Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

This clinical study synopsis is provided in line with **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

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:		**EudraCT No.:**		
Name of active ingredient: telmisartan and amlodipine		**Page:**	**Number:**	**Synopsis No.:**
Ref. to Documentation:	**Module:**	**Volume:**		
Report date: 30 November 2007	**Trial No. /U No.:** 1235.1/ U07-3503-02	**Date of trial:** 04 APR 2006 – 12 MAR 2007		**Date of revision:** 2 April 2008

Title of trial:	A randomized, double-blind, double-dummy placebo-controlled, 4x4 factorial design trial to evaluate telmisartan 20, 40 and 80 mg tablets in combination with amlodipine 2.5, 5 and 10 mg capsules after eight weeks of treatment in patients with Stage I or II hypertension, with an ABPM sub-study
Principal/Coordinating Investigator:	[redacted]
Trial sites:	Multicentre Study, cf. Appendix 16.1.4
Publication (reference):	Data of this study have not been published
Clinical phase:	III
Objectives:	To demonstrate that for both active therapies of telmisartan and amlodipine there exists an overall dose response, thereby showing that combinations of telmisartan and amlodipine are more effective in reducing diastolic blood pressure than each of the respective monotherapies in patients with Stage I or II hypertension.
Methodology:	Randomized, double-blind, double-dummy, placebo-controlled, international, multi-centre, parallel group, 4x4 factorial design comparison trial of 16 treatments over eight weeks with an ambulatory blood pressure monitoring (ABPM) sub-study.

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No. of subjects:

planned: Approximately 1280 randomized patients

actual: 2607 patients enrolled; 1461 randomized to one of 16 treatments

	Placebo	Amlodipine 2.5	Amlodipine 5	Amlodipine 10
Placebo	46	50	140	129
Telmisartan 20	42	44	46	44
Telmisartan 40	130	47	143	129
Telmisartan 80	135	48	146	142

Diagnosis and main criteria for inclusion: Male and female patients ≥18 years of age with Stage I or II hypertension defined as: a mean seated cuff diastolic blood pressure (DBP) ≥95 and ≤119 mmHg.

Test product: Telmisartan (T) and amlodipine (A) combination therapy

doses: Telmisartan: 20, 40 or 80 mg. and

Amlodipine: 2.5, 5 or 10 mg. Patients assigned to treatment with amlodipine 10 mg were dosed with amlodipine 5 mg for the first two weeks and up-titrated to target dose for the remaining six weeks of treatment

Patients randomized to combination therapy received one of nine treatment combinations:

T20+A2.5 or T20+A5 or T20+A10 or

T40+A2.5 or T40+A5 or T40+A10 or

T80+A2.5 or T80+A5 or T80+A10

(A10 mg was supplied as two 5 mg capsules)

mode of admin.: Oral

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batch nos.:	T20 - PD-2677
	T40 – PD-2679
	T80 – PD-2681
	A2.5 – PD-2682
	A5 – PD-2683
Reference therapies:	Placebo (matching), telmisartan monotherapy and amlodipine monotherapy
dose:	Placebo (matching) - N/A;
	Telmisartan: 20, 40 or 80 mg;
	Amlodipine: 2.5, 5 or 10 mg. Patients assigned to treatment with amlodipine 10 mg were dosed with amlodipine 5 mg for the first two weeks and up-titrated to target dose for the remaining six weeks of treatment
mode of admin.:	Oral
batch nos.:	T20 Matching Placebo – PD-2749
	T40 Matching Placebo – PD-2746
	T80 Matching Placebo – PD-2751
	T20 - PD-2677
	T40 – PD-2679
	T80 – PD-2681
	A2.5 and 5 Matching Placebo – PD-2687
	A2.5 – PD-2682
	A5 – PD-2683
Duration of treatment:	Eight weeks

