Figure 3.4

Study G2 Platelet Aggregation
Epiephrine Stimulated

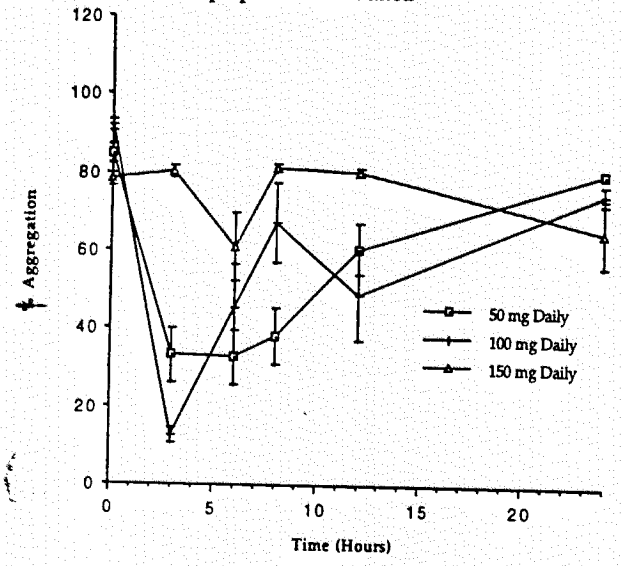
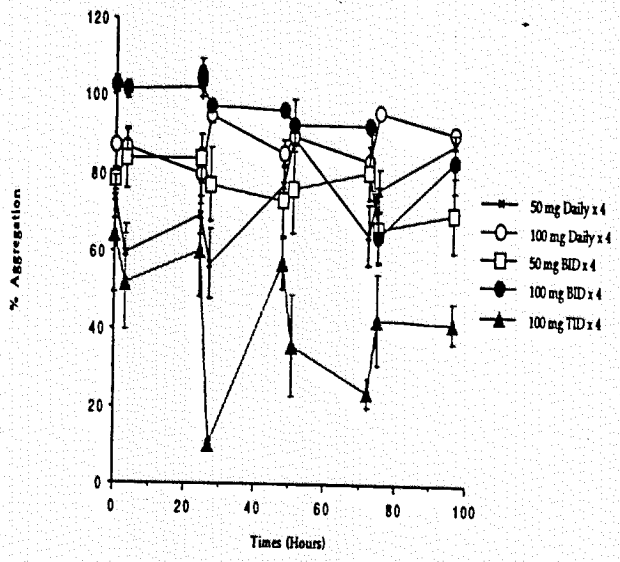


Figure 3.5

Study G2 Platelet Aggregation
Epinephrine Induced (1ug/ml)



exposure appears to show a trough in platelet aggregation somewhere between 3-6 hours. The multiple dose studies, however, show minimal effect at 3 hours post dose

