

Appendix:

Table 2-1. Relative survival by tyrosine kinase inhibitor and cumulative response within 1 year

Group	No. at 5y	5-y Absolute OS [95% CI]	5-y Relative OS [95% CI]	5-y OS in GP	No. at 10y	10-y Absolute OS [95% CI]	10-y Relative OS [95% CI]	10-y OS in GP
All TKI Group								
All N=483	312	92.7 [90.1-95.3]	94.8 [92.1-97.4]	97.8	127	83.5 [79.2-87.9]	88.3 [83.7-92.9]	94.6
CCyR N=425	284	94.5 [92.1-96.9]	96.6 [94.2-99.1]	97.8	115	87.1 [82.7-91.4]	92.1 [87.4-96.6]	94.6
MMR N=349	234	96.5 [94.4-98.7]	98.7 [96.5-100.9]	97.8	91	89.0 [84.5-93.7]	94.1 [89.3-99.0]	94.6
MR4.5 N=162	105	95.8 [92.1-99.4]	98.1 [94.3-101.7]	97.7	47	88.5 [81.9-95.0]	93.9 [86.9-100.8]	94.2
CMR N=84	53	98.6[95.8-100]	100.9[98.1-102.4]	97.7	21	91.7 [82.2-100]	97.3 [87.3-106.2]	94.2
Imatinib Group								
All N=271	239	92.4 [89.2-95.6]	94.5 [91.2-97.8]	97.8	127	83.3 [78.5-88.0]	88.0 [82.9-92.9]	94.7
CCyR N=229	212	94.7 [91.8-97.6]	96.9 [94.0-99.9]	97.7	115	87.4 [82.8-92.0]	92.8 [87.9-97.7]	94.2
MMR N=184	176	97.3 [94.9-99.6]	99.5 [97.0-101.8]	97.8	91	90.0 [85.2-94.8]	95.1 [90.1-100.2]	94.6
MR4.5 N=81	78	97.5 [94.1-100]	100.1 [96.6-102.7]	97.4	47	89.7 [82.9-96.5]	95.6 [88.4-102.9]	93.8
CMR N=34	33	100	102.5	97.6	21	93.1 [83.7-100]	99.0 [89.0-106.4]	94.0
Dasatinib Group								
All N=107	40	97.6 [94.1-100]	99.6 [96.0-102]	98.0	0	NA	NA	95.1
CCyR N=99	39	97.4 [93.7-100]	99.6 [95.8-102.2]	97.8	0	NA	NA	94.7
MMR N=79	30	98.7 [96.1-100]	100.9 [98.3-102.2]	97.8	0	NA	NA	94.7
MR4.5 N=38	12	100	102.1	97.9	0	NA	NA	94.9
CMR N=27	9	100	102.2	97.8	0	NA	NA	94.7
Nilotinib Group								
All N=105	33	87.6 [78.5-96.7]	89.6 [80.3-98.9]	97.8	0	NA	NA	94.6
CCyR N=97	33	89.8 [81.0-98.6]	91.9 [82.9-100.9]	97.7	0	NA	NA	94.3
MMR N=86	28	90.9 [82.0-99.9]	93.0 [83.9-102.2]	97.7	0	NA	NA	94.4
MR4.5 N=43	15	85.6 [70.2-100]	87.7 [71.9-102.5]	97.6	0	NA	NA	94.1
CMR N=23	11	94.1 [82.9-100]	96.4 [84.9-102.5]	97.6	0	NA	NA	94.2

Abbreviations: OS, overall survival; GP, general population; CI, confidence interval; CCyR, complete cytogenetic response; MMR, major molecular response; MR4.5, molecular response with 4.5 log reduction by international scale; CMR, complete molecular response; NA, not applicable.