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Criteria for evaluation:	
Efficacy / clinical pharmacology:	Primary: Change from baseline in the in-clinic seated trough cuff DBP after eight weeks of treatment Secondary: Change from baseline in the in-clinic seated trough cuff systolic blood pressure (SBP) after eight weeks of treatment; Percentage of patients responding to treatment based on in-clinic mean seated trough cuff BP measurements at the end of the eight week active treatment period; Changes from baseline in the in-clinic standing trough cuff DBP and SBP after eight weeks of treatment ABPM Sub-study: Changes from baseline in DBP and SBP hourly means over the 24-hour dosing interval as measured by ABPM after eight weeks of treatment; Changes from baseline in the 24-hour ABPM mean (relative to dosetime) for DBP and SBP after eight weeks of treatment
Safety:	Adverse events (AEs), laboratory parameters, electrocardiogram (ECG), orthostatic changes in SBP and DBP, and pulse rate
Statistical methods:	Analysis of covariance with main effects of treatment with telmisartan, treatment with amlodipine, and country/region, with baseline as a covariate; response surface analysis; Mantel-Haenszel test.

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SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results:

Overall

Primary: There was a significant difference in the change from baseline in seated trough cuff DBP among dosages of telmisartan (T: $p<0.0001$) and among dosages of amlodipine (A: $p<0.0001$), with no significant ($p=0.1777$) T-by-A interaction when excluding placebo patients, concluding that combination therapy with T+A is superior to either monotherapy in lowering seated trough cuff DBP in patients with Stage I or II hypertension.

Secondary: Treatment with each of four key combinations (T40+A5, T40+A10, T80+A5, and T80+A10) had significantly ($p<0.003$) greater reductions in seated trough cuff DBP than each respective monotherapy. There was a significant difference in the change from baseline in seated trough cuff SBP among dosages of telmisartan ($p<0.0001$) and among dosages of amlodipine ($p<0.0001$), with no

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Efficacy / clinical pharmacology results (continued):

significant (p=0.4970) T-by-A interaction when excluding placebo patients. Treatment with each of the four key combinations had significantly ($p \leq 0.02$) greater reductions in seated trough cuff SBP than each respective monotherapy. Response rates for DBP control, DBP response, SBP response and BP control were greater for combination therapy than the respective monotherapies. There were no significant ($p > 0.05$) interactions of treatment-by-subgroup when evaluating age group (<65, ≥65), gender, or race on changes from baseline in seated trough cuff DBP. ABPM hourly mean reductions in DBP and SBP over the 24-hour dosing interval for combination therapy were consistently of a greater magnitude than the respective monotherapies. Increasing dosage of telmisartan and increasing dosage of amlodipine both resulted in greater reductions in the 24-hour ABPM mean DBP and SBP, with the reductions for the four key combinations being greater than the respective monotherapies.

Moderate or severe hypertensive patients at baseline (Stage II hypertension as defined by Joint National Committee (JNC) VII guidelines)

There was a significant difference in the change from baseline in seated trough cuff DBP among dosages of telmisartan (T: $p < 0.0001$) and among dosages of amlodipine (A: $p < 0.0001$), with no significant (p=0.2299) T-by-A interaction when excluding placebo patients, concluding that combination therapy with T+A is superior to either monotherapy in lowering seated trough cuff DBP in patients with moderate or severe hypertension at baseline.

Overall, the results observed in this subset of patients with moderate or severe hypertension at baseline were similar to those observed in the overall patient population.

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Safety results:

This study confirmed the favorable safety profile and tolerability of telmisartan and amlodipine when administered as both mono and combination therapies.

Overall

AEs occurred in 37.3% of treated patients and the occurrence of AEs was well balanced between active treatment groupings. The most frequently reported AEs were headache and oedema peripheral. Headache was most commonly reported to occur in placebo patients and the incidence of oedema peripheral was most commonly reported to occur in A10 patients. The incidence rate of oedema on amlodipine 10 mg was less in the combination cells with telmisartan (6.2 – 11.3% in combination vs. 17.8% A10 monotherapy). Serious adverse events were reported in eight patients. One patient treated with T80 experienced a non-drug related, fatal event of choking. No unexpected changes in laboratory values, physical examinations, pulse rate or ECG readings were reported. Orthostatic changes as determined from in-clinic BPs were observed in 7.0% of patients and only infrequently reported as an adverse event.

