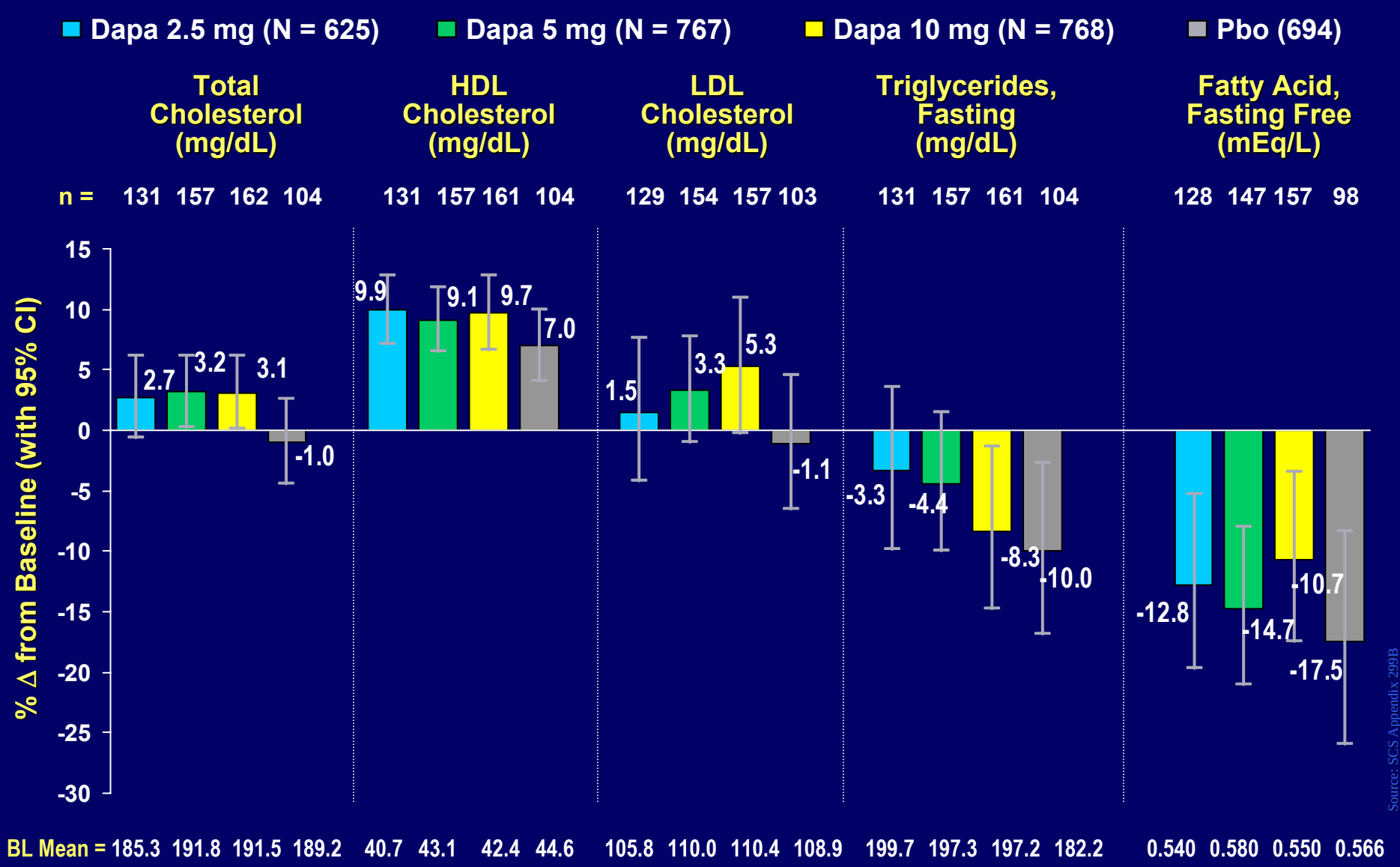
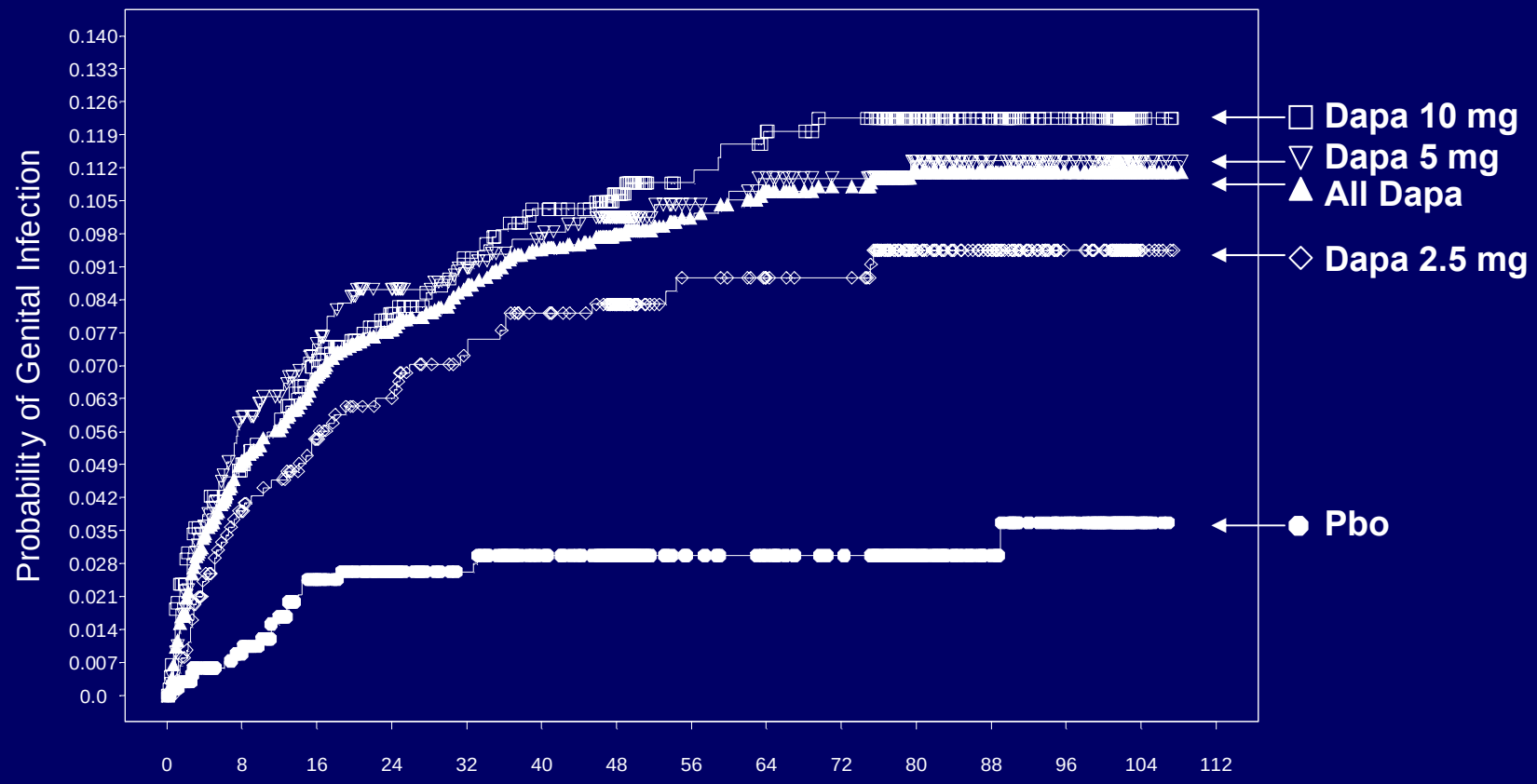
Lipids Percent Change from Baseline at Week 102