Table 3-1. Cause of death by cumulative response within 1 year in age 15-44

Age 15-44	All N= 197	CCyR* N= 165	MMR* N=136	MR4·5* N=62	CMR N=34
Number of death, (%)	12 (6)	4 (2)	3 (2)	1 (1)	0
Progression to AP/BP, (%)	5 (42)	0	0	0	0
SCT complications, (%)	3 (25)	1 (25)	1 (33)	0	0
Cardiovascular events, (%)	1 (8)	1 (25)	0	0	0
Car accident, No. (%)	2 (17)	1 (25)	1 (33)	0	0
Other, No. (%)	1 (8)	1 (25)	1 (33)	1 (100)	0
Type of TKI, No. (%)					
Imatinib	12 (100)	4 (100)	3 (100)	1 (100)	0
Dasatinib	0	0	0	0	0
Nilotinib	0	0	0	0	0
Overall cumulative response, No. (%)					
CCyR	4 (33)	4 (100)	3 (100)	1 (100)	0
MMR	3 (25)	3 (75)	3 (100)	1 (100)	0
MR4·5	2 (17)	2 (50)	2 (67)	1 (100)	0
CMR	1 (8)	1 (25)	1 (33)	1 (100)	0
Disease status** at the time of death, No. (%)					
CML-AP/BP	3 (25)	0	0	0	0
CHR	1 (8)	0	0	0	0
CCyR	1 (8)	0	0	0	0
MMR	1 (8)	1 (25)	1 (33)	0	0
MR4·5	1 (8)	1 (25)	1 (33)	1 (100)	0
CMR	3 (25)	2 (50)	1 (33)	0	0
Unknown	2 (17)	0	0	0	0

*: CCyR includes CCyR or better; MMR includes MMR or better; MR4·5 includes MR4·5 or better.

** : Each status represents the best category of response or disease status at the time of death.

Abbreviations: AP, accelerated phase; BP, blast phase; CP, chronic phase; CCyR, complete cytogenetic response; MMR, major molecular response; MR4·5, molecular response by a 4·5 log reduction on the international scale; CMR, complete molecular response; SCT, stem cell transplant; TKI, tyrosine kinase inhibitor; CML, chronic myeloid leukemia.

Table 3-2. Cause of death by cumulative response within 1 year in age 45-64

Age 45-64	All N= 222	CCyR* N= 202	MMR* N=169	MR4·5* N=75	CMR N=40
Number of death, No. (%)	19 (9)	12 (6)	7 (4)	3 (2)	0
Progression to AP/BP, No. (%)	5 (26)	3 (25)	1 (14)	0	0
SCT complications, No. (%)	2 (11)	0	0	0	0
Secondary malignancy, No. (%)	4 (21)	3 (25)	2 (29)	1 (33)	0
Cardiovascular events, No. (%)	1 (5)	1 (8)	1 (14)	0	0
Sepsis, No. (%)	1 (5)	1 (8)	0	0	0
Dementia, No. (%)	1 (5)	1 (8)	1 (14)	1 (33)	0
Surgical complications, No. (%)	1 (5)	1 (8)	1 (14)	0	0
HCV cirrhosis, No. (%)	1 (5)	0	0	0	0
Unknown, No. (%)	3 (16)	2 (17)	1 (14)	1 (33)	0
Type of TKI, No. (%)					
Imatinib	15 (79)	10 (83)	6 (86)	3 (100)	0
Dasatinib	1 (5)	1 (8)	1 (14)	0	0
Nilotinib	3 (16)	1 (8)	0	0	0
Overall cumulative response, No. (%)					
CCyR	14 (74)	12 (100)	7 (100)	3 (100)	0
MMR	11 (58)	9 (75)	7 (100)	3 (100)	0
MR4·5	5 (26)	4 (33)	3 (43)	3 (100)	0
CMR	3 (16)	2 (17)	1 (14)	1 (33)	0
Disease status** at the time of death, No. (%)					
CML-AP/BP	5 (26)	3 (25)	1 (14)	0	0
CML-CP	1 (5)	1 (8)	0	0	0
CCyR	1 (5)	1 (8)	1 (14)	0	0
MMR	3 (16)	3 (25)	2 (29)	0	0
MR4·5	2 (11)	2 (17)	2 (29)	2 (67)	0
CMR	5 (26)	1 (8)	0	0	0
Unknown	2 (11)	1 (8)	1 (14)	1 (33)	0

*: CCyR includes CCyR or better; MMR includes MMR or better; MR4·5 includes MR4·5 or better.