Moderate or severe hypertensive patients at baseline (Stage II hypertension as defined by JNC VII guidelines)

For the subset of patients with moderate to severe hypertension at baseline adverse events occurred in 36.1% of patients with the incidence well balanced among active treatment groupings. The safety results observed in the subset of patients was similar to that reported in the overall patient population

No unexpected changes in laboratory values, physical examination, pulse rate or ECG readings were reported. Orthostatic changes were observed in 6.6% of patients and infrequently reported as an adverse event.

No unusual safety concerns were reported in the trial.

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Conclusions:	Combination treatments of telmisartan 40 and 80 mg with amlodipine 5 and 10 mg were associated with additive blood pressure lowering effects that were both statistically and clinically significant. Similar effects were seen in a subset of patients with moderate or severe hypertension suggesting that these combinations could be used effectively as first-line agents. The overall safety profile of these combinations treatments was comparable to their monocomponents. The dose-limiting side effect of oedema peripheral caused by amlodipine 10 mg was substantially less with the co-administration of telmisartan. This study confirmed the efficacy and safety of combination treatment with telmisartan and amlodipine in patients with Stage I and Stage II hypertension.

Trial Synopsis - Appendix

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

Note that not all endpoints defined in the trial protocol are presented in this synopsis because their number was too large to allow meaningful presentation in this format.

Results for	**presented in**
Patient Disposition	Table 15.1.1: 2 Table 15.1.1: 3
Change from Baseline in Seated Trough DBP at 8 weeks (Primary Endpoint)	Table 15.2.1.1.1: 1 Table 15.2.1.1.1: 2 Table 15.2.1.1.1: 3
Treatment effects on Change from Baseline Seated Trough Cuff DBP at 8 weeks (Secondary Endpoint)	Table 15.2.1.1.1: 4
Change from Baseline in Seated Trough SBP at 8 weeks (Secondary Endpoint)	Table 15.2.2.1.1: 2
Treatment effects on Change from Baseline Seated trough cuff SBP at 8 weeks (Secondary Endpoint)	Table 15.2.2.1.1: 4
Response rate for DBP control at 8 weeks (Secondary Endpoint) Response rate for DBP response at 8 weeks (Secondary Endpoint) Response Rate for SBP response at 8 weeks (Secondary Endpoint) Response rate for BP control at 8 weeks (Secondary Endpoint)	Table 15.2.2.4.1: 1

Table 15.1.1: 2 Conclusion of patient participation - overall

	Total	
	N	(%)
Enrolled	2607	(100.0)
Not randomised	1146	(44.0)
Randomised	1461	(56.0)
Not treated	0	(0.0)
Treated	1461	(100.0)
Planned time reached	1344	(92.0)
Prematurely discontinued	117	(8.0)
Adverse event	38	(2.6)
AE study dis. worse	6	(0.4)
AE-oth. dis. worse	4	(0.3)
AE-other	28	(1.9)
Lack of efficacy	16	(1.1)
Non compliant with protocol	13	(0.9)
Lost to follow-up	10	(0.7)
Consent withdrawn	27	(1.8)
Other	13	(0.9)

Source data: Appendix 16.2, Listing 1.2

Table 15.1.1: 3 Conclusion of patient participation by treatment group (Treated set)

