Evidence Tables

Alphaglu_AntiD: Is the alphaglucosidase inhibitor acarbose as monotherapy or in combination with oral antidiabetic drugs effective in the control of blood glucose in people with type 2 diabetes compared to other oral antidiabetic drugs regimens or placebo?

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect size	Source of funding
Goke B, German Pioglitazone Study Group. Improved glycemic control and lipid profile in a randomized study of pioglitazone compared with acarbose in patients with type 2 diabetes mellitus. Treatments in Endocrinology 2002; 1(5):329-336. Ref ID: 44	RCT 1++	N=271 patients from 47 study centres in Germany	Inclusion criteria: Newly diagnosed type 2 diabetes patients or those who had received previous treatment with oral anthyperglycemic agents (but these were stopped 2 mths prior to the study). HbA1c levels between 7,5 and 11.5% and fasting blood glucose levels of 140mg/dl or more. BMI 25 to 43 kg/m2. 54% were male with a	N=129 Pioglitazone once daily 45mg/day.	N=136 Acarbose starting with 50mg once daily titrated to 300mg/day as 3 equal doses.	26 weeks	Change in HbA1c, changes in serum triglyceride and cholesterol levels, Insulin and C peptide ;eve;s, blood pressure and adverse events	Mean HbA1c was reduced from 8.98 ± 1.2% to 7.82 ± 1.95% with pioglitazone treatment and from 9.03 ± 1.32% to 8.55 ± 1.96% with acarbose treatment during the 26 week study. The change from baseline to endpoint was significantly greater for pioglitazone compared with acarbose for all patients ($p<0.001$) and for those who had ($p=0.009$) or had not ($p<0.001$) received previous medication for diabetes. Fasting plasma glucose (mg/dl) –56.41 ± 73.6 change from baseline for pioglitazone and –22.54 ± 65.86 for acarbose ($p<0.001$) Fasting insulin (mU/L) –7.21 ± 10.27 change from baseline for pioglitazone and –3.82 ± 19.32 for acarbose ($p<0.001$) C-peptide (ug/L) –1.34 ± 2.03 change from baseline for pioglitazone and –0.51 ± 2.08 for acarbose ($p<0.001$). No significant difference was found between treatments in terms of total cholesterol and LDL-cholesterol. Triglycerides were decreased by 71.1 ± 184.1mg/dl with pioglitazone compared with 38.1 ± 171.3 mg/dl with acarbose ($p=0.001$). HDL-cholesterol level was increased by 7.8 ± 10.2 mg/dl with	Takeda

			mean age of 60 years and mean BMI of 31 kg/m2. Mean HbA1c was 9%.					pioglitazone compared with a decrease of 0.8 ± 24.1 wth acarbose (p<0.001).Decrease from baseline in very low density lipoprotein cholesterol was significantly greater with pioglitazone than with acarbose (-11.1 ± 26.3 vs –7.1 ± 26.1, p=0.037). Body weight increased with pioglitazone treatment and decreased with acarbose treatment (1.23 ±5.42 kg vs –2.09 ± 3.58 kg, p<0.001). Both systolic and diastolic blood pressure decreased in the pioglitazone treated patients compared with those on acarbose but only significantly for systolic blood pressure (-5.6 ± 17.7 vs 0.4 ± 18.4, p<0.001). Treatment emergent adverse events possibly related to study medication occurred in 13 (10%) of patients receiving pioglitazone (including 6 cases of edema) and in 54 (40%) of patients receiving acarbose with 46 reporting abdominal distension and flatulence.	
Van del Laar FA, Lucassen PLBJ, Akkermans RP, Van de Lisdonk, Rutten GEHM, Van Weel C. Alpha-glucodase inhibitors for type 2 diabetes mellitus. The Cochrane Database of Systematic Reviews 2005, Issue 2. ID 1136	Cochrane systematic review 1++	N=30 acarbose RCTs (search until April 2003).	Patients with new or existing type 2 diabetes.	Monotherapy with alpha-glucosidase inhibitors (only acarbose results reported here).	Any other intervention.	Minimum duration12 weeks	Mortality, diabetes related complications, quality of life, glycaemic control, plasma lipids, fasting and post-load insulin and c-peptide levels, body weight,	***Acarbose vs placebo (N=28 studies)*** Significant differences were found in terms of: Change in glycated haemoglobin (%) weighted mean difference (WMD) = -0.77 (95%CI –0.9 to –0.64) Change in fasting blood glucose (mmol) WMD =-1.09 (95%CI –1.36 to –0.83). Change in post-load blood glucose (mmol/l) WMD=-2.32 (95%CI –2.73 to –1.92) Changes in post load insulin levels (pmol/l) WMD=-40.82 (%%CI –60.64 to –21.01). Change in BMI (kg/m2) WMD= -0.17 (95%CI –0.25 to –0.08) Occurrence of adverse effects OR=3.37 (95%CI 2.6 to 4.36)	N/A

