Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

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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: TWYNSTA		**EudraCT No.:** 2008-000873-40	
Name of active ingredient: Telmisartan and amlodipine		**Page:** 1 of 7	**Synopsis No.:**
Module:		**Volume:** {hyperlink }	
Report date: 12 May 2010	**Trial No. / U No.:** 1235.0020 / U10-3292-01	**Date of trial:** 09 MAR 2009 - 11 DEC 2009	**Date of revision:** Not applicable

Title of trial:	**TE**lmisartan 80 mg plus **AM**lodipine 10 mg fixed-dose combination tablet **ST**udy versus **A**mlodipine 10 mg over encapsulated tablets or telmisartan 80 mg tablets as first line therapy in patients with **severe H**yper**T**ensio**N**: A Phase III, 8-week, randomised, double-blind, double-dummy, forced-titration comparison (TEAMSTA severe HTN)
Coordinating Investigator:	[redacted] MD
Trial sites:	Multicentre study, cf. Appendix 16.1.4
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 seated trough cuff systolic blood pressure (SBP) compared to both of the respective monotherapies of telmisartan 80 mg (T80) and amlodipine 10 mg (A10) in patients with severe hypertension. A key secondary objective was to identify the duration of treatment required to demonstrate the superiority of the FDC over both monotherapies.
Methodology:	Randomised, double-blind, double-dummy, forced-titration, parallel group with eight weeks of treatment
No. of subjects:	
planned:	Enrolled: 1520 Entered (randomized): 760
actual:	Enrolled: 1315 Entered (randomized): 858 Telmisartan 80 mg and Amlodipine 10 mg fixed-dose combination: 421 entered Telmisartan 80 mg: 217 entered Amlodipine 10 mg: 220 entered

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Name of finished product: TWYNSTA		EudraCT No.: 2008-000873-40	
Name of active ingredient: Telmisartan and amlodipine		Page: 2 of 7	Synopsis No.:
Module:		Volume: {hyperlink }	
Report date: 12 May 2010	Trial No. / U No.: 1235.0020 / U10-3292-01	Date of trial: 09 MAR 2009 - 11 DEC 2009	Date of revision: Not applicable

Diagnosis and main criteria for inclusion:	Male or female patients with severe hypertension (defined as mean seated cuff SBP ≥180 mmHg and DBP ≥95 mm Hg) 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
mode of admin.:	Oral
batch no.:	B083000678
Test product:	Telmisartan 80 mg plus amlodipine 10 mg (T80/A10 FDC) tablet
dose:	Once-daily for the final six weeks of randomised treatment
mode of admin.:	Oral
batch no.:	B083000677
Reference therapy:	Telmisartan 80 mg (T80) tablet
dose:	Once-daily for the entire eight weeks of randomised treatment
mode of admin.:	Oral
batch no.:	B083000833 and B093000499
Reference therapy:	Amlodipine 5 mg (A5) over-encapsulated tablet
dose:	Once-daily for the first two weeks of randomised treatment
mode of admin.:	Oral
batch no.:	B083000763
Reference therapy:	Amlodipine 10 mg (A10) as two 5 mg over-encapsulated tablets
dose:	Once-daily for the final six weeks of randomised treatment
mode of admin.:	Oral
batch no.:	B083000763
Reference therapy:	Placebo tablets (matching T80/A5)
dose:	Once-daily for the first two weeks of randomised treatment
mode of admin.:	Oral

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Name of finished product: TWYNSTA		EudraCT No.: 2008-000873-40	
Name of active ingredient: Telmisartan and amlodipine		Page: 3 of 7	Synopsis No.:
Module:		Volume: {hyperlink }	
Report date: 12 May 2010	Trial No. / U No.: 1235.0020 / U10-3292-01	Date of trial: 09 MAR 2009 - 11 DEC 2009	Date of revision: Not applicable