	A0		A2.5		A5		A10		Total	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
T0										
Treated	46	(100.0)	50	(100.0)	140	(100.0)	129	(100.0)	365	(100.0)
Planned time reached	39	(84.8)	43	(86.0)	133	(95.0)	116	(89.9)	331	(90.7)
Prematurely discontinued	7	(15.2)	7	(14.0)	7	(5.0)	13	(10.1)	34	(9.3)
T20										
Treated	42	(100.0)	44	(100.0)	46	(100.0)	44	(100.0)	176	(100.0)
Planned time reached	41	(97.6)	40	(90.9)	43	(93.5)	39	(88.6)	163	(92.6)
Prematurely discontinued	1	(2.4)	4	(9.1)	3	(6.5)	5	(11.4)	13	(7.4)
T40										
Treated	130	(100.0)	47	(100.0)	143	(100.0)	129	(100.0)	449	(100.0)
Planned time reached	125	(96.2)	46	(97.9)	135	(94.4)	117	(90.7)	423	(94.2)
Prematurely discontinued	5	(3.8)	1	(2.1)	8	(5.6)	12	(9.3)	26	(5.8)
T80										
Treated	135	(100.0)	48	(100.0)	146	(100.0)	142	(100.0)	471	(100.0)
Planned time reached	118	(87.4)	44	(91.7)	136	(93.2)	129	(90.8)	427	(90.7)
Prematurely discontinued	17	(12.6)	4	(8.3)	10	(6.8)	13	(9.2)	44	(9.3)
Total										
Treated	353	(100.0)	189	(100.0)	475	(100.0)	444	(100.0)	1461	(100.0)
Planned time reached	323	(91.5)	173	(91.5)	447	(94.1)	401	(90.3)	1344	(92.0)
Prematurely discontinued	30	(8.5)	16	(8.5)	28	(5.9)	43	(9.7)	117	(8.0)

Table 15.2.1.1.1: 1 Summary of in-clinic seated trough DBP - LOCF (FAS-TC)

			A0	A2.5	A5	A10	Total
T0		N	46	48	137	124	355
	Baseline	Mean (SD)	102.5 (4.79)	102.5 (4.59)	102.4 (4.47)	101.2 (4.00)	102.0 (4.40)
	End of study	Mean (SD)	96.6 (11.25)	92.2 (9.85)	89.3 (9.28)	84.7 (7.96)	89.0 (9.98)
	Change	Mean (SD)	-5.9 (9.41)	-10.4 (9.85)	-13.0 (7.87)	-16.5 (7.06)	-13.0 (8.78)
T20		N	42	44	45	40	171
	Baseline	Mean (SD)	101.6 (3.45)	102.3 (4.79)	102.8 (5.27)	101.1 (3.76)	102.0 (4.42)
	End of study	Mean (SD)	88.4 (9.01)	84.3 (9.36)	87.0 (8.83)	82.4 (7.41)	85.6 (8.94)
	Change	Mean (SD)	-13.2 (8.97)	-18.0 (7.79)	-15.7 (6.46)	-18.7 (6.97)	-16.4 (7.83)
T40		N	129	47	141	123	440
	Baseline	Mean (SD)	102.2 (4.69)	101.1 (3.98)	101.6 (4.15)	101.6 (3.76)	101.7 (4.20)
	End of study	Mean (SD)	89.1 (10.28)	84.9 (7.55)	85.7 (7.69)	82.0 (8.30)	85.6 (9.07)
	Change	Mean (SD)	-13.1 (10.09)	-16.2 (8.15)	-16.0 (7.63)	-19.6 (7.88)	-16.2 (8.87)
T80		N	132	46	143	136	457
	Baseline	Mean (SD)	101.5 (4.50)	101.5 (3.86)	101.8 (4.55)	101.3 (3.93)	101.5 (4.28)
	End of study	Mean (SD)	87.9 (9.27)	86.1 (7.89)	84.0 (8.85)	81.7 (7.89)	84.7 (8.93)
	Change	Mean (SD)	-13.6 (8.70)	-15.3 (7.53)	-17.8 (8.52)	-19.6 (7.85)	-16.9 (8.60)
Total		N	349	185	466	423	1423
	Baseline	Mean (SD)	101.9 (4.50)	101.8 (4.33)	102.0 (4.49)	101.3 (3.88)	101.8 (4.30)
	End of study	Mean (SD)	89.6 (10.25)	86.9 (9.21)	86.4 (8.88)	82.7 (8.06)	86.1 (9.39)
	Change	Mean (SD)	-12.3 (9.66)	-14.9 (8.81)	-15.6 (8.07)	-18.6 (7.66)	-15.6 (8.77)

