



## Clinical trial results: Immune response to COVID-19 Vaccination in people with Diabetes Mellitus - COVAC-DM study

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2021-001459-15 |
| Trial protocol           | AT             |
| Global end of trial date | 24 June 2022   |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 15 November 2023 |
| First version publication date | 15 November 2023 |

### Trial information

#### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | HS-2021-02 |
|-----------------------|------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Medical University of Graz  |
| Sponsor organisation address | Neue Stiftingtalstrasse 6, Graz, Austria, 8010  |
| Public contact               | Dr. Caren Sourij (Sub-Investigator), Medical University of Graz, 43 316385 78038, caren.sourij@medunigraz.at            |
| Scientific contact           | Prof. Harald Sourij, MBA (Principal Investigator), Medical University of Graz, 43 316385 81310, ha.sourij@medunigraz.at |

Notes:

### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                |
|--|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 30 August 2022 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 24 June 2022   |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 24 June 2022   |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective is to investigate the short and mid-term humoral immune response to COVID-19 vaccines as assessed by anti-spike protein antibodies in people with diabetes as compared to healthy controls.

Protection of trial subjects:

physical examination at the first visit

assessment of general health status of each participant (e.g. general appearance, neck/thyroid, chest/lung., etc.)

Systolic and diastolic blood pressure (mmHg), pulse (bpm),

minimal invasive blood samples will be taken for laboratory safety variables (hematology, biochemistry coagulation, urinalysis)

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 16 April 2021 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Austria: 161 |
| Worldwide total number of subjects   | 161          |
| EEA total number of subjects         | 161          |

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) | 146 |
| From 65 to 84 years  | 15  |
| 85 years and over    | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Subjects will be recruited from the participant database kept at the trial site

### Pre-assignment

Screening details:

Screening Visit: oral and written infos. After signing IC at the screening Visit participants will be screened for eligibility (inclusion/exclusion criteria), physical examination, Discussion of all procedures.

### Period 1

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

### Arms

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Antibody response |
|------------------|-------------------|

Arm description:

Antibody response after vaccinations

|  |                                |
|--|--------------------------------|
| Arm type                               | Active comparator              |
| Investigational medicinal product name | Comirnaty/ Spykevax/ Vaxzevria |
| Investigational medicinal product code |                                |
| Other name                             |                                |
| Pharmaceutical forms                   | Solution for injection         |
| Routes of administration               | Injection                      |

Dosage and administration details:

0.3 ml of the vaccine is injected into the deltoid muscle of the upper arm

| Number of subjects in period 1          | Antibody response |
|---|-------------------|
| Started                                 | 161               |
| Completed                               | 150               |
| Not completed                           | 11                |
| Consent withdrawn by subject            | 2                 |
| postpone vaccination                    | 6                 |
| subjects knowingly know having COVID-19 | 3                 |

## Baseline characteristics

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Antibody response |
|-----------------------|-------------------|

Reporting group description:

18 - 80 years

| Reporting group values                             | Antibody response | Total |  |
|--|-------------------|-------|--|
| Number of subjects                                 | 161               | 161   |  |
| Age categorical                                    |                   |       |  |
| 18 - 64 years                                      |                   |       |  |
| Units: Subjects                                    |                   |       |  |
| In utero   | 0                 | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                 | 0     |  |
| Newborns (0-27 days)                               | 0                 | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0                 | 0     |  |
| Children (2-11 years)                              | 0                 | 0     |  |
| Adolescents (12-17 years)                          | 0                 | 0     |  |
| Adults (18-64 years)                               | 146               | 146   |  |
| From 65-84 years                                   | 15                | 15    |  |
| 85 years and over                                  | 0                 | 0     |  |
| Gender categorical                                 |                   |       |  |
| Male and Female                                    |                   |       |  |
| Units: Subjects                                    |                   |       |  |
| Female   | 71                | 71    |  |
| Male   | 90                | 90    |  |

## End points

### End points reporting groups

|   |                              |
|---|------------------------------|
| Reporting group title   | Antibody response            |
| Reporting group description:<br>Antibody response after vaccinations                                    |                              |
| Subject analysis set title  | T1D HbA1c $\leq$ 58 mmol/mol |
| Subject analysis set type   | Sub-group analysis           |
| Subject analysis set description:<br>Subjects with Type 1 Diabetes with a lower HbA1c under 58mmol/mol  |                              |
| Subject analysis set title  | T1D HbA1c $>$ 58 mmol/mol    |
| Subject analysis set type   | Sub-group analysis           |
| Subject analysis set description:<br>Subjects with Type 1 Diabetes with a higher HbA1c over 58 mmol/mol |                              |
| Subject analysis set title  | T2D HbA1c $\leq$ 58 mmol/mol |
| Subject analysis set type   | Sub-group analysis           |
| Subject analysis set description:<br>Subjects with Type 2 Diabetes with a lower HbA1c under 58 mmol/mol |                              |
| Subject analysis set title  | T2D HbA1c $>$ 58 mmol/mol    |
| Subject analysis set type   | Sub-group analysis           |
| Subject analysis set description:<br>Subjects with Type 2 Diabetes with a higher HbA1c over 58 mmol/mol |                              |

### Primary: CoV-2 S Antibody level

|   |                        |
|---|------------------------|
| End point title   | CoV-2 S Antibody level |
| End point description:  |                        |
|   |                        |
| End point type  | Primary                |
| End point timeframe:  |                        |
| Level of antibodies At 7 to 14 days after the first vaccination |                        |

| End point values                     | T1D HbA1c $\leq$ 58 mmol/mol | T1D HbA1c $>$ 58 mmol/mol | T2D HbA1c $\leq$ 58 mmol/mol | T2D HbA1c $>$ 58 mmol/mol |
|--------------------------------------|------------------------------|---------------------------|------------------------------|---------------------------|
| Subject group type                   | Subject analysis set         | Subject analysis set      | Subject analysis set         | Subject analysis set      |
| Number of subjects analysed          | 49                           | 26                        | 37                           | 38                        |
| Units: antibody unit(s)              |                              |                           |                              |                           |
| arithmetic mean (standard deviation) | 8696.0 ( $\pm$ 7095.8)       | 5822.2 ( $\pm$ 4144.5)    | 4204.6 ( $\pm$ 3961.7)       | 5804.1 ( $\pm$ 6522.9)    |

### Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | Antibody response  |
| Comparison groups          | T1D HbA1c $\leq$ 58 mmol/mol v T1D HbA1c $>$ 58 mmol/mol v<br>T2D HbA1c $\leq$ 58 mmol/mol v T2D HbA1c $>$ 58 mmol/mol |

|   |                                  |
|---|----------------------------------|
| Number of subjects included in analysis | 150                              |
| Analysis specification                  | Pre-specified                    |
| Analysis type                           | other <sup>[1]</sup>             |
| P-value                                 | < 0.05                           |
| Method                                  | Chi-squared                      |
| Parameter estimate                      | Median difference (final values) |
| Confidence interval                     |                                  |
| level                                   | 95 %                             |
| sides                                   | 2-sided                          |

Notes:

[1] - Categorical variables were summarized as frequencies and percentages (%). Quantitative variables were summarized as means and standard deviations ( $\pm$ SD). Categorical variables were compared with diabetes groups using chi-squared or Fisher's exact tests, Postvaccination, side effects were compared between people with type 1 diabetes and type 2 diabetes using chi-squared or Fisher's exacts tests, multiple comparisons using post-hoc Bonferroni correction, or Wilcoxon's signed-rank test.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

16. April 2021 until 31. March 2023

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Temperature 37-37,9 °C |
|-----------------------|------------------------|

Reporting group description: -

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Temperature >38 °C |
|-----------------------|--------------------|

Reporting group description: -

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | injection site reaction |
|-----------------------|-------------------------|

Reporting group description: -

|                       |          |
|-----------------------|----------|
| Reporting group title | Swelling |
|-----------------------|----------|

Reporting group description: -

|                       |         |
|-----------------------|---------|
| Reporting group title | Redness |
|-----------------------|---------|

Reporting group description: -

|                       |      |
|-----------------------|------|
| Reporting group title | Pain |
|-----------------------|------|

Reporting group description: -

|                       |          |
|-----------------------|----------|
| Reporting group title | Headache |
|-----------------------|----------|

Reporting group description: -

|                       |         |
|-----------------------|---------|
| Reporting group title | Fatigue |
|-----------------------|---------|

Reporting group description: -

|                       |            |
|-----------------------|------------|
| Reporting group title | Arthralgia |
|-----------------------|------------|

Reporting group description: -

|                       |          |
|-----------------------|----------|
| Reporting group title | Covid-19 |
|-----------------------|----------|

Reporting group description: -

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | Hepatocellular Carcinoma |
|-----------------------|--------------------------|

Reporting group description: -

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Hypertensive crisis |
|-----------------------|---------------------|

Reporting group description: -

|                       |              |
|-----------------------|--------------|
| Reporting group title | Minor stroke |
|-----------------------|--------------|

Reporting group description: -

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Dyspnea and oedema |
|-----------------------|--------------------|

Reporting group description: -

|                       |              |
|-----------------------|--------------|
| Reporting group title | AV Block III |
|-----------------------|--------------|

Reporting group description: -

|                       |               |
|-----------------------|---------------|
| Reporting group title | Urteic stones |
|-----------------------|---------------|

Reporting group description: -

|                       |         |
|-----------------------|---------|
| Reporting group title | Syncope |
|-----------------------|---------|

Reporting group description: -

|                       |              |
|-----------------------|--------------|
| Reporting group title | Ovarian cyst |
|-----------------------|--------------|

Reporting group description: -

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Chest pain (coronary heart disease) |
|-----------------------|-------------------------------------|

Reporting group description: -

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Periradicular infiltration |
|-----------------------|----------------------------|



|                                |                       |
|--------------------------------|-----------------------|
| Reporting group description: - |                       |
| Reporting group title          | Cerebellar infarction |
| Reporting group description: - |                       |
| Reporting group title          | NSTEMI                |
| Reporting group description: - |                       |
| Reporting group title          | Sick sinus syndrome   |
| Reporting group description: - |                       |
| Reporting group title          | Enteritis             |
| Reporting group description: - |                       |
| Reporting group title          | Acute pancreatitis    |
| Reporting group description: - |                       |
| Reporting group title          | Surgery (shoulder)    |
| Reporting group description: - |                       |
| Reporting group title          | EPU/ablation          |
| Reporting group description: - |                       |
| Reporting group title          | angina pectoris       |
| Reporting group description: - |                       |
| Reporting group title          | Elective surgery      |
| Reporting group description: - |                       |

