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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 6 Food consumption (females)

Sex: Female		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
-4	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
-3	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
-2	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
-1	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
1	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
2	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
3	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 6 Food consumption (females)

Sex: Female		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
4	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
5	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
6	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
7	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
8	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
9	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
10	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 6 Food consumption (females)

Sex: Female		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
11	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
12	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
13	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
14	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
15	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
16	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
17	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 6 Food consumption (females)

Food consumption (g/day)

Sex: Female		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
18	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
19	Mean	100	100	100	100	100	50
	S.D.	0	0	0	0	0	71
	N	4	4	4	4	4	2
20	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	.
	N	4	4	4	4	4	1
21	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	.
	N	4	4	4	4	4	1
22	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	.
	N	4	4	4	4	4	1
23	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	.
	N	4	4	4	4	4	1
24	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	.
	N	4	4	4	4	4	1

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 6 Food consumption (females)

Food consumption (g/day)

Sex: Female		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
25	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	.
	N	4	4	4	4	4	1
26	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	.
	N	4	4	4	4	4	1
27	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	.
	N	4	4	4	4	4	1
28	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	.
	N	4	4	4	4	4	1

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 7 Stool occult blood test (males)

Group	Animal No.	1 week prior to the start of dosing	Additional examination	Week 4 of dosing
Control	RP1M01	-	.	-
0.5%CMC-Na	RP1M02	-	.	-
	RP1M03	-	.	-
	RP1M04	-	.	-
Low	RP2M01	-	.	-
	TM5509	-	.	-
	2	-	.	-
	mg/kg/day	-	.	-
Low-Mid	RP3M01	-	.	-
	TM5509	-	.	-
	6	-	.	-
	mg/kg/day	-	.	-
Mid	RP4M01	-	.	-
	TM5509	-	.	-
	20	-	.	-
	mg/kg/day	-	.	-
Mid-High	RP5M01	-	.	-
	TM5509	-	- (Day 11)	-
	80	-	.	-
	mg/kg/day	-	.	-
High	RP6M01	-	+ (Day 11)	-
	TM5509	-	+ (Day 11)	. ^{a)}
	300	-	+ (Day 10)	+ -
	mg/kg/day	-	- (Day 10)	-

General Footnote: -: Negative + -: Trace +: Positive

^{a)} Died on Day 16 of dosing

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 8 Stool occult blood test (females)

Group	Animal No.	1 week prior to the start of dosing	Additional examination	Week 4 of dosing
Control	RP1F01	-	.	-
0.5%CMC-Na	RP1F02	-	.	-
	RP1F03	-	.	-
	RP1F04	-	.	-
Low TM5509 2 mg/kg/day	RP2F01	-	.	-
	RP2F02	-	.	-
	RP2F03	-	.	-
	RP2F04	-	.	-
Low-Mid TM5509 6 mg/kg/day	RP3F01	-	.	-
	RP3F02	-	.	-
	RP3F03	-	.	-
	RP3F04	-	.	-
Mid TM5509 20 mg/kg/day	RP4F01	-	.	-
	RP4F02	-	.	-
	RP4F03	-	.	-
	RP4F04	-	.	-
Mid-High TM5509 80 mg/kg/day	RP5F01	-	.	-
	RP5F02	-	.	-
	RP5F03	-	.	-
	RP5F04	-	.	-
High TM5509 300 mg/kg/day	RP6F01	-	- (Day 9)	. ^{a)}
	RP6F02	-	- (Day 9)	-
	RP6F03	-	+~ (Day 8)	. ^{b)}
	RP6F04	-	- (Day 8)	. ^{b)}

General Footnote: -: Negative +~: Trace

^{a)} Died on Day 20 of dosing^{b)} Necropsied on Day 19 of dosing due to a moribund condition

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 9 Hematology - List of abbreviations -

Abbreviation	Expansion
RBC	Red blood cell count
HGB	Hemoglobin concentration
HCT	Hematocrit
MCV	Mean corpuscular volume
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
Retic	Reticulocytes
PLT	Platelet count
WBC	White blood cell count
Neut	Neutrophils
Lymph	Lymphocytes
Mono	Monocytes
Eos	Eosinophils
Baso	Basophils
LUC	Large unstained cells
PT	Prothrombin time
APTT	Activated partial thromboplastin time
Fib	Fibrinogen
%	Ratio
#	Absolute count
RC	Result comment