							adverse effects.	Occurrence of gastrointestinal adverse effects OR=3.30 (95%CI 2.31 to 4.71) Change in post-load blood glucose (mmol/l) (2 hours) WMD=-2.27 (95%CI –2.67 to –1.88). No significant differences were found in terms of change in total, HDL, LDL cholesterol or triglycerides, change in fasting insulin levels, changes in fasting and post load C-peptide levels, body weight or total deaths. ***Acarbose vs sulphonylurea (N=8)*** Significant differences were found in terms of: Change in fasting blood glucose (mmol/l) WMD=0.69 (95%CI0.16 to 1.23) Change in fasting insulin levels (p/mol) WMD=-24.78 (95%C|l –43.30 to –6.26) Change in post-load insulin levels (p/mol) WMD=133.17 (95%CI-184.53 to –81.82) Total deaths OR=0.32 (95%CI 0.01 to 8.08) Disease related deaths OR=0.32 (95%CI 0.01 to 8.08) Occurrence of adverse effects OR=3.95 (95%CI 2.00 to 7.80) Occurrence of gastro intestinal effects OR=7.70 (95%CI 3.64 to 16.31). Change in post-load insulin levels (pmol/l) (2 hours). WMD=-115.84 (95%CI –152.52 to –79.15). Significant differences were not found in terms of change in glycated haemoglobin, change in post load blood glucose, change in total, HDL., LDL cholesterol and triglycerides, change in fasting and post load C-peptide levels, change in body weight and BMI and change in post load blood glucose (2 hours). NB The overall comparison in respect of glycated haemoglobin was non-significant, however the results in the subgroup “acarbose 100mg TID vs glibenclamide 3.5mg TID” were	

								not consistent with the other comparisons and there was significant heterogeneity. Leaving the entire sub-group out of the analysis would give an overall effect of 0.6% (95%CI 0.3 to 1.0) in favour of sulphonylurea with a non-significant test for heterogeneity. Acarbose vs meformin (N=1) Significant differences were found in terms of: Change in fasting blood glucose (mmol/l) WMD=-0.39 (95%CI-0.74 to –0.04) Change in post-load blood glucose (mmol/l) WM D=-0.39 (95%CI-0.74 to –0.04) Change in total cholesterol (mmol/l) WMD= -0.94 (95%CI –1.66 to –0.22) Change in LDL cholesterol (mmol/l) WMD= -0.94 (95%CI –1.52 to –0.36) Occurrence of adverse events OR=15.00 (95%CI3.06 to 73.58). Significant differences were not found in terms of change in glycated haemoglobin, change in HDL cholesterol and triglycerides, change in fasting and post load insulin levels and change in body weight. ***Acarbose vs nateglinide (N=1)*** Significant differences were found in terms of: Change in body weight (kg) WMD=-0.68 (95%CI-1.30 to –0.06) Occurrence of adverse effects OR=1.92 (95%CI 1.05 to 3.5) Occurrence of gastrointestinal effects OR=3.22 ((%%CI 1.66 to 6.24). Significant differences were not found in terms of change in glycated haemoglobin and change in fasting blood glucose.	
Bachmann W, Petzinna D, Raptis SA, Wascher T,	RCT 1+	N=373 patients from 42	Inclusion criteria: patients with	N=164 Acarbose titrated up to 100mg 3	N=166 Placebo	78 weeks	Change in HbA1c value from	Acarbose significantly improved HbA1c levels compared with placebo (9.07 vs. 9.61, least square mean (LS mean) difference –0.54,	Bayer

