |
| Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly. |                                  |
| <b>Arm title</b>   | Paclical 190 mg/m2               |
| Arm description: -   |                                  |
| Arm type   | Experimental                     |
| Investigational medicinal product name   | Paclical                         |
| Investigational medicinal product code   |                                  |
| Other name   |                                  |
| Pharmaceutical forms   | Powder for solution for infusion |
| Routes of administration   | Intravenous use                  |
| Dosage and administration details:   |                                  |
| Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly. |                                  |
| <b>Arm title</b>   | Paclical 210 mg/m2               |
| Arm description: -   |                                  |
| Arm type   | Experimental                     |
| Investigational medicinal product name   | Paclical                         |
| Investigational medicinal product code   |                                  |
| Other name   |                                  |
| Pharmaceutical forms   | Powder for solution for infusion |
| Routes of administration   | Intravenous use                  |
| Dosage and administration details:   |                                  |
| Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly. |                                  |

treatment was administered over approximately 30 minutes once weekly.

|  |                                  |
|--|----------------------------------|
| <b>Arm title</b>                       | Paclical 230 mg/m2               |
| Arm description: -                     |                                  |
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Paclical                         |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

|  |                                  |
|--|----------------------------------|
| <b>Arm title</b>                       | Paclical 240 mg/m2               |
| Arm description: -                     |                                  |
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Paclical                         |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer's solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

| <b>Number of subjects in period 1</b>             | Paclical 100 mg/m2 | Paclical 110 mg/m2 | Paclical 120 mg/m2 |
|---|--------------------|--------------------|--------------------|
| Started   | 3                  | 3                  | 2                  |
| Completed   | 2                  | 1                  | 1                  |
| Not completed                                     | 1                  | 2                  | 1                  |
| Adverse event, serious fatal                      | -                  | 1                  | -                  |
| Physician decision                                | -                  | 1                  | -                  |
| Consent withdrawn by subject                      | -                  | -                  | -                  |
| Protocol violation, fulfilling exclusion criteria | -                  | -                  | -                  |
| Adverse event, non-fatal                          | 1                  | -                  | 1                  |

| <b>Number of subjects in period 1</b> | Paclical 130 mg/m2 | Paclical 140 mg/m2 | Paclical 150 mg/m2 |
|---------------------------------------|--------------------|--------------------|--------------------|
| Started                               | 3                  | 2                  | 2                  |
| Completed                             | 2                  | 0                  | 0                  |
| Not completed                         | 1                  | 2                  | 2                  |
| Adverse event, serious fatal          | -                  | -                  | -                  |

|   |   |   |   |
|---|---|---|---|
| Physician decision                                | - | - | - |
| Consent withdrawn by subject                      | 1 | - | 1 |
| Protocol violation, fulfilling exclusion criteria | - | 1 | - |
| Adverse event, non-fatal                          | - | 1 | 1 |

| <b>Number of subjects in period 1</b>             | Paclical 160 mg/m2 | Paclical 170 mg/m2 | Paclical 180 mg/m2 |
|---|--------------------|--------------------|--------------------|
| Started   | 3                  | 3                  | 2                  |
| Completed   | 1                  | 0                  | 0                  |
| Not completed                                     | 2                  | 3                  | 2                  |
| Adverse event, serious fatal                      | 1                  | -                  | -                  |
| Physician decision                                | -                  | -                  | -                  |
| Consent withdrawn by subject                      | 1                  | 3                  | 1                  |
| Protocol violation, fulfilling exclusion criteria | -                  | -                  | -                  |
| Adverse event, non-fatal                          | -                  | -                  | 1                  |

| <b>Number of subjects in period 1</b>             | Paclical 190 mg/m2 | Paclical 210 mg/m2 | Paclical 230 mg/m2 |
|---|--------------------|--------------------|--------------------|
| Started   | 1                  | 1                  | 2                  |
| Completed   | 0                  | 0                  | 0                  |
| Not completed                                     | 1                  | 1                  | 2                  |
| Adverse event, serious fatal                      | -                  | -                  | -                  |
| Physician decision                                | -                  | -                  | 1                  |
| Consent withdrawn by subject                      | -                  | 1                  | 1                  |
| Protocol violation, fulfilling exclusion criteria | -                  | -                  | -                  |
| Adverse event, non-fatal                          | 1                  | -                  | -                  |

| <b>Number of subjects in period 1</b>             | Paclical 240 mg/m2 |
|---|--------------------|
| Started   | 2                  |
| Completed   | 0                  |
| Not completed                                     | 2                  |
| Adverse event, serious fatal                      | -                  |
| Physician decision                                | 1                  |
| Consent withdrawn by subject                      | 1                  |
| Protocol violation, fulfilling exclusion criteria | -                  |
| Adverse event, non-fatal                          | -                  |