Data Set: Treated Patients

Placebo-controlled Pool – ST + LT Treatment Period

Time to First Event Suggestive of Vulvovaginitis, Balanitis and Other Infections



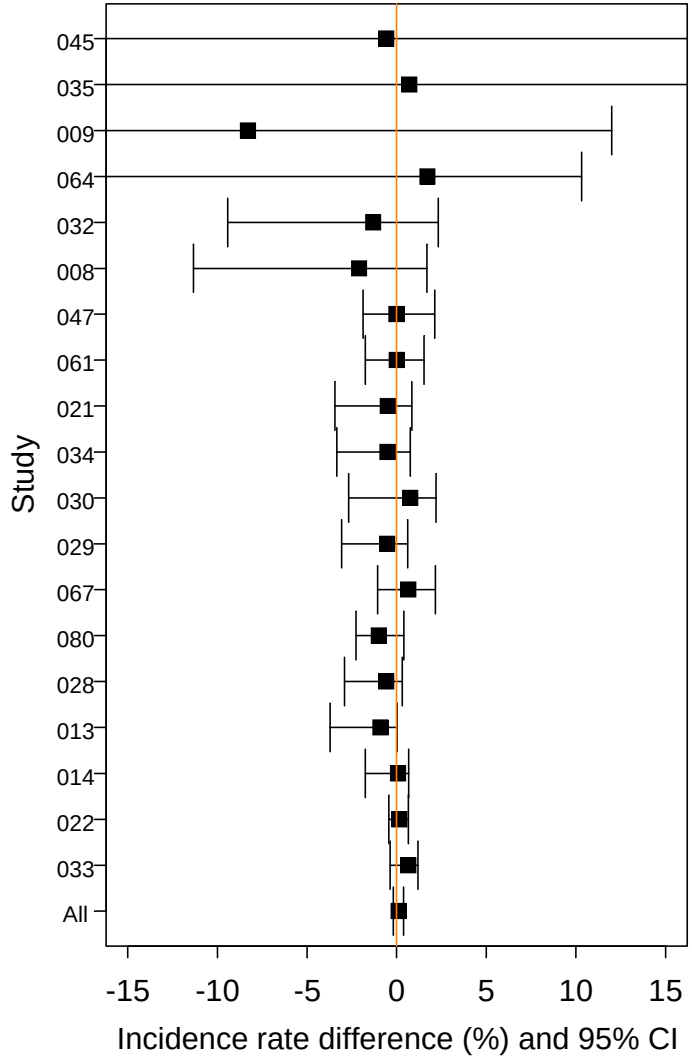
Number of Patients at Risk

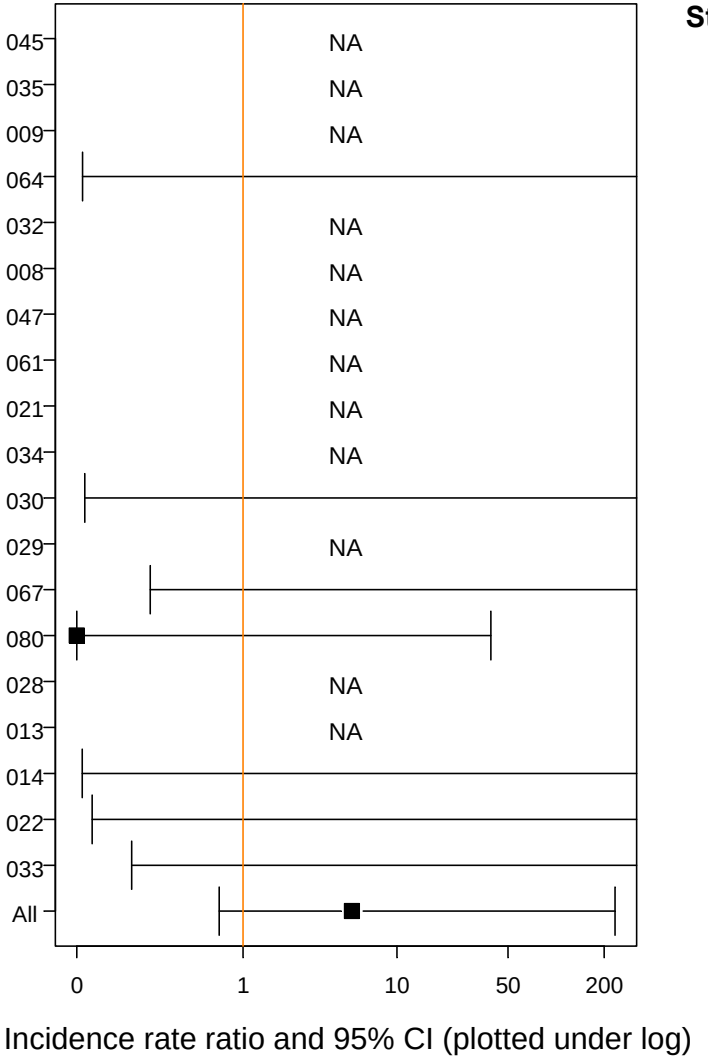
Dapa 2.5 mg	625	574	550	530	510	498	464	326	319	314	237	194	154	11	0
Dapa 5 mg	767	681	650	623	602	588	511	321	313	302	240	191	163	8	0
Dapa 10 mg	768	702	667	637	614	596	519	326	320	314	250	198	172	9	0
All Dapa	2160	1957	1867	1790	1726	1682	1494	973	952	930	727	583	489	28	0
Pbo	694	650	608	583	564	545	470	262	257	248	190	145	123	12	0

SCS Fig 2; page 183

All Phase 2b and 3 Pool, All Cases as of May 2011, including 3 cases from 2 blinded studies

