



## Clinical trial results:

### Systemic hypotension following intravenous administration of contrast medium during computed tomography.

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2013-002051-15 |
| Trial protocol           | AT             |
| Global end of trial date | 22 July 2015   |

#### Results information

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v1 (current)      |
| This version publication date  | 26 September 2020 |
| First version publication date | 26 September 2020 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | KM-HYPO |
|-----------------------|---------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |                                                                                                                                                                           |
|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Medical University Innsbruck                                                                                                                                              |
| Sponsor organisation address | Christoph-Probst-Platz 1, Innrain 52 A, Innsbruck, Austria, 6020                                                                                                          |
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| Scientific contact           | Priv.Do. Dr. Mag. Gerlig Widmann, Innsbruck Medical University, Department of Radiology, Section of Microinvasive Therapy, +43 (0)51250422761, gerlig.widmann@i-med.ac.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:

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**Results analysis stage**

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|                                                      |              |
|------------------------------------------------------|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 22 July 2015 |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 22 July 2015 |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 22 July 2015 |
| Was the trial ended prematurely?                     | No           |

Notes:

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**General information about the trial**

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Main objective of the trial:

Primary goal of this study is to quantify changes in systolic and diastolic blood pressure, heart rate and pO<sub>2</sub> before and after i.v. administration of either IOCM or LOCM. In particular the occurrence of clinically relevant drops in systolic and diastolic blood pressure after IOCM or LOCM administration is investigated.

Protection of trial subjects:

If sudden undesired clinical relevant events occur during the infusion of the study drug, the infusion should be stopped immediately and the events have to be treated properly. Very rarely, allergic reactions may occur. In case of severe skin rashes, angioedema, and/or bronchospasm, combined with tachycardia and hypotension and unexplained by other causes, infusion will be stopped and treatment will be implemented immediately. If thromboembolism to pulmonary, cerebral, coronary arteries or to other organs is diagnosed (CT scan, ECG, Echocardiography). Individually appropriate treatment will be implemented immediately.

Background therapy:

Basically all patients were hydrated with crystalloid solution at a rate of 3-5 ml/kg body weight (250–500 mL) per hour during general anesthesia.

Administration of vasopressors during the procedure was documented.

All patients received oral premedication with midazolam (Dormicum; Roche Pharmaceuticals) 30 minutes prior to intervention at doses between 3.75 and 7.5 mg.

Evidence for comparator:

LOCM (low-osmolar contrast medium) was reported to significantly decrease average renal blood flow and affect heart rate and left ventricular end-diastolic pressure during coronary ventriculography and angiography. In this trial IOCM (iso-osmolar contrast medium) iodixanol and LOCM iopromide, both FDA approved, were compared to systematically quantify the hemodynamic effects of intravenous CM (contrast medium) application in patients under general anesthesia with continuous invasive blood pressure monitoring.

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment                          | 27 October 2014 |
| 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 | Austria: 40 |
| Worldwide total number of subjects   | 40          |
| EEA total number of subjects         | 40          |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|-------------------------------------------|----|
| 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)                      | 19 |
| From 65 to 84 years                       | 21 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

#### Recruitment details:

Patients having both radiological interventions with CM and continuous blood pressure measurement during general anesthesia were within the sampling frame of our study population. Consequently, we focused on patients with liver tumors undergoing RFA, in whom invasive blood pressure is measured routinely at our institution.

### Pre-assignment

#### Screening details:

During November 18, 2014, and May 5, 2015, 50 patients were consecutively screened for eligibility, 40 of whom (20 LOCM, 20 IOCM) were included in the study. Eight patients were excluded by the exclusion criteria and 2 patients because the procedure could not be performed.

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Treatment period        |
| Is this the baseline period? | Yes                     |
| Allocation method            | Randomised - controlled |
| Blinding used                | Double blind            |
| Roles blinded                | Investigator, Subject   |

#### Blinding implementation details:

The 2 different CMs to which individual patients were assigned were determined with a randomized schedule. Allocation ratio was 1:1. The randomization list was generated independently by the clinical investigator and sent to the staff responsible for labeling the IMPs. The randomization list was kept confidential and consulted only by the principal investigator for assignment on the day of treatment. Patients and anesthesiologists were blinded.

