Supplemental Table 1: Characteristics of 660 Primary GISTs without synchronous metastases

		Total (n=660)	Neo-IM (n=78)	No Neo-IM (n=582)	p-value
Survivor follow-up (yrs)	Median (range)	4.60 (0.00-27.7)	3.05 (0.01-14.3)	4.81 (0.00-27.7)	
Age at first surgery (yrs)	Median (range)	64.5 (8.07-94.7)	60.3 (23.0-86.2)	64.9 (8.07-94.7)	0.13
Sex	F	326 (49.4)	34 (43.6)	292 (50.2)	0.28
	M	334 (50.6)	44 (56.4)	290 (49.8)	
Primary tumor site	Stomach	467 (70.8)	40 (51.3)	427 (73.4)	<0.001
	Small Bowel	116 (17.6)	13 (16.7)	103 (17.7)	
	Rectum	44 (6.7)	20 (25.6)	24 (4.1)	
	Other	33 (5)	5 (6.4)	28 (4.8)	
Primary tumor size (cm)	≤5	327 (49.5)	18 (23.1)	309 (53.1)	<0.001
	5-10	195 (29.5)	24 (30.8)	171 (29.4)	
	>10	138 (20.9)	36 (46.2)	102 (17.5)	
Primary tumor mitotic rate per 50 HPF (pre-treatment or untreated)[a]	≤5	369 (66.2)	16 (53.3)	353 (67)	0.16
	>5	188 (33.8)	14 (46.7)	174 (33)	
	Unknown	103 (N/A)	48 (N/A)	55 (N/A)	
Histologic variant	Spindle	355 (76.8)	51 (78.5)	304 (76.6)	0.90
	Epithelioid	55 (11.9)	8 (12.3)	47 (11.8)	
	Mixed	52 (11.3)	6 (9.2)	46 (11.6)	
	Unknown	198 (N/A)	13 (N/A)	185 (N/A)	
Margin[b]	R0	597 (90.5)	64 (82.1)	533 (91.6)	0.015
	R1	47 (7.1)	12 (15.4)	35 (6)	
	R2	16 (2.4)	2 (2.6)	14 (2.4)	
Adjuvant imatinib	No	539 (81.7)	42 (53.8)	497 (85.4)	<0.001
	Yes	121 (18.3)	36 (46.2)	85 (14.6)	
Duration (years)	Median (range)	1.71 (0.01-11.6)	1.90 (0.01-7.31)	1.66 (0.17-11.6)	>0.95
	Median (IQR)	1.71 (0.80-3.47)	1.90 (0.86-3.05)	1.66 (0.73-3.47)	
Mutation[c]	KIT exon 9	13 (4.1)	5 (8.8)	8 (3)	N/A[d]
	KIT exon 11 deletion	128 (40)	23 (40.4)	105 (39.9)	
	KIT exon 11 other	76 (23.8)	12 (21.1)	64 (24.3)	
	KIT exon 13	4 (1.3)	2 (3.5)	2 (0.8)	
	KIT exon 17 only	1 (0.3)	0 (0)	1 (0.4)	
	KIT mult exons	7 (2.2)	2 (3.5)	5 (1.9)	
	PDGFRA D842V / D842I	20 (6.3)	5 (8.8)	15 (5.7)	
	PDGFRA other	20 (6.3)	1 (1.8)	19 (7.2)	

	Wild type (WT)	47 (14.7)	7 (12.3)	40 (15.2)	
	Unknown	340 (N/A)	21 (N/A)	319 (N/A)	

[a]For patients who underwent Neo-IM, only those who had pre-treatment mitotic rate available are listed, while the “No Neo-IM” values all reflect untreated tumors. Most patients in the Neo-IM group did not have a pre-treatment mitotic rate available, since this requires a core needle biopsy.

[b]R2 margins include incomplete resection and tumor rupture

[c]Mutational analysis in the earliest patients included only *KIT* and *PDGFRA*, thus some “wild type” may reflect alternate mutations/epimutations

[d]Descriptive only, too many variables for statistical comparison. Numbers listed reflect percentage of all patients in whom mutation was known.

Supplemental Table 2: Univariate analysis of OS in 69 patients with primary GIST without synchronous metastases undergoing Neo-IM.