SD - Standard Deviation

Table 15.2.1.1.1: 2 Analysis of change from baseline to end of study (LOCF) in in-clinic seated trough DBP (FAS-TC)

Model*		A0	A2.5	A5	A10	Total
T0	N	46	48	137	124	355
	Adj Mean (SE)	-6.2(1.19)	-10.6(1.17)	-13.4(0.69)	-17.1(0.73)	-12.5(0.45)
T20	N	42	44	45	40	171
	Adj Mean (SE)	-13.8(1.25)	-18.3(1.22)	-15.9(1.20)	-19.3(1.28)	-16.8(0.63)
T40	N	129	47	141	123	440
	Adj Mean (SE)	-13.4(0.71)	-16.9(1.18)	-16.5(0.68)	-20.2(0.73)	-16.6(0.41)
T80	N	132	46	143	136	457
	Adj Mean (SE)	-14.0(0.71)	-15.7(1.19)	-18.2(0.68)	-20.1(0.70)	-17.2(0.40)
			Telm x Amlo interaction effect**: p=0.0317		Telm effect*:	p<0.0001
Total	N	349	185	466	423	
	Adj Mean (SE)	-12.2(0.46)	-15.3(0.60)	-16.2(0.40)	-19.3(0.42)	Amlo effect*: p<0.0001

* Estimates from main effects model including dosage of telmisartan, dosage of amlodipine, and country/region with baseline value as a covariate
** Model that also includes a term for the Telm x Amlo interaction
SE - Standard Error

Table 15.2.1.1.1: 3 Analysis of change from baseline to end of study (LOCF) in in-clinic seated trough DBP excluding patients treated with placebo (FAS-TC)

Model*		A0	A2.5	A5	A10
T0	N		48	137	124
	Adj Mean (SE)		-10.6(1.16)	-13.4(0.69)	-17.1(0.72)
T20	N	42	44	45	40
	Adj Mean (SE)	-13.8(1.24)	-18.3(1.21)	-15.9(1.20)	-19.3(1.27)
T40	N	129	47	141	123
	Adj Mean (SE)	-13.4(0.71)	-16.9(1.17)	-16.5(0.68)	-20.2(0.73)
T80	N	132	46	143	136
	Adj Mean (SE)	-14.0(0.70)	-15.7(1.18)	-18.2(0.68)	-20.1(0.69)

Telm x Amlo interaction effect*: p=0.1777

* Model that also includes a term for the Telm x Amlo interaction
SE - Standard Error

Table 15.2.1.1.1: 4 Comparison of treatment effects on the change from baseline in in-clinic seated trough DBP (LOCF) for combination therapy versus the individual components (FAS-TC)

		A0	A2.5	A5	A10
T0	N	46	48	137	124
	Adj* mean (SE)	-6.2 (1.19)	-10.6 (1.17)	-13.4 (0.69)	-17.1 (0.73)
T20	N	42	44	45	40
	Adj* mean (SE)	-13.8 (1.25)	-18.3 (1.22)	-15.9 (1.20)	-19.3 (1.28)
	Diff versus T				
	Adj* mean (SE)		-4.6 (1.74)	-2.1 (1.73)	-5.5 (1.78)
	95% CI		(-8.0, -1.2)	(-5.5, 1.3)	(-9.0, -2.0)
	p-value		0.0085	0.2202	0.0021
	Diff versus A				
	Adj* mean (SE)		-7.8 (1.68)	-2.5 (1.38)	-2.2 (1.46)
	95% CI		(-11.1, -4.5)	(-5.2, 0.2)	(-5.1, 0.7)
	p-value		<0.0001	0.0705	0.1351
T40	N	129	47	141	123
	Adj* mean (SE)	-13.4 (0.71)	-16.9 (1.18)	-16.5 (0.68)	-20.2 (0.73)
	Diff versus T				
	Adj* mean (SE)		-3.5 (1.37)	-3.1 (0.98)	-6.8 (1.01)
	95% CI		(-6.2, -0.8)	(-5.0, -1.2)	(-8.8, -4.8)
	p-value		0.0116	0.0016	<0.0001
	Diff versus A				
	Adj* mean (SE)		-6.3 (1.65)	-3.1 (0.97)	-3.1 (1.02)
	95% CI		(-9.5, -3.0)	(-5.0, -1.2)	(-5.1, -1.1)
	p-value		0.0002	0.0013	0.0023
T80	N	132	46	143	136
	Adj* mean (SE)	-14.0 (0.71)	-15.7 (1.19)	-18.2 (0.68)	-20.1 (0.70)
	Diff versus T				
	Adj* mean (SE)		-1.7 (1.38)	-4.2 (0.97)	-6.1 (0.98)
	95% CI		(-4.4, 1.0)	(-6.1, -2.3)	(-8.0, -4.1)
	p-value		0.2244	<0.0001	<0.0001
	Diff versus A				
	Adj* mean (SE)		-5.1 (1.66)	-4.9 (0.96)	-3.0 (1.00)
	95% CI		(-8.4, -1.9)	(-6.7, -3.0)	(-5.0, -1.1)
	p-value		0.0020	<0.0001	0.0024