## Baseline characteristics

### Reporting groups

|                                |               |
|--------------------------------|---------------|
| Reporting group title          | Overall trial |
| Reporting group description: - |               |

| Reporting group values                                       | Overall trial | Total |  |
|--|---------------|-------|--|
| Number of subjects   | 29            | 29    |  |
| Age categorical  |               |       |  |
| Units: Subjects  |               |       |  |
| Adults (18-64 years)   | 22            | 22    |  |
| From 65-84 years   | 7             | 7     |  |
| Age continuous   |               |       |  |
| Units: years   |               |       |  |
| arithmetic mean  | 54.1          |       |  |
| standard deviation   | ± 10.6        | -     |  |
| Gender categorical   |               |       |  |
| Units: Subjects  |               |       |  |
| Female   | 29            | 29    |  |
| Male   | 0             | 0     |  |
| Child bearing potential                                      |               |       |  |
| Units: Subjects  |               |       |  |
| Yes  | 9             | 9     |  |
| No   | 20            | 20    |  |
| HER2 assessment  |               |       |  |
| Units: Subjects  |               |       |  |
| HER2 positive  | 8             | 8     |  |
| HER2 negative  | 21            | 21    |  |
| ECOG status  |               |       |  |
| ECOG = Eastern Cooperative Oncology Group performance status |               |       |  |
| Units: Subjects  |               |       |  |
| Status 0   | 26            | 26    |  |
| Status 1   | 3             | 3     |  |
| Status 2   | 0             | 0     |  |
| Status 3   | 0             | 0     |  |
| Status 4   | 0             | 0     |  |
| Status 5   | 0             | 0     |  |



## End points

### End points reporting groups

|   |                         |
|---|-------------------------|
| Reporting group title   | Paclical 100 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 110 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 120 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 130 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 140 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 150 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 160 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 170 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 180 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 190 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 210 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 230 mg/m2      |
| Reporting group description: -  |                         |
| Reporting group title   | Paclical 240 mg/m2      |
| Reporting group description: -  |                         |
| Subject analysis set title  | Entire study population |
| Subject analysis set type   | Intention-to-treat      |
| Subject analysis set description:   |                         |
| All included patients, irrespective of treatment dose   |                         |
| Subject analysis set title  | Completers              |
| Subject analysis set type   | Per protocol            |
| Subject analysis set description:   |                         |
| This data set includes the patients reaching an endpoint (i.e. complete response, disease progression, unacceptable toxicity). The 22 withdrawn patients are not included in this data set. |                         |

### Primary: Number of cycles for weekly treatment of Paclical

|  |   |
|--|---|
| End point title  | Number of cycles for weekly treatment of Paclical <sup>[1][2]</sup> |
| End point description:   |   |
| The number of treatment cycles for Paclical weekly treatment could not be obtained.                                  |   |
| End point type   | Primary   |
| End point timeframe:   |   |
| Assessment was made until a reason for completion (complete response, unacceptable toxicity or progressive disease). |   |
| 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: Given the exploratory nature (i.e. to determine the number of cycles for weekly administration), no statistical hypothesis testing was performed.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Due to withdrawal primary endpoint data were not available for all treatment arms.

| End point values              | Paclical 100 mg/m2 | Paclical 110 mg/m2 | Paclical 120 mg/m2 | Paclical 130 mg/m2 |
|-------------------------------|--------------------|--------------------|--------------------|--------------------|
| Subject group type            | Reporting group    | Reporting group    | Reporting group    | Reporting group    |
| Number of subjects analysed   | 2                  | 1                  | 1                  | 2                  |
| Units: Treatment cycles       |                    |                    |                    |                    |
| median (full range (min-max)) | 8 (8 to 8)         | 10 (10 to 10)      | 13 (13 to 13)      | 14 (8 to 20)       |

| End point values              | Paclical 160 mg/m2 |  |  |  |
|-------------------------------|--------------------|--|--|--|
| Subject group type            | Reporting group    |  |  |  |
| Number of subjects analysed   | 1                  |  |  |  |
| Units: Treatment cycles       |                    |  |  |  |
| median (full range (min-max)) | 15 (15 to 15)      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Reason for completion due to endpoint

|                 |                                       |
|-----------------|---------------------------------------|
| End point title | Reason for completion due to endpoint |
|-----------------|---------------------------------------|