Figure 3.8 Study G2 Single Dose Platelet Aggregation Arachadonic Acid

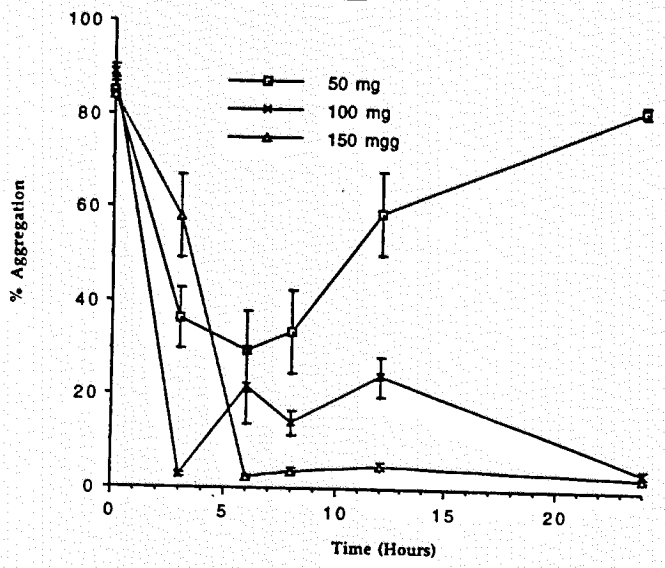
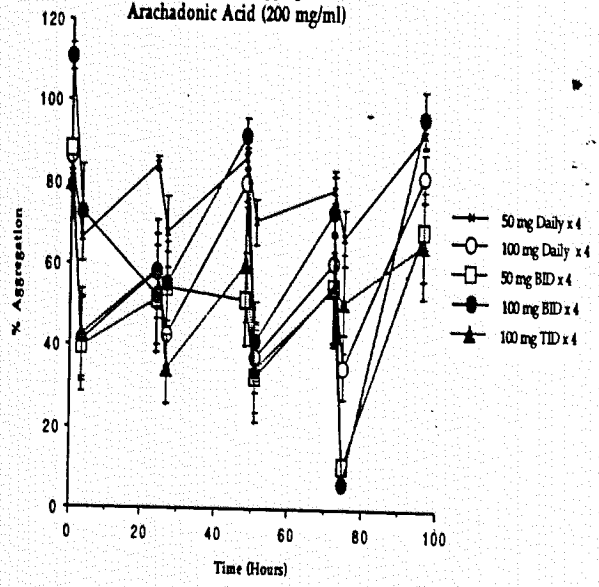


Figure 3.9 Study G2 Platelet Aggregation Arachadonic Acid (200 mg/ml)



compared to the single dose studies which show nearly complete inhibition of platelet aggregation. Concentrations of cilostazol, particularly for the BID and TID dosing regimens, at trough are comparable to the with 3 hour (peak) concentrations of cilostazol for a 50 mg single dose group. The inhibition of aggregation does not seem to correspond to serum concentrations.

Safety: No subject in the 50 mg/day dose complained of adverse events. Those treated with single doses of 100 mg and above and those treated with multiple dose regimens of cilostazol complained of headache. Dizziness occurred in all subjects in the two highest dose groups. Per sponsor, "[T]hese symptoms were not so severe and disappeared spontaneously within 12 hours". "Feverishness" occurred in 2 subjects in the single 150 mg dose and 6/19 subjects in the multiple dosing groups (no temperature was verified by thermometer measurements). Gastrointestinal symptoms occurred in all subjects in the 100 mg TID dose group, but were mild and disappeared spontaneously.

Vital Signs: There was no placebo group. The oscillations in blood pressure (mostly decrease in both systolic and diastolic blood pressure) may be drug related, diurnal rhythm related or random changes.

Laboratory: There were many minor deviations from normal values. None of these abnormalities had onset at first dose and persisted throughout the follow-up examinations. The most frequent abnormality was increased in either absolute neutrophil count or % neutrophils.

ECG: The sponsor claims no abnormalities in ECGs. No ECG interval data are presented.

[Comments: There was no placebo group. The results of this study both for inhibition of platelet aggregation as well as for safety are reflective of baseline changes.

In the listing of procedures there is reference to a treatment group designated as M-6. This is a multiple dose group that is treated with some unstated regimen of cilostazol. No data for this group is supplied in the study report.]

Conclusion: This is an open-label study. Those who analyzed the results of platelet aggregation may well have been aware as to the dose and the time point relative to dose.

The results of this study are not internally consistent with respect to the ability of OPC-13013 to inhibit ADP, epinephrine, arachidonic acid or collagen induced platelet aggregation. Although the single dose studies of OPC-13013 suggest early and rapid inhibition of platelet aggregation there is no convincing dose response.

The multiple dose studies, however, show much less, if any, effect in inhibiting induced platelet aggregation. In particular, the 100 mg TID at trough, generates concentrations of OPC-13013 equivalent to those seen at 3 hours with a single dose of 50 mg OPC-13013. Nevertheless, the single dose's effect on platelet aggregation is greater than that of the trough effect of the 100 mg TID effect. The effect on aggregation at each peak effect (hours 3,27, 51 and 75) were fairly small.