Westermeier T. Long-Term Improvement of Metabolic Control by Acarbose in Type 2 Diabetes Patients Poorly Controlled with Maximum Sulfonylurea Therapy. Clinical Drug Investigation 2003; 23(10):679-686. Ref ID: 141		sites in 6 European countries (N=330 patients in the ITT analysis due to no valid HbA1c data).	type 2 diabetes had to be treated with diet and sulfonylureaas for at least 3 years and with a maximum dose of either glibenclamide or glicazide. They had to have stable weight (BMI 25 to 35kg/m2) and an age in the range 50 to 75 years. Mean age 63 years with a mean BMI of 29kg/m2 and mean HbA1c of 9%. 48% were male in the acarbose group and 43% in the placebo group	times daily. Gibenclamide /gliclazide dose had to remain constant for the study duration except for reductions to prevent hypoglycaemia.	Gibenclamide /gliclazide dose had to remain constant for the study duration except for reductions to prevent hypoglycaemia.		baseline. Changes in fasting and 1h postprandial blood glucose and C peptide. Adverse events.	95%CI-0.86 to –0.22, p=0.001). Standard targets of 6.5 to 7.0% were reached by 11% of patients in the acarbose group and by 5% in the placebo group. There was a significant LS mean difference of –14.8 mg/dL (p=0.0195) in fasting blood glucose levels and significant differences in 1-hour-postprandial blood glucose (LS-mean difference –33.4 mg/dL p<0.0001) and in the rise in blood glucose from fasting to 1-h postprandial (LS-mean differ3ence –19.6 mg/dL, p=0.0001) all in favour of acarbose. Neither fasting nor 1h-postprandial C-peptide concentrations were affected by acarbose treatment. 61 drug-related adverse events (33.3%) occurred in the acarbose group and 30 (16% in the placebo group. Flatulence was reported by 48 patients (26.2%) in the acarbose group compared with 20 placebo recipients (10.6%) and diarrhoea occurred in seven acarbose recipients (3.8%) with no incidences reported in the placebo group.	
Feinbock C, Luger A, Klingler A, Egger T, Bielesz GK, Winkler F et al. Prospective multicentre trial comparing the efficacy of, and compliance with, glimepiride or acarbose treatment in patients with type 2	RCT 1+	N=219 from 17 centres in Austria	Inclusion criteria: Type 2 diabetics uncontrolled by diet alone. Patients had baseline HbA1c more than or equal to 7.8% with a	N=111 Glimepiride Titrated at weekly intervals (1mg/day) until target FBG of 7.8mmol/l achieved during a 6 week dose finding phase..	N=108 Acarbose Titrated at weekly intervals (50mg 3 times a day) until target FBG of 7.8mmol/l	26 weeks	Number of responder patients in each group (those with a FBG of 7.8mmol/l or less at the final study visit).	The glimepiride group had a significantly greater responder rate than acarbose (61 vs 34%, p<0.001) and a significantly greater decrease in HbA1c (2.5 ± 2.2% vs 1.8 ± 2.2%, p=0.014) and FBG (2.6 ± 2.6mmol/l vs 1.4 ± 2.8mmol/l, p=0.004). The glimepiride group had a decreased glucose response to breakfast compared with acarbose (area under curve end: 8.9 ± 2,7	Aventis