End point description:

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

End point timeframe:

From start of study (5th treatment cycle) until the patient discontinued the study due to any of the three pre-defined endpoints.

| End point values            | Completers           |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 7                    |  |  |  |
| Units: Patients             |                      |  |  |  |
| Complete response           | 1                    |  |  |  |
| Disease progression         | 2                    |  |  |  |
| Unacceptable toxicity       | 4                    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Tumour response**

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|                 |                 |
|-----------------|-----------------|
| End point title | Tumour response |
|-----------------|-----------------|

End point description:

Tumour response was assessed by CT evaluated according to RECIST 1.1 at the radiology department of the sites. The patient's last assessment is presented. The reason is that a limited number of patients were treated more than 8 cycles and that not all patients had an end of treatment assessment due to short interval between last scheduled CT and study withdrawal.

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

End point timeframe:

Tumour response was assessed at entry into the present follow-up study (treatment cycle 5) and every 8th week and at end of study.

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| End point values            | Entire study population |  |  |  |
|-----------------------------|-------------------------|--|--|--|
| Subject group type          | Subject analysis set    |  |  |  |
| Number of subjects analysed | 29                      |  |  |  |
| Units: Patients             |                         |  |  |  |
| Complete response           | 1                       |  |  |  |
| Partial response            | 9                       |  |  |  |
| Stable disease              | 16                      |  |  |  |
| Progressive disease         | 3                       |  |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first treatment administration in the follow-up study (cycle 5) until one week (7-9 days) after the last treatment or withdrawal.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 15.1 |
|--------------------|------|

### Reporting groups

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Entire study population |
|-----------------------|-------------------------|

Reporting group description:

All patients included in the study (one patient never received any treatment in this follow-up study but is still included in this safety data set).

| Serious adverse events  | Entire study population  |  |  |
|---|--|--|--|
| Total subjects affected by serious adverse events                   |  |  |  |
| subjects affected / exposed   | 3 / 28 (10.71%)  |  |  |
| number of deaths (all causes)                                       | 2  |  |  |
| number of deaths resulting from adverse events                      |  |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |
| Neoplasm progression  | Additional description: Relation to treatment assessed by investigator |  |  |
| alternative assessment type: Non-systematic                         |  |  |  |
| subjects affected / exposed   | 1 / 28 (3.57%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1  |  |  |
| deaths causally related to treatment / all                          | 0 / 1  |  |  |
| Cardiac disorders   |  |  |  |
| Cardiopulmonary failure   | Additional description: Relation to treatment assessed by investigator |  |  |
| alternative assessment type: Non-systematic                         |  |  |  |
| subjects affected / exposed   | 1 / 28 (3.57%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1  |  |  |
| deaths causally related to treatment / all                          | 0 / 1  |  |  |
| General disorders and administration site conditions                |  |  |  |
| Administration site abscess   | Additional description: Relation to treatment assessed by investigator |  |  |
| alternative assessment type: Non-systematic                         |  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 28 (3.57%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                     | Entire study population |  |  |
|---|-------------------------|--|--|
| Total subjects affected by non-serious adverse events |                         |  |  |
| subjects affected / exposed                           | 19 / 28 (67.86%)        |  |  |
| Vascular disorders                                    |                         |  |  |
| Phlebitis   |                         |  |  |
| subjects affected / exposed                           | 1 / 28 (3.57%)          |  |  |
| occurrences (all)                                     | 1                       |  |  |
| Nervous system disorders                              |                         |  |  |
| Hypoaesthesia   |                         |  |  |
| subjects affected / exposed                           | 4 / 28 (14.29%)         |  |  |
| occurrences (all)                                     | 4                       |  |  |
| Neuropathy peripheral                                 |                         |  |  |
| subjects affected / exposed                           | 2 / 28 (7.14%)          |  |  |
| occurrences (all)                                     | 2                       |  |  |
| Paraesthesia  |                         |  |  |
| subjects affected / exposed                           | 1 / 28 (3.57%)          |  |  |
| occurrences (all)                                     | 1                       |  |  |
| Peripheral sensory neuropathy                         |                         |  |  |
| subjects affected / exposed                           | 1 / 28 (3.57%)          |  |  |
| occurrences (all)                                     | 1                       |  |  |
| Blood and lymphatic system disorders                  |                         |  |  |
| Anaemia   |                         |  |  |
| subjects affected / exposed                           | 2 / 28 (7.14%)          |  |  |
| occurrences (all)                                     | 2                       |  |  |
| Leukocytosis  |                         |  |  |
| subjects affected / exposed                           | 1 / 28 (3.57%)          |  |  |
| occurrences (all)                                     | 1                       |  |  |
| Leukopenia  |                         |  |  |
| subjects affected / exposed                           | 4 / 28 (14.29%)         |  |  |
| occurrences (all)                                     | 4                       |  |  |

