Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

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The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country..

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's Policy on Transparency and Publication of Clinical Study Data**.

Name of company: Boehringer Ingelheim		**Tabulated Trial Report**	Boehringer Ingelheim
Name of finished product: Telmisartan (T) and Amlodipine (A) Fixed Dose Combination		**EudraCT No.:** 2008-000874-19	**Synopsis No.:**
Name of active ingredient: Telmisartan (T) and Amlodipine (A) Fixed Dose Combination		**Page:** 1 of 10	
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Title of trial:	TElmisartan 80 mg plus AMlodipine 10 mg fixed-dose combination tablet STudy versus Amlodipine 10 mg over-encapsulated tablets as first line therapy in patients with Type 2 Diabetes Mellitus and Stage 1 or 2 hypertension: a Phase III, eight week, randomised, double-blind, double-dummy, forced titration comparison with an ABPM sub-study
Coordinating Investigator:	[redacted]
Trial sites:	Multicentre Study, [redacted]
Publication (reference):	Data of this study has not been published
Clinical phase:	III
Objectives:	The primary objective of this trial was to demonstrate that following eight weeks of treatment the fixed-dose combination (FDC) of telmisartan 80 mg plus amlodipine 10 mg (T80/A10) was superior as first line therapy in reducing mean seated trough cuff systolic blood pressure (SBP) compared to amlodipine 10 mg (A10) in patients with type 2 diabetes mellitus and Stage 1 or 2 hypertension. A key secondary objective was to identify the duration of treatment required to demonstrate the superiority of the FDC over amlodipine monotherapy in patients with type 2 diabetes mellitus and Stage 1 or 2 hypertension
Methodology:	Randomised, double-blind, double-dummy, forced up-titration, international, multi-centre, parallel group trial; prospective comparison of two treatments after 8 weeks.

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No. of subjects:	
planned:	Enrolled: 1,000
	Entered: 520 (120 in ambulatory blood pressure monitor (ABPM) sub-study)
actual:	Enrolled: 981
	Entered (randomized): 706
	Telmisartan 80 mg plus amlodipine 10 mg entered: 352; treated: 352
	Amlodipine 10 mg entered: 354; treated: 354
Diagnosis and main criteria for inclusion:	Male or female patients ≥18 years of age with type 2 diabetes mellitus and Stage 1or 2 hypertension (defined as SBP>150 mmHg) at the randomisation visit
Test product:	Telmisartan 80 mg plus amlodipine 5 mg (T80/A5 FDC) tablet
dose:	Once daily for the first two weeks of randomised treatment for patients randomized to T80/A10
mode of admin.:	p.o.
batch no.:	B091002287 and G7853
Test product:	Telmisartan 80 mg plus amlodipine 10 mg (T80/A10 FDC) tablet
dose:	Once daily for the final six weeks of randomised treatment for patients randomized to T80/A10
mode of admin.:	p.o.
batch no.:	B091002289 and G86015

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Reference therapy:	Telmisartan 80 mg plus amlodipine 5 mg (T80/A5 FDC) matching placebo tablet
dose:	Once daily for the first two weeks of randomised treatment for patients randomized to A10
mode of admin.:	p.o.
batch no.:	B091001608 and GPL8617
Reference therapy:	Telmisartan 80 mg plus amlodipine 10 mg (T80/A10 FDC) matching placebo tablet
dose:	Once daily for the final six weeks of randomised treatment for patients randomized to A10
mode of admin.:	p.o.
batch no.:	B091001606 and GPL8618
Reference therapy:	Amlodipine 5 mg (A5) over encapsulated tablets
dose:	Once daily for the first two weeks of randomised treatment for patients randomized to A10
mode of admin.:	p.o.
batch no.:	B081004130 and B091003054

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Reference therapy:	Amlodipine 10 mg (A10) ** Dosed as two A5 over-encapsulated tablets **
dose:	Once daily for the final six weeks of randomised treatment for patients randomized to A10
mode of admin.:	p.o.
batch no.:	B081004130, B091003054
Reference therapy:	Placebo capsules (matching A5 and A10 [2 capsules])
dose:	Once daily for the first two weeks of randomised treatment for patients randomized to T80/A10
mode of admin.:	p.o.
batch no.:	B081001088, B081002638
Duration of treatment:	Eight weeks (forced up-titration after two weeks)