### Arms

|                              |           |
|------------------------------|-----------|
| Are arms mutually exclusive? | Yes       |
| <b>Arm title</b>             | Iopromide |

#### Arm description:

The intervention during which the study data were obtained followed the standard protocol for stereotactic radiofrequency ablation (SRFA). The SRFA procedure is performed in anesthetized patients in whom a CM-enhanced CT scan is required for planning of the ablation, a nonenhanced CT scan is obtained for verification of proper needle placement, and after ablation another CM-enhanced CT scan is performed for final verification of ablation size. LOCM iopromide was used for this procedure.

|                                        |                       |
|----------------------------------------|-----------------------|
| Arm type                               | Active comparator     |
| Investigational medicinal product name | Iopromide             |
| Investigational medicinal product code |                       |
| Other name                             | Ultravist 370 mg I/mL |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous bolus use |

#### Dosage and administration details:

We used LOCM iopromide (Ultravist 370 mg I/mL; Bayer Austria Ges.m.b.H., Vienna, Austria) for contrast enhancement.

CM was administered using an automatic injector at a flow of 3 mL/s via a separate peripheral temporary venous catheter with single access using 80–150 mL (2× bodyweight, minimum 80 mL, maximum 150 mL). For each patient, normal saline solution (NSS) was administered by automatic injector during the nonenhanced CT scan as a placebo control using exactly the same dose and injection rate as the previously given CM.

|                  |           |
|------------------|-----------|
| <b>Arm title</b> | Iodixanol |
|------------------|-----------|

#### Arm description:

The intervention during which the study data were obtained followed the standard protocol for stereotactic radiofrequency ablation (SRFA). The SRFA procedure is performed in anesthetized patients in whom a CM-enhanced CT scan is required for planning of the ablation, a nonenhanced CT scan is obtained for verification of proper needle placement, and after ablation another CM-enhanced CT scan is performed for final verification of ablation size. IOCM iodixanol was used for this procedure.

|                                        |                       |
|----------------------------------------|-----------------------|
| Arm type                               | Active comparator     |
| Investigational medicinal product name | Iodixanol             |
| Investigational medicinal product code |                       |
| Other name                             | Visipaque 320 mg I/mL |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous bolus use |

**Dosage and administration details:**

We used IOCM iodixanol (Visipaque 320 mg I/mL; GE Healthcare Handels GmbH, Vienna, Austria) for contrast enhancement.

CM was administered using an automatic injector at a flow of 3 mL/s via a separate peripheral temporary venous catheter with single access using 80–150 mL (2× bodyweight, minimum 80 mL, maximum 150 mL). For each patient, normal saline solution (NSS) was administered by automatic injector during the nonenhanced CT scan as a placebo control using exactly the same dose and injection rate as the previously given CM.

| <b>Number of subjects in period 1</b> | Iopromide | Iodixanol |
|---------------------------------------|-----------|-----------|
| Started                               | 20        | 20        |
| Completed                             | 20        | 20        |

**Period 2**

|                              |                         |
|------------------------------|-------------------------|
| Period 2 title               | Follow-up period        |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Double blind            |
| Roles blinded                | Subject, Investigator   |

**Blinding implementation details:**

The 2 different CMs to which individual patients were assigned were determined with a randomized schedule. Allocation ratio was 1:1. The randomization list was generated independently by the clinical investigator and sent to the staff responsible for labeling the IMPs. The randomization list was kept confidential and consulted only by the principal investigator for assignment on the day of treatment. Patients and anesthesiologists were blinded.

**Arms**

|                              |           |
|------------------------------|-----------|
| Are arms mutually exclusive? | Yes       |
| <b>Arm title</b>             | Iopromide |

**Arm description:**

Follow-up ended after completion of the study 30 days after inclusion into the study. In this time SAEs were evaluated.

|                                        |                       |
|----------------------------------------|-----------------------|
| Arm type                               | Active comparator     |
| Investigational medicinal product name | Iopromide             |
| Investigational medicinal product code |                       |
| Other name                             | Ultravist 370 mg I/mL |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous bolus use |

**Dosage and administration details:**

We used LOCM iopromide (Ultravist 370 mg I/mL; Bayer Austria Ges.m.b.H., Vienna, Austria) for contrast enhancement.