Bladder Cancer Analysis By Study





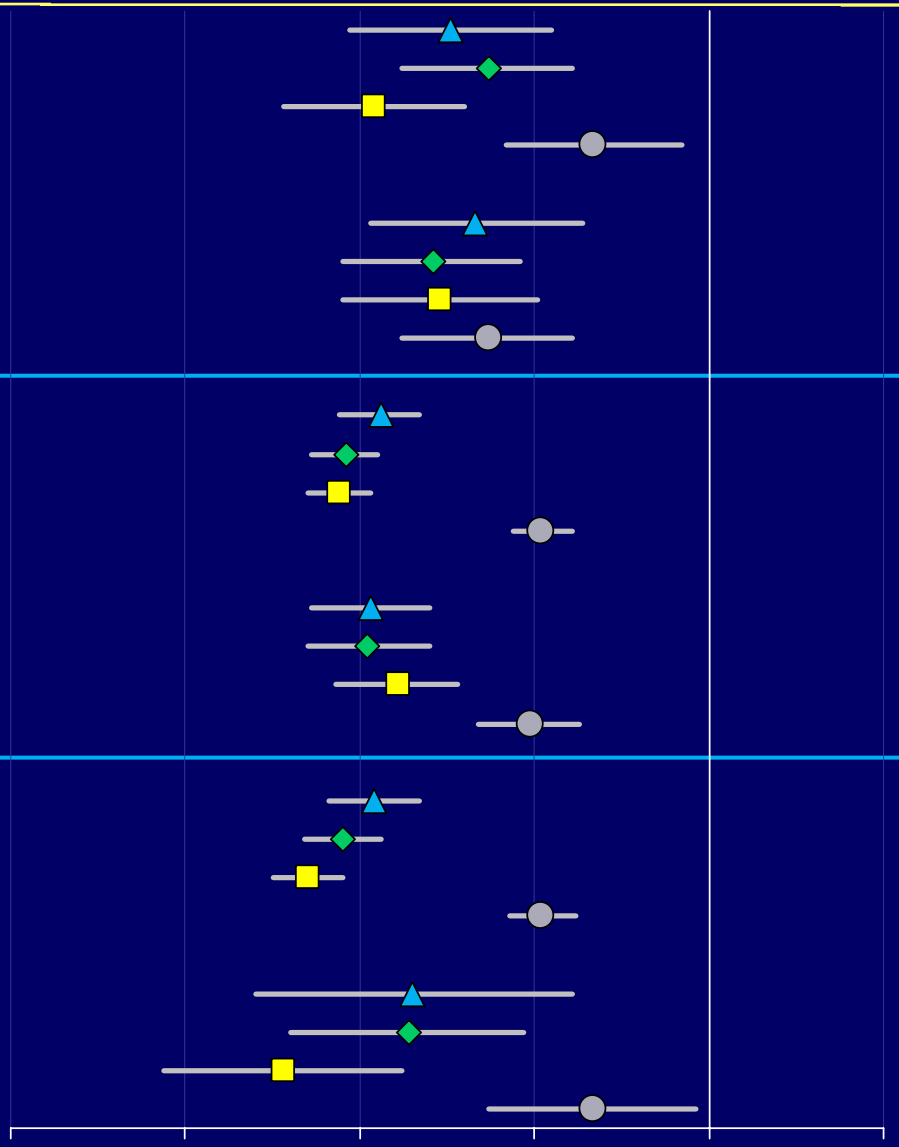
#Event/Pt-Year FU

Study	Dapa	Control
045	0/7.4	0/6.5
035	0/7.6	0/16.3
009	0/14.6	0/6.3
064	1/47.6	0/15.2
032	0/74.1	0/37
008	0/85.3	0/32.5
047	0/141.1	0/143.7
061	0/175.3	0/172.2
021	0/202.3	0/101.6
034	0/217.6	0/105.8
030	1/257.8	0/122.3
029	0/261.5	0/116
067	2/305.9	0/305.9
080	0/306.1	1/306.1
028	0/410.2	0/132.3
013	0/661.2	0/112.1
014	1/687.3	0/214.2
022	1/767.8	0/739
033	3/993.4	0/289.9
All	9/5624	1/2975

Adjusted Mean Change from Baseline in HbA1c (%) at Week 24 (LOCF) By eGFR and Age Category (9-study Pool)

Tx by subgroup interaction *p=0.2903*

BL eGFR	BL Age	Treatment	N	Point Est.
< 60*	< 65 Years	Dapa 2.5 mg	37	-0.74
		Dapa 5 mg	54	-0.63
		Dapa 10 mg	46	-0.96
		Pbo	50	-0.33
	≥ 65 Years	Dapa 2.5 mg	51	-0.67
		Dapa 5 mg	34	-0.79
		Dapa 10 mg	48	-0.77
		Pbo	39	-0.63
≥ 60* – < 90*	< 65 Years	Dapa 2.5 mg	531	-0.94
		Dapa 5 mg	272	-1.04
		Dapa 10 mg	439	-1.06
		Pbo	452	-0.48
	≥ 65 Years	Dapa 2.5 mg	157	-0.97
		Dapa 5 mg	115	-0.98
		Dapa 10 mg	106	-0.89
		Pbo	110	-0.51
> 90*	< 65 Years	Dapa 2.5 mg	407	-0.96
		Dapa 5 mg	212	-1.05
		Dapa 10 mg	325	-1.15
		Pbo	368	-0.48
	≥ 65 Years	Dapa 2.5 mg	36	-0.85
		Dapa 5 mg	15	-0.86
		Dapa 10 mg	28	-1.22
		Pbo	27	-0.33



*Units of eGFR are mL/min/1.73 m^2

Baseline Diabetes Characteristics

Duration of Type 2 Diabetes (years)	All Dapa N = 4287	All Control N = 1941
N#	4287	1940
Mean	6.09	5.92
Median	3.70	3.65
Min, max	0.0, 54.4	0.0, 46.3
Q1, Q3	0.70, 9.20	0.80, 8.80
Standard Deviation	6.931	6.734
	Number (%)	
<3 years	1918 (44.7)	868 (44.7)
≥3 years and ≤10 years	1419 (33.1)	663 (34.2)
>10 years	950 (22.2)	409 (21.1)
Not reported	0	1 (<0.1)
>8 years	1266 (29.5)	547 (28.2)

