GLOOCOSE Study Basic Result Summary

1. Participant Flow

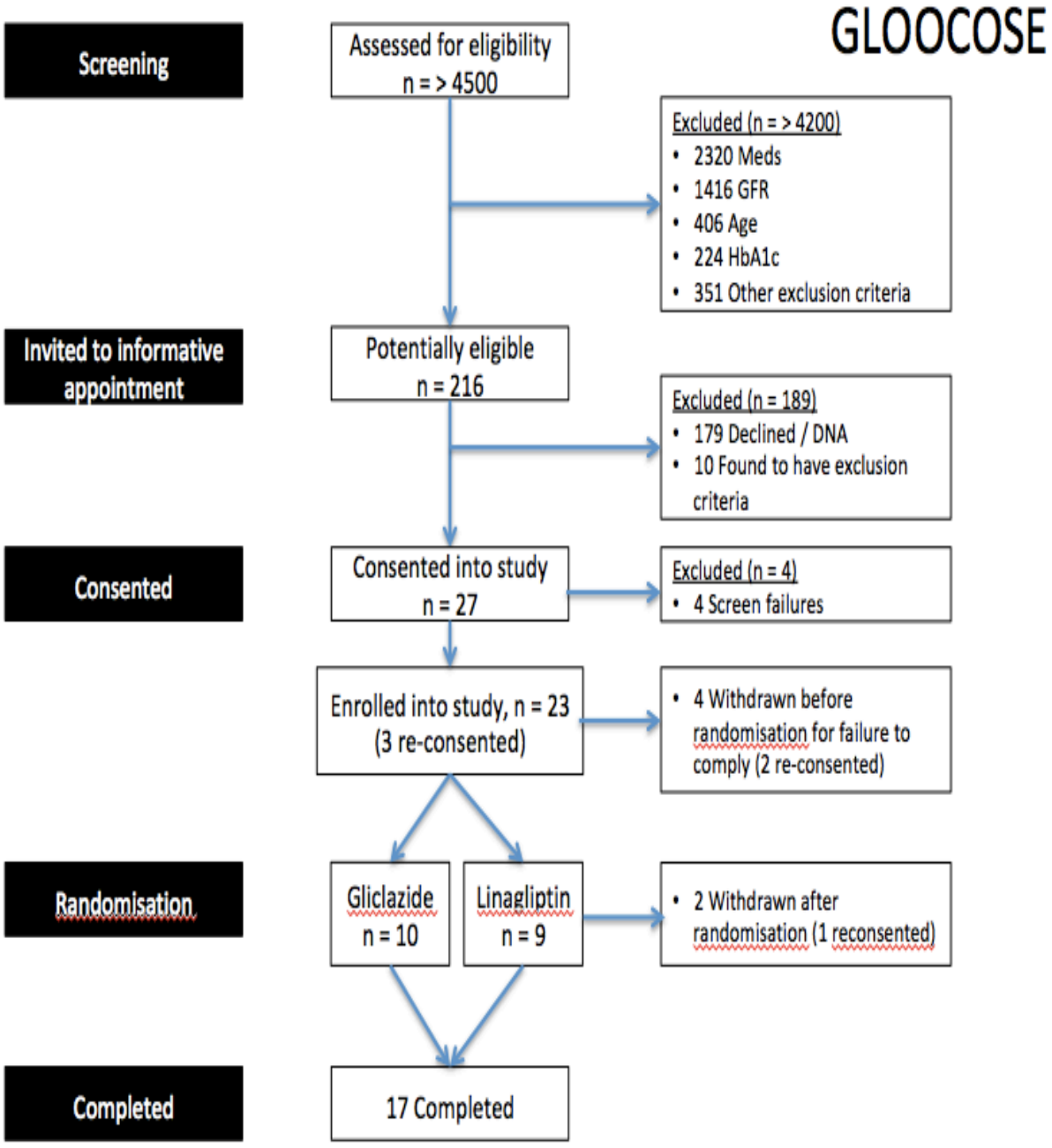

Figure 1: Number of patients screened, consented, randomised and completed study

2. Baseline Characteristics of Participants

Baseline Characteristics	Randomised to Gliclazide (n = 10)	Randomised to Linagliptin (n = 9)
Sex	Male 8 Female 2	Male 9 Female 0
Ethnicity	Caucasian 6 Afrocaribbean 1 Asian 2 Other/Mixed 1	Caucasian 6 Afrocaribbean 0 Asian 3 Other/Mixed 0
Age, y	72 (50 to 76)	71 (57 to 79)
Weight, kg	97.5 (60.8 to 116.6)	80.2 (64.8 to 103.8)
BMI, kg/m^2	33.1 (25.7 to 39.5)	29.4 (22.4 to 33.8)
Blood Pressure, mmHg	141 / 76 (99 to 173 / 59 to 91)	134 / 78 (94 to 153 / 56 to 94)
Duration of Diabetes, y	13 (6 to 23)	14 (3 to 30)
HbA1c, mmol/mol	55 (39 to 62)	52 (33 to 64)
Fasting CBG pre-randomisation, mmol/L	7.5 (5.6 to 10.3)	6.5 (4.7 to 10.9)
eGFR MDRD, ml/min/1.73m^2	37 (20 to 45)	32 (26 to 44)
Urine ACR, mg/mmol	35 (0 to 72)	6 (1 to 257)
Urine PCR, mg/mmol	58 (0 to 136)	16 (0 to 339)
Co-morbidities	Hypertension 10 Hyperlipidaemia 9 Ischaemic Heart Disease 6 Heart Failure 1 Retinopathy 2 Neuropathy 0	Hypertension 9 Hyperlipidaemia 9 Ischaemic Heart Disease 6 Heart Failure 4 Retinopathy 1 Neuropathy 0

