SUPPLEMENTARY MATERIAL

Table S1. Studies included in the analysis.

ClinicalTrials.gov ID	Study description	Treatment arms	Background therapy
	Placebo controlled pool		
Phase IIb studies (12 weeks)			
NCT00263276 [1]	**Monotherapy, dose-range**	DAPA 2.5, 5, 10, 20, 50 mg Placebo MET-XR 750–1,500 mg	Treatment-naïve
NCT00972244 [2]	**Monotherapy, Japanese patients**	DAPA 1, 2.5, 5, 10 mg Placebo	Treatment-naïve
NCT00357370 [3]	**Add-on to insulin**	DAPA 10, 20 mg Placebo	Insulin sensitizers (MET ± Thiazolidinedione) + 50% Original insulin
Phase III studies (24 weeks)			
NCT00528372 [4]	**Monotherapy**	DAPA 2.5, 5, 10 mg Placebo	Treatment-naïve
NCT00528879 [5]	**Add-on to MET**	DAPA 2.5, 5, 10 mg Placebo	MET ≥1,500 mg/day
NCT00855166 [6]	**Add-on to MET**	DAPA 10 mg Placebo	MET ≥1,500 mg/day
NCT00859898 [7]	**Initial combination with MET**	DAPA 10 mg + MET-XR DAPA 10 mg MET-XR ≤2,000 mg	Treatment-naïve
NCT00680745 [8]	**Add-on to sulfonylurea**	DAPA 2.5, 5, 10 mg Placebo	Glimepiride 4 mg/day
NCT00683878 [9]	**Add-on to thiazolidinedione**	DAPA 5, 10 mg Placebo	Pioglitazone 30 or 45 mg/day
NCT00984867 [10]	**Add-on to sitagliptin**	DAPA 10 mg Placebo	Sitagliptin 100 mg/day ± MET ≥1,500 mg/day
NCT00673231 [11]	**Add-on to insulin**	DAPA 2.5, 5, 10 mg Placebo	Insulin ≥30 IU/day ± maximum 2 OADs
NCT01031680 [12]	**High CV risk add-on to usual care**	DAPA 10 mg Placebo	OADs ± insulin
NCT01042977 [13]	**High CV risk add-on to usual care**	DAPA 10 mg Placebo	OADs ± insulin
	Renal impairment		
NCT00663260 [14]	**52-week moderate renal impairment study**	DAPA 5, 10 mg Placebo	Any except MET

CV, cardiovascular; DAPA, dapagliflozin; MET, metformin; OAD, oral antidiabetic drug; XR, extended release.

Supplementary References

1. List JF, Woo V, Morales E, Tang W, Fiedorek FT. Sodium-glucose cotransport inhibition with dapagliflozin in type 2 diabetes. *Diabetes Care* 2009; **32**(4): 650–657. DOI: 10.2337/dc08-1863.
2. Kaku K, Inoue S, Matsuoka O*, et al.* Efficacy and safety of dapagliflozin as a monotherapy for type 2 diabetes mellitus in Japanese patients with inadequate glycaemic control: a phase II multicentre, randomized, double-blind, placebo-controlled trial. *Diabetes Obes Metab* 2013; **15**(5): 432–440. DOI: 10.1111/dom.12047.
3. Wilding JP, Norwood P, T'Joen C, Bastien A, List JF, Fiedorek FT. A study of dapagliflozin in patients with type 2 diabetes receiving high doses of insulin plus insulin sensitizers: applicability of a novel insulin-independent treatment. *Diabetes Care* 2009; **32**(9): 1656–1662. DOI: 10.2337/dc09-0517.
4. Ferrannini E, Ramos SJ, Salsali A, Tang W, List JF. Dapagliflozin monotherapy in type 2 diabetic patients with inadequate glycemic control by diet and exercise: a randomized, double-blind, placebo-controlled, phase 3 trial. *Diabetes Care* 2010; **33**(10): 2217–2224. DOI: 10.2337/dc10-0612.
5. Bailey CJ, Gross JL, Pieters A, Bastien A, List JF. Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with metformin: a randomised, double-blind, placebo-controlled trial. *Lancet* 2010; **375**(9733): 2223–2233. DOI: 10.1016/S0140-6736(10)60407-2.
6. Bolinder J, Ljunggren O, Kullberg J*, et al.* Effects of dapagliflozin on body weight, total fat mass, and regional adipose tissue distribution in patients with type 2 diabetes mellitus with inadequate glycemic control on metformin. *J Clin Endocrinol Metab* 2012; **97**(3): 1020–1031. DOI: 10.1210/jc.2011-2260.
7. Henry RR, Murray AV, Marmolejo MH, Hennicken D, Ptaszynska A, List JF. Dapagliflozin, metformin XR, or both: initial pharmacotherapy for type 2 diabetes, a randomised controlled trial. *Int J Clin Pract* 2012; **66**(5): 446–456. DOI: 10.1111/j.1742-1241.2012.02911.x.
8. Strojek K, Yoon KH, Hruba V, Elze M, Langkilde AM, Parikh S. Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with glimepiride: a randomized, 24-week, double-blind, placebo-controlled trial. *Diabetes Obes Metab* 2011; **13**(10): 928–938. DOI: 10.1111/j.1463-1326.2011.01434.x.
9. Rosenstock J, Vico M, Wei L, Salsali A, List JF. Effects of dapagliflozin, an SGLT2 inhibitor, on HbA(1c), body weight, and hypoglycemia risk in patients with type 2 diabetes inadequately controlled on pioglitazone monotherapy. *Diabetes Care* 2012; **35**(7): 1473–1478. DOI: 10.2337/dc11-1693.
10. Jabbour SA, Hardy E, Sugg J, Parikh S. Dapagliflozin is effective as add-on therapy to sitagliptin with or without metformin: a 24-week, multicenter, randomized, double-blind, placebo-controlled study. *Diabetes Care* 2014; **37**(3): 740–750. DOI: 10.2337/dc13-0467.
11. Wilding JP, Woo V, Soler NG*, et al.* Long-term efficacy of dapagliflozin in patients with type 2 diabetes mellitus receiving high doses of insulin: a randomized trial. *Ann Intern Med* 2012; **156**(6): 405–415. DOI: 10.7326/0003-4819-156-6-201203200-00003.
12. Cefalu WT. Dapagliflozin Treatment for Type 2 Diabetes Mellitus Patients with Comorbid Cardiovascular Disease and Hypertension. *Diabetes* 2012; **61**(Suppl. 1): Abstr. 1056–P.
13. Leiter LA, Cefalu WT, de Bruin TW, Gause-Nilsson I, Sugg J, Parikh SJ. Dapagliflozin added to usual care in individuals with type 2 diabetes mellitus with preexisting cardiovascular disease: a 24-week, multicenter, randomized, double-blind, placebo-controlled study with a 28-week extension. *J Am Geriatr Soc* 2014; **62**(7): 1252–1262. DOI: 10.1111/jgs.12881.

14. Kohan DE, Fioretto P, Tang W, List JF. Long-term study of patients with type 2 diabetes and moderate renal impairment shows that dapagliflozin reduces weight and blood pressure but does not improve glycemic control. *Kidney Int* 2014; **85**(4): 962–971. DOI: 10.1038/ki.2013.356.