** : Each status represents the best category of response or disease status at the time of death.

Abbreviations: AP, accelerated phase; BP, blast phase; CP, chronic phase; CCyR, complete cytogenetic response; MMR, major molecular response; MR4·5, molecular response by a 4·5 log reduction on the international scale; CMR, complete molecular response; SCT, stem cell transplant; TKI, tyrosine kinase inhibitor; CML, chronic myeloid leukemia; HCV, hepatitis C virus.

Table 3-3. Cause of death by cumulative response within 1 year in age 65-84

Age 65-84	All N= 64	CCyR* N= 58	MMR* N=44	MR4·5* N=25	CMR N=11
Number of death, No. (%)	22 (34)	20 (34)	13 (25)	8 (17)	3 (9)
Progression to AP/BP, No. (%)	2 (9)	1 (5)	0	0	0
Secondary malignancy, No. (%)	5 (23)	5 (25)	3 (23)	2 (25)	1 (33)
Cardiovascular events, No. (%)	7 (32)	7 (35)	4 (31)	3 (6)	0
Sepsis, No. (%)	1 (5)	1(5)	1 (8)	1 (13)	1 (33)
Dementia, No. (%)	1 (5)	1 (5)	1 (8)	0	0
Surgical complications, No. (%)	1 (5)	1 (5)	1 (8)	0	0
Bowel obstruction, No. (%)	1 (5)	0	0	0	0
Gastrointestinal bleeding, No. (%)	1 (5)	1 (5)	0	0	0
Parkinson disease, No. (%)	1 (5)	1 (5)	1 (8)	0	0
Unknown, No. (%)	2 (9)	2 (10)	2 (15)	2 (25)	1 (33)
Type of TKI, No. (%)					
Imatinib	16 (73)	14 (70)	8 (62)	5 (63)	2 (67)
Dasatinib	2 (9)	2 (10)	1 (8)	0	0
Nilotinib	4 (18)	4 (20)	4 (31)	3 (38)	1 (33)
Overall cumulative response, No. (%)					
CCyR	20 (91)	20 (100)	13 (100)	8 (100)	3 (100)
MMR	14 (64)	14 (70)	13 (100)	8 (100)	3 (100)
MR4·5	12 (55)	12 (60)	11 (85)	8 (100)	3 (100)
CMR	8 (36)	8 (40)	7 (54)	5 (63)	3 (100)
Disease status** at the time of death, No. (%)					
CML-AP/BP	1 (5)	0	0	0	0
CML-CP	2 (9)	2 (10)	0	0	0
CHR	2 (9)	1 (5)	0	0	0
CCyR	1 (5)	1 (5)	0	0	0
MMR	3 (14)	3 (15)	2 (15)	1 (13)	1 (33)
MR4·5	4 (18)	4 (20)	4 (31)	3 (38)	0
CMR	5 (23)	5 (25)	4 (31)	2 (25)	1 (33)
Unknown	3 (14)	4 (20)	3 (23)	2 (25)	1 (33)

*: CCyR includes CCyR or better; MMR includes MMR or better; MR4·5 includes MR4·5 or better.

** : Each status represents the best category of response or disease status at the time of death.

Abbreviations: AP, accelerated phase; BP, blast phase; CP, chronic phase; CCyR, complete cytogenetic response; MMR, major molecular response; MR4·5, molecular response by a 4·5 log reduction on the international scale; CMR, complete molecular response; SCT, stem cell transplant; TKI, tyrosine kinase inhibitor; CML, chronic myeloid leukemia.