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
RBC (10 ⁶ /μL)	-1	Mean	5.86 ¹	5.86	6.31	5.56	6.13	5.57
		S.D.	0.70	0.51	0.36	0.25	0.62	0.22
		N	4	4	4	4	4	4
	1	Mean	5.58 ¹	5.27	5.97	5.19	5.51	5.33
		S.D.	0.69	0.34	0.28	0.22	0.50	0.50
		N	4	4	4	4	4	4
	2	Mean	5.58 ¹	5.37	5.96	5.19	5.36	5.05
		S.D.	0.73	0.26	0.35	0.24	0.50	0.59
		N	4	4	4	4	4	4
	3	Mean	5.51 ¹	5.30	6.04	5.29	5.43	4.94
		S.D.	0.59	0.26	0.28	0.12	0.45	0.28
		N	4	4	4	4	4	3
	4	Mean	5.57 ¹	5.31	5.96	5.35	5.43	4.92
		S.D.	0.67	0.20	0.21	0.16	0.36	0.10
		N	4	4	4	4	4	3

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
HGB (g/dL)	-1	Mean	14.5 I ¹	13.9	14.5	13.9	14.0	13.8
		S.D.	1.1	0.6	0.5	0.8	0.6	0.8
		N	4	4	4	4	4	4
	1	Mean	13.7 I ¹	12.6	13.7	12.8	12.8	13.2
		S.D.	1.1	0.6	0.7	0.4	0.4	1.5
		N	4	4	4	4	4	4
	2	Mean	13.8 I ¹	12.7	13.6	12.9	12.3	12.4
		S.D.	1.1	0.5	0.7	0.6	0.5	1.7
		N	4	4	4	4	4	4
	3	Mean	13.6 I ¹	12.7	13.8	13.0	12.6	12.4
		S.D.	0.8	0.3	0.8	0.3	0.6	0.9
		N	4	4	4	4	4	3
4	Mean	13.7 I ¹	12.7	13.7	13.1	12.6	12.2	
	S.D.	0.9	0.4	1.1	0.2	0.6	0.2	
	N	4	4	4	4	4	3	

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
HCT (%)	-1	Mean	47.7 ¹	46.6	48.1	45.2	46.7	43.9
		S.D.	4.5	3.3	0.5	3.8	4.0	2.4
		N	4	4	4	4	4	4
	1	Mean	45.8 ¹	42.3	45.0	41.2	41.7	41.7
		S.D.	4.3	3.9	0.8	1.9	2.6	4.9
		N	4	4	4	4	4	4
	2	Mean	45.5 ¹	43.7	45.4	42.1	41.0	39.1
		S.D.	4.5	3.5	1.0	3.1	2.4	6.1
		N	4	4	4	4	4	4
	3	Mean	45.5 ¹	42.8	46.4	42.4	42.5	38.8 ^{dd3}
		S.D.	3.4	2.8	0.6	1.4	2.3	2.4
		N	4	4	4	4	4	3
	4	Mean	45.6 ^{R2}	43.2	45.8	42.8	41.8	39.2
		S.D.	4.5	3.1	0.6	1.2	1.0	1.7
		N	4	4	4	4	4	3

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

2 [R - Automatic Transformation Selected: Rank]

3 [dd - Test: Dunnett 2 Sided p < 0.01]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
MCV (fL)	-1	Mean	81.6 ¹	79.8	76.5	81.1	76.4	78.8
		S.D.	4.1	3.8	3.8	3.2	5.8	3.2
		N	4	4	4	4	4	4
	1	Mean	82.4 ¹	80.2	75.4	79.5	75.9	78.3
		S.D.	4.4	6.0	3.2	2.0	4.9	4.6
		N	4	4	4	4	4	4
	2	Mean	82.1 ¹	81.5	76.3	81.1	76.7	77.2
		S.D.	4.7	7.1	2.8	2.7	4.8	4.8
		N	4	4	4	4	4	4
	3	Mean	82.9 ¹	80.8	76.9	80.3	78.5	78.5
		S.D.	4.2	6.2	3.4	3.1	4.2	0.9
		N	4	4	4	4	4	3
	4	Mean	82.1 ¹	81.3	76.9	80.1	77.3	79.6
		S.D.	3.4	6.7	3.0	3.4	5.2	2.8
		N	4	4	4	4	4	3

