

Appendix 1 Search strategies

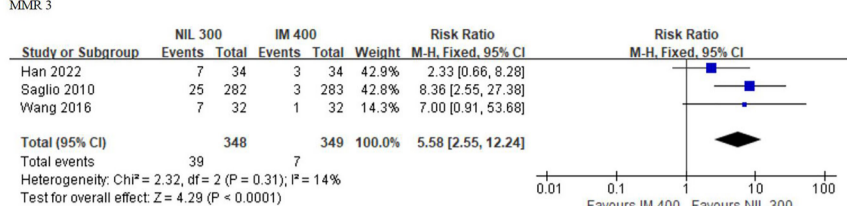
PubMed

Search	Query
#1	leukemia, myelogenous, chronic, bcr-abl positive [MeSH]
#2	CML [Title-Abstract] OR "chronic myelocytic leukemia*" [Title-Abstract] OR "chronic myelogenous leukemia*" [Title-Abstract] OR "chronic myeloid leukemia*" [Title-Abstract] OR "ph1 positive myeloid leukemia*" [Title-Abstract] OR "philadelphia positive myeloid leukemia*" [Title-Abstract] OR "chronic granulocytic leukemia*" [Title-Abstract]
#3	#1 OR #2
#4	Imatinib Mesylate [MeSH]
#5	Imatinib [Title-Abstract] OR STI571 [Title-Abstract] OR CGP57148 [Title-Abstract] OR Glivec [Title-Abstract] OR Gleevec [Title-Abstract]
#6	Dasatinib [MeSH]
#7	Dasatinib [Title-Abstract] OR BMS354825 [Title-Abstract] OR SPRYCEL [Title-Abstract]
#8	nilotinib [Supplementary Concept]
#9	nilotinib [Title-Abstract] OR AMN107 [Title-Abstract] OR Tasigna [Title-Abstract]
#10	flumatinib [Supplementary Concept]
#11	Flumatinib [Title-Abstract] OR HHGV678 [Title-Abstract] OR SPRYCEL [Title-Abstract]
#12	bosutinib [Supplementary Concept]
#13	bosutinib [Title-Abstract] OR SKI606 [Title-Abstract] OR Bosulif [Title-Abstract]
#14	radotinib [Title-Abstract] OR iy5511[Title-Abstract]
#15	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14
#16	randomized controlled trial [Publication Type] OR controlled clinical trial [Publication Type] OR random*[Title-Abstract] OR RCT [Title-Abstract]
#17	Animals [Mesh] NOT Humans [Mesh]
#18	#3 AND #15 AND #16 NOT #17