Results presented as Median with (Data Range: Minimum to Maximum)

Table 1: Baseline characteristics of all randomised patients, n = 19

3. Outcome Measures

3.1 Outcome Measure: Clinical Characteristics

Post randomisation value – Pre randomisation value	Randomised to Gliclazide (n = 10)	Randomised to Linagliptin (n = 7)	Test statistic U, p value
Change in weight, kg	+ 0.3 (-1.1 to +4.8)	- 0.5 (-3.8 to +0.1)	12.5, p = 0.025
Change in BMI, kg/m²	+ 0.1 (-0.4 to +1.7)	- 0.1 (-1.4 to 0.0)	13.0, p = 0.033
Change in BP, mmHg	+ 5.0 / + 0.5 (-29 to +22 / -10 to +14)	+ 3.0 / + 3.0 (-19 to +33 / -10 to +12)	37.0 / 43.5, p = 0.887 / p = 0.417
Change in HbA1c, mmol/mol	+ 1.5 (-2.0 to +11.0)	+ 8.0 (-2.0 to +18.0)	49.5, p = 0.161
Change in Fasting CBGs	+ 0.5 (-0.9 to +1.2)	+ 2.6 (+0.6 to +6.8)	65.5, p = 0.001
Change in eGFR MDRD	+ 1.0 (-2.0 to +9.0)	- 1.0 (-3.0 to +1.0)	15.0, p = 0.055
Change in Urine ACR	+ 3.1 (-19.1 to +130.2)	- 0.3[a] (-9.4 to +9.4)	21.0, p = 0.368
Change in Urine PCR	+ 8.0[b] (-22.0 to +157.0)	- 1.0[a] (-20.0 to +39.0)	20.5, p = 0.456

Results presented as Median with (Data Range: Minimum to Maximum)
[a] : Based on 6 patient samples, [b]: Based on 9 patient samples

Table 2: Change in clinical outcomes for participants randomised to Gliclazide or Linagliptin

3.2 Primary Outcome Measure: Hypoglycaemic Incidence and Severity

Post randomisation value – Pre randomisation value	Randomised to Gliclazide (n = 9)	Randomised to Linagliptin (n = 7)	Test statistic U, p value
Change in total number of hypoglycaemic episodes	- 1.0 (-8.0 to +16.0)	0.0 (-6.0 to 0.0)	30.0, p = 0.918
Change in total time spent in hypoglycaemia <3.9 mmol/L, (%)	0.0 (-4.0 to +9.0)	0.0 (-5.0 to 0.0)	24.5, p = 0.470
Change in number of Level 1 hypoglycaemic episodes	0.0 (-7.0 to +10.0)	0.0 (-5.0 to 0.0)	28.0, p = 0.758
Change in total time spent in Level 1 hypoglycaemia 3.0 – 3.8 mmol/L, (%)	0.0 (-4.0 to +4.0)	0.0 (-2.0 to 0.0)	29.0, p = 0.837
Change in number of Level 2 hypoglycaemic episodes	0.0 (-2.0 to +6.0)	0.0 (-2.0 to 0.0)	30.0, p = 0.918
Change in total time spent in Level 2 hypoglycaemia <3.0 mmol/L, (%)	0.0 (-1.0 to +5.0)	0.0 (-5.0 to 0.0)	22.5, p = 0.351

Results presented as Median with (Data Range: Minimum to Maximum)

Table 3: Change in hypoglycaemic incidence and severity for participants randomised to Gliclazide or Linagliptin