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Criteria for evaluation:

Efficacy / clinical pharmacology:

Primary endpoint:

- Change from baseline in mean seated trough cuff systolic blood pressure (SBP) following eight weeks of treatment

Key secondary endpoints:

- Change from baseline in mean seated trough cuff SBP following one, two, four and six weeks of treatment

Other secondary endpoints:

- Change from baseline in mean seated trough cuff diastolic blood pressure (DBP) after one, two, four, six, and eight weeks of treatment
- DBP control (mean seated DBP<80 mmHg) after one, two, four, six, and eight weeks of treatment
- Other response variables after one, two, four, six, and eight weeks of treatment:
  - BP control 130/80: SBP <130 mmHg and DBP <80 mmHg
  - BP control 140/90: SBP <140 mmHg and DBP <90 mmHg
  - SBP control 130: SBP <130 mmHg
  - SBP control 140: SBP <140 mmHg
  - SBP response 130: SBP <130 mmHg or a reduction of ≥10 mmHg
  - SBP response 140: SBP <140 mmHg or a reduction of ≥10 mmHg
  - BP normality:

    Optimal: SBP<120 mmHg and DBP<80 mmHg
    Normal: SBP<130 mmHg and DBP<85 mmHg but not optimal
    High normal: SBP<140 mmHg and DBP<90 mmHg but not normal
    High: SBP≥140 mmHg or DBP≥90 mmHg
- Change from baseline in urinary albumin:creatinine ratio (UACR) (measured in spot urine) after eight weeks of treatment

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	ABPM Sub-Study – Change from baseline in the 24-hour ABPM mean (relative to dose time) for SBP after eight weeks of treatment – Changes from baseline in DBP and SBP hourly means over the 24-hour dosing interval as measured by ABPM after eight weeks of treatment – Change from baseline in the last 6-hour ABPM mean (relative to dose time) for SBP after eight weeks of treatment – Changes from baseline in the 24-hour and last 6-hour ABPM mean (relative to dose time) for DBP after eight weeks of treatment – Proportion of patients achieving 24-hour study targets of mean SBP/DBP <130/80, <125/75, and <120/80 mmHg as assessed by ABPM after eight weeks of treatment – Proportion of patients achieving the BP thresholds of mean SBP/DBP <135/85 mmHg (daytime 8:00 a m.-4:00 p.m.) and mean SBP/DBP<120/70 mmHg (night time 12:00 a m.-6:00 a.m.) as assessed by ABPM after eight weeks of treatment
Safety:	Adverse events (AE), changes from baseline in pulse rate, changes in laboratory parameters, changes in 12-lead Electrocardiogram (ECG), incidence of peripheral oedema, orthostatic changes in SBP and DBP
Statistical methods:	Restricted maximum likelihood (REML) repeated measures analysis with baseline and baseline-by-visit as a covariates on the changes from baseline in mean seated trough cuff blood pressures; Analysis of covariance with baseline as a covariate for the change from baseline in UACR (measured in spot urine) performed on the log-transformed data; Mantel-Haenszel test comparing response rates for the response variable of DBP control; Mantel-Haenszel test comparing rates of peripheral oedema. ABPM Sub-study: Analysis of covariance with baseline as a covariate for the change from baseline in the 24-hour ABPM mean (relative to dose time) for SBP after eight weeks of treatment; Mantel-Haenszel test comparing response rates for 1) the proportion of patients achieving 24-hour study targets of mean

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SBP/DBP <130/80, <125/75, and <120/80 mmHg after eight weeks of treatment and 2) the proportion of patients achieving BP thresholds of mean SBP/DBP <135/85 mmHg (daytime 8:00 a.m.-4:00 p m.) and mean SBP/DBP <120/70 mmHg (night time 12:00 a.m.-6:00 a.m.) after eight weeks of treatment

SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results:

For the 706 patients randomized, the demographic and other baseline characteristics were comparable between the treatment groups. The mean age of the treated patients in the study was 60.5 years. Most patients were white (76.2%) and 51.7% were male. Patients had a mean duration of hypertension of 8.8 years and a mean duration of diabetes of 6.1 years.

Mean SBP at baseline was 160.8 mmHg with 51.2% of patients having baseline SBP of 151 to <160 mmHg, 28.9 % 160 to <170 mmHg and 17.3% ≥170 mmHg. Baseline SBP was well matched between the treatment groups.

