



Clinical trial results:

Renal and Cardiovascular Effects of SGLT2 inhibition in combination with loop diuretics in diabetic patients with chronic heart failure.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2016-003968-39 |
| Trial protocol | GB |
| Global end of trial date | 09 January 2019 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 03 January 2020 |
| First version publication date | 03 January 2020 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 2015CA02 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03226457 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Sponsor Reference: 2015CA02, REC: Regional Ethics Committee Reference: 16/ES/0137 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | University of Dundee & Tayside Health Board |
| Sponsor organisation address | George Pirie Way, Dundee, United Kingdom, DD1 9SY |
| Public contact | Professor Jacob George , University of Dundee & Tayside Health Board Tayside Medical Science Centre, Ninewells Hospital, 01382 383204, J.George@dundee.ac.uk |
| Scientific contact | Professor Jacob George , University of Dundee & Tayside Health Board Tayside Medical Science Centre, Ninewells Hospital, 01382 383204, J.George@dundee.ac.uk |

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 | 01 December 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 09 January 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 09 January 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective will be to assess whether empagliflozin (SGLT2 Inhibitor) can augment the effects of loop diuretics in diabetic patients with mild congestive heart failure with left ventricular systolic dysfunction (LVSD), as measured by urinary volume.

Protection of trial subjects:

Participants were recruited had both Type 2 Diabetes (T2D) and Heart Failure (HF). Whilst this co-morbidity can often lead to frailty, the inclusion/exclusion criteria ensured that participants with stable T2D and HF were recruited.

Participants were eligible if they were:

- Aged 18 to 80 years with previously diagnosed Type 2 Diabetes Mellitus.
- Diagnosed with NYHA Functional class II-III HF with prior echocardiographic evidence of LVSD.
- On stable doses of furosemide, or alternative loop diuretic for at least one month.
- Type 2 Diabetes
- eGFR \geq 45 ml/min.
- Had stable HF symptoms for at least three months prior to consent
- On stable HF therapy for at least three months prior to consent
- Had not been hospitalised for HF for at least three months prior to consent.
- Women of childbearing potential* (WoCBP) agreed to take precautions to avoid pregnancy throughout the trial and for 4 weeks after intake of the last dose.

Participants will be excluded if they had:

- A diagnosis of chronic liver disease and/or liver enzymes that are twice the upper limit of normal
- Systolic BP of <95mmHg at screening visit.
- HbA1c < 6.0%
- Participants on thiazide diuretics.
- Participants receiving renal dialysis
- Participants who had previously had an episode of diabetic ketoacidosis.
- Participants with type 1 diabetes mellitus
- Malignancy (receiving active treatment) or other life threatening disease.
- Pregnant or lactating women
- Participants with difficulty in micturition e.g. severe prostate enlargement
- Allergy to any SGLT2 inhibitor or lactose or galactose intolerance
- Past or current treatment with any SGLT2 inhibitor
- Participants who have participated in any other clinical interventional trial of an investigational medicinal product within 30 days.
- Participants who are unable to give informed consent
- Any other reason considered by the physician to be inappropriate for inclusion.

Background therapy:

Participants recruited were on HF medications (except for thiazide diuretics) and could be on T2D medications or have diet-controlled T2D.

Evidence for comparator:

The landmark EMPA-REG outcome study reported a striking 35% relative risk reduction in HF hospitalisations with empagliflozin providing supportive evidence for the beneficial effects of SGLT2 inhibition in the setting of chronic HF. The early separation curves on the Kaplan-Meier graphs and the effect on HF hospitalisations has led to the hypothesis that this outcome is seen due to a diuretic effect

of SGLT2 inhibition.

Data on the effect of SGLT2 inhibitor use with diuretics are limited, but given the relative frequency of both HF and T2D they are likely to be prescribed concurrently. The RECEDE-CHF trial sets out to explore this in more detail.

| | |
|---|------------------|
| Actual start date of recruitment | 30 November 2017 |
| 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 | United Kingdom: 23 |
| Worldwide total number of subjects | 23 |
| EEA total number of subjects | 23 |

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) | 5 |
| From 65 to 84 years | 18 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A high drop out rate was factored into the power calculations due to the high intensity of the patient visits. A minimum of 22 participants was required to meet the power calculations. There were no patient drop outs and 23 patients were recruited and completed participation in the trial.

Pre-assignment

Screening details:

At the screening visit, following informed consent, an initial medical history and clinical examination was performed and concomitant medication will be recorded. Participants had bloods taken for safety analysis and vital signs will be checked to confirm eligibility prior to enrolment.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Assessor |

Blinding implementation details:

Participants were randomised to either empagliflozin 25mg/ placebo or placebo/empagliflozin 25 mg in a double blind fashion.

The double blind medication (empagliflozin or placebo) was prepared, packaged and labelled by Tayside Pharmaceuticals.

The Clinical Trials Pharmacy, Ninewells Hospital were provided with a copy of the randomisation allocation for the purposes of 24 hour emergency unblinding.

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | No |
| Arm title | Placebo |

Arm description:

Placebo arm, one tablet once a day for 6 weeks

| | |
|--|---------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | Placebo |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo, one tablet once a day

| | |
|------------------|---------------------|
| Arm title | Empagliflozin 25 mg |
|------------------|---------------------|

Arm description:

Empagliflozin 25 mg, one tablet once a day for 6 weeks

| | |
|--|---------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Empagliflozin 25 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Empagliflozin 25 mg once daily, oral administration

| Number of subjects in period 1 | Placebo | Empagliflozin 25 mg |
|---------------------------------------|---------|---------------------|
| Started | 23 | 23 |
| Completed | 23 | 23 |

Baseline characteristics

Reporting groups

Reporting group title

Overall Trial

Reporting group description: -

| Reporting group values | Overall Trial | Total | |
|---|---------------|-------|--|
| Number of subjects | 23 | 23 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 69.8 | | |
| standard deviation | ± 5.6 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 6 | 6 | |
| Male | 17 | 17 | |

End points

End points reporting groups

| | |
|--|---------------------|
| Reporting group title | Placebo |
| Reporting group description: Placebo arm, one tablet once a day for 6 weeks | |
| Reporting group title | Empagliflozin 25 mg |
| Reporting group description: Empagliflozin 25 mg, one tablet once a day for 6 weeks | |

Primary: Change in 24 hour urine volume from baseline to day 3

| | |
|---|---|
| End point title | Change in 24 hour urine volume from baseline to day 3 |
| End point description: | |
| End point type | Primary |
| End point timeframe: Change in 24 hour urine volume from baseline to day 3 | |

| End point values | Placebo | Empagliflozin 25 mg | | |
|--|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 23 | | |
| Units: millilitres | | | | |
| least squares mean (confidence interval 95%) | -117.65 (-348.78 to 113.49) | 425.16 (118.26 to 662.07) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Change in 24 hour urine volume from baseline to D3 |
| Comparison groups | Placebo v Empagliflozin 25 mg |
| Number of subjects included in analysis | 46 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 ^[1] |
| Method | ANCOVA |

Notes:

[1] - Mean difference from placebo 549.30 mls (151.42 to 947.17; 95% CI), p value < 0.004

Primary: Change in 24 hour urine volume from baseline to week 6

| | |
|------------------------|--|
| End point title | Change in 24 hour urine volume from baseline to week 6 |
| End point description: | |

| | |
|--|---------|
| End point type | Primary |
| End point timeframe: | |
| Change in 24 hour urine volume from baseline to week 6 | |

| End point values | Placebo | Empagliflozin 25 mg | | |
|--|-----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 23 | | |
| Units: millilitre(s) | | | | |
| least squares mean (confidence interval 95%) | -117.65 (-348.78 to 113.49) | 425.16 (188.26 to 662.07) | | |

Statistical analyses

| Statistical analysis title | Change in 24h urinary volume from baseline to wk6 |
|---|---|
| Comparison groups | Placebo v Empagliflozin 25 mg |
| Number of subjects included in analysis | 46 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | ANCOVA |

Secondary: Change in 24 hour urinary sodium at week 6 from baseline

| | |
|--|--|
| End point title | Change in 24 hour urinary sodium at week 6 from baseline |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change in 24 hour urinary sodium at week 6 from baseline | |

| End point values | Placebo | Empagliflozin 25 mg | | |
|--|------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 23 | | |
| Units: millimole(s)/litre | | | | |
| least squares mean (confidence interval 95%) | 0.42 (-10.26 to 11.10) | -7.99 (-18.7 to 2.69) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Change in 24 hour urinary sodium at week 6 |
| Comparison groups | Placebo v Empagliflozin 25 mg |
| Number of subjects included in analysis | 46 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.81 |
| Method | ANCOVA |

Secondary: Change in serum creatinine at week 6 from baseline

| | |
|--|--|
| End point title | Change in serum creatinine at week 6 from baseline |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change in serum creatinine at week 6 from baseline | |

| End point values | Placebo | Empagliflozin 25 mg | | |
|--|-------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 23 | | |
| Units: millimole(s)/litre | | | | |
| least squares mean (confidence interval 95%) | -10.81 (-19.2 to -2.44) | -0.44 (-8.82 to 7.94) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Change in serum creatinine at week 6 from baseline |
| Comparison groups | Placebo v Empagliflozin 25 mg |
| Number of subjects included in analysis | 46 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.512 |
| Method | ANCOVA |

Secondary: Change in urinary Protein:Creatinine Ratio at week 6 from baseline

| | |
|--|--|
| End point title | Change in urinary Protein:Creatinine Ratio at week 6 from baseline |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change in urinary Protein:Creatinine Ratio at week 6 from baseline | |

| End point values | Placebo | Empagliflozin 25 mg | | |
|--|-----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 23 | | |
| Units: milligram/millimol | | | | |
| least squares mean (confidence interval 95%) | -3.05 (-7.05 to 0.97) | 2.26 (-1.75 to 6.28) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Change in urine PCR from baseline to wk6 |
| Comparison groups | Placebo v Empagliflozin 25 mg |
| Number of subjects included in analysis | 46 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.399 |
| Method | ANCOVA |

Secondary: Change in urinary Albumin:Creatinine Ratio at week 6 from baseline

| | |
|--|--|
| End point title | Change in urinary Albumin:Creatinine Ratio at week 6 from baseline |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change in urinary Albumin:Creatinine Ratio at week 6 from baseline | |

| End point values | Placebo | Empagliflozin 25 mg | | |
|--|-----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 23 | | |
| Units: milligram/millimol | | | | |
| least squares mean (confidence interval 95%) | -1.10 (-2.98 to 0.77) | 1.18 (-0.69 to 3.05) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | Change in uACR from baseline to week 6 |
| Comparison groups | Placebo v Empagliflozin 25 mg |

| | |
|---|---------------|
| Number of subjects included in analysis | 46 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.543 |
| Method | ANCOVA |

Secondary: Change in cystatin C from baseline to week 6

| | |
|--|--|
| End point title | Change in cystatin C from baseline to week 6 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change in cystatin C from baseline to week 6 | |

| End point values | Placebo | Empagliflozin 25 mg | | |
|--|--------------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 23 | | |
| Units: nanogram/millilitre | | | | |
| least squares mean (confidence interval 95%) | 22.50 (-91.52 to 136.52) | 31.35 (-80.07 to 142.75) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Change in cystatin C from baseline to week 6 |
| Comparison groups | Placebo v Empagliflozin 25 mg |
| Number of subjects included in analysis | 46 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.99 |
| Method | ANCOVA |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomisation to the last patient visit (visit 10), which was 4 weeks post discontinuation of investigational medicinal product (both treatment arms and last arm being either empagliflozin 25 mg od or placebo).