diabetes not controlled with diet alone. Diabetes, Nutrition & Metabolism - Clinical & Experimental 2003; 16(4):214-221. Ref ID: 32			BMI between 24 and 35kg/m2. Mean age was 57 years with a mean BMI of 29kg/m2. In the glimepiride group 66% were male, with a mean HbA1c of 9.1 and FBG of 10.3mmol/l. In the acarbose group 58% were male, with a mean HbA1c of 9.4 and FBG of 10.9mmol/l.	The dose was increased to 2,3,4 or 6 mg/day.	achieved during a 6 week dose finding phase. The dose was increased to 100, 150 or 200mg 3 times a day.		Secondary efficacy criteria included changes from baseline in HbA1c, weight, postprandial blood glucose and C-peptide levels. Adverse events.	mmol/l vs 11.3 ± 3.9 mmol/l, p=0.0001). Decreased glucose response to breakfast (intraindividual reduction) was 3.1 ± 3.1 mmol/l glimepiride vs 1.7 ± 3.5 mmol/l acarbose, p=0.004. The difference in C peptide profiles (intraindividual difference) was 0.53 ± 1.7 ng/ml glimepiride vs –0.31 ± 1.72 ng/ml for acarbose, p=0.001 The mean body weight of the glimepiride. group decreased by 0.4 ± 5.2kg (NS) and that of the acarbose group by 1.9 ± 3.9kg (p=0.001). More patients in the acarbose group reported adverse events (52% vs 81%, p=0.001). In the acarbose group 73% of the patients experienced adverse events thought to be drug related compared with 33% in the acarbose group. Hypoglycaemic episodes were experienced by 18% of the glimepiride group and 1.9% of the acarbose group (there were no severe episodes requiring external help).	
Hwu CM, Ho LT, Fuh MM, Siu SC, Sutanegara D, Piliang S et al. Acarbose improves glycemic control in insulin-treated Asian type 2 diabetic patients: results from a multinational, placebo-controlled study. Diabetes Research & Clinical Practice 2003;	RCT 1+	N=112 patients from 6 medical centres in Indonesia, Hong Kong and Taiwan	Inclusion criteria: Asian patients with type 2 diabetes treated with insulin (2 injections of intermediate insulin a day of at least 20IU/day) but inadequately	N=55 Acarbose 50gm tid with meals for 6 weeks then titrated to 100mg tid for 12 weeks. Usual insulin doses continued.	N=56 Matching placebo. Usual insulin doses continued.	18 weeks	Change in HbA1c, fasting blood glucose, one and two hour postprandial blood glucose and lipid levels. Adverse events	There was a significant difference in HbA1c between the two groups (-0.69%, 95%CI-0.18 to –0.2) in favour of acarbose. Differences between the treatment groups were significant for the 1-h postprandial blood glucose (-1.89 mmol/l, 95%CI –3.5 to –0.28),p=0.029) but failed to reach significance for the 2-h value. There were no differences between groups for the changes from baseline to study endpoint for fasting blood glucose, triglycerides, total cholesterol and LDL cholesterol. There was a	Bayer