Telmisartan 80 mg plus amlodipine 10 mg fixed-dose combination therapy resulted in statistically significant improvements in systolic blood pressure from baseline at all time points (Weeks 1, 2, 4, 6, and 8) when compared to amlodipine monotherapy. These improvements were all clinically meaningful.

Primary and Key Secondary Endpoints

The mean change from baseline in SBP at Week 8 was −29.0 mmHg in the T80/A10 group and −22.9 mmHg in the A10 group. The difference of the adjusted means for T80/A10 compared to A10 at Week 8 (-6.1 mmHg) was statistically significant (p<.0001). At each of Weeks 1, 2, 4 and 6 the adjusted mean reduction in SBP from baseline in the FDC group was significantly greater than in the group receiving A10. Therefore, evidence that the FDC was superior to monotherapy in reducing SBP was seen after just one week of treatment (difference of the adjusted means at Week 1 was -4.9 mmHg, p<.0001).

Secondary Endpoints

Changes in DBP were similar to those observed in SBP. A greater reduction in mean DBP was observed for patients treated with combination therapy

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	(-12.5 mmHg) compared with amlodipine monotherapy (-10.5 mmHg) at Week 8 as well as at Weeks 1-6. Higher proportions of patients in the FDC group achieved secondary endpoint goals for SBP and BP control, SBP response, and BP normality, compared to the A10 group. At Week 8, the proportion of patients in the FDC group who achieved BP control <140/90 mmHg was 71.4% compared to 53.8% in the A10 group. Additionally, there were almost double the number of FDC patients who achieved the widely recommended BP control <130/80 mmHg at Week 8 (36.4%) compared to the A10 group (17.9%). The SBP response rate was 93.1% in the FDC group; with FDC patients almost twice as likely to be SBP responders as A10 patients (odds ratio = 1.92, p = .0169). Patients in the T80/A10 had a geometric mean decrease in UACR of 0.36 mg/g, whereas those in the A10 experienced no change. In the APBM sub-study, BP was lowered consistently over the 24 hour interval, including the early morning hours, for both treatment groups. The mean change in 24-hour BP from baseline to Week 8, when adjusted for baseline, was statistically greater in the T80/A10 group for both SBP (p =.0044) and DBP (p =.0004) when compared to A10 alone. After eight weeks, 24-hour BP control (24h mean <130/80 mmHg) was achieved in more than half of the T80/A10 patients (52.9% vs. 39.1%, T80/A10 and A10, respectively). Subgroup analyses of SBP by gender, age, race, body mass index, and baseline SBP category were conducted. There were no notable treatment-by-subgroup interactions, except for the analysis by race, suggesting largely homogenous treatment effects across the subgroups.
Safety results:	The fixed-dose combination of telmisartan 80 mg and amlodipine 10 mg was well tolerated in these diabetic patients with hypertension. The incidence of AEs was similar between patients treated with combination therapy (41.8%) and those treated amlodipine monotherapies (41.2%). The most frequently reported AEs were peripheral oedema and headache, which is consistent with the known AE profiles of amlodipine plus telmisartan therapy. The reported incidence of peripheral oedema was numerically lower in patients treated with combination therapy (17.6%) compared to amlodipine monotherapy

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(20.1%). Headache was reported at a similar frequency in both treatment groups (T80/A10 2.0% and A10 2.5%).

The first onset of peripheral oedema was reported twice as frequently when patients were being treated with 10 mg amlodipine than with 5 mg amlodipine; both as monotherapy and when used in combination with telmisartan. This is consistent with the known dose-dependent occurrence of peripheral oedema with amlodipine.

Special attention was paid to adverse events that may occur with substantial decreases in blood pressure, such as dizziness, syncope, and orthostatic changes. In light of the reductions in blood pressure observed during the study, the occurrence of dizziness was low. The reported incidence of dizziness was numerically higher in patients treated with T80/A10 FDC therapy (2.3%) than with amlodipine monotherapy (1.1%). Hypotension and orthostatic hypotension were each reported by two patients (0.6%) in FDC therapy and none in monotherapy. There were no reports of syncope during the study. The occurrence of clinically meaningful changes in blood pressure was low during orthostatic testing (4% of patients overall), but numerically higher in the combination therapy group (5.7%) than in the amlodipine monotherapy group (2.3%). These were generally one-time, asymptomatic occurrences.