Table 4. Multivariate Cox proportional hazards analysis of overall survival

Variable	Univariate	Multivariate Analysis		
	<i>P</i>	<i>P</i>	HR	95% CI
Age at diagnosis	<0.0001	<0.0001	1.045	1.026-1.065
Clonal evolution at diagnosis	0.031	0.028	2.841	1.121-7.149
Sokal risk Score	0.15			
Type of TKIs	0.45			
Time from diagnosis to TKI	0.26			
Cumulative response with a time dependent variable*				
CCyR	<0.0001	<0.0001	6.250	3.367-11.494
MMR	<0.0001	<0.0001	6.579	3.745-11.628
MR4.5	<0.0001	<0.0001	5.154	2.841-9.346
CMR	<0.0001	0.0013	3.003	1.538-5.882

*: Each variable was compared to the counterpart no response category and calculated for multivariate analysis separately.

Abbreviations: TKI, tyrosine kinase inhibitor; HR, hazard ratio; CI, confidence interval; CCyR, complete cytogenetic response; MMR, major molecular response; MR4.5, molecular response with 4.5 log reduction by international scale; CMR, complete molecular response; OS, overall survival.

Table 5. One-year landmark by cumulative response within one year

Group	No. at 5y	5-y Absolute OS [95% CI]	5-y Relative OS [95% CI]	5-y OS in GP	No. at 10y	10-y Absolute OS [95% CI]	10-y Relative OS [95% CI]	10-y OS in GP
Age 15-84								
All N=465	312	93.5 [91.0-95.9]	95.1 [92.6-97.6]	98.3	127	84.2 [79.9-88.6]	88.4 [83.9-93.1]	95.2
CCyR N=413	284	95.2 [92.8-97.5]	97.0 [94.6-99.4]	98.1	115	87.7 [83.4-92.0]	92.3 [87.8-96.8]	95.0
MMR N=338	234	97.3 [95.4-99.3]	99.1 [97.1-101.1]	98.2	91	89.9 [85.3-94.4]	94.6 [89.8-99.4]	95.0
MR4.5 N=159	105	95.8 [92.1-99.4]	97.8 [94.0-101.4]	98.0	47	88.5 [81.9-95.0]	93.5 [86.5-100.3]	94.7
CMR N=81	53	98.6 [95.8-100]	100.5 [97.7-101.9]	98.1	21	91.7 [82.2-100]	96.8 [86.8-105.6]	94.7
Age 15-44								
All N=189	131	96.2 [93.2-99.2]	96.9 [93.9-99.9]	99.3	48	90.0 [84.4-95.6]	91.6 [85.9-97.4]	98.2
CCyR N=160	117	99.2 [97.7-100]	99.9 [98.4-100.7]	99.3	42	95.5 [90.9-100]	97.3 [92.6-101.8]	98.2
MMR N=131	95	99.1 [97.2-100]	99.8 [97.9-100.7]	99.3	34	96.0 [91.4-100]	97.9 [93.2-101.9]	98.1
MR4.5 N=60	41	100	100.7	99.3	19	97.0 [91.1-100]	99.0 [93.0-102.0]	98.0
CMR N=32	21	100	100.7	99.3	10	100	102.1	97.9
Age 45-64								
All N=214	140	94.4 [90.9-97.8]	97.0 [93.4-100.5]	97.3	58	88.0 [82.4-93.6]	94.7 [88.7-100.8]	92.9
CCyR N=196	130	96.1 [93.0-99.2]	98.8 [95.6-102.0]	97.3	54	92.0 [87.0-97.0]	99.0 [93.6-104.4]	92.9
MMR N=164	110	98.5 [96.5-100]	101.2 [99.2-102.8]	97.3	43	94.6 [89.7-99.4]	101.8 [96.6-107.0]	92.9
MR4.5 N=74	49	98.2 [94.8-100]	100.7 [97.2-102.6]	97.5	20	92.8 [84.7-100]	99.5 [90.8-107.2]	93.3
CMR N=39	24	100	102.8	97.3	7	100	107.6	92.9
Age 65-84								
All N=62	41	82.7 [72.4-93.0]	92.4 [80.9-103.9]	89.5	21	60.9 [46.2-75.5]	83.4 [63.6-104.0]	72.6
CCyR N=57	37	81.3 [70.2-92.3]	90.8 [78.4-103.1]	89.5	19	59.5 [44.0-74.9]	82.0 [60.6-103.2]	72.6
MMR N=43	29	88.3 [77.5-99.1]	99.7 [87.5-111.9]	88.6	14	61.9 [43.6-80.3]	88.9 [62.6-115.4]	69.6
MR4.5 N=25	15	80.0 [62.5-97.5]	88.5 [69.1-107.9]	90.4	8	61.7 [38.9-94.5]	82.6 [52.1-126.5]	74.7
CMR N=10	8	88.9 [68.4-100]	98.6 [75.8-110.9]	90.2	4	61.0 [25.6-96.3]	82.3 [34.5-130.0]	74.1