Reference 4. Study G-3

Submitted is a publication entitled: Effects of 6-[4-(1-Cyclohexy-5-Tetrazolyl)-Butoxy]-1, 2,-3,4-Tetrahydro-2-Oxo-Quinoline (OPC-13013) on Platelet Function. Arteriosclerosis, 12 (5), 1243-1249; (1984).

Investigator and Sites: Kawamura, M.; Naito, C.; Kooda, M.; Hayashi, H.; Miyazaki, S.; Hashimoto, Y.; and Kato, H.; Tokyo Teishen Hospital, Tokyo, Japan

Dates of Study: May-November 1982.

Study Summary: A total of 10 patients were enrolled into the study. The patients had cerebrovascular disease (8 with cerebral thrombosis, 1 with TIA and 1 with RIND) that occurred at least one month before entry. Only those patients who demonstrated a 50% increase in maximum aggregation rates after exposure to at least three of the following inducers: ADP, Collagen, Epinephrine or arachidonic acid (at respective concentrations of 1 uM, 0.5 ug/ml, 1 uM and 0.5 mM) were enrolled. Five of these patients were treated with OPC-13013 at doses of 50 mg BID and the other 5 were treated with 100 mg BID for 2 weeks.

The following parameters were measured three times prior to treatment and also after week one and week two of treatment. It is unclear whether patients were on concurrent therapies, particularly those which effect platelet function (i.e. aspirin). The timing of the measurements with respect to dosing is not stated.

Table 4.1 Methodology.

Test	Methodology
Platelet Aggregation	Measured in platelet poor and platelet rich fractions. The inducers ADP, collagen, epinephrine and arachidonic acid were used at the minimal concentrations needed to cause a 50% increase in maximum aggregation rate.
Platelet adhesiveness	Measured by the method of Salzman
B-thromboglobulin	Determined by RIA
Thromboxane B2	Detected by RIA
6-Keto-prostaglandin F1α	Determined by RIA.

Per the publication, there was no statistically significant decrease in platelet adhesiveness from baseline.

Platelet aggregation was only altered by arachidonic acid at 0.5 mM at 1 week and - collagen at 0.5 and 1 ug/ml at 2 weeks.

With respect to the 200 mg dose of OPC-10313, there was no change when epinephrine was the inducer. There was an apparent decrease in platelet aggregation at week 2 when arachidonic acid was the inducer (relative to baseline, uncorrected for multiple comparisons). There was an apparent decrease in aggregation when collagen (either at 0.05

or 1 uM) was the inducer. When ADP at 1 uM was the inducer there was an apparent decrease in aggregation at 2 weeks. There was no statistical difference when the concentration of ADP, as the inducer, was 2 uM.

Safety: No evaluation of safety was provided. No deaths, discontinuations or dropouts are described (nor is the absence of such events stated). There is no description of adverse events, vital signs, ECG changes or laboratory abnormalities.

Conclusion: This study was submitted without protocol, all measurements were baseline controlled, and the study was unblinded. There did not appear to be a stipulation that medications which might effect platelet function were kept constant during the course of the study. There was no primary end-point to the study and measurements were made under multiple conditions: platelet rich and platelet poor plasma, different inducers, different doses of inducers and different time points. Consequently, the study adds little to definition of the activity of OPC-13013 and its effect on platelet function.

Reference 5. Study G-4

Title of Study: Clinical Effects of Oral Cilostazol on Suppression of Platelet Function in Patients with Cerebrovascular Disease. Arzneim-Forsch/Drug Res. 35 (II); 1186-1188, (1985).

Investigators and Sites: Yasunaga, K.; and Mase, K.; Kansai Medical University, Osaka, Japan.