CM was administered using an automatic injector at a flow of 3 mL/s via a separate peripheral temporary venous catheter with single access using 80–150 mL (2× bodyweight, minimum 80 mL, maximum 150 mL). For each patient, normal saline solution (NSS) was administered by automatic injector during the nonenhanced CT scan as a placebo control using exactly the same dose and injection rate as the previously given CM.

|                  |           |
|------------------|-----------|
| <b>Arm title</b> | Iodixanol |
|------------------|-----------|

**Arm description:**

Follow-up ended after completion of the study 30 days after inclusion into the study. In this time SAEs were evaluated.

|                                        |                       |
|----------------------------------------|-----------------------|
| Arm type                               | Active comparator     |
| Investigational medicinal product name | Iodixanol             |
| Investigational medicinal product code |                       |
| Other name                             | Visipaque 320 mg I/mL |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous bolus use |

**Dosage and administration details:**

We used IOCM iodixanol (Visipaque 320 mg I/mL; GE Healthcare Handels GmbH, Vienna, Austria) for contrast enhancement.

CM was administered using an automatic injector at a flow of 3 mL/s via a separate peripheral temporary venous catheter with single access using 80–150 mL (2× bodyweight, minimum 80 mL, maximum 150 mL). For each patient, normal saline solution (NSS) was administered by automatic injector during the nonenhanced CT scan as a placebo control using exactly the same dose and injection rate as the previously given CM.

| <b>Number of subjects in period 2</b> | Iopromide | Iodixanol |
|---------------------------------------|-----------|-----------|
| Started                               | 20        | 20        |
| Completed                             | 20        | 20        |

## Baseline characteristics

### Reporting groups

|                       |           |
|-----------------------|-----------|
| Reporting group title | Iopromide |
|-----------------------|-----------|

Reporting group description:

The intervention during which the study data were obtained followed the standard protocol for stereotactic radiofrequency ablation (SRFA). The SRFA procedure is performed in anesthetized patients in whom a CM-enhanced CT scan is required for planning of the ablation, a nonenhanced CT scan is obtained for verification of proper needle placement, and after ablation another CM-enhanced CT scan is performed for final verification of ablation size. LOCM iopromide was used for this procedure.

|                       |           |
|-----------------------|-----------|
| Reporting group title | Iodixanol |
|-----------------------|-----------|

Reporting group description:

The intervention during which the study data were obtained followed the standard protocol for stereotactic radiofrequency ablation (SRFA). The SRFA procedure is performed in anesthetized patients in whom a CM-enhanced CT scan is required for planning of the ablation, a nonenhanced CT scan is obtained for verification of proper needle placement, and after ablation another CM-enhanced CT scan is performed for final verification of ablation size. IOCM iodixanol was used for this procedure.