There was no difference between the treatment groups in the incidence of investigator-categorized drug-related adverse events, with 20% of patients in both groups having reported related AEs. Only two preferred terms were attributed to study drug in at least 1% of patients in either treatment group; peripheral oedema and joint swelling. There was no difference between groups in the reports of peripheral oedema attributed to study drug. Joint swelling occurred at a slightly higher rate in the amlodipine monotherapy group (1.1%) than in the fixed dose combination group (0.3%).

Patients in the A10 group discontinued study treatment due to AEs at nearly twice the rate of those in the fixed dose combination group (5.4% vs. 2.8%, respectively). The main reason for premature discontinuation was peripheral oedema (2.8% A10 vs. 1.4% FDC). The intensity of peripheral oedema was generally more pronounced with A10 monotherapy than with FDC therapy, with 4.5% (A10) vs. 1.7% (FDC) of patients experiencing moderate to severe

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peripheral oedema.

SAEs occurred infrequently; 7 patients (3 FDC; 4 A10) experienced 12 SAEs. Two SAEs in one patient were mild, the remainder were moderate to severe in intensity. Two patients discontinued study treatment due to one or more SAEs. None of the SAEs were considered related to study medication. One patient in the A10 group died during the study. Her death resulted from hypokalemia associated with a previously undiagnosed bronchus carcinoma. The death and all of the AEs associated with her hospitalization were considered unrelated to study medication.

Changes in laboratory measures were consistent with a diabetic patient population and were generally not clinically significant. There were no clinically meaningful changes in mean pulse rate or ECG.

Conclusions:

Treatment with the fixed-dose combination of 80 mg telmisartan and 10 mg amlodipine is superior at reducing blood pressure and in obtaining blood pressure control compared to treatment with amlodipine monotherapy in diabetic patients with hypertension. In this population, significantly greater reductions in SBP and DBP were demonstrated with the fixed-dose combination compared to monotherapy after only one week of treatment; these significant reductions persisted throughout the 8-week trial.

Treatment with the fixed-dose combination of 80 mg telmisartan and 10 mg amlodipine is safe and well tolerated in diabetic patients with hypertension. Adverse event data, clinical laboratory, vital signs, and orthostatic changes in blood pressure are consistent with the established safety profile for telmisartan plus amlodipine combination therapy.

In light of these results for efficacy and safety, the balance between benefit and risk appears to be advantageous for the use of T80/A10 combination therapy in the treatment of patients with Type II diabetes and hypertension.

Trial Synopsis - Appendix

The appended tables on the following pages supplement the trial results presented in the Trial Synopsis. They provide disposition results and results of primary and secondary endpoints of the trial.

Results for	**presented in**
Patient Disposition	Table 15.1.1: 1
Change from baseline in trough seated SBP at weeks 1 through 8 (primary and secondary endpoints)	Table 15.2.1.1: 2 Table 15.2.1.1: 3
Trough DBP at each visit and change from baseline by treatment group (secondary endpoint)	Table 15.2.2.1: 1
Response rates for trough DBP response, DBP control (secondary endpoint)	Table 15.2.2.3: 1
Response rates for trough BP control, SBP control, and SBP response at each time point (secondary endpoint)	Table 15.2.2.2: 1
Proportion of patients within each normal BP classification at each time point (secondary endpoint)	Table 15.2.2.2: 10
Urine albumin:creatinine ratio (UACR) (secondary endpoint)	Table 15.2.2.4: 1

Table 15.1.1: 1 Disposition of patients by treatment group

	T80/A10 N (%)	A10 N (%)	Total N (%)
Enrolled			981
Not entered/randomised			275
Entered/randomised	352	354	706
Not Treated	0	0	0
Treated	352 (100.0)	354 (100.0)	706 (100.0)
Not prematurely discontinued from trial medication	332 (94.3)	319 (90.1)	651 (92.2)
Prematurely discontinued from trial medication	20 (5.7)	35 (9.9)	55 (7.8)
Adverse event	11 (3.1)	20 (5.6)	31 (4.4)
Worsening of disease under study	1 (0.3)	0 (0.0)	1 (0.1)
Worsening of other pre-existing disease	2 (0.6)	1 (0.3)	3 (0.4)
Other adverse event	8 (2.3)	19 (5.4)	27 (3.8)
Lack of efficacy	0 (0.0)	1 (0.3)	1 (0.1)
Non compliant with protocol	3 (0.9)	3 (0.8)	6 (0.8)
Lost to follow-up	0 (0.0)	1 (0.3)	1 (0.1)
Consent withdrawn not due to adverse events	4 (1.1)	4 (1.1)	8 (1.1)
Other	2 (0.6)	6 (1.7)	8 (1.1)