| <b>Serious adverse events</b>                                       | Temperature 37-37,9 °C | Temperature >38 °C | injection site reaction |
|---|------------------------|--------------------|-------------------------|
| Total subjects affected by serious adverse events                   |                        |                    |                         |
| subjects affected / exposed   | 0 / 150 (0.00%)        | 0 / 150 (0.00%)    | 0 / 150 (0.00%)         |
| number of deaths (all causes)                                       | 0                      | 0                  | 0                       |
| number of deaths resulting from adverse events                      |                        |                    |                         |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                        |                    |                         |
| Hepatocellular carcinoma  |                        |                    |                         |
| alternative assessment type: Non-systematic                         |                        |                    |                         |
| subjects affected / exposed   | 0 / 150 (0.00%)        | 0 / 150 (0.00%)    | 0 / 150 (0.00%)         |
| occurrences causally related to treatment / all                     | 0 / 0                  | 0 / 0              | 0 / 0                   |
| deaths causally related to treatment / all                          | 0 / 0                  | 0 / 0              | 0 / 0                   |
| Ovarian cyst  |                        |                    |                         |
| alternative assessment type: Non-systematic                         |                        |                    |                         |
| subjects affected / exposed   | 0 / 150 (0.00%)        | 0 / 150 (0.00%)    | 0 / 150 (0.00%)         |
| occurrences causally related to treatment / all                     | 0 / 0                  | 0 / 0              | 0 / 0                   |
| deaths causally related to treatment / all                          | 0 / 0                  | 0 / 0              | 0 / 0                   |
| Cardiac disorders   |                        |                    |                         |
| AV Block III  |                        |                    |                         |
| alternative assessment type: Non-systematic                         |                        |                    |                         |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Chest pain (coronary heart disease)<br>alternative assessment type: Non-systematic                            |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| NSTEMI<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Sick sinus syndrome<br>alternative assessment type: Non-systematic  |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| EPU/ablation<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| angina pectoris<br>alternative assessment type: Non-systematic  |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgical and medical procedures<br>Periradikuläre Infiltration<br>alternative assessment type: Non-systematic |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgery (shoulder)                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Elective surgery                                |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Hypertensive crisis                             |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| minor stroke                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebellar infarction                           |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Enteritis                                       |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Dyspnea and oedema                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Urteic stones                                   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Acute pancreatitis                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| COVID-19  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

| <b>Serious adverse events</b>                                       | Swelling        | Redness         | Pain            |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events                   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| number of deaths (all causes)                                       | 0               | 0               | 0               |
| number of deaths resulting from adverse events                      |                 |                 |                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |                 |
| Hepatocellular carcinoma  |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Ovarian cyst  |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac disorders   |                 |                 |                 |
| AV Block III  |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Chest pain (coronary heart disease)                                 |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| NSTEMI  |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Sick sinus syndrome   |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| EPU/ablation                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| angina pectoris                                 |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgical and medical procedures                 |                 |                 |                 |
| Periradikuläre Infiltration                     |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgery (shoulder)                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Elective surgery                                |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Hypertensive crisis                             |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| minor stroke                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebellar infarction                           |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Enteritis                                       |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Dyspnea and oedema                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Urteic stones                                   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Acute pancreatitis                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| COVID-19  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

| <b>Serious adverse events</b>                                       | Headache        | Fatigue         | Arthralgia      |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events                   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| number of deaths (all causes)                                       | 0               | 0               | 0               |
| number of deaths resulting from adverse events                      |                 |                 |                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |                 |
| Hepatocellular carcinoma  |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Ovarian cyst  |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac disorders   |                 |                 |                 |
| AV Block III  |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Chest pain (coronary heart disease)<br>alternative assessment type: Non-systematic                            |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| NSTEMI<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Sick sinus syndrome<br>alternative assessment type: Non-systematic  |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| EPU/ablation<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| angina pectoris<br>alternative assessment type: Non-systematic  |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgical and medical procedures<br>Periradikuläre Infiltration<br>alternative assessment type: Non-systematic |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgery (shoulder)                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Elective surgery                                |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Hypertensive crisis                             |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| minor stroke                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebellar infarction                           |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Enteritis                                       |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Dyspnea and oedema                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Urteic stones                                   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Acute pancreatitis                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| COVID-19  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

| Serious adverse events  | Covid-19        | Hepatocellular Carcinoma | Hypertensive crisis |
|---|-----------------|--------------------------|---------------------|
| Total subjects affected by serious adverse events                   |                 |                          |                     |
| subjects affected / exposed   | 8 / 150 (5.33%) | 1 / 150 (0.67%)          | 1 / 150 (0.67%)     |
| number of deaths (all causes)                                       | 0               | 0                        | 0                   |
| number of deaths resulting from adverse events                      |                 |                          |                     |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                          |                     |
| Hepatocellular carcinoma  |                 |                          |                     |
| alternative assessment type: Non-systematic                         |                 |                          |                     |
| subjects affected / exposed   | 0 / 150 (0.00%) | 1 / 150 (0.67%)          | 0 / 150 (0.00%)     |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0                    | 0 / 0               |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0                    | 0 / 0               |
| Ovarian cyst  |                 |                          |                     |
| alternative assessment type: Non-systematic                         |                 |                          |                     |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0                    | 0 / 0               |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0                    | 0 / 0               |
| Cardiac disorders   |                 |                          |                     |
| AV Block III  |                 |                          |                     |
| alternative assessment type: Non-systematic                         |                 |                          |                     |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0                    | 0 / 0               |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0                    | 0 / 0               |
| Chest pain (coronary heart disease)                                 |                 |                          |                     |
| alternative assessment type: Non-systematic                         |                 |                          |                     |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0                    | 0 / 0               |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0                    | 0 / 0               |
| NSTEMI  |                 |                          |                     |
| alternative assessment type: Non-systematic                         |                 |                          |                     |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0                    | 0 / 0               |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0                    | 0 / 0               |
| Sick sinus syndrome   |                 |                          |                     |
| alternative assessment type: Non-systematic                         |                 |                          |                     |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| EPU/ablation                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| angina pectoris                                 |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgical and medical procedures                 |                 |                 |                 |
| Periradikuläre Infiltration                     |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgery (shoulder)                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Elective surgery                                |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Hypertensive crisis                             |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| minor stroke                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebellar infarction                           |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Enteritis                                       |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Dyspnea and oedema                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Urteic stones                                   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Acute pancreatitis                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| COVID-19  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 8 / 150 (5.33%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