	Univariate				
Parameter	**Class Value**	**Reference**	**HR**	**CI**	**p-value**
Age at first surgery (yrs)	N/A	N/A	1.06	1.01-1.11	0.017
Sex	M	F	1.80	0.56-5.76	0.32
Primary tumor site	Small Bowel	Stomach	2.33	0.65-8.30	0.19
	Rectum	Stomach	0.67	0.08-5.65	0.71
	Other	Stomach	6.30	1.45-27.5	0.014
Primary tumor size (cm)	>10	≤5	3.25	0.40-26.1	0.27
	5-10	≤5	2.48	0.26-24.0	0.43
Histologic variant	Epithelioid	Spindle	2.34	0.58-9.46	0.23
	Mixed	Spindle	1.44	0.29-7.23	0.66
Margin	R1	R0	0.36	0.05-2.80	0.33
	R2	R0	N/A	N/A	N/A
Primary tumor post-treatment mitotic rate per 50 HPF	>5	⩽5	3.22	0.98-10.6	0.055
Primary tumor viability	>50%	⩽50%	3.03	0.98-9.38	0.054
Primary tumor mRECIST	PD	SD	0.31	0.04-2.43	0.26
	PR	SD	0.47	0.10-2.18	0.33
Adjuvant imatinib	Yes	No	0.52	0.16-1.67	0.27

Supplemental Table 3: Characteristics of 128 Primary GISTs with synchronous metastases

		Total (n=128)	Neo-IM (n=72)	No Neo-IM (n=56)	p-value
Survivor follow-up (yrs)	Median (range)	4.44 (0.20-21.7)	4.56 (0.20-12.5)	3.77 (0.77-21.7)	
Age at first surgery (yrs)	Median (range)	56.6 (22.6-85.3)	57.1 (24.6-85.3)	54.9 (22.6-84.5)	0.65
Sex	F	47 (36.7)	27 (37.5)	20 (35.7)	0.86
	M	81 (63.3)	45 (62.5)	36 (64.3)	
Primary tumor site	Stomach	59 (46.1)	34 (47.2)	25 (44.6)	0.90
	Small Bowel	55 (43)	31 (43.1)	24 (42.9)	
	Other	14 (10.9)	7 (9.7)	7 (12.5)	
Primary tumor size (cm)	≤5	17 (13.5)	10 (14.1)	7 (12.7)	0.85
	5-10	40 (31.7)	21 (29.6)	19 (34.5)	
	>10	69 (54.8)	40 (56.3)	29 (52.7)	
	Unknown	2 (N/A)	1 (N/A)	1 (N/A)	
Primary tumor mitotic rate per 50 HPF (pre-treatment or untreated)[a]	≤5	8 (20.5)	3 (20)	5 (20.8)	>0.95
	>5	31 (79.5)	12 (80)	19 (79.2)	
	Unknown	89 (N/A)	57 (N/A)	32 (N/A)	
Histologic variant	Spindle	59 (67)	44 (69.8)	15 (60)	0.68
	Epithelioid	12 (13.6)	8 (12.7)	4 (16)	
	Mixed	17 (19.3)	11 (17.5)	6 (24)	
	Unknown	40 (N/A)	9 (N/A)	31 (N/A)	
Margin[b]	R0	49 (38.6)	31 (43.1)	18 (32.7)	0.12
	R1	22 (17.3)	15 (20.8)	7 (12.7)	
	R2	56 (44.1)	26 (36.1)	30 (54.5)	
	Unknown	1 (N/A)	0 (N/A)	1 (N/A)	
Adjuvant imatinib	No	52 (40.9)	16 (22.5)	36 (64.3)	<0.001
	Yes	75 (59.1)	55 (77.5)	20 (35.7)	
	Unknown	1 (N/A)	1 (N/A)	0 (N/A)	
Duration (years)	Median (range)	2.56 (0.16-9.51)	2.72 (0.16-9.45)	2.44 (0.28-9.51)	0.88
	Median (IQR)	2.56 (0.97-4.44)	2.72 (0.97-4.44)	2.44 (1.24-4.53)	
Mutation[c]	KIT exon 9	11 (10.9)	8 (12.5)	3 (8.1)	N/A[d]
	KIT exon 11 deletion	43 (42.6)	30 (46.9)	13 (35.1)	
	KIT exon 11 other	11 (10.9)	6 (9.4)	5 (13.5)	
	KIT exon 13	3 (3)	1 (1.6)	2 (5.4)	
	KIT mult exons	16 (15.8)	13 (20.3)	3 (8.1)	
	PDGFRA other	3 (3)	2 (3.1)	1 (2.7)	
	SDH	2 (2)	0 (0)	2 (5.4)	
	Wild type (WT)	12 (11.9)	4 (6.3)	8 (21.6)	
	Unknown	27 (N/A)	8 (N/A)	19 (N/A)	