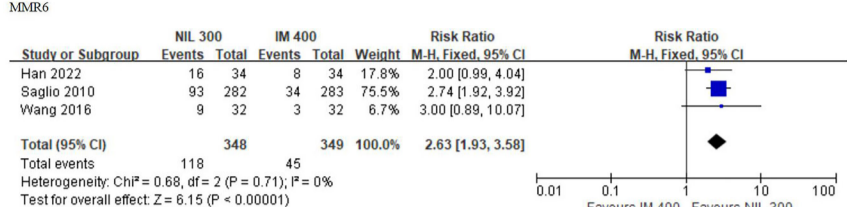
Cochrane Library

Search	Query
#1	MeSH descriptor: [leukemia, myelogenous, chronic, bcr-abl positive] explode all trees
#2	(CML):ti, ab, kw OR (chronic myelocytic leukemia*):ti, ab, kw OR (chronic myelogenous leukemia*):ti, ab, kw OR (chronic myeloid leukemia*):ti, ab, kw OR (ph1 positive myeloid leukemia*):ti, ab, kw OR (philadelphia positive myeloid leukemia*):ti, ab, kw OR (chronic granulocytic leukemia*):ti, ab, kw
#3	#1 OR #2
#4	MeSH descriptor: [Imatinib Mesylate] explode all trees
#5	(Imatinib):ti, ab, kw OR (STI571):ti, ab, kw OR (CGP57148):ti, ab, kw OR (Glivec):ti, ab, kw OR (Gleevec):ti, ab, kw
#6	MeSH descriptor: [Dasatinib] explode all trees
#7	(Dasatinib):ti, ab, kw OR (BMS354825):ti, ab, kw OR (SPRYCEL):ti, ab, kw
#8	(nilotinib):ti, ab, kw OR (AMN107):ti, ab, kw OR (Tasigna):ti, ab, kw
#9	(Flumatinib):ti, ab, kw OR (HHGV678):ti, ab, kw
#10	(Bosutinib):ti, ab, kw OR (SKI606):ti, ab, kw OR (Bosulif):ti, ab, kw
#11	(Radotinib):ti, ab, kw OR (iy5511):ti, ab, kw
#12	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
#13	(Controlled clinical trial):pt
#14	(Randomised controlled trial):pt
#15	#13 OR #14
#16	#3 AND #12 AND #15