Study Summary. The submission consists of a publication with selected line listings. No protocol, randomization code (if any existed) were submitted.

A total of 15 subjects with cerebrovascular disease, who were not receiving any drug that modifies platelet function were enrolled. Of these, 11 had a history of cerebral arteriosclerosis, 2 had TIAs and 2 had cerebral thrombosis. These patients were allocated (not randomized) to receive 2-weeks of cilostazol at a daily dose of 75, 150 and 300 mg divided TID.

Platelet aggregation was determined after the addition of the following inducers (concentration): ADP (1 umol/l), collagen (5 ug/ml) and epinephrine (1 umol/l).

The effect of the various aggregation inducers on platelet aggregation is tabulated below.

Table 5.1 Effect of Inducers of Platelet Aggregation

	Cilostazol 75 mg			Cilostazol 150 mg			Cilostazol 300 mg		
	pre	During	% decrease	pre	During	% decrease	pre	During	% decrease
ADP	73.8 ± 0.8	55.0 ± 5	25.5 ± 5.8	66.9 ± 2.8	43.5 ± 4.1	34.2 ± 5.2	77.5 ± 0.2	29.2 ± 3.5	62.1 ± 4.6
Collagen	73.9 ± 1.0	46.2 ± 2.5	36.5 ± 7.1	69.6 ± 1.5	34.6 ± 2.6	50.7 ± 6.5	76.1 ± 0.6	21.3 ± 4.2	71.7 ± 5.8
Epinephrine	77.8 ± 1.4	69.2 ± 7.5	10.9 ± 2.3	63.4 ± 3.7	33.5 ± 5.0	48.0 ± 5.5	76.6 ± 0.3	39.8 ± 6.7	48.2 ± 8.7

There is a dose related increase in inhibition of platelet aggregation at two weeks, independent of the inducing stimulus.

Bleeding time in the cilostazol treated patients was variable (decreased on 150 mg/day) and increased slightly in the 75 and 300 mg/day doses. With respect to platelet adhesiveness, there was a decrease, for the high dose group only, relative to baseline (the p-value was not corrected for multiple comparisons).

Safety: The sponsor notes no adverse events. Five of 16 subjects, however, did not have both baseline and on-treatment measurements of vital signs.

Laboratory values were occasionally missing (the number of missing labs differed depending on the specific lab value). One subject had increases in liver function test as below:

Table 5.2 Laboratory Values Representing Liver Dysfunction

	GOT	GPT	T-Bili	ALP	γ-GTP
Pre	14	7	0.7	158	13
2 weeks of therapy	136	64	1.0	517	101

No further laboratory values are available for this individual. The increase in γ-GTP suggest a cholestatic mechanism is responsible for the increase LFTs.

Conclusion: The study suggests, relative to baseline, that platelet aggregation in response to any of several stimuli is inhibited in a dose-related manner.

Reference 6. Study G5

Title of Study : Platelet Aggregation Inhibitory Effect of Cilostazol in Patients with Cerebrovascular Disease.

Table 6.1 Investigators and Sites:

Abe, T. Teiko U. Schl Med	Kazama, M Teiko U. Schl Med	Kinoshita, T Teiko U. Schl Med	Onodera, K Hirosaki U. Schl Med
Metoki, H Hirosaki U. Schl Med	Terashi, A Nihon Med Schl	Okamota, F Nihon Med Schl	Maezawa, H Tokyo Med Dental U Schl Med
Numono, F. Tokyo Med Dental U Schl Med	Hiyamuta, E Kanto Teishin Hosp	Shintani, K Kanto Teishin Hosp	Igata, A Kagoshima U Schl Med
Ohkastu, Y Ohkatsu Hospital			

No Protocol, CRFs and line listings were submitted.

Subjects were enrolled between September 1982 and February 1983.