[a]For patients who underwent Neo-IM, only those who had pre-treatment mitotic rate available are listed, while the “No Neo-IM” values all reflect untreated tumors. Most patients in the Neo-IM group did not have a pre-treatment mitotic rate available, since this requires a core needle biopsy.
[b]R2 margins include incomplete resection and tumor rupture
[c]Mutational analysis in the earliest patients included only *KIT* and *PDGFRA*, thus some “wild type” may reflect alternate mutations/epimutations
[d]Descriptive only, too many variables for statistical comparison. Numbers listed reflect percentage of all patients in whom mutation was known.

Supplemental Table 4: Univariate analysis of OS in 56 patients with primary GIST with synchronous metastases undergoing Neo-IM.

	Univariate				
Parameter	**Class Value**	**Reference**	**HR**	**CI**	**p-value**
Age at first surgery (yrs)	N/A	N/A	1.05	1.00-1.09	0.039
Sex	M	F	1.16	0.47-2.88	0.74
Primary tumor site	Small Bowel	Stomach	1.05	0.40-2.73	0.92
	Other	Stomach	2.17	0.65-7.23	0.21
Primary tumor size (cm)	>10	≤5	0.82	0.23-2.93	0.76
	5-10	≤5	0.78	0.19-3.17	0.73
Histologic variant	Epithelioid	Spindle	0.81	0.18-3.61	0.78
	Mixed	Spindle	1.79	0.62-5.13	0.28
Margin	R1	R0	3.26	0.93-11.4	0.064
	R2	R0	4.76	1.65-13.7	0.004
Primary tumor post-treatment mitotic rate per 50 HPF	>5	≤5	4.39	1.67-11.5	0.003
Primary tumor viability	>50%	≤50%	1.02	0.39-2.70	>0.95
Primary tumor mRECIST	PD	SD	6.35	1.22-33.0	0.028
	PR	SD	1.26	0.49-3.26	0.63
Adjuvant imatinib	Yes	No	0.20	0.08-0.52	<0.001

Supplemental Table 5: Mutational analysis by response category.

	Mitotic rate / 50 HPF			Tumor viability %			mRECIST				
Mutation*	**>5**	**≤5**	**% >5**	**>50**	**≤50**	**% >50**	**PD**	**SD**	**PR**	**% PD**	**% PR**
KIT exon 9	4	7	30.7	7	4	63.6	1	7	4	8.3	33.3
KIT exon 11 del	12	31	27.9	13	36	26.5	4	23	20	8.5	42.6
KIT exon 11 other	3	11	21.4	2	12	14.2	1	9	9	5.3	47.4
KIT exon 13	1	2	33.3	2	1	66.6	0	1	1	0.0	50.0
KIT mult exon	6	6	50.0	5	8	50.0	1	4	4	11.1	44.4
PGDFRA D842V/I	1	4	20.0	2	2	50.0	3	2	2	42.9	28.6
PDGFRA other	1	1	50.0	0	3	0.0	0	2	2	0.0	50.0

*The first two columns for each parameter show the number of patients in that group. In the additional column(s), percentages reflect proportion of listed mutation for that parameter. For example, % >5 mitoses/50HPF for KIT exon 9 is 4 of 11, or 30.7%. Numbers vary slightly for each parameter due to different numbers of patients evaluable for each parameter. Wild type was excluded from this analysis since early “wild types” were only tested for KIT and PDGFRA and not alternate mutations/epimutations.