MMR 3



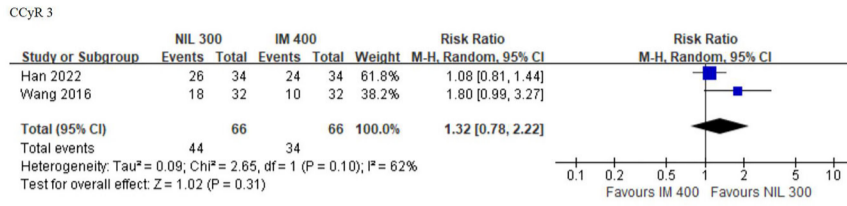
MMR6



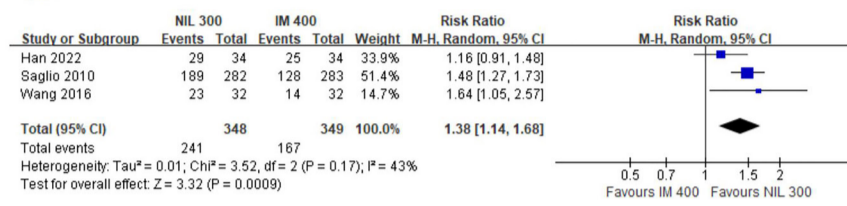
MMR12



CCyR 3



CCyR 6

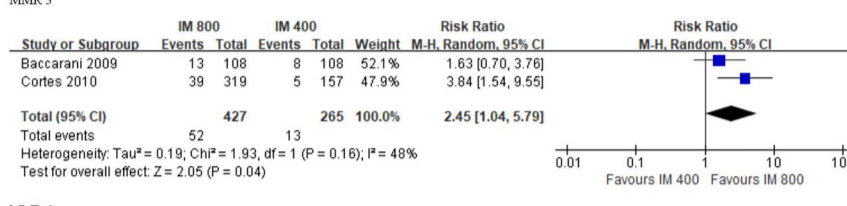


CCyR 12

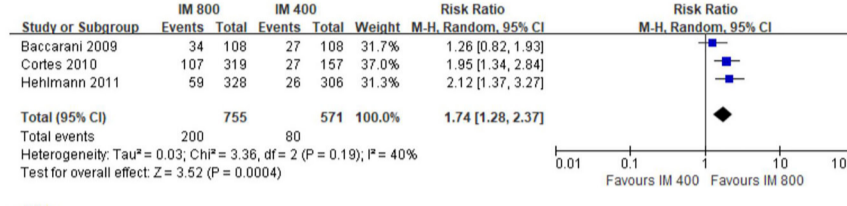


IM 800 vs. IM 400

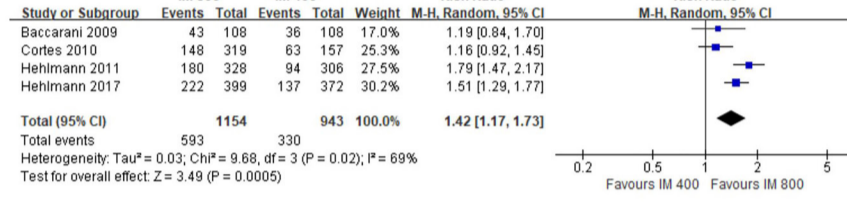
MMR 3



MMR 6



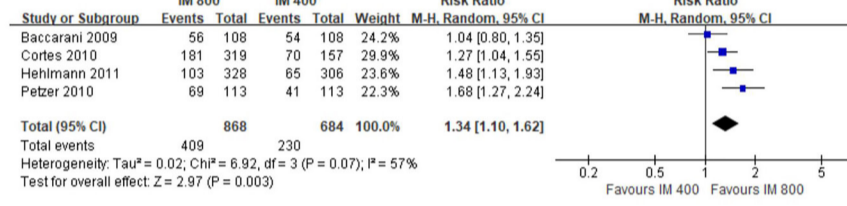
MMR 12



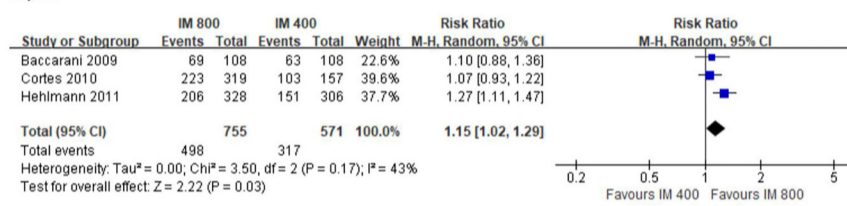
CCyR 3



CCyR 6

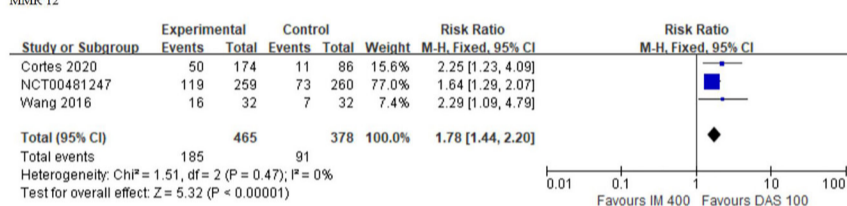


CCyR 12

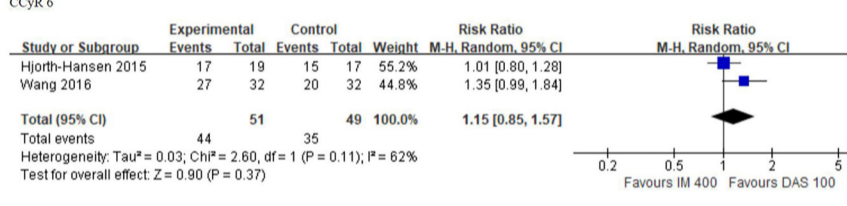


DAS 100 vs. IM 400

MMR 12



CCyR 6



CCyR 12



A												
IM 400mg QD	4.45 (1.05,18.90)	4.92 (1.94,12.50)	3.11 (0.91,10.60)	2.45 (0.61,9.86)	2.14 (0.68,6.70)	4.10 (0.41,41.28)	8.00 (0.88,72.41)	2.45 (1.06,5.64)				
0.22 (0.05,0.95)	DAS 100mg QD	1.10 (0.33,3.74)	0.70 (0.15,3.30)	0.55 (0.07,4.09)	0.48 (0.08,3.03)	0.92 (0.06,14.03)	1.80 (0.13,25.03)	0.55 (0.10,2.91)				
0.20 (0.08,0.52)	0.91 (0.27,3.06)	NIL 300mg BID	0.63 (0.23,1.73)	0.50 (0.09,2.66)	0.44 (0.10,1.90)	0.83 (0.07,10.06)	1.63 (0.15,17.78)	0.50 (0.14,1.74)				
0.32 (0.09,1.09)	1.43 (0.30,6.76)	1.58 (0.58,4.32)	NIL 400mg BID	0.79 (0.12,5.03)	0.69 (0.13,3.67)	1.32 (0.10,17.99)	2.57 (0.21,31.97)	0.79 (0.18,3.45)				
0.41 (0.10,1.64)	1.82 (0.24,13.53)	2.01 (0.38,10.74)	1.27 (0.20,8.12)	BOS 400mg QD	0.87 (0.14,5.29)	1.67 (0.11,24.83)	3.27 (0.24,44.24)	1.00 (0.20,5.07)				
0.47 (0.15,1.46)	2.08 (0.33,13.11)	2.30 (0.53,10.03)	1.45 (0.27,7.75)	1.14 (0.19,6.92)	BOS 500mg QD	1.91 (0.15,25.15)	3.73 (0.31,44.63)	1.14 (0.28,4.70)				
0.24 (0.02,2.45)	1.09 (0.07,16.55)	1.20 (0.10,14.47)	0.76 (0.06,10.36)	0.60 (0.04,8.85)	0.52 (0.04,6.86)	RAD 300mg BID	1.95 (0.48,7.94)	0.60 (0.05,6.96)				