Study Summary: A total of 52 patients were enrolled; 47 of those had histories of cerebral thrombosis, 2 had cerebral embolism, 2 had TIAs and 1 had reversible neurological deficit (RIND). These patients were allocated to two weeks of treatment with cilostazol at daily doses of 100 or 200 mg/day, divided into two equal doses or 150 or 300 mg/day divided into three equal doses. Measured parameters included: platelet aggregation and adhesiveness, bleeding time and plasma beta-thromboglobulin concentrations. All parameters were measured before dosing and after 1 and 2 weeks of therapy.

Platelet rich plasma was used to test platelet aggregation with the following inducers of aggregation (and their concentrations): ADP (1, 2, 3, and 10 uM), collagen (0.5, 1, and 2 ug/ml), epinephrine (0.1 and 1 ug/ml) and arachidonic acid (100 and 200 ug/ml). The timing of the platelet tests, relative to dose is not stated. Platelet adhesiveness was determined by the glass beads method. Bleeding time was determined by Duke's method. Plasma concentration of beta-thromboglobulin were measured by RIA.

The number of patients, at baseline, with > 30% and > 50% aggregation at the various doses of inducers is shown below:

Table 6.2 Effect of Concentration of Inducers on Aggregation Prior to Cilostazol Treatment

Inducer	ADP uM				Collagen ug/ml			Epinephrine ug/ml		Arach Acid ug/ml	
conc	1	2	3	10	0.5	1	2	0.1	1	100	200
# tested Aggregation	47	46	6	48	39	3	51	46	51	42	53
# ≥ 30% Aggregation	16	38	6	48	15	3	50	19	44	26	45
#≥ 50%	7	24	4	46	12	3	49	18	39	24	41

Generally, a greater fraction of patients had more extensive aggregation at the

higher range of each of the inducers. Whereas only 34% who were exposed to 1 uM ADP had ≥ 30% aggregation, the numbers increased to 100 % by 3 uM and 10 uM. The fraction of patients with ≥ 50% aggregation also increased in direct relationship to the concentration of ADP. This pattern of more extensive aggregation, with higher inducer concentrations was consistently noted across all of the inducers.

The effect of cilostazol treatment on aggregation ability, in association with the various inducers, are shown below. This table is limited to the aggregation measurements where there was a substantial fraction of the randomized group tested. The data for the 3 uM ADP is not included (there were between 0-3 subjects/cilostazol dose).

Table 6.3 Percent Aggregation

Cilostazol Dose	ADP Induction of Aggregation %									Epinephrine Induction Aggregation %					
	1 uM			2 uM			10 uM			0.1 ug/ml			1 ug/ml		
	pre	1 week	2 week	pre	1 week	2 week	pre	1 week	2 week	pre	1 week	2 week	pre	1 week	2 week
100 mg	29.2 ± 6.9 (n=12)	20.6 ± 7.0 (n=10)	20.8 ± 7.4 (n=12)	55.9 ± 5.4 (n=11)	44.8 ± 9.6 (n=9)	40.1 ± 7.1 (n=11)	74.7 ± 3.9 (n=12)	65.1 ± 7.1 (n=11)	65.6 ± 5.8 (n=12)	43.7 ± 9.4 (n=12)	22.3 ± 6.1 (n=10)	26.0 6.1 (n=11)	63.5 ± 6.1 (n=11)	65.1 ± 6.5 (n=11)	49.4 ± 9.6 (n=13)
150 mg	18.6 ± 4.5 (n=12)	24.9 6.6 (n=10)	23.7 ± 6.6 (n=13)	45.5 ± 5.8 (n=13)	47.9 ± 9.2 (n=10)	46.5 ± 6.8 (n=13)	68.1 ± 4.0 (n=13)	73.2 ± 2.8 (n=10)	68.6 ± 3.4 (n=13)	23.8 ± 7.0 (n=11)	50.6 ± 11.2 (n=10)	37.1 ± 9.4 (n=12)	62.0 ± 4.3 (n=13)	71.1 ± 5.3 (n=10)	67.6 ± 3.6 (n=13)
200 mg	25.7 ± 5.4 (n=13)	13.7 ± 6.0 (n=11)	20.7 ± 5.8 (n=13)	52.2 ± 7.2 (n=11)	34.7 ± 10.1 (n=9)	42.1 ± 6.8 (n=11)	73.5 ± 2.2 (n=13)	67.9 ± 5.1 (n=12)	71.3 ± 3.3 (n=13)	37.0 ± 8.6 (n=13)	31.9 ± 8.7 (n=12)	20.1 ± 7.2 (n=14)	59.4 ± 7.8 (n=14)	56.9 ± 8.9 (n=12)	52.9 ± 7.8 (n=14)
300 mg	33.1 ± 9.3 (n=10)	16.7 ± 4,2 (n=10)	25.5 ± 9.5 (n=12)	53.5 ± 6.9 (n=11)	37.0 ± 7.4 (n=9)	27.1 ± 7.4 (n=11)	69.5 ± 2.9 (n=10)	69.0 ± 4.2 (n=10)	58.8 ± 6.6 (n=12)	37.6 ± 9.2 (n=10)	33.1 ± 8.8 (n=10)	34.6 ± 9.5 (n=12)	63.4 ± 5.9 (n=12)	53.9 ± 8.7 (n=10)	51.9 ± 9.3 (n=12)