Table 15.2.2.1.1: 2 Analysis of change from baseline to end of study (LOCF) in in-clinic seated trough SBP (FAS-TC)

Model*		A0	A2.5	A5	A10	Total
T0	N	46	48	137	124	355
	Adj Mean (SE)	-2.5(1.82)	-11.4(1.79)	-15.4(1.06)	-20.7(1.11)	-13.3(0.69)
T20	N	42	44	45	40	171
	Adj Mean (SE)	-15.1(1.91)	-18.8(1.87)	-21.0(1.85)	-24.4(1.96)	-19.9(0.96)
T40	N	129	47	141	123	440
	Adj Mean (SE)	-14.6(1.09)	-21.9(1.81)	-21.8(1.05)	-24.7(1.12)	-20.3(0.62)
T80	N	132	46	143	136	457
	Adj Mean (SE)	-14.3(1.08)	-17.4(1.82)	-22.1(1.04)	-26.4(1.07)	-20.4(0.61)
			Telm x Amlo interaction effect**: p=0.0950		Telm effect*:	p<0.0001
Total	N	349	185	466	423	
	Adj Mean (SE)	-12.0(0.70)	-17.4(0.92)	-20.2(0.61)	-24.3(0.64)	Amlo effect*: p<0.0001

* Estimates from main effects model including dosage of telmisartan, dosage of amlodipine, and country/region with baseline value as a covariate
** Model that also includes a term for the Telm x Amlo interaction
SE - Standard Error

Table 15.2.2.1.1: 4 Comparison of treatment effects on the change from baseline in in-clinic seated trough SBP (LOCF) for combination therapy versus the individual components (FAS-TC)