0.12 (0.01,1.13)	0.56 (0.04,7.76)	0.62 (0.06,6.73)	0.39 (0.03,4.84)	0.31 (0.02,4.15)	0.27 (0.02,3.20)	0.51 (0.13,2.09)	RAD 400mg BID	0.31 (0.03,3.23)				
0.41 (0.18,0.94)	1.82 (0.34,9.63)	2.01 (0.57,7.02)	1.27 (0.29,5.56)	1.00 (0.20,5.07)	0.87 (0.21,3.59)	1.67 (0.14,19.50)	3.27 (0.31,34.44)	IM 800mg QD				
B												
IM 400mg QD	1.19 (0.91,1.56)	1.33 (1.08,1.64)	1.31 (0.98,1.75)	1.25 (0.60,2.58)	1.43 (1.03,1.98)	1.20 (0.76,1.90)	/	1.22 (0.89,1.68)	1.27 (0.89,1.80)	1.17 (0.81,1.68)	1.33 (1.11,1.61)	1.37 (0.92,2.04)
0.24 (0.12,0.49)	DAS 100mg QD	1.12 (0.83,1.51)	1.10 (0.76,1.60)	1.05 (0.48,2.29)	1.20 (0.79,1.85)	1.01 (0.70,1.46)	/	1.03 (0.68,1.56)	1.06 (0.68,1.66)	0.98 (0.63,1.55)	1.12 (0.81,1.56)	1.15 (0.71,1.87)
0.39 (0.27,0.55)	1.61 (0.83,3.13)	NIL 300mg BID	0.99 (0.75,1.30)	0.94 (0.44,2.00)	1.08 (0.73,1.58)	0.90 (0.56,1.45)	/	0.92 (0.63,1.34)	0.95 (0.63,1.44)	0.88 (0.58,1.34)	1.00 (0.76,1.33)	1.03 (0.66,1.62)
0.42 (0.28,0.62)	1.74 (0.84,3.60)	1.08 (0.78,1.49)	NIL 400mg BID	0.95 (0.43,2.08)	1.09 (0.71,1.69)	0.91 (0.54,1.55)	/	0.93 (0.61,1.43)	0.96 (0.61,1.52)	0.89 (0.56,1.42)	1.02 (0.72,1.43)	1.05 (0.64,1.71)
\	\	\	\	FLT3 400mg QD	1.15 (0.57,2.33)	0.96 (0.41,2.28)	/	0.98 (0.44,2.17)	1.01 (0.45,2.28)	0.94 (0.42,2.12)	1.07 (0.50,2.27)	1.10 (0.48,2.52)
0.54 (0.36,0.82)	2.25 (0.98,5.14)	1.40 (0.81,2.41)	1.29 (0.73,2.28)	\	FLT3 600mg QD	0.84 (0.48,1.48)	/	0.85 (0.54,1.35)	0.88 (0.55,1.43)	0.82 (0.50,1.33)	0.93 (0.64,1.36)	0.96 (0.57,1.60)
0.23 (0.09,0.60)	0.95 (0.50,1.81)	0.59 (0.24,1.49)	0.55 (0.21,1.44)	\	0.42 (0.15,1.21)	DAS 70mg QD	/	1.02 (0.58,1.79)	1.06 (0.59,1.89)	0.98 (0.54,1.75)	1.11 (0.68,1.83)	1.14 (0.62,2.10)