Table 6.3 Continued

Cilostazol Dose	Collagen-Induced Aggregation %						Arachidonic Acid-Induced Aggregation %					
	0.5 ug/ml			2 ug/ml			100 ug/ml			200 ug/ml		
	pre	1 week	2 week	pre	1 week	2 week	pre	1 week	2 week	pre	1 week	2 week
100 mg	24.6 ± 7.7 (n=9)	14.8 ± 7.2 (n=9)	17.9 ± 9.4 (n=9)	67.6 ± 4.3 (n=12)	57.3 ± 8.4 (n=9)	45.7 ± 7.5 (n=12)	41.2 ± 11.7 (n=10)	14.2 ± 9.9 (n=9)	9.0 ± 8.0 (n=9)	62.8 ± 8.4 (n=13)	51.7 ± 10.9 (n=11)	34.6 ± 10.7 (n=13)
150 mg	28.5 ± 8.6 (n=10)	28.8 ± 9.8 (n=10)	27.2 ± 10.2 (n=10)	67.8 ± 2.7 (n=13)	66.9 ± 7.6 (n=10)	69.6 ± 5.2 (n=13)	35.6 ± 10.8 (n=11)	25.9 ± 10.7 (n=10)	25.1 ± 10.4 (n=12)	50.6 ± 7.7 (n=13)	44.0 ± 12.1 (n=10)	42.9 ± 10.9 (n=12)
200 mg	19.2 ± 6.5 (n=11)	26.8 ± 8.9 (n=10)	11.0 ± 5.3 (n=11)	67.1 ± 4.2 (n=14)	47.4 ± 8.2 (n=12)	49.0 ± 8.2 (n=14)	50.0 ± 10.6 (n=12)	15.6 ±8.3 (n=11)	24.6 ± 9.4 (n=12)	73.1 ± 5.9 (n=14)	50.3 ± 10.8 (n=12)	44.3 ± 9.0 (n=14)
300 mg	40.7 ± 11.7 (n=9)	11.7 ± 7.0 (n=9)	14.6 ± 7.4 (n=9)	67.8 ± 2.8 (n=12)	52.4 ± 9.0 (n=10)	36.6 ± 8.6 (n=12)	46.1 ± 11.8 (n=9)	8.5 ± 8.1 (n=10)	9.2 ± 8.0 (n=9)	68.9 ± 4.0 (n=11)	6.2 ± 4.6 (n=10)	21.1 ± 9.4 (n=12)

It is difficult to determine whether there is an effect of cilostazol on platelet aggregation. There are a large number of inducers, a large number of doses of these inducers, two weeks of measurement, four doses of cilostazol and missing data for the

measured parameters. None of the analyses were designated as the study's primary end point. Any conclusion should, therefore, be taken with some skepticism.