		A0	A2.5	A5	A10
T0	N	46	48	137	124
	Adj* mean (SE)	-2.5 (1.82)	-11.4 (1.79)	-15.4 (1.06)	-20.7 (1.11)
T20	N	42	44	45	40
	Adj* mean (SE)	-15.1 (1.91)	-18.8 (1.87)	-21.0 (1.85)	-24.4 (1.96)
	Diff versus T				
	Adj* mean (SE)		-3.7 (2.67)	-5.8 (2.65)	-9.3 (2.73)
	95% CI		(-8.9, 1.5)	(-11.1, -0.6)	(-14.7, -4.0)
	p-value		0.1641	0.0276	0.0006
	Diff versus A				
	Adj* mean (SE)		-7.4 (2.57)	-5.6 (2.12)	-3.8 (2.24)
	95% CI		(-12.5, -2.4)	(-9.7, -1.4)	(-8.2, 0.6)
	p-value		0.0039	0.0090	0.0930
T40	N	129	47	141	123
	Adj* mean (SE)	-14.6 (1.09)	-21.9 (1.81)	-21.8 (1.05)	-24.7 (1.12)
	Diff versus T				
	Adj* mean (SE)		-7.4 (2.10)	-7.2 (1.50)	-10.1 (1.55)
	95% CI		(-11.5, -3.2)	(-10.2, -4.3)	(-13.2, -7.1)
	p-value		0.0005	<0.0001	<0.0001
	Diff versus A				
	Adj* mean (SE)		-10.6 (2.54)	-6.4 (1.48)	-4.0 (1.57)
	95% CI		(-15.5, -5.6)	(-9.3, -3.5)	(-7.1, -0.9)
	p-value		<0.0001	<0.0001	0.0108
T80	N	132	46	143	136
	Adj* mean (SE)	-14.3 (1.08)	-17.4 (1.82)	-22.1 (1.04)	-26.4 (1.07)
	Diff versus T				
	Adj* mean (SE)		-3.2 (2.11)	-7.8 (1.49)	-12.1 (1.51)
	95% CI		(-7.3, 1.0)	(-10.8, -4.9)	(-15.1, -9.2)
	p-value		0.1343	<0.0001	<0.0001
	Diff versus A				
	Adj* mean (SE)		-6.1 (2.55)	-6.7 (1.47)	-5.7 (1.53)
	95% CI		(-11.1, -1.1)	(-9.6, -3.8)	(-8.7, -2.7)
	p-value		0.0175	<0.0001	0.0002

Source data: Appendix 16.1.9.2, Statdoc 6.2.1.4 t15glm3.sas 17OCT2007

Table 15.2.2.4.1: 1 Analysis of in-clinic blood pressure control and response (FAS-TC)

	Number of patients with response (%)				
	DBP control	DBP response	SBP response	SBP response 3	BP control
Placebo	14 (30.4)	18 (39.1)	17 (37.0)	15 (32.6)	9 (19.6)
T20	23 (54.8)	27 (64.3)	30 (71.4)	27 (64.3)	17 (40.5)
T20+A2.5	33 (75.0)	40 (90.9)	38 (86.4)	37 (84.1)	23 (52.3)
T20+A5	29 (64.4)	36 (80.0)	40 (88.9)	35 (77.8)	23 (51.1)
T20+A10	34 (85.0)	37 (92.5)	37 (92.5)	35 (87.5)	28 (70.0)
T40	69 (53.5)	90 (69.8)	89 (69.0)	82 (63.6)	55 (42.6)
T40+A2.5	34 (72.3)	41 (87.2)	40 (85.1)	39 (83.0)	31 (66.0)
T40+A5	101 (71.6)	114 (80.9)	129 (91.5)	125 (88.7)	83 (58.9)
T40+A10	101 (82.1)	113 (91.9)	119 (96.7)	113 (91.9)	93 (75.6)
T80	80 (60.6)	103 (78.0)	90 (68.2)	86 (65.2)	55 (41.7)
T80+A2.5	32 (69.6)	34 (73.9)	37 (80.4)	35 (76.1)	26 (56.5)
T80+A5	107 (74.8)	127 (88.8)	125 (87.4)	120 (83.9)	94 (65.7)
T80+A10	116 (85.3)	124 (91.2)	129 (94.9)	123 (90.4)	104 (76.5)
A2.5	16 (33.3)	25 (52.1)	31 (64.6)	23 (47.9)	12 (25.0)
A5	72 (52.6)	93 (67.9)	107 (78.1)	100 (73.0)	58 (42.3)
A10	91 (73.4)	106 (85.5)	110 (88.7)	102 (82.3)	78 (62.9)
	p<0.0001	p<0.0001	p<0.0001	p<0.0001	p<0.0001

DBP control: DBP < 90 mmHg
DBP response: DBP < 90 mmHg or >= 10 mmHg reduction in DBP
SBP response: SBP < 140 mmHg or >= 10 mmHg reduction in SBP
SBP response 3: SBP < 140 mmHg or >= 15 mmHg reduction in SBP
BP Control: SBP < 140 mmHg and DBP < 90 mmHg