| Serious adverse events  | Minor stroke    | Dyspnea and oedema | AV Block III    |
|---|-----------------|--------------------|-----------------|
| Total subjects affected by serious adverse events                   |                 |                    |                 |
| subjects affected / exposed   | 1 / 150 (0.67%) | 1 / 150 (0.67%)    | 1 / 150 (0.67%) |
| number of deaths (all causes)                                       | 0               | 0                  | 0               |
| number of deaths resulting from adverse events                      |                 |                    |                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                    |                 |
| Hepatocellular carcinoma  |                 |                    |                 |
| alternative assessment type: Non-systematic                         |                 |                    |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)    | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0              | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0              | 0 / 0           |
| Ovarian cyst  |                 |                    |                 |
| alternative assessment type: Non-systematic                         |                 |                    |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)    | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0              | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0              | 0 / 0           |
| Cardiac disorders   |                 |                    |                 |
| AV Block III  |                 |                    |                 |
| alternative assessment type: Non-systematic                         |                 |                    |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Chest pain (coronary heart disease)<br>alternative assessment type: Non-systematic                            |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| NSTEMI<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Sick sinus syndrome<br>alternative assessment type: Non-systematic  |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| EPU/ablation<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| angina pectoris<br>alternative assessment type: Non-systematic  |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgical and medical procedures<br>Periradikuläre Infiltration<br>alternative assessment type: Non-systematic |                 |                 |                 |



|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgery (shoulder)<br>alternative assessment type: Non-systematic    |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Elective surgery<br>alternative assessment type: Non-systematic      |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders   |                 |                 |                 |
| Hypertensive crisis<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| minor stroke<br>alternative assessment type: Non-systematic          |                 |                 |                 |
| subjects affected / exposed  | 1 / 150 (0.67%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope<br>alternative assessment type: Non-systematic               |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebellar infarction<br>alternative assessment type: Non-systematic |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Enteritis                                       |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Dyspnea and oedema                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 1 / 150 (0.67%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Urteic stones                                   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Acute pancreatitis                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| COVID-19  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

| <b>Serious adverse events</b>                                       | Urteic stones   | Syncope         | Ovarian cyst    |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events                   |                 |                 |                 |
| subjects affected / exposed   | 1 / 150 (0.67%) | 1 / 150 (0.67%) | 1 / 150 (0.67%) |
| number of deaths (all causes)                                       | 0               | 0               | 0               |
| number of deaths resulting from adverse events                      |                 |                 |                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |                 |
| Hepatocellular carcinoma  |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Ovarian cyst  |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac disorders   |                 |                 |                 |
| AV Block III  |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Chest pain (coronary heart disease)                                 |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| NSTEMI  |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Sick sinus syndrome   |                 |                 |                 |
| alternative assessment type: Non-systematic                         |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| EPU/ablation                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| angina pectoris                                 |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgical and medical procedures                 |                 |                 |                 |
| Periradikuläre Infiltration                     |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgery (shoulder)                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Elective surgery                                |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Hypertensive crisis                             |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| minor stroke                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 1 / 150 (0.67%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebellar infarction                           |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Enteritis                                       |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Dyspnea and oedema                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Urteic stones                                   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 150 (0.67%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Acute pancreatitis                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| COVID-19  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

| <b>Serious adverse events</b>                                       | Chest pain (coronary heart disease) | Periradicular infiltration | Cerebellar infarction |
|---|-------------------------------------|----------------------------|-----------------------|
| Total subjects affected by serious adverse events                   |                                     |                            |                       |
| subjects affected / exposed   | 1 / 150 (0.67%)                     | 1 / 150 (0.67%)            | 1 / 150 (0.67%)       |
| number of deaths (all causes)                                       | 0                                   | 0                          | 0                     |
| number of deaths resulting from adverse events                      |                                     |                            |                       |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                     |                            |                       |
| Hepatocellular carcinoma  |                                     |                            |                       |
| alternative assessment type: Non-systematic                         |                                     |                            |                       |
| subjects affected / exposed   | 0 / 150 (0.00%)                     | 0 / 150 (0.00%)            | 0 / 150 (0.00%)       |
| occurrences causally related to treatment / all                     | 0 / 0                               | 0 / 0                      | 0 / 0                 |
| deaths causally related to treatment / all                          | 0 / 0                               | 0 / 0                      | 0 / 0                 |
| Ovarian cyst  |                                     |                            |                       |
| alternative assessment type: Non-systematic                         |                                     |                            |                       |
| subjects affected / exposed   | 0 / 150 (0.00%)                     | 0 / 150 (0.00%)            | 0 / 150 (0.00%)       |
| occurrences causally related to treatment / all                     | 0 / 0                               | 0 / 0                      | 0 / 0                 |
| deaths causally related to treatment / all                          | 0 / 0                               | 0 / 0                      | 0 / 0                 |
| Cardiac disorders   |                                     |                            |                       |
| AV Block III  |                                     |                            |                       |
| alternative assessment type: Non-systematic                         |                                     |                            |                       |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Chest pain (coronary heart disease)<br>alternative assessment type: Non-systematic                            |                 |                 |                 |
| subjects affected / exposed   | 1 / 150 (0.67%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| NSTEMI<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Sick sinus syndrome<br>alternative assessment type: Non-systematic  |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| EPU/ablation<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| angina pectoris<br>alternative assessment type: Non-systematic  |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgical and medical procedures<br>Periradikuläre Infiltration<br>alternative assessment type: Non-systematic |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed  | 0 / 150 (0.00%) | 1 / 150 (0.67%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgery (shoulder)<br>alternative assessment type: Non-systematic    |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Elective surgery<br>alternative assessment type: Non-systematic      |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders   |                 |                 |                 |
| Hypertensive crisis<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| minor stroke<br>alternative assessment type: Non-systematic          |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope<br>alternative assessment type: Non-systematic               |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebellar infarction<br>alternative assessment type: Non-systematic |                 |                 |                 |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Enteritis                                       |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Dyspnea and oedema                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Urteic stones                                   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Acute pancreatitis                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| COVID-19  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