Since baseline measurements were likely easily identified, a convincing effect would need to establish a dose related effect while on therapy. In this respect, there did not appear a convincing effect of cilostazol on ADP, epinephrine or collagen induced aggregation. There appears to be a strong effect of the highest dose of cilostazol on arachidonic acid induced aggregation but the other doses are less convincing of an effect.

The platelet adhesiveness is shown below:

Table 6.4 Platelet Adhesiveness.

Cilostazol Dose	Pre	1 Week	2 Weeks
100 mg	59.02 ± 5.58 (n=11)	40.57 ± 5.73 (n=11)	37.05 ± 6.83 (n=11)
150 mg	47.34 ± 5.45 (n=8)	47.53 ± 6.74 (n=8)	47.88 ± 7.57 (n=8)
200 mg	47.99 ± 5.56 (n=11)	42.62 ± 5.65 (n=11)	39.73 ± 4.66 (n=11)
300 mg	54.80 ± 9.12 (n=6)	39.30 ± 9.31(n=6)	37.68 ± 6.65 (n=6)

Platelet adhesiveness, bleeding time or beta thromboglobulin information did not appear to have been collected from every subject. No clear dose response effect is evident.

Table 6.5 Bleeding Time and Beta Thromboglobulin

Dose	Bleeding time			Bet a-thromboglobulin (ng/ml)		
	Pre	1 week	2 week	pre	1 week	2 weeks
100 mg	194 ± 24 (n=7)	175 ± 35.0 (n=6)	176 ± 19 (n=7)	411.5 ± 159 (n=13)	625 ± 408 (n=11)	293 ± 138 (n=13)
150 mg	190 ± 22 (n=9)	180 ± 47 (n=5)	203 ± 28 (n=8)	366 ± 135 (n=12)	344 ± 191 (n=9)	290 ±149 (n=11)
200 mg	160 ± 27 (n=6)	233 ± 50 (n=4)	204 ± 18 (n=5)	243 ± 104 (n=13)	666 ± 325 (n=11)	306 ± 154 (n=13)
300 mg	150 ± 13 (n=8)	130 ± 15 (n=6)	139 ± 16 (n=8)	178 ± 72 (n=11)	302 ± 182 (n=9)	245 ± 116 (n=11)

Safety: No line listings of adverse events were supplied

Deaths Dropouts and Discontinuations: The sponsor notes that there were no deaths among those treated. One patient with chronic renal insufficiency discontinued due to worsening of renal function (creatinine increased and BUN increased and potassium dropped This subject also complained of appetite loss, nausea and vomiting.

Adverse Events: The sponsor notes that there were six patients who had tachycardia, though none discontinued. Four of these patients were in the 200 mg dose group and two were in the 300 mg dose group.

Vital Signs. Measurements of vital signs displayed substantial heterogeneity among patients. It is unclear when, during the dosing, vital signs were measured. At the highest

dose group there was an apparent increase in heart rate of 8.3 BPM. Changes in group mean blood pressure either in DBP or SBP were small (generally < 2 mm Hg).

ECGs: ECGs were tabulated as either abnormal or normal. I have no idea how the sponsor defined an ECG as abnormal. For the 100 mg dose, there were three subjects with either baseline or on therapy ECGs missing. None of the patients at this dose had transitions from normal to abnormal, one patient had transition of abnormal to normal. For the 150 mg dose there were 4 subjects with missing ECGs. None in this dose group had transitions from normal to abnormal or abnormal to normal. For the 200 mg dose, there were three subjects with missing data. For the 300 mg dose, There were three subjects with missing data, there were no transitions from normal to abnormal or visa versa.