batch no.:	BB083000764
Reference therapy:	Placebo tablets (matching T80/A10)
dose:	Once-daily for the final six weeks of randomised treatment
mode of admin.:	Oral
batch no.:	B083000756
Reference therapy:	Placebo capsules (matching A5 and A10 [2 capsules])
dose:	Once-daily for the first two weeks of randomized treatment (A5) or final six weeks of randomised treatment (A10)
mode of admin.:	Oral
batch no.:	B083000770 and B093000503
Duration of treatment:	Eight weeks (forced up-titration after two weeks for the T80/A10 and A10 treatment groups; T80 did not require titration)
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<90 mmHg, <80 mmHg) after one, two, four, six, and eight weeks of treatment • SBP control (mean seated DBP<140 mmHg, <130 mmHg) after one, two, four, six, and eight weeks of treatment • Other measures of BP control and response variables after one, two,

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Name of finished product: TWYNSTA		EudraCT No.: 2008-000873-40	
Name of active ingredient: Telmisartan and amlodipine		Page: 4 of 7	Synopsis No.:
Module:		Volume: {hyperlink }	
Report date: 12 May 2010	Trial No. / U No.: 1235.0020 / U10-3292-01	Date of trial: 09 MAR 2009 - 11 DEC 2009	Date of revision: Not applicable

	four, six, and eight weeks of treatment. All BP related endpoints were required to be trough measurements (i.e. 20-30 hours past last intake of study medication)
Safety:	Adverse events (AE); incidence of peripheral oedema; changes from baseline in pulse rate; changes in laboratory parameters; changes in 12-lead electrocardiogram (ECG); orthostatic changes (seated to standing) in SBP and DBP
Statistical methods:	Analysis of covariance (ANCOVA) utilising a restricted maximum likelihood (REML) repeated measures analysis with baseline and baseline-by-visit as covariates on the changes from baseline in mean seated trough cuff SBP and DBP. The following hierarchical was used: At each time point during the treatment period beginning with 8 weeks then followed by 6 weeks, 4 weeks, 2 weeks and finally 1 week, comparisons of adjusted mean reductions from baseline SBP between T80/A10 to both T80 and A10 were done. A conclusion of superiority of T80/A10 over the respective monotherapies (T80 and A10) following 8 weeks of treatment was only made if the FDC was significantly more effective than both monotherapies in reducing SBP. An identification of the duration of treatment required to show this superiority could only be done if superiority if T80/A10 was significantly more effective than both monotherapies at the 8 week time point. If so, then testing progressed in the order stated above for the other time points. The duration of treatment required to show this superiority was the earliest point in which the FDC of T80/A10 or T80/A5 was significantly more effective than both monotherapies. Logistic regression with baseline as a covariate was employed to analyse the SBP and DBP control endpoints. Frequencies and percentages were reported for other SBP, DBP response and BP control endpoints. Logistic regression analysis was also performed to compare rates of peripheral oedema.

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Name of finished product: TWYNSTA		EudraCT No.: 2008-000873-40	
Name of active ingredient: Telmisartan and amlodipine		Page: 5 of 7	Synopsis No.:
Module:		Volume: {hyperlink }	
Report date: 12 May 2010	Trial No. / U No.: 1235.0020 / U10-3292-01	Date of trial: 09 MAR 2009 - 11 DEC 2009	Date of revision: Not applicable

SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results:

All of the 858 patients randomised had received at least one dose of trial medication. Mean age was 58.2 years and the majority of patients were under 65 years-of-age. Approximately half of the patients were male (51.9%) and 86.0% of patients were white. Baseline efficacy parameters of SBP/DBP mean (SD) were 185.4 (4.5)/103.3 (6.4) mm Hg. All demographic and baseline characteristics were well-matched across all three treatment groups. The majority of patients completed the trial (93.0%).