3.3 Secondary Outcome Measure: Glycaemic Outcomes

Post randomisation value – Pre randomisation value	Randomised to Gliclazide (n = 9)	Randomised to Linagliptin (n = 7)	Test statistic U, p value
Change in mean CGM glucose (mmol/L)	+ 0.1 (-1.1 to +1.1)	+ 1.5 (-0.4 to +6.8)	53.0, p = 0.023
Change in estimated CGM HbA1c (mmol/mol)	0.0 (-8.0 to +7.0)	+ 10.0 (-2.0 to +47.0)	54.0, p = 0.016
Change in time spent in normoglycaemia 3.9 – 10.0 mmol/L, (%)	- 3.2 (-12.9 to +6.1)	- 12.0 (-64.0 to +10.4)	21.0, p = 0.299
Change in Co-efficient of Variation CV, (%)	- 0.7 (-12.1 to +12.9)	- 9.2 (-15.7 to +6.3)	14.0, p = 0.071
Change in Standard Deviation SD	0.0 (-1.0 to +0.8)	- 0.6 (-0.9 to +0.6)	26.0, p = 0.606
Change in Continuous Overall Net Glycaemic Action (CONGA-1)	- 0.3 (-0.8 to +0.7)	0.0 (-0.7 to +0.7)	33.0, p = 0.918
Change in Mean Absolute Glucose (MAG)	- 0.2 (-0.4 to +0.5)	+ 0.1 (-0.5 to +0.5)	36.0, p = 0.681
Change in Mean of Daily Differences (MODD)	- 0.2 (-1.5 to +0.2)	- 0.4 (-0.7 to +0.3)	29.0, p = 0.837
Change in Mean Amplitude of Glucose Excursions (MAGE)	+ 0.3 (-1.9 to +3.3)	- 1.4 (-2.5 to +1.7)	19.0, p = 0.210

Results presented as Median with (Data Range: Minimum to Maximum)

Table 4: Change in overall glycaemic control and glycaemic variability outcomes for participants randomised to Gliclazide or Linagliptin

Post randomisation value – Pre randomisation value	Randomised to Gliclazide (n = 9)	Randomised to Linagliptin (n = 7)	Test statistic U, p value
Change in time spent in hyperglycaemia >10.0 mmol/L, (%)	+ 2.6 (-5.3 to +13.7)	+ 11.3 (-10.2 to +69.0)	41.0, p = 0.351
Change in time spent in hyperglycaemia >13.9 mmol/L, (%)	+ 0.6 (-10.5 to +4.6)	+ 0.8 (-2.7 to +61.9)	38.0, p = 0.536
Change in Low Blood Glucose Index (LBGI)	0.0 (-0.7 to +2.1)	- 0.2 (-2.3 to 0.0)	16.0, p = 0.114
Change in High Blood Glucose Index (HBGI)	+ 0.3 (-2.8 to +3.0)	+ 1.7 (-1.6 to +22.8)	45.0, p = 0.174

Results presented as Median with (Data Range: Minimum to Maximum)

Table 5: Change in time spent in hyperglycaemic thresholds and risk indices for participants randomised to Gliclazide or Linagliptin

3.4 Secondary Outcome Measure: Serum and Urine Biomarkers

Post randomisation value – Pre randomisation value	Randomised to Gliclazide (n = 10)	Randomised to Linagliptin (n = 7)	Test statistic U, p value
Change in serum MCP-1 (pg/ml)	- 12.1 (-55.2 to +14.0)	- 18.1 (-47.5 to +20.9)	31.0, p = 0.740
Change in urine MCP-1 (pg/ml)	- 15.9 (-363.5 to +10.0)	- 7.3 (-123.8 to +154.4)	42.0, p = 0.536
Change in urine MCP-1/ creatinine ratio	- 4.4 (-30.6 to +1.5)	+ 3.4 (-1.0 to +6.1)	65.0, p = 0.002
Change in serum TGF-β1 (ng/ml)	+ 2.6 (-1.9 to +7.9)	+ 2.6 (-0.3 to +6.0)	37.0, p = 0.887
Change in urine TGF-β1 (pg/ml)	0.0 (-198.5 to +72.6)	0.0 (-88.0 to +1023.4)	36.0, p = 1.000
Change in urine TGF-β1/ creatinine ratio	0.0 (-39.7 to +5.3)	0.0 (-4.7 to +47.6)	36.0, p = 1.000

Results presented as Median with (Data Range: Minimum to Maximum)

Table 6: Change in serum and urine biomarkers for participants randomised to Gliclazide or Linagliptin

3.5 Secondary Outcome Measure: Patient Satisfaction (DTSQ Scores)

Post randomisation value – Pre randomisation value	Randomised to Gliclazide (n = 10)	Randomised to Linagliptin (n = 7)	Test statistic U, p value
Change in overall DTSQ score	+ 0.5 (-6.0 to +4.0)	+ 2.0 (-6.0 to +10.0)	41.5, p = 0.536
Change in Question 2 DTSQ	0.0 (-3.0 to +1.0)	0.0 (-2.0 to +4.0)	35.5, p = 1.000
Change in Question 3 DTSQ	+ 0.5 (-1.0 to +1.0)	0.0 (-2.0 to +1.0)	21.5, p = 0.193

Results presented as Median with (Data Range: Minimum to Maximum)

Table 7: Change in DTSQ scores for participants randomised to Gliclazide or Linagliptin

4. Adverse Events

There were no serious adverse events associated with this trial. There was one adverse event of special interest (AESI) reported in a participant randomised to Linagliptin (deranged liver function tests).