Labs: One patient discontinued for abnormalities (see above). There was sporadic abnormalities or changes from baseline among the various lab values. Most frequent of these lab abnormalities were increases in creatinine. The number of those whose creatinine increased by $\geq$ 0.2 mg/dl or decreased by $\geq$ 0.2 mg/dl are shown below. There is a modest trend towards increases in creatinine with dose.

Table 6.6 Categorical Assessment of Creatinine Changes

	100 mg	150 mg	200 mg	300 mg
Increase in Cr $\geq$ 0.2 mg/dl	1	2	4	3
Decrease in Cr $\geq$ 0.2 mg/dl	2	2	2	0

Conclusion: This is a fairly large dose ranging study (either 50 mg Bid, 50 mg TID, 100 mg BID or 100 mg TID) of cilostazol's effect on platelet function in patients who have cerebrovascular disease. Although the measurements on treatment all showed a decrease from baseline in platelet aggregation as induced by ADP, epinephrine, collagen or epinephrine, there was no convincing dose related inhibition of platelet function.

Reference 7. Study G-6

Title of Study: Comparison of the Inhibitory Effects of Cilostazol, Acetylsalicylic Acid and Ticlopidine on Platelet Function Ex-Vivo- Randomized, Double-Blind Cross-Over Study.
Publication: Arzneim-Forsh/Drug Res 37 ; (1) 5; 563-566; (1987).

Investigator and Sites. Ikeda, Y.; Kikuchi, M.; Murakami, H.; Satoh, K.; Murata, M.; Watanabe, K.; and Ando, Y.; Keio University, Tokyo, Japan.
No protocol, CRFs or line listings were supplied

Study Summary: This was a cross-over study in nine patients with cerebral thrombosis, randomized to 1 week of treatment with either aspirin 500 mg/d; ticlopidine 300 mg/d or cilostazol at 200 mg/d. There was a one week placebo washout phase between active regimens. Platelet aggregation was studied both before and after treatments. Aggregation studies were done approximately 12 hours after the last dose. Aggregation of platelet rich plasma was induced by ADP (2 and 10 umol/l), epinephrine (1 ug/ml), collagen (2 ug/ml) and arachidonic acid (200 ug/ml).

Any statistical significance of cilostazol's effect on platelet aggregation was based on the results of a paired t-test. The analysis of variance for the latin square design was performed to assess the effect of the placebo during wash-out in all nine patients. Duncan's multiple range test was used to compare the anti-aggregating activities of the three drugs. (I spoke with Dr. Kun Jin, one of the Division's statisticians, about the proposed analytic plan. It is unclear if this analysis corrects for any carry-over effects).

No raw data was shown. Graphical displays of the data, however were included. Relative to baseline (I presume this is the baseline immediately prior to each treatment and not the original baseline), platelet aggregation induced by 2 uM ADP was less complete than when induced by 10 uM ADP. All three treatments (cilostazol, aspirin and ticlopidine) decreased platelet aggregation induced by ADP (at either concentrations), but pre-treatment with cilostazol and ticlopidine statistically differed from baseline. Although aspirin decreased aggregation, the inhibition was not statistically different from baseline. At 2 uM ADP, both cilostazol and ticlopidine differed from aspirin. At 10 uM only ticlopidine differed from aspirin.

When epinephrine (1 ug/ml), served as the inducer, relative to baseline, only aspirin statistically decreased aggregation.

When collagen was the inducer (2 ug/ml), all three treatments inhibited aggregation. There was no difference among the 3 treatments when the inducer was either collagen or epinephrine.

When arachidonic acid served as the inducer (200 ug/ml), all three pre-treatments statistically differed from baseline. Aggregation, however, was nearly completely

inhibited by cilostazol. The effect on platelet aggregation (change from baseline) differed statistically for cilostazol and aspirin, relative to ticlopidine.

Safety: No safety information was supplied.