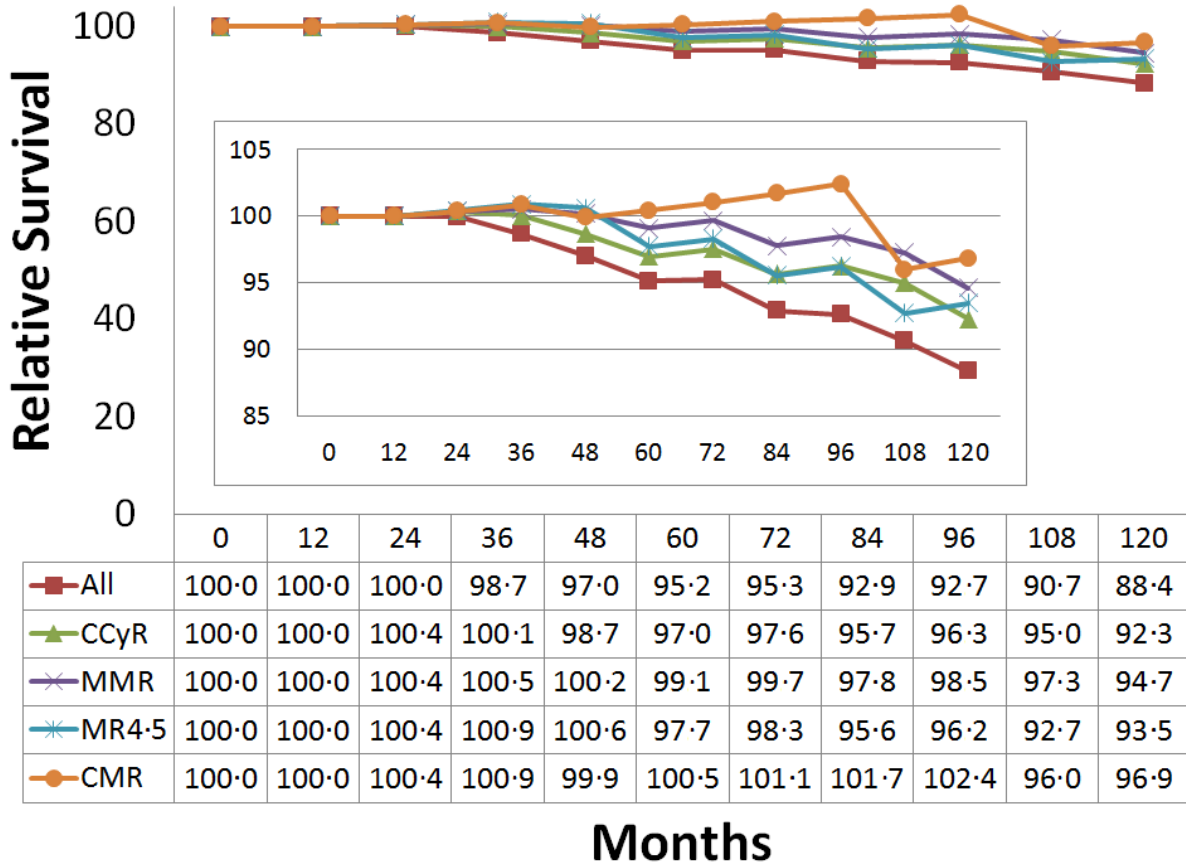
Abbreviations: OS, overall survival; GP, general population; CI, confidence interval; CCyR, complete cytogenetic response; MMR, major molecular response; MR4.5, molecular response with 4.5 log reduction by international scale; CMR, complete molecular response.