Primary/key secondary endpoints

After 8 weeks of treatment, the mean change from baseline in SBP adjusted for baseline SBP was - 47.5 mmHg in the T80/A10 group. This was a greater reduction from baseline than the adjusted means observed in both the T80 (-36.9 mmHg) and the A10 (-43.2 mmHg) groups. The difference in adjusted means between the T80/A10 and the T80 groups -10.6 mmHg (95% CI: -12.9, -8.3) achieved statistical significance ($p<0.0001$) as did the differences in adjusted means between the T80/A10 and A10 groups ($p=0.0002$), with a difference of -4.4 mmHg (95% CI: -6.7, -2.1). At all other time points in which BP measurements were collected (Weeks 6, 4, 2, and 1), the differences in the adjusted mean SBP observed in the FDC group were greater than in both of the monotherapies and these differences were statistically significant. With these results it was concluded that the FDC of T80/A10 is superior to both T80 and A10 at all timepoints. Evidence of this superiority was observed after one week of treatment. This result was confirmed for the sensitivity analysis using a last observation carried forward method to impute missing efficacy data.

Secondary endpoints:

In the analysis of DBP at week 8, an adjusted mean change of -18.7 mmHg for the T80/A10 group was observed compared to changes of -13.8 mmHg for the T80 group and -16.3 mmHg for the A10 group. The differences in the adjusted means for T80/A10 compared with both T80 (-5.0 mmHg (95% CI: -6.4, -3.6)) and A10 (-2.4 mmHg (95% CI: -3.8, -1.0)) indicated additional reduction in mean trough DBP in the T80/A10 group over the two monotherapies. Statistically, the results in the analyses of DBP mirrored those in the analyses of SBP where, at all time points, the differences in the adjusted mean DBP observed in the FDC group were greater than in both of the monotherapies and these differences were statistically significant.

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Name of finished product: TWYNSTA		EudraCT No.: 2008-000873-40	
Name of active ingredient: Telmisartan and amlodipine		Page: 6 of 7	Synopsis No.:
Module:		Volume: {hyperlink }	
Report date: 12 May 2010	Trial No. / U No.: 1235.0020 / U10-3292-01	Date of trial: 09 MAR 2009 - 11 DEC 2009	Date of revision: Not applicable

	In all measures of the other secondary endpoints of achieving SBP, DBP and BP control, SBP and DBP response, and in attaining normal BP levels, higher proportions of patients in the T80/A10 group compared to T80 and A10 were consistently observed, supporting the analyses of the reductions from baseline in SBP and DBP. For example, at week 8, the proportion of patients who achieved SBP control (<140 mm Hg) in the T80/A10 group was 57.0% compared to 29.2% of patients in the T80 group and 44.9% in the A10 group. Additionally, there were almost double the number of patients who achieved SBP control at week 1 in the T80/A10 group (18.1%) compared to the T80 (8.7%) and A5 (10.6%) groups.
Safety results:	Overall, 283 (33.0%) patients reported AEs during the study. Patients treated with combination therapy reported a similar rate of AEs (32.8%) compared with telmisartan monotherapy (33.2%) and amlodipine monotherapy (33.2%). The most frequently occurring AEs across all treatment groups were peripheral oedema (11.2%) and headache (5.4%). Combination therapy resulted in a lower rate of peripheral oedema (13.1%) compared with amlodipine monotherapy (15.0%); 3.7% of patients treated with telmisartan monotherapy reported peripheral oedema. The rate of headache was lowest for combination therapy (3.8% T80/A10; 8.3% T80; 5.5% A10). Related AEs occurred in 12.6%, 6.9%, and 16.4% of patients treated with combination therapy, telmisartan monotherapy, and amlodipine monotherapy, respectively. Patients treated with combination therapy had the lowest rate of discontinuation due to AEs (2.1% T80/A10; 2.8% T80; and 3.2% A10). Serious AEs occurred infrequently (0.8%) and none were fatal. AEs associated with a decrease in blood pressure occurred infrequently and were similar between treatment groups. Clinically meaningful orthostatic changes in blood pressure were also infrequent during orthostatic testing (2.2% T80/A10; 3.3% T80; and 1.9% A10). Changes in clinical laboratory measures were consistent with the known effects of telmisartan and amlodipine monotherapies and were generally not clinically significant. There were no clinically meaningful changes in pulse rate or ECG.
Conclusions:	*Efficacy conclusions:* • Significantly greater reductions from baseline SBP were achieved for T80/A10 patients compared with both monotherapies of T80 and A10

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Name of finished product: TWYNSTA		EudraCT No.: 2008-000873-40	
Name of active ingredient: Telmisartan and amlodipine		Page: 7 of 7	Synopsis No.:
Module:		Volume: {hyperlink }	
Report date: 12 May 2010	Trial No. / U No.: 1235.0020 / U10-3292-01	Date of trial: 09 MAR 2009 - 11 DEC 2009	Date of revision: Not applicable

after 8 weeks of treatment and at all other time points in the trial.