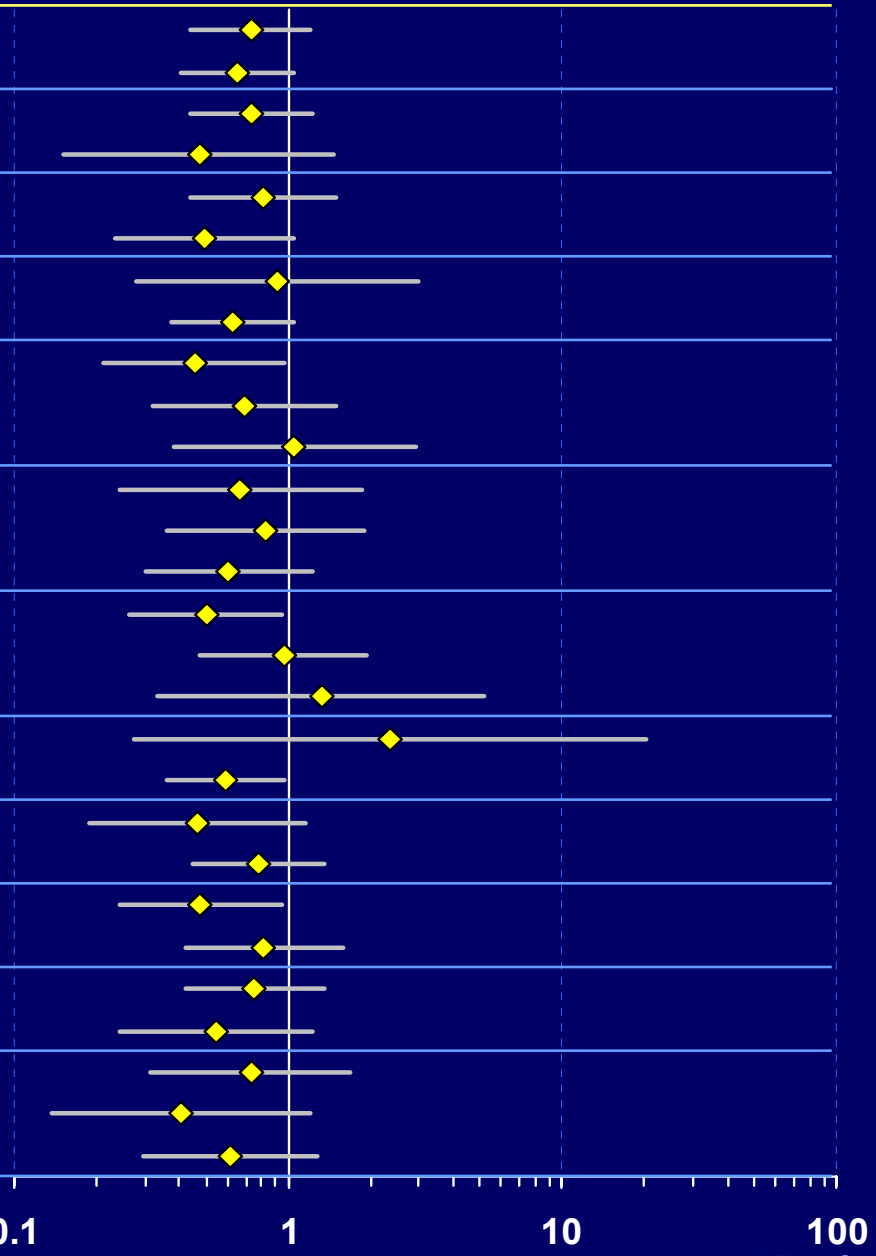
Source: SCS Table 23

Primary CV Composite Endpoint by Subgroups

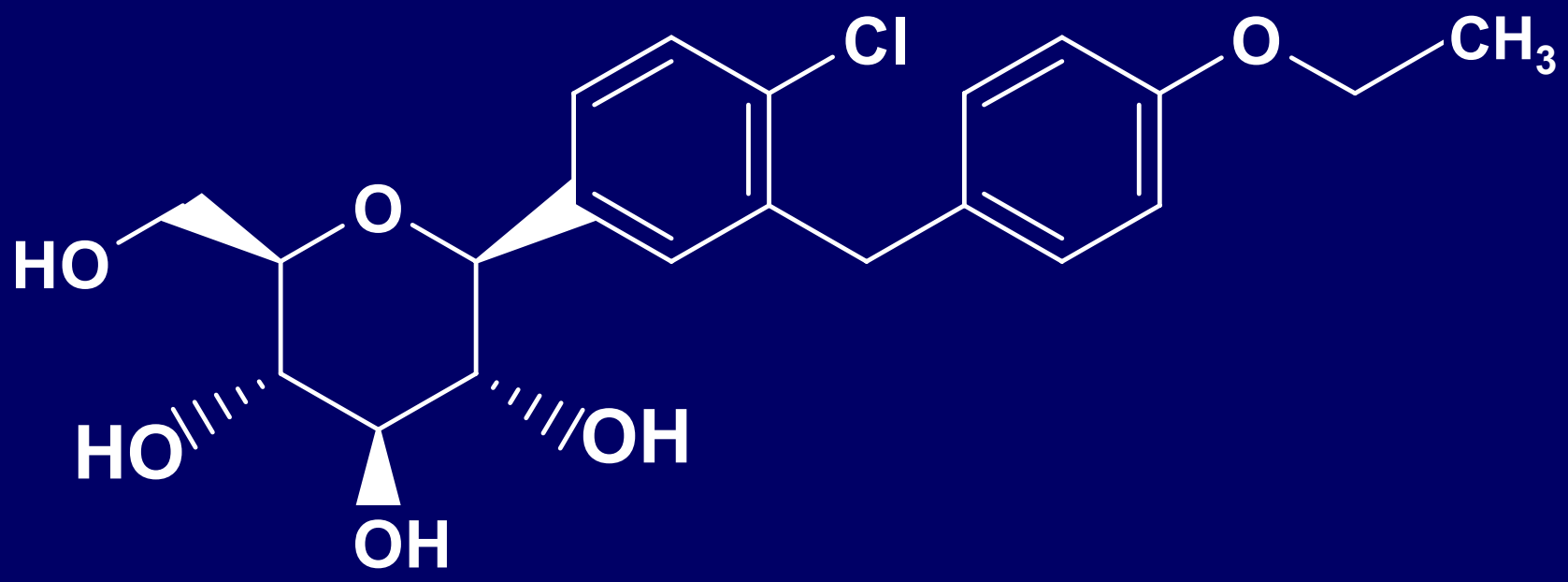
Hazard Ratio with 95% CI

Dapa better ⟷ Ctrl better

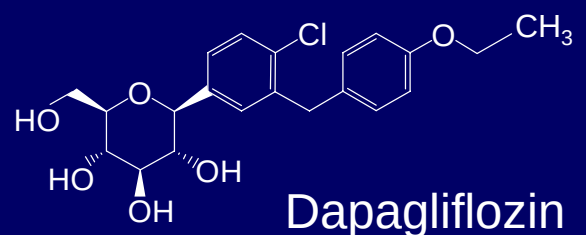
		Dapa	Ctrl
CV Risk Factors in addition to T2DM	≥ 2	44	25
	≥ 1	47	30
Hypertension	Yes	41	24
	No	7	6
Hyperchol./Dyslipidemia	Yes	32	17
	No	16	13
Current Smoking	Yes	11	4
	No	37	26
Baseline eGFR (mL/min/1.73 m^2)	≥30 – <60	17	13
	≥60 – <90	19	11
	≥90	12	6
Duration of Diabetes (yrs)	<3	11	6
	≥3 – ≤10	17	9
	>10	20	15
Age (yrs)	< 65	22	17
	≥ 65	26	13
	≥ 75	7	3
History of heart failure	Yes	8	1
	No	40	29
Family history of premature CVD	Yes	11	9
	No	37	21
Prior CV Disease	Yes	22	15
	No	26	15
Gender	Male	34	19
	Female	14	11
Region	North America	19	8
	Latin America	6	8
	Europe	18	14



Structure of Dapagliflozin



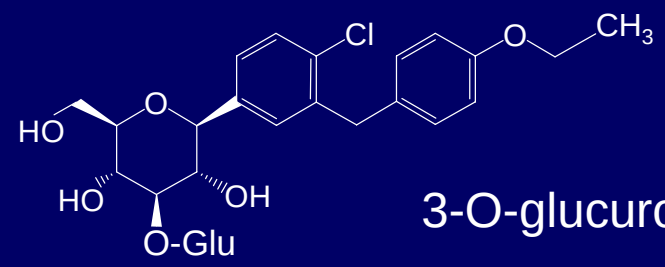