|  |                      |  |  |
|--|----------------------|--|--|
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)  | 5 / 28 (17.86%)<br>6 |  |  |
| Neutrophilia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 28 (3.57%)<br>1  |  |  |
| General disorders and administration site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all) | 7 / 28 (25.00%)<br>8 |  |  |
| Infusion site phlebitis<br>subjects affected / exposed<br>occurrences (all)  | 5 / 28 (17.86%)<br>6 |  |  |
| Injection site extravasation<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 28 (3.57%)<br>1  |  |  |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)  | 1 / 28 (3.57%)<br>1  |  |  |
| Spinal pain<br>subjects affected / exposed<br>occurrences (all)  | 1 / 28 (3.57%)<br>1  |  |  |
| Ear and labyrinth disorders<br>Vertigo<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 28 (3.57%)<br>1  |  |  |
| Eye disorders<br>Lacrimation increased<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 28 (3.57%)<br>1  |  |  |
| Visual acuity reduced<br>subjects affected / exposed<br>occurrences (all)  | 1 / 28 (3.57%)<br>1  |  |  |
| Gastrointestinal disorders<br>Stomatitis   |                      |  |  |

|   |  |  |  |
|---|--|--|--|
| subjects affected / exposed<br>occurrences (all)  | 1 / 28 (3.57%)<br>1  |  |  |
| Hepatobiliary disorders<br>Hepatotoxicity<br>subjects affected / exposed<br>occurrences (all)   | 1 / 28 (3.57%)<br>1  |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Epistaxis<br>subjects affected / exposed<br>occurrences (all)<br><br>Pneumothorax<br>subjects affected / exposed<br>occurrences (all)  | 1 / 28 (3.57%)<br>1<br><br>1 / 28 (3.57%)<br>1   |  |  |
| Skin and subcutaneous tissue disorders<br>Nail discolouration<br>subjects affected / exposed<br>occurrences (all)<br><br>Nail disorder<br>subjects affected / exposed<br>occurrences (all)<br><br>Onychoclasia<br>subjects affected / exposed<br>occurrences (all)<br><br>Skin erosion<br>subjects affected / exposed<br>occurrences (all)<br><br>Skin ulcer<br>subjects affected / exposed<br>occurrences (all)<br><br>Onychomadesis<br>subjects affected / exposed<br>occurrences (all) | 2 / 28 (7.14%)<br>2<br><br>1 / 28 (3.57%)<br>1<br><br>1 / 28 (3.57%)<br>1<br><br>1 / 28 (3.57%)<br>1<br><br>1 / 28 (3.57%)<br>1<br><br>1 / 28 (3.57%)<br>1 |  |  |
| Renal and urinary disorders<br>Enuresis<br>subjects affected / exposed<br>occurrences (all)   | 1 / 28 (3.57%)<br>1  |  |  |

|  |                     |  |  |
|--|---------------------|--|--|
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 1 / 28 (3.57%)<br>1 |  |  |
|--|---------------------|--|--|



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date           | Amendment  |
|----------------|--|
| 10 August 2012 | This is a follow-up of a study intended to be a phase I/II (OAS-11PAC-W). When the phase II part of the main study was removed this also warranted changes in the present follow-up study. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

Since no MTD was established in OAS-11PAC-W, patients in the present follow-up were treated with different doses. A high withdrawal rate resulting in a small sample size limits the possibility to draw conclusions regarding number of treatment cycles.

Notes: