**Appendix 1**. Other cardiac measures of function and structure

|  |
| --- |
| * Peak Systolic Strain
* Left Ventricular Ejection Fraction
* Stroke volume
* LV end-diastolic volume
* LV end-systolic volume
* LV end-diastolic mass
* Left Ventricular End Diastolic Mass/volume ratio
* Pre-and post contrast T1 mapping to calculate volume of distribution, a marker of diffuse cardiac fibrosis
* Myocardial Perfusion Reserve ( a measure of microvascular function)
 |

**Appendix 2 –** Secondary outcome measures

|  |
| --- |
| * HbA1c
* Lipid profile including total-, LDL- and HDL-cholesterol and triglycerides
* Liver Function Tests
* Renal Function Tests
* Thyroid function tests
* Complete Blood Count (Hematocrit)
* Vitamin D
* Endothelial function (EPCs & SDF-1α)
* Measures of inflammation (hs-CRP)
* Anthropometirc measures – body weight, height, BMI, blood pressure
* Cardiorespiratory fitness (V02 max)
* Level of physical activity (accelerometer/inclinometer)
* 7-point glucose profile
* Treatment satisfaction & quality of life
* Thoracic and abdominal subcutaneous and visceral fat assessment
 |

**Appendix 3** – Participant flow chart

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**Appendix 4** – Examination and measures

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Visit | Consent /Screening (Visit 0) | Baseline (Visit 1) | Baseline (Visit 2) | Baseline (Visit 3) |  Follow Up Contact |  Follow Up Contact | Pre-Visit 4 Self Reporting | 1st Follow Up, 2nd Dispensing (Visit 4 )  | Pre-Visit 6 Self Reporting | Follow Up MRI (Visit 5)  | 2nd Follow Up (Visit 6) |
| Time-point | n/a | n/a | n/a | Week 0 | Weeks 1,2,3 | Weeks 4,6,9 | 11 weeks\* | 12 weeks | 25 weeks\* | 26 weeks(< or > v6) | 26 weeks(< or > v5) |
| Visit Window  | n/a |  n/a | n/a | n/a | +/- 7 days | +/- 7 days | +/- 7 days | +/- 14 days | +/- 7 days | +/- 14 days | +/- 14 days |
| HbA1C Finger prick Test | √ |  |  |  |  |  |  |  |  |  |  |
| Cardiac MRI  |  |  | √ |  |  |  |  |  |  | √ |  |
| Standard Biochemical variables |  | √ |  |  |  |  |  | √ |  |  | √ |
| Other Biochemical measures i.e. chronic low-grade inflammation |  | √ |  |  |  |  |  | √ |  |  | √ |
| Anthropometric variables |  | √ |  |  |  |  |  | √ |  |   | √ |
| Blood Pressure |  | √ |  |  |  |  |  | √ |  |   | √ |
| Smoking, Medical & Family History |  | √ |  |  |  |  |  |  |  |  |  |
| Pregnancy Test |  | √ |  | √ |  |  |  | √ |  |   | √ |
| Endothelial function |  | √ |  |  |  |  |  |  |  |  | √ |
| Vitamin D |  | √ |  |  |  |  |  |  |  |  | √ |
| Cardio-respiratory fitness (graded VO2 max test) |  |  |  | √ (+2 weeks) |  |  |  |  |  |  | √ |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Visit | Consent /Screening (Visit 0) | Baseline (Visit 1) | Baseline (Visit 2) | Baseline (Visit 3) |  (Follow Up Contact |  (Follow Up Contact | Pre-Visit 4 Self Reporting | 1st Follow Up, 2nd Dispensing (Visit 4 )  | Pre-Visit 6 Self Reporting | Follow Up MRI (Visit 5)  | 2nd Follow Up (Visit 6) |
| Time-point | Any | n/a | n/a | Week 0 | Weeks 1,2,3 | Weeks 4,6,9 | 11 weeks\* | 12 weeks | 25 weeks\* | 26 weeks(< or > v6) | 26 weeks (< or > v5) |
| Visit Window  | n/a | n/a | n/a | n/a | +/- 7 days | +/- 7 days | +/- 7 days | +/- 14 days | +/- 7 days | +/- 14days | +/- 14 days |
| Physical Activity and Sitting Time\*\* |  | √ |  |  |  |  |  | √ |  |  | √ |
| Quality of life and depression |  | √ |  |  |  |  |  | √ |  |  | √ |
| Treatment satisfaction |  | √ |  |  |  |  |  | √ |  |  | √ |
| 7-point G profile\* |  |  | √ |  |  |  | √ |  | √ |  |  |
| Hypoglycaemia Diary\*\*\* |  |  |  |  |  |  |  | √ |  |  | √ |
| Adverse events |  | √ |  |  | √ | √ |  | √ |  |  | √ |

**Key:** (\*) The 7-point glucose profile is self-reported by the participant at (-)2 weeks, 11 weeks and 25 weeks prior to the visits 3, 4 and 6 in which the data is collected.

(\*\*) An accelerometer and inclinometer are setup for 7 days at visit 1 to be returned in the post or at visit 3 and then setup at visits 4 and 6 and returned in the post.

(\*\*\*) The hypoglycaemia diary is self-reported by the patient throughout the 26 weeks of drug treatment and a copy of this taken at visit 4 and visit 6.