Table 15.2.1.1: 2 Presentation of MMRM results at nominal Weeks 4, 6, and 8 (high dose) by treatment group regarding change from baseline in in-clinic mean seated trough cuff SBP - treated set

				Comparison vs. T80/A10		
Change from Baseline	Treatment	N	Adjusted* Mean (SE)	Difference (SE) of adjusted* means	95% CI	p-value
Week 8	T80/A10	320	-29.0 (0.66)			
	A10	311	-22.9 (0.67)	-6.1 (0.94)	(-7.9, -4.2)	< 0.0001
Week 6	T80/A10	326	-29.7 (0.62)			
	A10	317	-22.6 (0.63)	-7.1 (0.88)	(-8.9, -5.4)	< 0.0001
Week 4	T80/A10	329	-27.7 (0.62)			
	A10	326	-21.1 (0.62)	-6.6 (0.88)	(-8.3, -4.9)	< 0.0001
Interaction treatment and week:						0.2300
Interaction baseline and week:						0.0004

*adjusted for baseline as a covariate. Significance tests are based on Least Squares (LS) means.The statistical model includes the fixed, categorical effects of treatment, week, and treatment-by-week interaction, with the continuous covariate of baseline mean seated trough cuff SBP (at Visit 3) and baseline-by-week interaction.

Source data: Appendix 16.1.9.2, Statdoc 6.1.1.1 ctr\eot_t4.sas 09MAR2011

Table 15.2.1.1: 3 Presentation of MMRM results at nominal Weeks 1 and 2 (low dose) by treatment group regarding change from baseline in in-clinic mean seated trough cuff SBP - treated set

				Comparison vs. T80/A5		
Change from Baseline	Treatment	N	Adjusted* Mean (SE)	Difference (SE) of adjusted* means	95% CI	p-value
Week 2	T80/A5	333	-22.4 (0.65)			
	A5	332	-16.4 (0.65)	-6.1 (0.92)	(-7.9, -4.3)	< 0.0001
Week 1	T80/A5	334	-17.5 (0.61)			
	A5	336	-12.6 (0.61)	-4.9 (0.86)	(-6.6, -3.2)	< 0.0001
Interaction treatment and week:						0.1666
Interaction baseline and week:						0.3621

*adjusted for baseline as a covariate. Significance tests are based on Least Squares (LS) means.The statistical model includes the fixed, categorical effects of treatment, week, and treatment-by-week interaction, with the continuous covariate of baseline mean seated trough cuff SBP (at Visit 3) and baseline-by-week interaction.

Source data: Appendix 16.1.9.2, Statdoc 6.1.1.2 ctr\eot_t4.sas 09MAR2011

Table 15.2.2.1: 1 Summary of in-clinic mean seated trough DBP at each visit and change from baseline by treatment group - treated set (OBS, LOCF)