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
MCH (pg)	-1	Mean	24.9 I ¹	23.8	23.0	25.0	23.0	24.8
		S.D.	1.6	0.9	2.1	0.7	2.2	1.1
		N	4	4	4	4	4	4
	1	Mean	24.8 I ¹	23.9	23.0	24.7	23.4	24.6
		S.D.	1.5	0.8	2.1	0.8	2.1	0.8
		N	4	4	4	4	4	4
	2	Mean	24.8 I ¹	23.8	23.0	24.8	23.2	24.6
		S.D.	1.5	1.0	2.0	0.9	2.3	0.6
		N	4	4	4	4	4	4
	3	Mean	24.8 I ¹	24.0	23.0	24.6	23.3	25.1
		S.D.	1.5	1.0	2.1	0.8	2.2	0.4
		N	4	4	4	4	4	3
	4	Mean	24.7 I ¹	23.9	23.1	24.4	23.4	24.8
		S.D.	1.6	0.8	2.1	0.9	2.2	0.2
		N	4	4	4	4	4	3

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
MCHC (g/dL)	-1	Mean	30.4 I ¹	29.8	30.1	30.8	30.1	31.5
		S.D.	0.7	1.1	1.4	0.9	1.7	0.2
		N	4	4	4	4	4	4
	1	Mean	30.0 I ¹	29.9	30.5	31.0	30.7	31.5
		S.D.	0.6	1.8	1.7	0.7	1.5	1.0
		N	4	4	4	4	4	4
	2	Mean	30.2 I ¹	29.3	30.0	30.6	30.1	31.9
		S.D.	0.5	1.7	1.8	1.1	1.4	1.6
		N	4	4	4	4	4	4
	3	Mean	30.0 R ²	29.8	29.9	30.7	29.7	32.0
		S.D.	0.4	1.5	2.1	0.3	1.6	0.4
		N	4	4	4	4	4	3
	4	Mean	30.1 I ¹	29.5	30.0	30.5	30.2	31.2
		S.D.	1.0	1.9	2.3	0.5	1.0	1.0
		N	4	4	4	4	4	3

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

2 [R - Automatic Transformation Selected: Rank]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
%Retic (%)	-1	Mean	1.3 ¹	1.0	1.1	1.1	1.2	1.3
		S.D.	0.3	0.2	0.4	0.3	0.5	0.4
		N	4	4	4	4	4	4
	1	Mean	2.5 ¹	2.8	2.4	2.2	2.2	2.0
		S.D.	0.8	1.0	0.6	0.3	0.2	0.6
		N	4	4	4	4	4	4
	2	Mean	2.3 ¹	2.3	2.0	2.0	2.0	2.4
		S.D.	0.5	0.5	0.3	0.2	0.7	0.7
		N	4	4	4	4	4	4
	3	Mean	2.4 ¹	2.1	1.8	2.0	2.1	2.8
		S.D.	0.9	0.6	0.4	0.5	0.3	0.8
		N	4	4	4	4	4	3
	4	Mean	2.3 ¹	1.8	1.6	1.9	1.7	3.2
		S.D.	0.8	0.6	0.3	0.6	0.6	0.4
		N	4	4	4	4	4	3

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
#Retic (10 ⁹ /L)	-1	Mean	73.1 I ¹	60.0	66.8	61.5	68.7	71.5
		S.D.	15.7	11.2	19.6	19.4	26.9	23.0
		N	4	4	4	4	4	4
	1	Mean	134.5 I ¹	145.2	140.2	112.4	120.4	102.5
		S.D.	40.0	45.5	34.5	21.7	14.1	24.5
		N	4	4	4	4	4	4
	2	Mean	124.1 I ¹	123.8	118.5	105.0	107.0	117.8
		S.D.	16.7	22.5	10.4	8.9	35.6	23.6
		N	4	4	4	4	4	4
	3	Mean	130.7 I ¹	109.5	109.5	105.9	112.9	139.0
		S.D.	44.3	27.1	17.4	24.6	15.5	29.6
		N	4	4	4	4	4	3
	4	Mean	126.8 I ¹	93.8	97.0	100.0	94.8	159.1
		S.D.	30.6	36.0	17.8	29.5	28.0	16.8
		N	4	4	4	4	4	3