- Significantly greater reductions from baseline DBP were achieved for T80/A10 patients compared with both monotherapies of T80 and A10 after 8 weeks of treatment and at all other time points in the trial.
- Proportions of patients achieving SBP, DBP response, SBP, DBP, BP control, and normal levels of BP were consistently higher in the T80/A10 group compared to both monotherapies.

Safety conclusions

- T80/A10 combination therapy resulted in a similar rate of AEs compared with the individual monotherapies.
- The incidence of peripheral oedema and headache, the most frequently occurring AEs, was numerically lower in patients treated with combination therapy when compared to amlodipine monotherapy.
- The occurrence of AEs related to decreases in blood pressure and the occurrence of orthostatic changes were infrequent and generally similar between treatment groups.
- No clinically meaningful differences were observed between combination therapy and monotherapies in clinically laboratory measures, pulse rate, or ECG.

Overall 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 either telmisartan or amlodipine monotherapy in patients with severe hypertension. In this population, significantly greater reductions from baseline SBP and DBP were demonstrated after one week of treatment with the fixed-dose combination compared to the respective monotherapies and persisted throughout the trial.

Treatment with the fixed-dose combination of T80/A10 is well tolerated in patients with severe hypertension. Adverse event data, clinical laboratory, vital signs, and orthostatic changes in blood pressure are consistent with the established safety profile for telmisartan and amlodipine monotherapies.

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
Change from baseline in trough seated DBP at weeks 1 through 8 (secondary endpoints)	Table 15.2.2.1: 2 Table 15.2.2.1: 3
Proportion of patients achieving SBP, DBP control at each time point (secondary endpoint)	Table 15.2.2.2.1: 1
Proportion of patients achieving SBP, DPB response at each time point (secondary endpoint)	Table 15.2.2.2.2: 1
Proportion of patients achieving BP control at each time point (secondary endpoint)	Table 15.2.2.2.2: 2
Proportion of patients achieving normal BP at each time point (secondary endpoint)	Table 15.2.2.2.2: 3

Table 15.1.1: 1 Disposition of patients by treatment group

	T80/A10 N (%)	T80 N (%)	A10 N (%)	Total N (%)
Enrolled				1315
Not entered/randomised				457
Entered/randomised	421	217	220	858
Not Treated	0	0	0	0
Treated	421 (100.0)	217 (100.0)	220 (100.0)	858 (100.0)
Not prematurely discontinued from trial medication	401 (95.2)	195 (89.9)	202 (91.8)	798 (93.0)
Prematurely discontinued from trial medication	20 (4.8)	22 (10.1)	18 (8.2)	60 (7.0)
Adverse event	9 (2.1)	6 (2.8)	7 (3.2)	22 (2.6)
Worsening of disease under study	0 (0.0)	2 (0.9)	1 (0.5)	3 (0.3)
Worsening of other pre-existing disease	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.2)
Other adverse event	7 (1.7)	4 (1.8)	6 (2.7)	17 (2.0)
Lack of efficacy	0 (0.0)	4 (1.8)	3 (1.4)	7 (0.8)
Non compliant with protocol	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.1)
Lost to follow-up	2 (0.5)	0 (0.0)	1 (0.5)	3 (0.3)
Consent withdrawn not due to adverse events	4 (1.0)	8 (3.7)	6 (2.7)	18 (2.1)
Other	5 (1.2)	3 (1.4)	1 (0.5)	9 (1.0)

Table 15.2.1.1: 2 Presentation of repeated measure ANCOVA 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 - FAS

				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	379	-47.5 (0.69)			
	T80	189	-36.9 (0.96)	-10.6 (1.18)	(-12.9, -8.3)	< 0.0001
	A10	195	-43.2 (0.95)	-4.4 (1.18)	(-6.7, -2.1)	0.0002
Week 6	T80/A10	390	-46.9 (0.73)			
	T80	197	-36.3 (1.01)	-10.6 (1.25)	(-13.1, -8.2)	< 0.0001
	A10	201	-42.1 (1.01)	-4.8 (1.24)	(-7.3, -2.4)	0.0001
Week 4	T80/A10	392	-44.5 (0.73)			
	T80	202	-34.4 (1.01)	-10.2 (1.24)	(-12.6, -7.7)	< 0.0001
	A10	203	-39.8 (1.01)	-4.8 (1.24)	(-7.2, -2.4)	0.0001
Interaction treatment and week:						
p-value						0.0376
Interaction baseline and week:						
p-value						0.2544

*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 27APR2010

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

				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	395	-37.9 (0.71)			
	T80	208	-30.1 (0.97)	-7.8 (1.20)	(-10.2, -5.4)	< 0.0001
	A5	204	-33.3 (0.98)	-4.6 (1.21)	(-7.0, -2.3)	0.0001
Week 1	T80/A5	387	-31.9 (0.72)			
	T80	207	-25.4 (0.99)	-6.4 (1.23)	(-8.8, -4.0)	< 0.0001
	A5	207	-28.6 (0.99)	-3.3 (1.23)	(-5.7, -0.9)	0.0077
Interaction treatment and week:						
p-value						0.2794
Interaction baseline and week:						
p-value						0.2359

*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 27APR2010

Table 15.2.2.1: 2 Presentation of repeated measure ANCOVA results at nominal Weeks 4, 6, and 8 (high dose) by treatment group regarding change from baseline in in-clinic mean seated trough cuff DBP - FAS

				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	379	-18.7 (0.41)			
	T80	189	-13.8 (0.58)	-5.0 (0.71)	(-6.4, -3.6)	< 0.0001
	A10	195	-16.3 (0.58)	-2.4 (0.71)	(-3.8, -1.0)	0.0006
Week 6	T80/A10	390	-18.3 (0.41)			
	T80	197	-13.5 (0.57)	-4.9 (0.70)	(-6.2, -3.5)	< 0.0001
	A10	201	-15.7 (0.57)	-2.6 (0.70)	(-4.0, -1.3)	0.0002
Week 4	T80/A10	392	-17.0 (0.43)			
	T80	202	-12.1 (0.60)	-5.0 (0.74)	(-6.4, -3.5)	< 0.0001
	A10	203	-14.2 (0.60)	-2.8 (0.74)	(-4.3, -1.4)	0.0001
Interaction treatment and week:						
p-value						0.0015
Interaction baseline and week:						
p-value						0.2426

*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 6.2.1 ctr\eot_t4.sas 27APR2010

Table 15.2.2.1: 3 Presentation of repeated measure ANCOVA results at nominal Weeks 1 and 2 (low dose) by treatment group regarding change from baseline in in-clinic mean seated trough cuff DBP - FAS

				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	395	-13.2 (0.40)			
	T80	208	-10.4 (0.56)	-2.8 (0.69)	(-4.2, -1.5)	< 0.0001
	A5	204	-11.4 (0.56)	-1.8 (0.69)	(-3.2, -0.5)	0.0089
Week 1	T80/A5	387	-10.9 (0.37)			
	T80	207	-8.2 (0.50)	-2.7 (0.62)	(-3.9, -1.5)	< 0.0001
	A5	207	-9.6 (0.50)	-1.4 (0.62)	(-2.6, -0.1)	0.0301
Interaction treatment and week:						
p-value						0.7482
Interaction baseline and week:						
p-value						0.9062

*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 6.2.2 ctr\eot_t4.sas 27APR2010

Table 15.2.2.2.1: 1 Proportion of patients achieving SBP, DBP control at each time point - FAS (LOCF)

Week	Treatment	SBP control (<140 mmHg) n	(%)	N	SBP control 2 (<130 mmHg) n	(%)	N	DBP control (<90 mmHg) n	(%)	N	DBP control 2 (<80 mmHg) n	(%)	N
Week 1	T80/A5	70	(18.1)	387	17	(4.4)	387	147	(38.0)	387	18	(4.7)	387
	T80	18	(8.7)	207	3	(1.4)	207	61	(29.5)	207	6	(2.9)	207
	A5	22	(10.6)	207	5	(2.4)	207	64	(30.9)	207	7	(3.4)	207
Week 2	T80/A5	108	(26.7)	405	37	(9.1)	405	205	(50.6)	405	38	(9.4)	405
	T80	35	(16.5)	212	8	(3.8)	212	87	(41.0)	212	14	(6.6)	212
	A5	36	(17.0)	212	6	(2.8)	212	91	(42.9)	212	13	(6.1)	212
Week 4	T80/A10	179	(45.7)	392	79	(20.2)	392	268	(68.4)	392	89	(22.7)	392
	T80	60	(28.3)	212	20	(9.4)	212	106	(50.0)	212	24	(11.3)	212
	A10	69	(34.0)	203	24	(11.8)	203	109	(53.7)	203	27	(13.3)	203
Week 6	T80/A10	211	(53.6)	394	105	(26.6)	394	290	(73.6)	394	106	(26.9)	394
	T80	63	(29.7)	212	26	(12.3)	212	110	(51.9)	212	34	(16.0)	212
	A10	92	(44.9)	205	26	(12.7)	205	128	(62.4)	205	32	(15.6)	205
Week 8	T80/A10	225	(57.0)	395	109	(27.6)	395	291	(73.7)	395	116	(29.4)	395
	T80	62	(29.2)	212	25	(11.8)	212	112	(52.8)	212	25	(11.8)	212
	A10	92	(44.9)	205	37	(18.0)	205	131	(63.9)	205	35	(17.1)	205

Table 15.2.2.2.2: 1 Proportion of patients achieving SBP, DPB response at each time point - FAS (LOCF)

Week	Treatment	SBP response n	(%)	N	SBP response 2 n	(%)	N	SBP response 3 n	(%)	N	SBP response 4 n	(%)	N	SBP response 5 n	(%)	N	SBP response 6 n	(%)	N	SBP response 7 n	(%)	N
Week 1	T80/A5	338	(87.3)	387	361	(93.3)	387	311	(80.4)	387	220	(56.8)	387	120	(31.0)	387	220	(56.8)	387	120	(31.0)	387
	T80	164	(79.2)	207	177	(85.5)	207	130	(62.8)	207	80	(38.6)	207	38	(18.4)	207	80	(38.6)	207	38	(18.4)	207
	A5	173	(83.6)	207	190	(91.8)	207	150	(72.5)	207	97	(46.9)	207	43	(20.8)	207	97	(46.9)	207	43	(20.8)	207
Week 2	T80/A5	387	(95.6)	405	397	(98.0)	405	364	(89.9)	405	292	(72.1)	405	176	(43.5)	405	292	(72.1)	405	176	(43.5)	405
	T80	169	(79.7)	212	187	(88.2)	212	153	(72.2)	212	117	(55.2)	212	60	(28.3)	212	117	(55.2)	212	59	(27.8)	212
	A5	189	(89.2)	212	202	(95.3)	212	178	(84.0)	212	128	(60.4)	212	72	(34.0)	212	127	(59.9)	212	71	(33.5)	212
Week 4	T80/A10	388	(99.0)	392	389	(99.2)	392	380	(96.9)	392	339	(86.5)	392	259	(66.1)	392	339	(86.5)	392	258	(65.8)	392
	T80	180	(84.9)	212	190	(89.6)	212	174	(82.1)	212	133	(62.7)	212	82	(38.7)	212	133	(62.7)	212	82	(38.7)	212
	A10	194	(95.6)	203	199	(98.0)	203	185	(91.1)	203	157	(77.3)	203	110	(54.2)	203	157	(77.3)	203	110	(54.2)	203
Week 6	T80/A10	388	(98.5)	394	392	(99.5)	394	384	(97.5)	394	359	(91.1)	394	280	(71.1)	394	359	(91.1)	394	279	(70.8)	394
	T80	184	(86.8)	212	193	(91.0)	212	171	(80.7)	212	138	(65.1)	212	97	(45.8)	212	138	(65.1)	212	97	(45.8)	212
	A10	201	(98.0)	205	203	(99.0)	205	194	(94.6)	205	171	(83.4)	205	124	(60.5)	205	170	(82.9)	205	123	(60.0)	205
Week 8	T80/A10	391	(99.0)	395	394	(99.7)	395	389	(98.5)	395	361	(91.4)	395	295	(74.7)	395	361	(91.4)	395	294	(74.4)	395
	T80	188	(88.7)	212	194	(91.5)	212	174	(82.1)	212	140	(66.0)	212	100	(47.2)	212	140	(66.0)	212	100	(47.2)	212
	A10	202	(98.5)	205	202	(98.5)	205	196	(95.6)	205	175	(85.4)	205	127	(62.0)	205	174	(84.9)	205	126	(61.5)	205