	T80/A10						A10					
	N	Mean	SD	Min	Median	Max	N	Mean	SD	Min	Median	Max
Number of patients [N]	352						354					
Diastolic blood pressure [mmHg] (OBS)												
Baseline	344	90.5	8.3	58	91.3	112	345	91.4	7.8	68	91.7	109
Week 1	340	83.5	9.0	53	83.7	109	344	86.3	8.6	60	86.7	109
Week 2	339	81.8	8.9	53	82.0	107	339	84.2	9.1	53	84.0	107
Week 4	336	78.3	8.8	47	79.0	106	334	82.0	8.7	55	81.3	107
Week 6	333	77.1	8.9	45	78.0	106	324	81.1	8.1	60	80.5	105
Week 8	327	78.1	8.7	56	78.3	107	317	80.8	8.0	59	80.7	104
Change from baseline Week 1	334	-7.1	6.9	-26	-6.7	11	336	-5.0	7.4	-39	-4.0	16
Change from baseline Week 2	333	-8.9	7.5	-39	-9.0	13	332	-7.0	8.0	-35	-6.7	20
Change from baseline Week 4	329	-12.3	7.5	-40	-12.3	12	326	-9.4	8.3	-35	-9.0	12
Change from baseline Week 6	326	-13.5	7.7	-42	-13.3	8	317	-10.3	8.1	-33	-10.0	13
Change from baseline Week 8	320	-12.5	8.0	-51	-11.7	8	311	-10.5	8.2	-35	-10.0	16
Diastolic blood pressure [mmHg] (LOCF)												
Baseline	344	90.5	8.3	58	91.3	112	345	91.4	7.8	68	91.7	109
Week 1	340	83.5	9.0	53	83.7	109	344	86.3	8.6	60	86.7	109
Week 2	343	81.7	9.0	53	82.0	107	349	84.4	9.1	53	84.0	107
Week 4	336	78.3	8.8	47	79.0	106	334	82.0	8.7	55	81.3	107
Week 6	340	77.1	8.9	45	78.0	106	336	81.2	8.3	55	80.7	105
Week 8	340	78.2	8.6	56	78.5	107	337	81.0	8.4	55	80.7	104
Change from baseline Week 1	334	-7.1	6.9	-26	-6.7	11	336	-5.0	7.4	-39	-4.0	16
Change from baseline Week 2	337	-8.9	7.5	-39	-9.0	13	341	-7.0	7.9	-35	-6.7	20
Change from baseline Week 4	329	-12.3	7.5	-40	-12.3	12	326	-9.4	8.3	-35	-9.0	12
Change from baseline Week 6	332	-13.6	7.7	-42	-13.3	8	328	-10.2	8.1	-33	-10.0	13
Change from baseline Week 8	332	-12.5	8.0	-51	-11.7	8	329	-10.5	8.3	-35	-10.0	16

Weeks 1 and 2 are at low dose amlodipine

Source data: Appendix 16.2, Listing 6.1

Table 15.2.2.3: 1 Response rates for trough DBP response, DBP control- treated set (LOCF) - treated set

Week	Treatment	DBP control n	(%)	N	DBP response n	(%)	N
Week 1	T80/A5	110	(32.9)	334	165	(49.4)	334
	A5	71	(21.1)	336	113	(33.6)	336
Week 2	T80/A5	126	(37.4)	337	206	(61.1)	337
	A5	102	(29.9)	341	166	(48.7)	341
Week 4	T80/A10	175	(53.2)	329	250	(76.0)	329
	A10	111	(34.0)	326	190	(58.3)	326
Week 6	T80/A10	198	(59.6)	332	275	(82.8)	332
	A10	149	(45.4)	328	214	(65.2)	328
Week 8	T80/A10	185	(55.7)	332	253	(76.2)	332
	A10	142	(43.2)	329	214	(65.0)	329

DBP control (mean seated DBP < 80 mmHg)
DBP response (mean seated DBP < 80 mmHg or a reduction of >= 10 mmHg)
n (number of responders); N (sample size at that visit)

Source data: Appendix 16.2, Listing 6.2 ctr\bprsp.sas 09MAR2011

Table 15.2.2.2: 1 Response rates for trough BP control, SBP control, and SBP response at each time point - treated set (LOCF)

Week	Treatment	BP control n (%) N	BP control 2 n (%) N	SBP control n (%) N	SBP control 2 n (%) N	SBP response n (%) N	SBP response 2 n (%) N
Week 1	T80/A5	130 (38.9) 334	35 (10.5) 334	141 (42.2) 334	50 (15.0) 334	253 (75.7) 334	253 (75.7) 334
	A5	72 (21.4) 336	12 (3.6) 336	81 (24.1) 336	26 (7.7) 336	201 (59.8) 336	199 (59.2) 336
Week 2	T80/A5	184 (54.6) 337	58 (17.2) 337	193 (57.3) 337	92 (27.3) 337	297 (88.1) 337	297 (88.1) 337
	A5	103 (30.2) 341	23 (6.7) 341	112 (32.8) 341	42 (12.3) 341	246 (72.1) 341	246 (72.1) 341
Week 4	T80/A10	235 (71.4) 329	94 (28.6) 329	243 (73.9) 329	137 (41.6) 329	309 (93.9) 329	309 (93.9) 329
	A10	155 (47.5) 326	38 (11.7) 326	163 (50.0) 326	70 (21.5) 326	274 (84.0) 326	274 (84.0) 326
Week 6	T80/A10	245 (73.8) 332	134 (40.4) 332	251 (75.6) 332	164 (49.4) 332	318 (95.8) 332	318 (95.8) 332
	A10	168 (51.2) 328	60 (18.3) 328	177 (54.0) 328	81 (24.7) 328	286 (87.2) 328	286 (87.2) 328
Week 8	T80/A10	237 (71.4) 332	121 (36.4) 332	243 (73.2) 332	157 (47.3) 332	309 (93.1) 332	309 (93.1) 332
	A10	177 (53.8) 329	59 (17.9) 329	187 (56.8) 329	89 (27.1) 329	288 (87.5) 329	288 (87.5) 329