60(2):111-118. Ref ID: 1150			controlled (HbA1c level 8 to 11%). Mean BMI was 24kg/m2, 50% were male, HbA1c was 9.5% and mean age was 54.5 in the placebo group and 58.1 in the acarbose group. Mean FBG was 9.67 in the placebo group and 11.39 in the acarbose group.					significant decrease in HDL cholesterol values in the acarbose arm (-1 ± 9 vs –3 ± 7, p=0.049). Incidence of drug-related treatment emergent adverse events were similar in the two treatment groups except for flatulence owing to acarbose (28.6% vs 16.4% for placebo).	
Lin BJ, Wu HP, Huang HS, Huarng J, Sison A, bin Abdul Kadir DK et al. Efficacy and tolerability of acarbose in Asian patients with type 2 diabetes inadequately controlled with diet and sulfonylureas. Journal of Diabetes & its Complications 2003; 17(4):179-185. Ref ID: 202	RCT 1+	N=69 (N=64 in ITT population) from 6 centres in Asia	Inclusion criteria: Type 2 diabetes patients whose previous treatment with diet and sulfonylureas proved inadequate. HbA1c value of 7-10%, a history of diabetes for at least 3 months, age between 35 and 70 with a stable body	N=32 Acarbose 50mg tid for 4 weeks titrated to 100mg tid for 20 weeks. Concomitant treatment remained unchanged.	N=32 Placebo Concomitant treatment remained unchanged.	24 weeks of treatment	Change in HbA1c. Change in blood glucose (fasting and 1 hour post prandial), serum insulin (fasting and 1 hour post-prandial and urinary glucose). Change in body weight. Adverse events.	Acarbose treatment was associated with significantly greater reductions in HbA1c (-0.91% vs. placebo 0.13%,p=0.0018) and 1-h post-prandial blood glucose levels (-2.84 mmol/l vs. placebo –0.28 mmoll/l, p=0.002). There were no significant differences between the groups regarding changes in fasting blood glucose, fasting or 1-h post prandial serum insulin, urinary glucose or body weight. Drug-related gastrointestinal side effects were reported more frequently with acarbose: flatulence 33.3% vs 6.3%, abdominal pain 9.1% vs 3.1%, diarrhoea 9.1% vs 0%, dyspepsia 9.1% vs 0%, and abdomen enlarged 6.1% vs 0%. (significance tests not performed).	Bayer

			weight and a BMI of 35 or below. Mean age 58 yrs in the acarbose group and 55yrs in the placebo group. 53% and 38% were male in the acarbose and placebo groups respectively. Mean BMI was 25kg/m2 and mean HbjA1c was 9% in each group.						
Phillips P, Karrasch J, Scott R, Wilson D, Moses R. Acarbose improves glycemic control in overweight type 2 diabetic patients insufficiently treated with metformin. Diabetes Care 2003; 26(2):269-273. Ref ID: 40	RCT 1+	N=83 from 5 centres in Australia and New Zealand	Inclusion criteria: Patients had type 2 diabetes and were 40 years or more with a BMI of 25 to 35 kg/m2 and an HbA1c of 7 to 10% at screening. Mean age 58 in the acarbose group and 62 in the placebo group. 65% and 77% were	N=40 50mg acarbose bid for 2 weeks followed by a 22 week period on 100mg acarbose bid. If this was not well tolerated the dose could be reduced to 50mg bid. Patients continued their normal metformin dose throughout the study period (mean daily dose 1700mg)	N=43 Matching placebo Patients continued their normal metformin dose throughout the study period (mean daily dose 1700mg)	4 week run in and 24 weeks of treatment	Change in HbA1c. Change in fasting blood glucose. Proportion of "treatment responders" defined as those with HbA1c levels showing a 5% or more relative reduction from baseline to	Statistically significant differences between acarbose and placebo were found in HbA1c (1.02%; 95%CI 0.543 to 1.497; p=0.0001) and fasting blood glucose (1.132 mmol/l; 95% CI 0.056 to 2.208; p=0.0395) . 18 patients (47%) in the acarbose group were classifed as responders compared to 6 (14%) in the placebo group (p=0.001). There was a small mean weight reduction in both groups which was not significantly different Treatment emergent adverse events were reported by 75% of acarbose patients and 55.8% of placebo patients (NS) There was a significant difference in the proportion of	Bayer