Clearance Pathways for Dapagliflozin and Its Metabolites in Humans



Dapagliflozin

Urine: 1.2 %
Feces: 15.6%

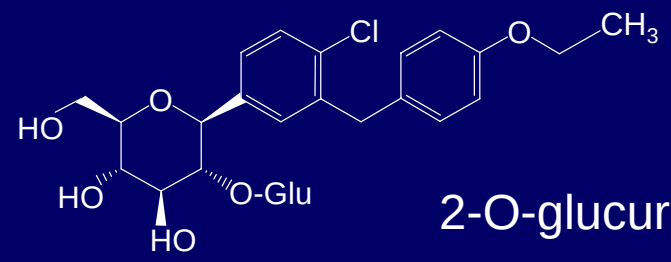
UGT1A9



3-O-glucuronide

Urine: 60.6%

UGT2B7



2-O-glucuronide

Urine: 5.4%

Other minor metabolites (<5% each)

Urine + Feces: 9.3%

Efficacy (HbA1c) in Patients ≥65 years:
Individual Studies With Greatest Numbers of Patients ≥65 yr

Study/ comparator		Age ≥65 years	
		Comparator	Dapa 10 mg
Active comparison vs SU/ glipizide	N#	120	100
	Adjusted Mean Δ from BL (%, 95CI)	-0.6 (-0.74, -0.45)	-0.48 (-0.64, -0.33)
Add-on to SU/ placebo	N#	52	36
	Adjusted Mean Δ from BL (%, 95CI)	-0.13 (-0.33, 0.08)	-0.72 (-0.97, -0.48)
	Diff vs Pbo (%, 95CI)	-	-0.60 (-0.92, -0.28)
Add-on to Insulin/ placebo	N#	49	47
	Adjusted Mean Δ from BL (%, 95CI)	-0.25 (-0.45, -0.05)	-0.79 (-1.00, -0.59)
	Diff vs Pbo (%, 95CI)	-	-0.54 (-0.83, -0.26)