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 21.1 |

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo arm, one tablet once a day for 6 weeks

| | |
|-----------------------|---------------------|
| Reporting group title | Empagliflozin 25 mg |
|-----------------------|---------------------|

Reporting group description:

Empagliflozin 25 mg, one tablet once a day for 6 weeks

| Serious adverse events | Placebo | Empagliflozin 25 mg | |
|---|--|---------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 23 (13.04%) | 2 / 23 (8.70%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 23 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardiac failure congestive | Additional description: 2 x cases of Cardiac Failure (congestive), 1 on placebo (after washout period following treatment of empagliflozin) and 1 on discontinuation of empagliflozin. | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 1 / 23 (4.35%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Rectal Haemorrhage | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 1 / 23 (4.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|--|----------------|--|
| Psychiatric disorders | | | |
| Delerium | Additional description: In relation to sepsis caused by cellulitis | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 23 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 23 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 23 (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: 5 %

| Non-serious adverse events | Placebo | Empagliflozin 25 mg | |
|---|-----------------|---------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 23 (39.13%) | 13 / 23 (56.52%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lipoma | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 23 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 1 / 23 (4.35%) | |
| occurrences (all) | 1 | 1 | |
| Vascular disorders | | | |
| hypotension | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | 0 / 23 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 23 (0.00%) | 1 / 23 (4.35%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|---|---|--|
| Dizziness subjects affected / exposed occurrences (all) | 0 / 23 (0.00%) 0 | 1 / 23 (4.35%) 1 | |
| General disorders and administration site conditions Thirst subjects affected / exposed occurrences (all) | 0 / 23 (0.00%) 0 | 1 / 23 (4.35%) 1 | |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Rectal haemorrhage subjects affected / exposed occurrences (all) | 0 / 23 (0.00%) 0 0 / 23 (0.00%) 0 | 2 / 23 (8.70%) 2 1 / 23 (4.35%) 1 | |
| Respiratory, thoracic and mediastinal disorders Lower respiratory tract infection subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) | 1 / 23 (4.35%) 1 1 / 23 (4.35%) 2 | 1 / 23 (4.35%) 1 0 / 23 (0.00%) 0 | |
| Renal and urinary disorders Renal impairment subjects affected / exposed occurrences (all) Dysuria subjects affected / exposed occurrences (all) Pollakiuria subjects affected / exposed occurrences (all) | 0 / 23 (0.00%) 0 0 / 23 (0.00%) 0 1 / 23 (4.35%) 1 | 2 / 23 (8.70%) 3 1 / 23 (4.35%) 1 0 / 23 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all) | 0 / 23 (0.00%) 0 | 1 / 23 (4.35%) 1 | |
| Infections and infestations | | | |

| | | | |
|---|---------------------|----------------------|--|
| Viral upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 23 (0.00%) 0 | 3 / 23 (13.04%) 3 | |
| Balanitis candida subjects affected / exposed occurrences (all) | 1 / 23 (4.35%) 1 | 1 / 23 (4.35%) 1 | |
| Sinusitis subjects affected / exposed occurrences (all) | 1 / 23 (4.35%) 1 | 0 / 23 (0.00%) 0 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 23 (4.35%) 1 | 0 / 23 (0.00%) 0 | |
| Metabolism and nutrition disorders | | | |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 1 / 23 (4.35%) 1 | 0 / 23 (0.00%) 0 | |
| Hypoglycaemia subjects affected / exposed occurrences (all) | 0 / 23 (0.00%) 0 | 1 / 23 (4.35%) 2 | |
| Gout subjects affected / exposed occurrences (all) | 1 / 23 (4.35%) 1 | 2 / 23 (8.70%) 2 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 22 January 2018 | Participant selection and enrolment: the addition of the Scottish Diabetes Research Network including GoDARTS database. Inclusion criteria was changed from HbA1c in the last 3 months of 6.5% < and <10.0%, to exclusion criteria of HbA1c < 6.0%. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29042392>