| Reporting group values                             | Iopromide | Iodixanol | Total |
|----------------------------------------------------|-----------|-----------|-------|
| Number of subjects                                 | 20        | 20        | 40    |
| Age categorical                                    |           |           |       |
| Units: Subjects                                    |           |           |       |
| In utero                                           | 0         | 0         | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0         | 0         | 0     |
| Newborns (0-27 days)                               | 0         | 0         | 0     |
| Infants and toddlers (28 days-23 months)           | 0         | 0         | 0     |
| Children (2-11 years)                              | 0         | 0         | 0     |
| Adolescents (12-17 years)                          | 0         | 0         | 0     |
| Adults (18-64 years)                               | 9         | 10        | 19    |
| From 65-84 years                                   | 11        | 10        | 21    |
| 85 years and over                                  | 0         | 0         | 0     |
| Age continuous                                     |           |           |       |
| Units: years                                       |           |           |       |
| arithmetic mean                                    | 62.5      | 61.1      |       |
| standard deviation                                 | ± 10.3    | ± 12.4    | -     |
| Gender categorical                                 |           |           |       |
| Units: Subjects                                    |           |           |       |
| Female                                             | 7         | 9         | 16    |
| Male                                               | 13        | 11        | 24    |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |           |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Iopromide |
| Reporting group description:<br>The intervention during which the study data were obtained followed the standard protocol for stereotactic radiofrequency ablation (SRFA). The SRFA procedure is performed in anesthetized patients in whom a CM-enhanced CT scan is required for planning of the ablation, a nonenhanced CT scan is obtained for verification of proper needle placement, and after ablation another CM-enhanced CT scan is performed for final verification of ablation size. LOCM iopromide was used for this procedure. |           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Iodixanol |
| Reporting group description:<br>The intervention during which the study data were obtained followed the standard protocol for stereotactic radiofrequency ablation (SRFA). The SRFA procedure is performed in anesthetized patients in whom a CM-enhanced CT scan is required for planning of the ablation, a nonenhanced CT scan is obtained for verification of proper needle placement, and after ablation another CM-enhanced CT scan is performed for final verification of ablation size. IOCM iodixanol was used for this procedure. |           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Iopromide |
| Reporting group description:<br>Follow-up ended after completion of the study 30 days after inclusion into the study. In this time SAEs were evaluated.                                                                                                                                                                                                                                                                                                                                                                                     |           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Iodixanol |
| Reporting group description:<br>Follow-up ended after completion of the study 30 days after inclusion into the study. In this time SAEs were evaluated.                                                                                                                                                                                                                                                                                                                                                                                     |           |

### Primary: Systolic blood pressure

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Systolic blood pressure |
| End point description:<br>After administration of CM systemic blood pressure showed a typical hemodynamic temporal course. Compared to the initial value obtained 1 minute before administration, systemic blood pressure first showed a slight increase, followed by a variable decrease and after 3 minutes recovery to initial and compensatory levels higher than initial. We did not alter the infusion or administer additional vasopressors so as to not skew the data.<br>Time from onset of decline in blood pressure to normotension was $105 \pm 61$ seconds (range, 25–300 seconds) for LOCM and $112 \pm 20$ seconds (range, 90–145 seconds) for IOCM. |                         |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Primary                 |
| End point timeframe:<br>Day 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                         |

| End point values                     | Iopromide             | Iodixanol           |  |  |
|--------------------------------------|-----------------------|---------------------|--|--|
| Subject group type                   | Reporting group       | Reporting group     |  |  |
| Number of subjects analysed          | 20                    | 20                  |  |  |
| Units: mm Hg                         |                       |                     |  |  |
| arithmetic mean (standard deviation) | 78.57 ( $\pm$ 19.934) | 119 ( $\pm$ 15.492) |  |  |

## Statistical analyses

|                                         |                       |
|-----------------------------------------|-----------------------|
| <b>Statistical analysis title</b>       | Systemic hypotension  |
| Comparison groups                       | Iodixanol v Iopromide |
| Number of subjects included in analysis | 40                    |
| Analysis specification                  | Pre-specified         |
| Analysis type                           | superiority           |
| P-value                                 | < 0.001               |
| Method                                  | t-test, 2-sided       |

## Primary: Diastolic blood pressure

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                          |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Diastolic blood pressure |
| End point description:<br>After administration of CM systemic blood pressure showed a typical hemodynamic temporal course. Compared to the initial value obtained 1 minute before administration, systemic blood pressure first showed a slight increase, followed by a variable decrease and after 3 minutes recovery to initial and compensatory levels higher than initial. We did not alter the infusion or administer additional vasopressors so as to not skew the data.<br>Time from onset of decline in blood pressure to normotension was $105 \pm 61$ seconds (range, 25–300 seconds) for LOCM and $112 \pm 20$ seconds (range, 90–145 seconds) for IOCM. |                          |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Primary                  |
| End point timeframe:<br>Day 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                          |

|                                      |                      |                      |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| <b>End point values</b>              | Iopromide            | Iodixanol            |  |  |
| Subject group type                   | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed          | 20                   | 20                   |  |  |
| Units: mm Hg                         |                      |                      |  |  |
| arithmetic mean (standard deviation) | 43.14 ( $\pm$ 8.946) | 61.86 ( $\pm$ 7.330) |  |  |