| <b>Serious adverse events</b>                                       | NSTEMI          | Sick sinus syndrome | Enteritis       |
|---|-----------------|---------------------|-----------------|
| Total subjects affected by serious adverse events                   |                 |                     |                 |
| subjects affected / exposed   | 1 / 150 (0.67%) | 1 / 150 (0.67%)     | 1 / 150 (0.67%) |
| number of deaths (all causes)                                       | 0               | 0                   | 0               |
| number of deaths resulting from adverse events                      |                 |                     |                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                     |                 |
| Hepatocellular carcinoma  |                 |                     |                 |
| alternative assessment type: Non-systematic                         |                 |                     |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)     | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0               | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0               | 0 / 0           |
| Ovarian cyst  |                 |                     |                 |
| alternative assessment type: Non-systematic                         |                 |                     |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)     | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0               | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0               | 0 / 0           |
| Cardiac disorders   |                 |                     |                 |
| AV Block III  |                 |                     |                 |
| alternative assessment type: Non-systematic                         |                 |                     |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)     | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0               | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0               | 0 / 0           |
| Chest pain (coronary heart disease)                                 |                 |                     |                 |
| alternative assessment type: Non-systematic                         |                 |                     |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)     | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0               | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0               | 0 / 0           |
| NSTEMI  |                 |                     |                 |
| alternative assessment type: Non-systematic                         |                 |                     |                 |
| subjects affected / exposed   | 1 / 150 (0.67%) | 0 / 150 (0.00%)     | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0               | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0               | 0 / 0           |
| Sick sinus syndrome   |                 |                     |                 |
| alternative assessment type: Non-systematic                         |                 |                     |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 1 / 150 (0.67%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| EPU/ablation                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| angina pectoris                                 |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgical and medical procedures                 |                 |                 |                 |
| Periradikuläre Infiltration                     |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgery (shoulder)                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Elective surgery                                |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Hypertensive crisis                             |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| minor stroke                                    |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebellar infarction                           |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Enteritis                                       |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Dyspnea and oedema                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Urteic stones                                   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Acute pancreatitis                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| COVID-19  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

| <b>Serious adverse events</b>                                       | Acute pancreatitis | Surgery (shoulder) | EPU/ablation    |
|---|--------------------|--------------------|-----------------|
| Total subjects affected by serious adverse events                   |                    |                    |                 |
| subjects affected / exposed   | 1 / 150 (0.67%)    | 1 / 150 (0.67%)    | 1 / 150 (0.67%) |
| number of deaths (all causes)                                       | 0                  | 0                  | 0               |
| number of deaths resulting from adverse events                      |                    |                    |                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                    |                    |                 |
| Hepatocellular carcinoma  |                    |                    |                 |
| alternative assessment type: Non-systematic                         |                    |                    |                 |
| subjects affected / exposed   | 0 / 150 (0.00%)    | 0 / 150 (0.00%)    | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0              | 0 / 0              | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0              | 0 / 0              | 0 / 0           |
| Ovarian cyst  |                    |                    |                 |
| alternative assessment type: Non-systematic                         |                    |                    |                 |
| subjects affected / exposed   | 0 / 150 (0.00%)    | 0 / 150 (0.00%)    | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0              | 0 / 0              | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0              | 0 / 0              | 0 / 0           |
| Cardiac disorders   |                    |                    |                 |
| AV Block III  |                    |                    |                 |
| alternative assessment type: Non-systematic                         |                    |                    |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Chest pain (coronary heart disease)<br>alternative assessment type: Non-systematic                            |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| NSTEMI<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Sick sinus syndrome<br>alternative assessment type: Non-systematic  |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| EPU/ablation<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| angina pectoris<br>alternative assessment type: Non-systematic  |                 |                 |                 |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgical and medical procedures<br>Periradikuläre Infiltration<br>alternative assessment type: Non-systematic |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgery (shoulder)<br>alternative assessment type: Non-systematic    |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 1 / 150 (0.67%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Elective surgery<br>alternative assessment type: Non-systematic      |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders   |                 |                 |                 |
| Hypertensive crisis<br>alternative assessment type: Non-systematic   |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| minor stroke<br>alternative assessment type: Non-systematic          |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope<br>alternative assessment type: Non-systematic               |                 |                 |                 |
| subjects affected / exposed  | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all                      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                           | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebellar infarction<br>alternative assessment type: Non-systematic |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Enteritis                                       |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Dyspnea and oedema                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Urteic stones                                   |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Acute pancreatitis                              |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 150 (0.67%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| COVID-19  |                 |                 |                 |
| alternative assessment type: Non-systematic     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |



| <b>Serious adverse events</b>                                       | angina pectoris | Elective surgery |  |
|---|-----------------|------------------|--|
| Total subjects affected by serious adverse events                   |                 |                  |  |
| subjects affected / exposed   | 1 / 150 (0.67%) | 2 / 150 (1.33%)  |  |
| number of deaths (all causes)                                       | 0               | 0                |  |
| number of deaths resulting from adverse events                      |                 |                  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                  |  |
| Hepatocellular carcinoma  |                 |                  |  |
| alternative assessment type: Non-systematic                         |                 |                  |  |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0            |  |
| Ovarian cyst  |                 |                  |  |
| alternative assessment type: Non-systematic                         |                 |                  |  |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0            |  |
| Cardiac disorders   |                 |                  |  |
| AV Block III  |                 |                  |  |
| alternative assessment type: Non-systematic                         |                 |                  |  |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0            |  |
| Chest pain (coronary heart disease)                                 |                 |                  |  |
| alternative assessment type: Non-systematic                         |                 |                  |  |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0            |  |
| NSTEMI  |                 |                  |  |
| alternative assessment type: Non-systematic                         |                 |                  |  |
| subjects affected / exposed   | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0            |  |
| Sick sinus syndrome   |                 |                  |  |
| alternative assessment type: Non-systematic                         |                 |                  |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| EPU/ablation                                    |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| angina pectoris                                 |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 1 / 150 (0.67%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Surgical and medical procedures                 |                 |                 |  |
| Periradikuläre Infiltration                     |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Surgery (shoulder)                              |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Elective surgery                                |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 1 / 150 (0.67%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nervous system disorders                        |                 |                 |  |
| Hypertensive crisis                             |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| minor stroke                                    |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Syncope   |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cerebellar infarction                           |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Enteritis                                       |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Dyspnea and oedema                              |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Urteic stones                                   |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Endocrine disorders                             |                 |                 |  |
| Acute pancreatitis                              |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| COVID-19  |                 |                 |  |
| alternative assessment type: Non-systematic     |                 |                 |  |
| subjects affected / exposed                     | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

Frequency threshold for reporting non-serious adverse events: 3 %

| <b>Non-serious adverse events</b>                     | Temperature 37-37,9 °C | Temperature >38 °C | injection site reaction |
|---|------------------------|--------------------|-------------------------|
| Total subjects affected by non-serious adverse events |                        |                    |                         |
| subjects affected / exposed                           | 12 / 150 (8.00%)       | 2 / 150 (1.33%)    | 104 / 150 (69.33%)      |
| Investigations  |                        |                    |                         |
| Injection site reaction                               |                        |                    |                         |
| alternative assessment type: Non-systematic           |                        |                    |                         |
| subjects affected / exposed                           | 0 / 150 (0.00%)        | 0 / 150 (0.00%)    | 104 / 150 (69.33%)      |
| occurrences (all)                                     | 0                      | 0                  | 104                     |
| Temperature 37 - 37,9                                 |                        |                    |                         |
| alternative assessment type: Non-systematic           |                        |                    |                         |
| subjects affected / exposed                           | 12 / 150 (8.00%)       | 0 / 150 (0.00%)    | 0 / 150 (0.00%)         |
| occurrences (all)                                     | 12                     | 0                  | 0                       |
| Temperature >38                                       |                        |                    |                         |
| alternative assessment type: Non-systematic           |                        |                    |                         |
| subjects affected / exposed                           | 0 / 150 (0.00%)        | 2 / 150 (1.33%)    | 0 / 150 (0.00%)         |
| occurrences (all)                                     | 0                      | 2                  | 0                       |
| Swelling  |                        |                    |                         |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Redness                                     |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Pain  |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Headache                                    |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Fatigue                                     |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Arthralgia                                  |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |

| Non-serious adverse events                            | Swelling          | Redness         | Pain              |
|---|-------------------|-----------------|-------------------|
| Total subjects affected by non-serious adverse events |                   |                 |                   |
| subjects affected / exposed                           | 16 / 150 (10.67%) | 9 / 150 (6.00%) | 98 / 150 (65.33%) |
| Investigations  |                   |                 |                   |
| Injection site reaction                               |                   |                 |                   |
| alternative assessment type: Non-systematic           |                   |                 |                   |
| subjects affected / exposed                           | 0 / 150 (0.00%)   | 0 / 150 (0.00%) | 0 / 150 (0.00%)   |
| occurrences (all)                                     | 0                 | 0               | 0                 |
| Temperature 37 - 37,9                                 |                   |                 |                   |
| alternative assessment type: Non-systematic           |                   |                 |                   |

|   |                   |                 |                   |
|---|-------------------|-----------------|-------------------|
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%) | 0 / 150 (0.00%)   |
| occurrences (all)                           | 0                 | 0               | 0                 |
| Temperature >38                             |                   |                 |                   |
| alternative assessment type: Non-systematic |                   |                 |                   |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%) | 0 / 150 (0.00%)   |
| occurrences (all)                           | 0                 | 0               | 0                 |
| Swelling                                    |                   |                 |                   |
| alternative assessment type: Non-systematic |                   |                 |                   |
| subjects affected / exposed                 | 16 / 150 (10.67%) | 0 / 150 (0.00%) | 0 / 150 (0.00%)   |
| occurrences (all)                           | 16                | 0               | 0                 |
| Redness                                     |                   |                 |                   |
| alternative assessment type: Non-systematic |                   |                 |                   |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 9 / 150 (6.00%) | 0 / 150 (0.00%)   |
| occurrences (all)                           | 0                 | 9               | 0                 |
| Pain  |                   |                 |                   |
| alternative assessment type: Non-systematic |                   |                 |                   |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%) | 98 / 150 (65.33%) |
| occurrences (all)                           | 0                 | 0               | 98                |
| Headache                                    |                   |                 |                   |
| alternative assessment type: Non-systematic |                   |                 |                   |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%) | 0 / 150 (0.00%)   |
| occurrences (all)                           | 0                 | 0               | 0                 |
| Fatigue                                     |                   |                 |                   |
| alternative assessment type: Non-systematic |                   |                 |                   |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%) | 0 / 150 (0.00%)   |
| occurrences (all)                           | 0                 | 0               | 0                 |
| Arthralgia                                  |                   |                 |                   |
| alternative assessment type: Non-systematic |                   |                 |                   |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%) | 0 / 150 (0.00%)   |
| occurrences (all)                           | 0                 | 0               | 0                 |

| <b>Non-serious adverse events</b>                     | Headache          | Fatigue           | Arthralgia        |
|---|-------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events |                   |                   |                   |
| subjects affected / exposed                           | 33 / 150 (22.00%) | 45 / 150 (30.00%) | 15 / 150 (10.00%) |

