SUPPLEMENTARY DATA

Supplementary Table 1. 24-week clinical trials included in the pooled analysis in which subjects received either placebo or 5 mg/day linagliptin as monotherapy or in combination with other oral glucose-lowering agents either placebo or 5 mg/day linagliptin as monotherapy or in combination with other oral glucose-lowering agents.

ClinicalTrials.gov	**Background treatment**	**Treatment groups**	**Pooled analysis set***		**Reference**
Registration Number					
			Linagliptin	**Placebo**	
			n=162	**n=55**	
NCT00621140	None	Linagliptin; placebo	16 (9.9%)	10 (18.2%)	Del Prato, 2011
NCT00798161	None	Linagliptin; placebo	10 (6.2%)	4 (7.3%)	Haak, 2012[†]
NCT00601250	Metformin	Linagliptin; placebo	47 (29.0%)	14 (25.5%)	Taskinen, 2011
NCT00602472	Metformin + sulfonylurea	Linagliptin; placebo	89 (54.9%)	27 (49.1%)	Owens, 2011

*Pooled analysis set includes randomized patients who received at least one dose of treatment, *had a baseline* UACR between 30–3000 mg/g Cr, a *baseline* eGFR ≥ 30 mL/min per 1.73m^2, and had been receiving stable doses of ACEIs, ARBs, or both for at least 4 weeks prior to study conduct and from baseline to date of last UACR on-treatment measurement within the 24 week treatment period. [†]Data from other treatment groups (i.e., metformin 500 mg, linagliptin 2.5 mg + metformin 500 mg, metformin 1000 mg, and linagliptin 2.5 mg + metformin 1000 mg) were not included in the pooled analysis reported here.

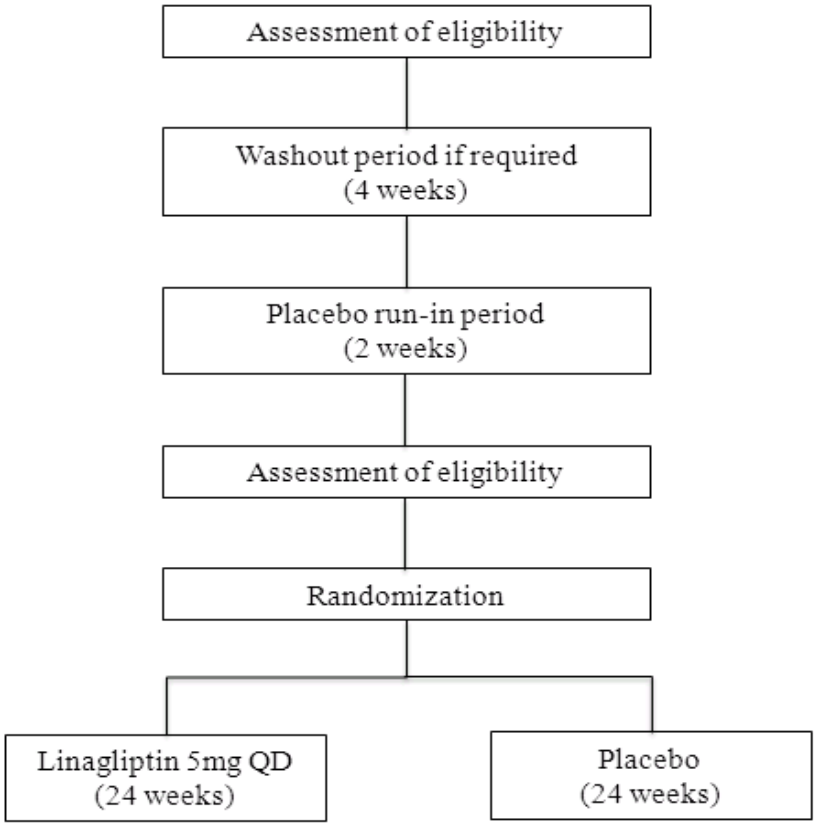
Supplementary Table 2. Summary of clinical adverse events.

	Linagliptin (n=162)	**Placebo (n=55)**
Any AE	61.1	63.6
Drug-related AEs	13.0	5.5
AEs leading to discontinuation	0.6	1.8
Serious AEs	2.5	5.5
Deaths	0.0	0.0
Most common AEs (>5% in any treatment group) by preferred term		
Hyperglycemia	8.0	21.8
Hypoglycemia	14.2	0.0
Upper respiratory tract infection	1.9	9.1
Back pain	1.2	5.5
Nasopharyngitis	6.2	5.5
Headache	5.6	3.6
Hypertension	2.5	5.5
Dizziness	3.7	5.5
AEs of special interest by system organ class		
Gastrointestinal disorders	12.3	23.6
Renal and urinary disorders	4.3	5.5
Skin/subcutaneous tissue disorders	1.9	3.6

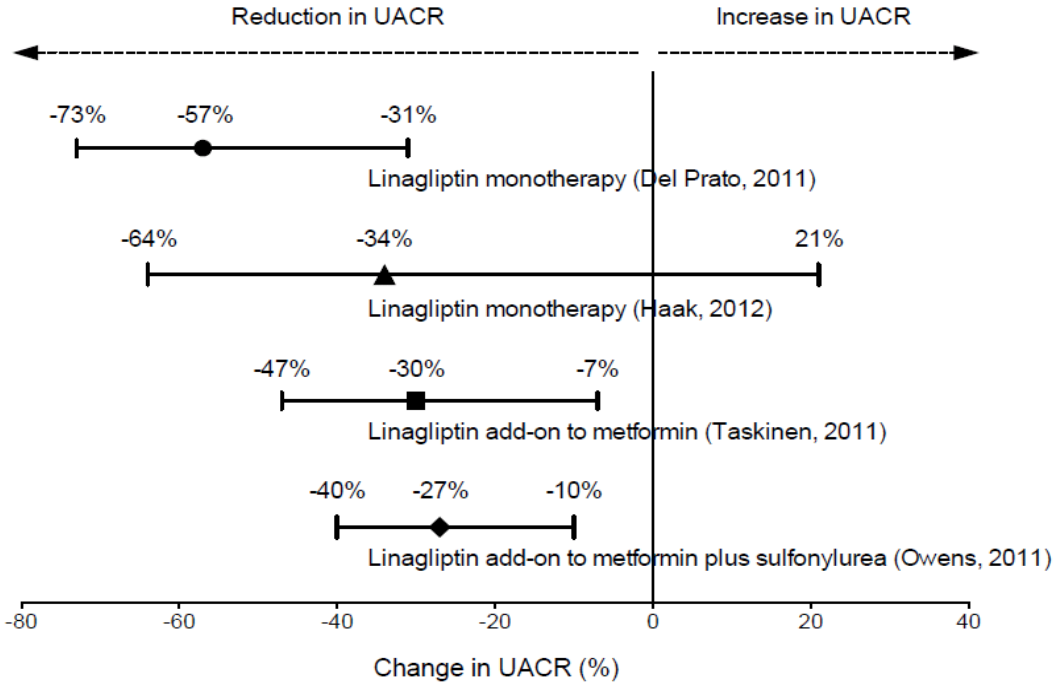
Data are expressed as percentages. Investigator-reported hypoglycemia was observed in 14.8% in the linagliptin group versus 0.0% in the placebo group. All subjects who experienced investigator-reported hypoglycemia in the linagliptin group were on sulfonylurea background therapy. No investigator-reported hypoglycemic events were reported in patients treated with linagliptin as monotherapy or add-on to metformin.

SUPPLEMENTARY DATA

Supplementary Figure 1. Schematic diagram of clinical trial design used in all four studies included in the pooled analysis.



Supplementary Figure 2. Adjusted geometric mean of percentage change in UACR from baseline to week 24 in the linagliptin group stratified by clinical trials*.



*. Black circle, linagliptin (Del Prato, 2011): n = 16; black triangle, linagliptin (Haak, 2012): n = 10; black square, linagliptin add-on to metformin (Taskinen, 2011): n = 47; black diamond, linagliptin add-on to metformin plus sulfonylurea (Owens, 2011): n = 89. Error bars represent 95% CIs.*Adjusted geometric mean of percentage change in UACR from baseline to week 24 in the placebo group stratified by clinical trials were respectively +26% ([95% CI: −31, +132], n = 10) with placebo (Del Prato, 2011), +168% ([95% CI: +2, +601], n = 4) with placebo (Haak, 2012), −14% ([95% CI: −49, +43], n = 14) with placebo add-on to metformin (Taskinen, 2011) and −25% ([95% CI: −48, +9], n = 27) with placebo add-on to metformin plus sulfonylurea (Owens, 2011).
The treatment x study interaction was significant (P = 0.0277). This interaction might be attributable to high between-study variance of the placebo UACR response, ranging from −25% to +168%, probably due to small sample sizes (ranging from 4 to 27). In contrast, the linagliptin UACR response showed consistent reductions across the trials, ranging from −27% to −57% alongside larger sample sizes (ranging from 10 to 89).