BP control (mean seated SBP < 140 mmHg and mean seated DBP < 90 mmHg)
BP control 2 (mean seated SBP < 130 mmHg and mean seated DBP < 80 mmHg)
SBP control (mean seated SBP < 140 mmHg)
SBP control 2 (mean seated SBP < 130 mmHg)
SBP response (mean seated SBP < 140 mmHg or a reduction of >= 10 mmHg)
SBP response 2 (mean seated SBP < 130 mmHg or a reduction of >= 10 mmHg)
n (number of responders); N (sample size at that visit)

Source data: Appendix 16.2, Listing 6.2 ctr\bprsp.sas 09MAR2011

Table 15.2.2.2: 10 Proportion of patients within each normal BP classification at each time point - treated set (LOCF)

Week	Treatment	Optimal n (%) N	Normal n (%) N	High normal n (%) N	High n (%) N
Week 1	T80/A5	11 (3.3) 334	33 (9.9) 334	86 (25.7) 334	204 (61.1) 334
	A5	4 (1.2) 336	15 (4.5) 336	53 (15.8) 336	264 (78.6) 336
Week 2	T80/A5	21 (6.2) 337	61 (18.1) 337	102 (30.3) 337	153 (45.4) 337
	A5	8 (2.3) 341	25 (7.3) 341	70 (20.5) 341	238 (69.8) 341
Week 4	T80/A10	39 (11.9) 329	88 (26.7) 329	108 (32.8) 329	94 (28.6) 329
	A10	11 (3.4) 326	53 (16.3) 326	91 (27.9) 326	171 (52.5) 326
Week 6	T80/A10	55 (16.6) 332	104 (31.3) 332	86 (25.9) 332	87 (26.2) 332
	A10	22 (6.7) 328	52 (15.9) 328	94 (28.7) 328	160 (48.8) 328
Week 8	T80/A10	53 (16.0) 332	93 (28.0) 332	91 (27.4) 332	95 (28.6) 332
	A10	14 (4.3) 329	65 (19.8) 329	98 (29.8) 329	152 (46.2) 329

Optimal (mean seated SBP < 120 mmHg and mean seated DBP < 80 mmHg)
Normal (mean seated SBP < 130 mmHg and mean seated DBP < 85 mmHg but not optimal)
High normal (mean seated SBP < 140 mmHg and mean seated DBP < 90 mmHg but not normal)
High (mean seated SBP >=140 mmHg and mean seated DBP >= 90 mmHg)
n (number of responders); N (sample size at that visit)

Source data: Appendix 16.2, Listing 6.2 ctr\bprsp.sas 09MAR2011

Table 15.2.2.4: 1 Summary statistics of log-transformed urine albumin:creatinine ratio (UACR) - treated set

	T80/A10	A10
Number of Patients in TS	352	354
Number of analyzed patients	334	333
Baseline		
Mean (SD)*	2.0 (1.91)	2.1 (1.93)
Geometric mean	7.3	7.9
Week 8		
Mean (SD)*	1.6 (1.78)	2.1 (1.91)
Geometric mean	5.1	8.2
Change from Baseline		
Mean (SD)*	-0.36 (0.79)	0.04 (0.92)
Geometric mean	0.70	1.04
95% Confidence interval	(0.64 , 0.76)	(0.95 , 1.15)
Q1	0.50	0.69
Median	0.76	1.08
Q3	1.08	1.69
Interquartile Range	0.58	1.00

* Log scale
Source data: Appendix 16.2, Listing 8.4