SBP response (mean seated SBP < 140 mmHg or a reduction of = 15 mmHg)
SBP response 2 (mean seated SBP < 140 mmHg or a reduction of = 10 mmHg)
SBP response 3 (mean seated SBP < 140 mmHg or a reduction of = 20 mmHg)
SBP response 4 (mean seated SBP < 140 mmHg or a reduction of = 30 mmHg)
SBP response 5 (mean seated SBP < 140 mmHg or a reduction of = 40 mmHg)
SBP response 6 (reduction from baseline of = 30 mmHg)
SBP response 7 (reduction from baseline of = 40 mmHg)
DBP response (mean seated DBP < 90 mmHg or a reduction of = 10 mmHg)

Source data: Appendix 16.2, Listing 6.3 ctr\binarypcts.sas 22APR2010

Table 15.2.2.2.2: 1 Proportion of patients achieving SBP, DPB response at each time point - FAS (LOCF)

Week	Treatment	DBP response n	(%)	N
Week 1	T80/A5	232	(59.9)	387
	T80	95	(45.9)	207
	A5	100	(48.3)	207
Week 2	T80/A5	289	(71.4)	405
	T80	123	(58.0)	212
	A5	128	(60.4)	212
Week 4	T80/A10	339	(86.5)	392
	T80	132	(62.3)	212
	A10	151	(74.4)	203
Week 6	T80/A10	356	(90.4)	394
	T80	144	(67.9)	212
	A10	168	(82.0)	205
Week 8	T80/A10	361	(91.4)	395
	T80	147	(69.3)	212
	A10	172	(83.9)	205

SBP response (mean seated SBP < 140 mmHg or a reduction of = 15 mmHg)
SBP response 2 (mean seated SBP < 140 mmHg or a reduction of = 10 mmHg)
SBP response 3 (mean seated SBP < 140 mmHg or a reduction of = 20 mmHg)
SBP response 4 (mean seated SBP < 140 mmHg or a reduction of = 30 mmHg)
SBP response 5 (mean seated SBP < 140 mmHg or a reduction of = 40 mmHg)
SBP response 6 (reduction from baseline of = 30 mmHg)
SBP response 7 (reduction from baseline of = 40 mmHg)
DBP response (mean seated DBP < 90 mmHg or a reduction of = 10 mmHg)

Source data: Appendix 16.2, Listing 6.3 ctr\binarypcts.sas 22APR2010

Table 15.2.2.2.2: 2 Proportion of patients achieving BP control at each time point - FAS (LOCF)