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
PLT (10 ³ /μL)	-1	Mean	418 1 ¹	405	396	371	510	391
		S.D.	67	44	47	45	125	82
		N	4	4	4	4	4	4
	1	Mean	405 1 ¹	440	398	332	442	388
		S.D.	49	30	61	52	14	51
		N	4	4	4	4	4	4
	2	Mean	390 1 ¹	461	420	385	474	533 dd ²
		S.D.	44	33	34	57	37	81
		N	4	4	4	4	4	4
	3	Mean	375 1 ¹	431	397	362	453	448
		S.D.	54	22	35	61	48	53
		N	4	4	4	4	4	3
	4	Mean	380 1 ¹	437	386	360	458	483
		S.D.	51	34	41	49	45	106
		N	4	4	4	4	4	3

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

2 [dd - Test: Dunnett 2 Sided p < 0.01]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
WBC (10 ³ /μL)	-1	Mean	11.19 I ¹	9.59	12.55	10.81	11.27	8.21
		S.D.	2.92	2.23	5.00	2.30	1.73	1.65
		N	4	4	4	4	4	4
	1	Mean	10.48 I ¹	9.09	9.94	9.78	7.74	7.11
		S.D.	2.52	2.88	4.03	1.92	0.98	3.29
		N	4	4	4	4	4	4
	2	Mean	10.62 I ¹	8.63	11.63	11.89	9.26	8.94
		S.D.	2.17	2.78	4.61	1.75	1.71	2.11
		N	4	4	4	4	4	4
	3	Mean	13.51 R ²	7.37	11.40	10.05	8.84	10.97
		S.D.	1.38	3.08	5.22	0.41	2.46	6.20
		N	4	4	4	4	4	3
	4	Mean	12.31 I ¹	9.19	10.75	10.91	8.41	9.98
		S.D.	1.44	2.77	5.06	1.13	1.69	4.10
		N	4	4	4	4	4	3

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

2 [R - Automatic Transformation Selected: Rank]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
%Neut (%)	-1	Mean	42.9 ¹	28.8	34.0	36.4	27.4	23.4
		S.D.	11.9	18.0	6.2	9.3	5.2	8.2
		N	4	4	4	4	4	4
	1	Mean	42.9 ¹	39.4	35.9	43.9	41.9	50.0
		S.D.	18.8	20.6	9.3	9.4	8.5	5.5
		N	4	4	4	4	4	4
	2	Mean	40.2 ¹	28.7	42.3	37.9	38.1	55.7
		S.D.	8.2	10.9	10.0	14.9	13.3	16.2
		N	4	4	4	4	4	4
	3	Mean	54.8 ¹	30.0 ^{d2}	44.4	34.9	41.2	56.9
		S.D.	14.7	9.1	4.7	9.8	15.8	11.9
		N	4	4	4	4	4	3
	4	Mean	54.1 ¹	38.0	39.4	37.5	34.9	55.1
		S.D.	9.9	14.7	3.7	14.5	10.2	15.6
		N	4	4	4	4	4	3

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

2 [d - Test: Dunnett 2 Sided p < 0.05]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 10 Hematology (males)

Sex: Male			Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Week(s) Relative to Start Date								
%Lymph (%)	-1	Mean	52.3 I ¹	65.4	61.1	58.9	67.3	72.6 d ²
		S.D.	11.0	17.1	6.6	9.8	6.2	7.5
		N	4	4	4	4	4	4
	1	Mean	51.8 I ¹	55.9	59.6	51.6	54.0	45.9
		S.D.	17.1	19.8	8.9	8.7	8.8	4.8
		N	4	4	4	4	4	4
	2	Mean	54.4 I ¹	66.1	53.4	57.5	57.0	39.6
		S.D.	7.9	10.1	8.9	14.5	12.5	15.2
		N	4	4	4	4	4	4
	3	Mean	40.7 I ¹	64.7 d ²	51.5	60.9	54.1	39.4
		S.D.	13.5	8.7	4.1	10.0	13.7	10.9
		N	4	4	4	4	4	3
	4	Mean	41.3 I ¹	56.0	56.0	58.3	60.3	40.4
		S.D.	8.8	15.3	3.7	14.1	8.8	12.6
		N	4	4	4	4	4	3

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

2 [d - Test: Dunnett 2 Sided p < 0.05]