## Statistical analyses

|                                         |                       |
|-----------------------------------------|-----------------------|
| <b>Statistical analysis title</b>       | Systemic hypotension  |
| Comparison groups                       | Iopromide v Iodixanol |
| Number of subjects included in analysis | 40                    |
| Analysis specification                  | Pre-specified         |
| Analysis type                           | superiority           |
| P-value                                 | < 0.001               |
| Method                                  | t-test, 2-sided       |

## Primary: Heart rate

|                                                                                                                                                           |            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| End point title                                                                                                                                           | Heart rate |
| End point description:<br>Administration of CM was associated with an increase of heart rate measured during the lowest value of systemic blood pressure. |            |
| End point type                                                                                                                                            | Primary    |
| End point timeframe:<br>Day 2                                                                                                                             |            |

| End point values                     | Iopromide          | Iodixanol          |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 20                 | 20                 |  |  |
| Units: bpm                           |                    |                    |  |  |
| arithmetic mean (standard deviation) | 62.9 ( $\pm$ 11.7) | 55.7 ( $\pm$ 10.3) |  |  |

### Statistical analyses

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Influence of CM on heart rate |
| Comparison groups                       | Iopromide v Iodixanol         |
| Number of subjects included in analysis | 40                            |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | superiority                   |
| P-value                                 | = 0.042                       |
| Method                                  | t-test, 2-sided               |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 2- day 30

Adverse event reporting additional description:

No suspected expected SAEs (SESAEs) and suspected unexpected SAEs (SUSAEs) were observed during treatment and follow-up

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

### Dictionary used

|                 |       |
|-----------------|-------|
| Dictionary name | CTCAE |
|-----------------|-------|

|                    |     |
|--------------------|-----|
| Dictionary version | 4.0 |
|--------------------|-----|

### Reporting groups

|                       |           |
|-----------------------|-----------|
| Reporting group title | Iopromide |
|-----------------------|-----------|

Reporting group description:

The intervention during which the study data were obtained followed the standard protocol for stereotactic radiofrequency ablation (SRFA). The SRFA procedure is performed in anesthetized patients in whom a CM-enhanced CT scan is required for planning of the ablation, a nonenhanced CT scan is obtained for verification of proper needle placement, and after ablation another CM-enhanced CT scan is performed for final verification of ablation size. LOCM iopromide was used for this procedure.

|                       |           |
|-----------------------|-----------|
| Reporting group title | Iodixanol |
|-----------------------|-----------|

Reporting group description:

The intervention during which the study data were obtained followed the standard protocol for stereotactic radiofrequency ablation (SRFA). The SRFA procedure is performed in anesthetized patients in whom a CM-enhanced CT scan is required for planning of the ablation, a nonenhanced CT scan is obtained for verification of proper needle placement, and after ablation another CM-enhanced CT scan is performed for final verification of ablation size. IOCM iodixanol was used for this procedure.

| Serious adverse events                            | Iopromide      | Iodixanol      |  |
|---------------------------------------------------|----------------|----------------|--|
| Total subjects affected by serious adverse events |                |                |  |
| subjects affected / exposed                       | 0 / 20 (0.00%) | 0 / 20 (0.00%) |  |
| number of deaths (all causes)                     | 0              | 0              |  |
| number of deaths resulting from adverse events    | 0              | 0              |  |

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

| Non-serious adverse events                            | Iopromide      | Iodixanol       |  |
|-------------------------------------------------------|----------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                |                 |  |
| subjects affected / exposed                           | 0 / 20 (0.00%) | 2 / 20 (10.00%) |  |
| Injury, poisoning and procedural complications        |                |                 |  |
| Perihepatic bleeding                                  |                |                 |  |
| subjects affected / exposed                           | 0 / 20 (0.00%) | 1 / 20 (5.00%)  |  |
| occurrences (all)                                     | 0              | 1               |  |

|                                                                      |                     |                     |  |
|----------------------------------------------------------------------|---------------------|---------------------|--|
| Hepatic bleeding<br>subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0 | 1 / 20 (5.00%)<br>1 |  |
|----------------------------------------------------------------------|---------------------|---------------------|--|

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28806208>