|   |                   |                   |                 |
|---|-------------------|-------------------|-----------------|
| Investigations                              |                   |                   |                 |
| Injection site reaction                     |                   |                   |                 |
| alternative assessment type: Non-systematic |                   |                   |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%)   | 0 / 150 (0.00%) |
| occurrences (all)                           | 0                 | 0                 | 0               |
| Temperature 37 - 37,9                       |                   |                   |                 |
| alternative assessment type: Non-systematic |                   |                   |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%)   | 0 / 150 (0.00%) |
| occurrences (all)                           | 0                 | 0                 | 0               |
| Temperature >38                             |                   |                   |                 |
| alternative assessment type: Non-systematic |                   |                   |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%)   | 0 / 150 (0.00%) |
| occurrences (all)                           | 0                 | 0                 | 0               |
| Swelling                                    |                   |                   |                 |
| alternative assessment type: Non-systematic |                   |                   |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%)   | 0 / 150 (0.00%) |
| occurrences (all)                           | 0                 | 0                 | 0               |
| Redness                                     |                   |                   |                 |
| alternative assessment type: Non-systematic |                   |                   |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%)   | 0 / 150 (0.00%) |
| occurrences (all)                           | 0                 | 0                 | 0               |
| Pain  |                   |                   |                 |
| alternative assessment type: Non-systematic |                   |                   |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 0 / 150 (0.00%)   | 0 / 150 (0.00%) |
| occurrences (all)                           | 0                 | 0                 | 0               |
| Headache                                    |                   |                   |                 |
| alternative assessment type: Non-systematic |                   |                   |                 |
| subjects affected / exposed                 | 33 / 150 (22.00%) | 0 / 150 (0.00%)   | 0 / 150 (0.00%) |
| occurrences (all)                           | 33                | 0                 | 0               |
| Fatigue                                     |                   |                   |                 |
| alternative assessment type: Non-systematic |                   |                   |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%)   | 45 / 150 (30.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0                 | 45                | 0               |
| Arthralgia                                  |                   |                   |                 |
| alternative assessment type: Non-systematic |                   |                   |                 |

|                             |                 |                 |                   |
|-----------------------------|-----------------|-----------------|-------------------|
| subjects affected / exposed | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 15 / 150 (10.00%) |
| occurrences (all)           | 0               | 0               | 15                |

| <b>Non-serious adverse events</b>                     | Covid-19        | Hepatocellular Carcinoma | Hypertensive crisis |
|---|-----------------|--------------------------|---------------------|
| Total subjects affected by non-serious adverse events |                 |                          |                     |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| Investigations  |                 |                          |                     |
| Injection site reaction                               |                 |                          |                     |
| alternative assessment type: Non-systematic           |                 |                          |                     |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| occurrences (all)                                     | 0               | 0                        | 0                   |
| Temperature 37 - 37,9                                 |                 |                          |                     |
| alternative assessment type: Non-systematic           |                 |                          |                     |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| occurrences (all)                                     | 0               | 0                        | 0                   |
| Temperature >38                                       |                 |                          |                     |
| alternative assessment type: Non-systematic           |                 |                          |                     |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| occurrences (all)                                     | 0               | 0                        | 0                   |
| Swelling  |                 |                          |                     |
| alternative assessment type: Non-systematic           |                 |                          |                     |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| occurrences (all)                                     | 0               | 0                        | 0                   |
| Redness   |                 |                          |                     |
| alternative assessment type: Non-systematic           |                 |                          |                     |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| occurrences (all)                                     | 0               | 0                        | 0                   |
| Pain  |                 |                          |                     |
| alternative assessment type: Non-systematic           |                 |                          |                     |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| occurrences (all)                                     | 0               | 0                        | 0                   |
| Headache  |                 |                          |                     |
| alternative assessment type: Non-systematic           |                 |                          |                     |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)          | 0 / 150 (0.00%)     |
| occurrences (all)                                     | 0               | 0                        | 0                   |



|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Fatigue                                     |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Arthralgia                                  |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |

| <b>Non-serious adverse events</b>                     | Minor stroke    | Dyspnea and oedema | AV Block III    |
|---|-----------------|--------------------|-----------------|
| Total subjects affected by non-serious adverse events |                 |                    |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)    | 0 / 150 (0.00%) |
| Investigations  |                 |                    |                 |
| Injection site reaction                               |                 |                    |                 |
| alternative assessment type: Non-systematic           |                 |                    |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)    | 0 / 150 (0.00%) |
| occurrences (all)                                     | 0               | 0                  | 0               |
| Temperature 37 - 37,9                                 |                 |                    |                 |
| alternative assessment type: Non-systematic           |                 |                    |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)    | 0 / 150 (0.00%) |
| occurrences (all)                                     | 0               | 0                  | 0               |
| Temperature >38                                       |                 |                    |                 |
| alternative assessment type: Non-systematic           |                 |                    |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)    | 0 / 150 (0.00%) |
| occurrences (all)                                     | 0               | 0                  | 0               |
| Swelling  |                 |                    |                 |
| alternative assessment type: Non-systematic           |                 |                    |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)    | 0 / 150 (0.00%) |
| occurrences (all)                                     | 0               | 0                  | 0               |
| Redness   |                 |                    |                 |
| alternative assessment type: Non-systematic           |                 |                    |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)    | 0 / 150 (0.00%) |
| occurrences (all)                                     | 0               | 0                  | 0               |
| Pain  |                 |                    |                 |
| alternative assessment type: Non-systematic           |                 |                    |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Headache                                    |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Fatigue                                     |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Arthralgia                                  |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |

| <b>Non-serious adverse events</b>                     | Urteic stones   | Syncope         | Ovarian cyst    |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by non-serious adverse events |                 |                 |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| Investigations  |                 |                 |                 |
| Injection site reaction                               |                 |                 |                 |
| alternative assessment type: Non-systematic           |                 |                 |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                                     | 0               | 0               | 0               |
| Temperature 37 - 37,9                                 |                 |                 |                 |
| alternative assessment type: Non-systematic           |                 |                 |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                                     | 0               | 0               | 0               |
| Temperature >38                                       |                 |                 |                 |
| alternative assessment type: Non-systematic           |                 |                 |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                                     | 0               | 0               | 0               |
| Swelling  |                 |                 |                 |
| alternative assessment type: Non-systematic           |                 |                 |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                                     | 0               | 0               | 0               |

|   |                      |                      |                      |
|---|----------------------|----------------------|----------------------|
| Redness<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)    | 0 / 150 (0.00%)<br>0 | 0 / 150 (0.00%)<br>0 | 0 / 150 (0.00%)<br>0 |
| Pain<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)       | 0 / 150 (0.00%)<br>0 | 0 / 150 (0.00%)<br>0 | 0 / 150 (0.00%)<br>0 |
| Headache<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)   | 0 / 150 (0.00%)<br>0 | 0 / 150 (0.00%)<br>0 | 0 / 150 (0.00%)<br>0 |
| Fatigue<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)    | 0 / 150 (0.00%)<br>0 | 0 / 150 (0.00%)<br>0 | 0 / 150 (0.00%)<br>0 |
| Arthralgia<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all) | 0 / 150 (0.00%)<br>0 | 0 / 150 (0.00%)<br>0 | 0 / 150 (0.00%)<br>0 |

| Non-serious adverse events   | Chest pain (coronary heart disease) | Periradicular infiltration | Cerebellar infarction |
|--|-------------------------------------|----------------------------|-----------------------|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed   | 0 / 150 (0.00%)                     | 0 / 150 (0.00%)            | 0 / 150 (0.00%)       |
| Investigations<br>Injection site reaction<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all) | 0 / 150 (0.00%)<br>0                | 0 / 150 (0.00%)<br>0       | 0 / 150 (0.00%)<br>0  |
| Temperature 37 - 37,9<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 150 (0.00%)<br>0                | 0 / 150 (0.00%)<br>0       | 0 / 150 (0.00%)<br>0  |
| Temperature >38<br>alternative assessment type: Non-systematic   |                                     |                            |                       |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Swelling                                    |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Redness                                     |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Pain  |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Headache                                    |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Fatigue                                     |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Arthralgia                                  |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |

| Non-serious adverse events                            | NSTEMI          | Sick sinus syndrome | Enteritis       |
|---|-----------------|---------------------|-----------------|
| Total subjects affected by non-serious adverse events |                 |                     |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)     | 0 / 150 (0.00%) |
| Investigations  |                 |                     |                 |
| Injection site reaction                               |                 |                     |                 |
| alternative assessment type: Non-systematic           |                 |                     |                 |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)     | 0 / 150 (0.00%) |
| occurrences (all)                                     | 0               | 0                   | 0               |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Temperature 37 - 37,9                       |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Temperature >38                             |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Swelling                                    |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Redness                                     |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Pain  |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Headache                                    |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Fatigue                                     |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Arthralgia                                  |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |

| Non-serious adverse events                            | Acute pancreatitis | Surgery (shoulder) | EPU/ablation |
|---|--------------------|--------------------|--------------|
| Total subjects affected by non-serious adverse events |                    |                    |              |

| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
|---|-----------------|-----------------|-----------------|
| Investigations                              |                 |                 |                 |
| Injection site reaction                     |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Temperature 37 - 37,9                       |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Temperature >38                             |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Swelling                                    |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Redness                                     |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Pain  |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Headache                                    |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Fatigue                                     |                 |                 |                 |
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |
| Arthralgia                                  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| alternative assessment type: Non-systematic |                 |                 |                 |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) | 0 / 150 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0               |

| <b>Non-serious adverse events</b>                     | angina pectoris | Elective surgery |  |
|---|-----------------|------------------|--|
| Total subjects affected by non-serious adverse events |                 |                  |  |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| Investigations  |                 |                  |  |
| Injection site reaction                               |                 |                  |  |
| alternative assessment type: Non-systematic           |                 |                  |  |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| occurrences (all)                                     | 0               | 0                |  |
| Temperature 37 - 37,9                                 |                 |                  |  |
| alternative assessment type: Non-systematic           |                 |                  |  |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| occurrences (all)                                     | 0               | 0                |  |
| Temperature >38                                       |                 |                  |  |
| alternative assessment type: Non-systematic           |                 |                  |  |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| occurrences (all)                                     | 0               | 0                |  |
| Swelling  |                 |                  |  |
| alternative assessment type: Non-systematic           |                 |                  |  |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| occurrences (all)                                     | 0               | 0                |  |
| Redness   |                 |                  |  |
| alternative assessment type: Non-systematic           |                 |                  |  |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| occurrences (all)                                     | 0               | 0                |  |
| Pain  |                 |                  |  |
| alternative assessment type: Non-systematic           |                 |                  |  |
| subjects affected / exposed                           | 0 / 150 (0.00%) | 0 / 150 (0.00%)  |  |
| occurrences (all)                                     | 0               | 0                |  |
| Headache  |                 |                  |  |
| alternative assessment type: Non-systematic           |                 |                  |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences (all)                           | 0               | 0               |  |
| Fatigue                                     |                 |                 |  |
| alternative assessment type: Non-systematic |                 |                 |  |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences (all)                           | 0               | 0               |  |
| Arthralgia                                  |                 |                 |  |
| alternative assessment type: Non-systematic |                 |                 |  |
| subjects affected / exposed                 | 0 / 150 (0.00%) | 0 / 150 (0.00%) |  |
| occurrences (all)                           | 0               | 0               |  |



## 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/34984802>