			male in the placebo and acarbose groups respectively.				study end. Adverse events.	patients reporting flatulence :57.5% in the acarbose group and 27.9% in the placebo group (p=0.0064).	
Ko GTC, Tsang CC, Ng CW, Wai HPS, Kan ECY. Use of acarbose or bedtime insulin after failure of treatment with conventional oral antidiabetics: A one-year randomised clinical trial. Clinical Drug Investigation 2001; 21(6):401-408. Ref ID: 194	RCT 1-	N=57 chinese patients from a single centre in Hong Kong.	Inclusion criteria: Type 2 diabetes with secondary oral antidiabetic drug failure. This is despite treatment with sulphonylurea and metformin (unless the latter was contraindicated). Persistent OAD failure was persistne thyperglycaemi a with HbA1c of more than or equal to 9.0% for 6 months or more despite maximal dosage of OADs. 33% were men and mean age was 59 years. 89%received both metformin and sulphonylurea. Mean BMI 24.6, mean	N=30 Bedtime insulin commenced as 6 units and titrated 4 weeks later with an increment of 2 to 4 units. This was adjusted at each visit aiming for an HbA1c of less than 8.5% ((type of insulin not specified). Original antidiabetic medication remained the same.	N=27 Acarbose started at 50mg 3 times a day for 2 weeks then increased to 100mg 3 times a day. Increased to the maximum dose of 200mg 3 times a day if tolerated and if HbA1c remained at or more than 8.5%. Original antidiabetic medication remained the same.	52 weeks	Fasting plasma glucose, glycated haemoglobin , 2-hour blood glucose, BMI, adverse events.	Insulin compared with acarbose gave a greater reduction in the fasting plasma glucose levels at 6 ($p<0.01$) and 12 ($p<0.05$) months after treatment. The improvements in 2 hour blood glucose and HbA1c showed no significant difference between the two groups. BMI was significantly different between the two groups at 3 months but not after this. 5/27 patients in the acarbose group developed adverse events (flatulence, diarrhoea and abdominal colic and discontinued treatment). None of the insulin treated patients developed adverse events ($p=0.008$).	Dept Research Fund

			HbA1c 10.3%.						
Segal P, Eliahou HE, Petzinna D, Neuser D, Bruckner A, Spengler M. Long-term efficacy and tolerability of acarbose treatment in patients with type 2 diabetes mellitus. Clinical Drug Investigation 2005; 25(9):589-595. Ref ID: 236	RCT 1-	N=139, single centre study, Israel	Inclusion criteria: patients aged 33 to 65 years with type 2 diabetes for 3 years or more, a fasting blood glucose value (1h-ppBG) of >200mg/dL, a fasting C-peptide level >0.6 ng/mL, systolic blood pressure <170mmHg and diastolic<100mmHg. Median diabetes duration was 11 years, diabetes was poorly controlled (median HbA1 11%) and patients were overweight (median BMI 28kg/m2). Median age was 54 in the acarbose group (54% male) and 56	N=69 Acarbose During the first 4 weeks, patients received 50mg of acarbose three times daily which was then titrated up to 300mg three times a day in weeks 5 to 8. Concomitant antidiabetic medication could be modified during treatment if required.	N=70 Placebo Concomitant antidiabetic medication could be modified during treatment if required.	78 weeks	Change in HbA1c, blood glucose and lipid levels. Adverse events.	NB The “efficacy analysis” only included N=88 patients (63% of the total study population) with 44 in each group. Acarbose significantly improved fasting (-33.7 vs 2 mg/dl p=0.039) and 1 hour postprandial (-34.4 vs. 14.9 mg/dL, p=0.009) blood glucose levels compared to placebo . There was no significant difference in terms of HbA1 compared with placebo (adjusted mean 9.6% in the acabose group and 10.6% in the placebo group, p=0.057). Adverse events were reported in 63.8% of acarbose and 32.9% of the placebo group. The difference mainly owing to gastrointestincal events, all of which occurred more frequently in the acarbose group: flatulence 62.3% vs30%, abdominal pain, 21.7% vs 4.3% and diarrhoea 10.1% vs 8.6%.	Bayer

			in the placebo group (60% male).						