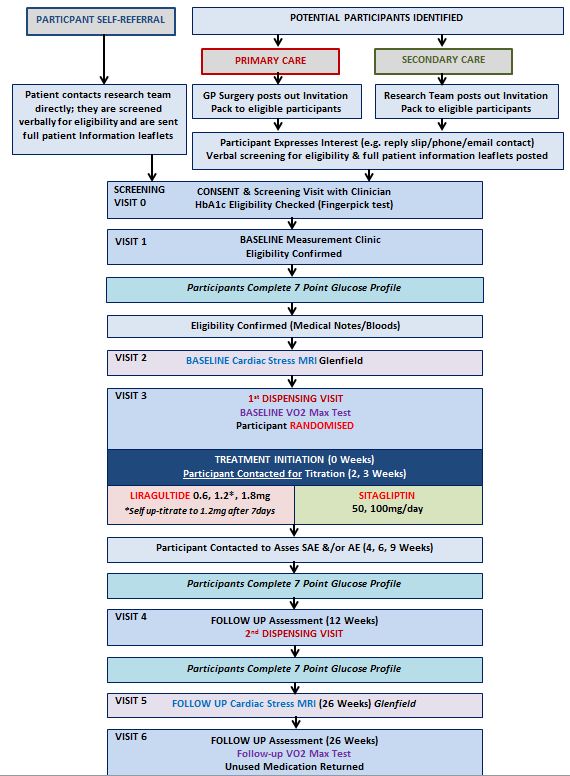
**Appendix 1**. Other cardiac measures of function and structure

|  |
| --- |
| * 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.