Table 6. One-year landmark by tyrosine kinase inhibitor and cumulative response within 1 year

Group	No. at 5y	5-y Absolute OS [95% CI]	5-y Relative OS [95% CI]	5-y OS in GP	No. at 10y	10-y Absolute OS [95% CI]	10-y Relative OS [95% CI]	10-y OS in GP
All TKI Group								
All N=465	312	93.5 [91.0-95.9]	95.1 [92.6-97.6]	98.3	127	84.2 [79.9-88.6]	88.4 [83.9-93.1]	95.2
CCyR N=413	284	95.2 [92.8-97.5]	97.0 [94.6-99.4]	98.1	115	87.7 [83.4-92.0]	92.3 [87.8-96.8]	95.0
MMR N=338	234	97.3 [95.4-99.3]	99.1 [97.1-101.1]	98.2	91	89.9 [85.3-94.4]	94.6 [89.8-99.4]	95.0
MR4.5 N=159	105	95.8 [92.1-99.4]	97.8 [94.0-101.4]	98.0	47	88.5 [81.9-95.0]	93.5 [86.5-100.3]	94.7
CMR N=81	53	98.6 [95.8-100]	100.5 [97.7-101.9]	98.1	21	91.7 [82.2-100]	96.8 [86.8-105.6]	94.7
Imatinib Group								
All N=266	239	93.1 [90.0-96.2]	94.7 [91.6-97.9]	98.3	127	83.9 [79.2-88.6]	88.1 [83.2-93.1]	95.2
CCyR N=228	212	95.1 [92.3-97.9]	96.9 [94.1-99.8]	98.1	115	87.8 [83.2-92.3]	92.6 [87.8-97.4]	94.8
MMR N=183	176	97.8 [95.7-99.9]	99.6 [97.5-101.7]	98.2	91	90.5 [85.8-95.2]	95.3 [90.3-100.2]	95.0
MR4.5 N=81	78	97.5 [94.1-100]	99.6 [96.1-102.5]	97.9	47	89.7 [82.9-96.5]	95.2 [88.0-102.4]	94.2
CMR N=34	33	100	102.0	98.0	21	93.1 [83.7-100]	98.5 [88.6-105.8]	94.5
Dasatinib Group								
All N=101	40	98.5 [95.6-100]	100.1 [97.2-101.6]	98.4	0	NA	NA	95.4
CCyR N=94	39	98.4 [95.3-100]	100.0 [96.8-101.6]	98.4	0	NA	NA	95.4
MMR N=75	30	100	101.9	98.1	0	NA	NA	94.7
MR4.5 N=37	12	100	101.8	98.2	0	NA	NA	95.1
CMR N= 26	9	100	101.8	98.2	0	NA	NA	94.9
Nilotinib Group								
All N=98	33	88.5 [79.4-97.5]	90.1 [80.9-99.3]	98.2	0	NA	NA	95.0
CCyR N=91	33	90.7 [82.0-99.5]	92.5 [83.6-101.4]	98.1	0	NA	NA	94.7
MMR N=80	28	92.0 [83.3-100]	93.7 [84.8-101.8]	98.2	0	NA	NA	94.8
MR4.5 N=41	15	85.6 [70.2-100]	87.3 [71.6-102.0]	98.0	0	NA	NA	94.6
CMR N=21	11	94.1 [82.9-100]	95.9 [84.5-101.9]	98.1	0	NA	NA	94.7

Abbreviations: OS, overall survival; GP, general population; CI, confidence interval; CCyR, complete cytogenetic response; MMR, major molecular response; MR4.5, molecular response with 4.5 log reduction by international scale; CMR, complete molecular response; NA, not applicable.

Figure 2-1. One-year landmark: Relative survival in patients with chronic myeloid leukemia by cumulative response within 1 year



Abbreviations: CCyR, complete cytogenetic response; MMR, major molecular response; MR4·5, molecular response by a 4·5 log reduction on the international scale; CMR, complete molecular response.