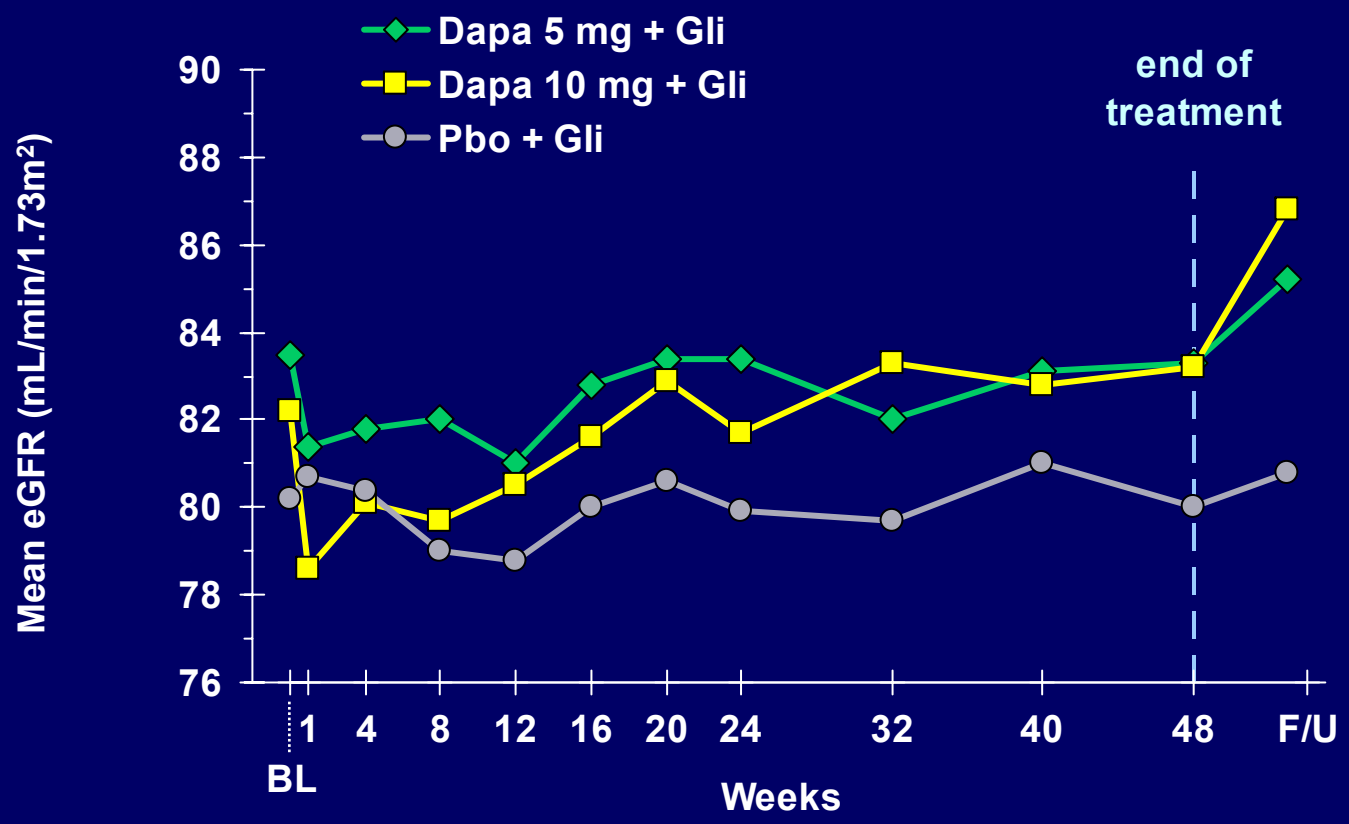
Subgroup analyses, adjusted mean change from baseline using ANCOVA, excluding data after rescue where applicable (LOCF)

Efficacy (HbA1c) in Patients ≥65 years:
Combination with Metformin XR Studies

Study/ comparator		Age ≥ 65 years	
		Met XR mono-therapy	Dapa 10 mg
Dapa 10 mg initial comb. With met XR/ metformin monotherapy	N#	27	27
	HbA1c (%) Adjusted Mean Δ from BL	-1.46 (-1.87, -1.06)	-1.25 (-1.66, -0.84)

Subgroup analysis, adjusted mean change from baseline using ANCOVA, excluding data after rescue (LOCF)

Mean Estimated GFR



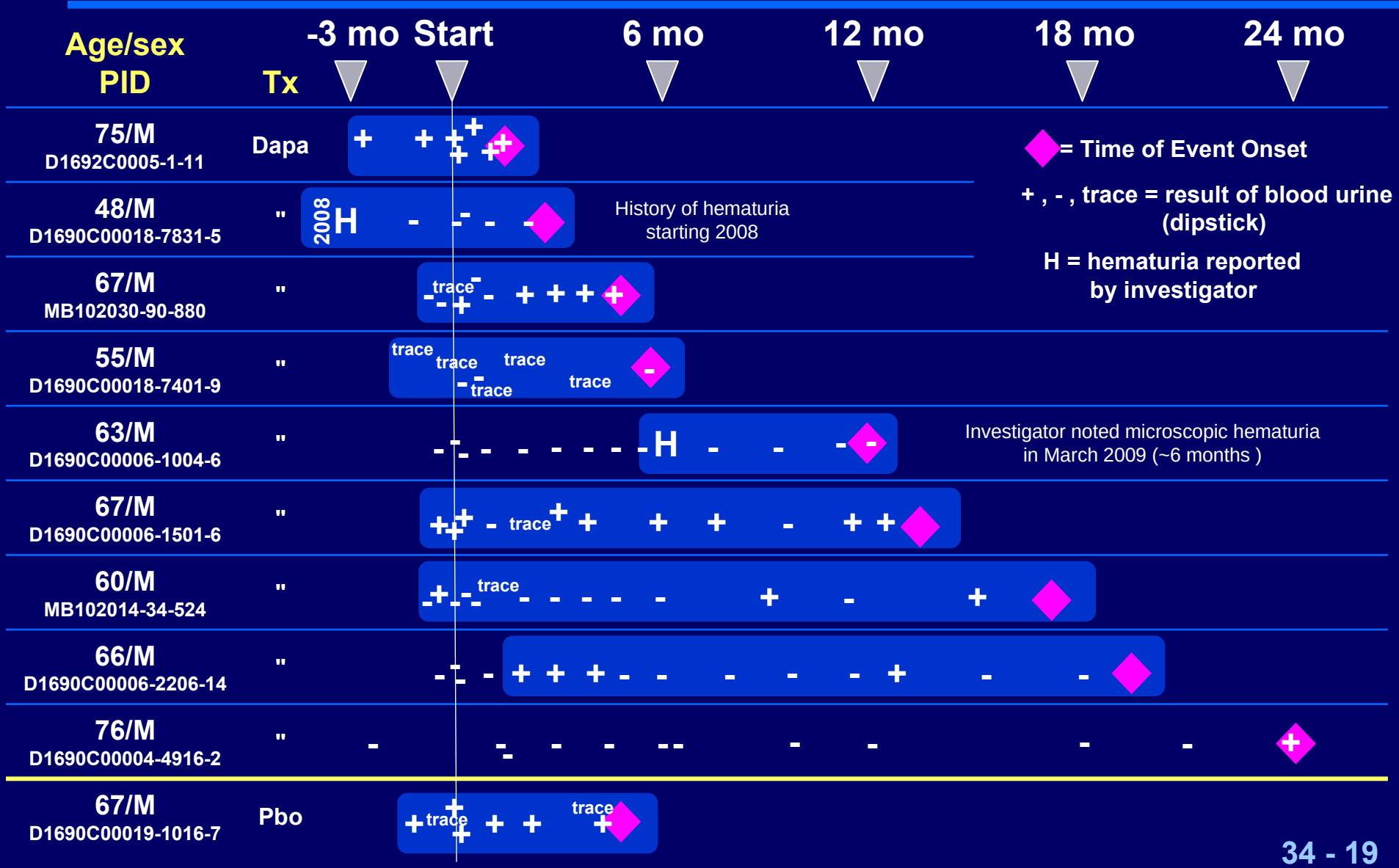
Number of Patients

Dapa 5 mg + Gli	145	140	140	139	138	135	136	132	132	127	127	134
Dapa 10 mg + Gli	151	149	149	148	145	142	142	140	138	135	132	137
Pbo + Gli	146	144	142	141	135	134	132	132	131	129	127	135

Source: Study 005 48wk Table 11.3.7.6.30

Breast Cancer: Patient Characteristics

Age / PID	Dapa Dose	Country	BMI Baseline	Other Risk Factors	Treatment	Outcome
63 D1690C00006-1403-2	2.5 mg	Germany	40		Mastectomy, axillary lymph node dissection, chemotherapy	Complete remission
53 MB102-021-59-482	5 mg	Mexico	24.2	Nulliparous	Mastectomy, chemotherapy	In remission
60 D1690C00004-4405-20**	2.5-10 mg	United Kingdom	29	Nulliparous	Wide local excision, radiotherapy	Resolved
61 D1690C00006-1005-18	10 mg	Austria	32	Nulliparous	Mastectomy, axillary lymphadenectomy, polychemotherapy, radiotherapy	Resolved with sequela
64 D1690C00012-202-4	10 mg	Czech Republic	29		Mastectomy, axillary lymph node dissection, chemotherapy, hormonal therapy, radiotherapy	No disease progression
64 MB102-014-50-151	10 mg	Canada	30.8	Benign prolif. Breast disease	Mastectomy, chemotherapy, radiotherapy	Resolved with sequela
58 D1690C00006-1803-7	2.5 mg	Russia	24		Mastectomy, hormonal therapy	Resolved with sequela
74 MB102-013-33-261	2.5 mg	United States	32.4	HRT x 15 yr, Breast calcifications	Lumpectomy, hormonal therapy, radiotherapy	Resolved
69 D1690C00005-4012-46 *	10 mg	Republic of Korea	25	None known	No treatment (surgery suggested) *	Not resolved *
73 D1690C00010-2009-3	Pbo	Germany	28	Breast Ca in aunt	Mastectomy, chemotherapy, radiotherapy, hormonal therapy	Not resolved

*Patient withdrew consent, no further info available
**Dapa dose for this patient was up-titrated from 2.5 to 5 to 10 mg

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