Week	Treatment	BP control n	(%)	N	BP control 2 n	(%)	N	BP control 3 n	(%)	N	BP control 4 n	(%)	N
Week 1	T80/A5	54	(14.0)	387	12	(3.1)	387	4	(1.0)	387	3	(0.8)	387
	T80	16	(7.7)	207	3	(1.4)	207	1	(0.5)	207	0	(0.0)	207
	A5	15	(7.2)	207	3	(1.4)	207	0	(0.0)	207	0	(0.0)	207
Week 2	T80/A5	88	(21.7)	405	27	(6.7)	405	14	(3.5)	405	6	(1.5)	405
	T80	30	(14.2)	212	7	(3.3)	212	4	(1.9)	212	0	(0.0)	212
	A5	28	(13.2)	212	5	(2.4)	212	4	(1.9)	212	0	(0.0)	212
Week 4	T80/A10	161	(41.1)	392	62	(15.8)	392	41	(10.5)	392	15	(3.8)	392
	T80	49	(23.1)	212	19	(9.0)	212	13	(6.1)	212	4	(1.9)	212
	A10	53	(26.1)	203	16	(7.9)	203	12	(5.9)	203	2	(1.0)	203
Week 6	T80/A10	196	(49.7)	394	90	(22.8)	394	58	(14.7)	394	17	(4.3)	394
	T80	54	(25.5)	212	24	(11.3)	212	17	(8.0)	212	5	(2.4)	212
	A10	77	(37.6)	205	21	(10.2)	205	14	(6.8)	205	3	(1.5)	205
Week 8	T80/A10	199	(50.4)	395	94	(23.8)	395	70	(17.7)	395	18	(4.6)	395
	T80	51	(24.1)	212	24	(11.3)	212	14	(6.6)	212	3	(1.4)	212
	A10	73	(35.6)	205	27	(13.2)	205	19	(9.3)	205	2	(1.0)	205

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 < 85 mmHg)
BP control 3 (mean seated SBP < 130 mmHg and mean seated DBP < 80 mmHg)
BP control 4 (mean seated SBP < 120 mmHg and mean seated DBP < 80 mmHg)

Source data: Appendix 16.2, Listing 6.4 ctr\binarypcts.sas 22APR2010

Table 15.2.2.2.2: 3 Proportion of patients achieving normal BP at each time point - FAS (LOCF)

Week	Treatment	Optimal n (%)	N	Normal n (%)	N	High normal n (%)	N	High n (%)	N
Week 1	T80/A5	3 (0.8)	387	9 (2.3)	387	42 (10.9)	387	333 (86.0)	387
	T80	0 (0.0)	207	3 (1.4)	207	13 (6.3)	207	191 (92.3)	207
	A5	0 (0.0)	207	3 (1.4)	207	12 (5.8)	207	192 (92.8)	207
Week 2	T80/A5	6 (1.5)	405	21 (5.2)	405	61 (15.1)	405	317 (78.3)	405
	T80	0 (0.0)	212	7 (3.3)	212	23 (10.8)	212	182 (85.8)	212
	A5	0 (0.0)	212	5 (2.4)	212	23 (10.8)	212	184 (86.8)	212
Week 4	T80/A10	15 (3.8)	392	47 (12.0)	392	99 (25.3)	392	231 (58.9)	392
	T80	4 (1.9)	212	15 (7.1)	212	30 (14.2)	212	163 (76.9)	212
	A10	2 (1.0)	203	14 (6.9)	203	37 (18.2)	203	150 (73.9)	203
Week 6	T80/A10	17 (4.3)	394	73 (18.5)	394	106 (26.9)	394	198 (50.3)	394
	T80	5 (2.4)	212	19 (9.0)	212	30 (14.2)	212	158 (74.5)	212
	A10	3 (1.5)	205	18 (8.8)	205	56 (27.3)	205	128 (62.4)	205
Week 8	T80/A10	18 (4.6)	395	76 (19.2)	395	105 (26.6)	395	196 (49.6)	395
	T80	3 (1.4)	212	21 (9.9)	212	27 (12.7)	212	161 (75.9)	212
	A10	2 (1.0)	205	25 (12.2)	205	46 (22.4)	205	132 (64.4)	205

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)

Source data: Appendix 16.2, Listing 6.5 ctr\binarypcts.sas 22APR2010