0.52 (0.36,0.77)	2.16 (0.96,4.87)	1.34 (0.80,2.26)	1.24 (0.72,2.15)	\	0.96 (0.55,1.69)	2.26 (0.81,6.35)	BOS 400mg QD	/	/	/	/	/
0.41 (0.26,0.65)	1.69 (0.72,3.95)	1.05 (0.59,1.88)	0.97 (0.53,1.77)	\	0.75 (0.41,1.40)	1.77 (0.61,5.12)	0.78 (0.43,1.42)	BOS 500mg QD	1.03 (0.64,1.67)	0.96 (0.59,1.55)	1.09 (0.76,1.58)	1.12 (0.67,1.87)
0.43 (0.22,0.84)	1.78 (0.67,4.74)	1.11 (0.52,2.36)	1.02 (0.47,2.22)	\	0.79 (0.36,1.74)	1.86 (0.58,6.00)	0.82 (0.38,1.78)	1.05 (0.47,2.37)	RAD 300mg BID	0.92 (0.66,1.30)	1.05 (0.71,1.57)	1.08 (0.64,1.85)
0.61 (0.30,1.25)	2.53 (0.92,6.97)	1.57 (0.71,3.50)	1.45 (0.64,3.29)	\	1.13 (0.49,2.58)	2.65 (0.80,8.77)	1.17 (0.52,2.64)	1.50 (0.64,3.50)	1.42 (0.81,2.50)	RAD 400mg BID	1.14 (0.76,1.71)	1.17 (0.68,2.01)
0.57 (0.44,0.75)	2.37 (1.11,5.09)	1.48 (0.95,2.30)	1.36 (0.85,2.19)	\	1.06 (0.64,1.73)	2.49 (0.92,6.72)	1.10 (0.69,1.75)	1.40 (0.82,2.39)	1.34 (0.65,2.76)	0.94 (0.44,2.02)	IM 800mg QD	1.03 (0.66,1.59)
\	\	\	\	\	\	\	\	\	\	\	\	IM 600mg QD
C												
IM 400mg QD	0.99 (0.76,1.29)	0.59 (0.40,0.88)	0.49 (0.32,0.75)	0.70 (0.47,1.04)	0.56 (0.32,0.97)	0.46 (0.30,0.69)	0.64 (0.36,1.13)	0.79 (0.47,1.33)	1.53 (1.06,2.20)			
0.62 (0.39,0.97)	DAS 100mg QD	0.60 (0.37,0.96)	0.49 (0.30,0.82)	0.71 (0.44,1.14)	0.56 (0.31,1.04)	0.46 (0.28,0.76)	0.65 (0.35,1.21)	0.80 (0.45,1.43)	1.54 (0.98,2.42)			
0.85 (0.49,1.49)	1.39 (0.68,2.84)	NIL 300mg BID	0.82 (0.51,1.33)	1.19 (0.68,2.07)	0.94 (0.48,1.86)	0.77 (0.43,1.37)	1.08 (0.54,2.16)	1.34 (0.70,2.57)	2.58 (1.51,4.42)			
0.72 (0.42,1.23)	1.17 (0.58,2.35)	0.84 (0.50,1.41)	NIL 400mg BID	1.44 (0.81,2.57)	1.14 (0.57,2.29)	0.93 (0.51,1.70)	1.31 (0.65,2.67)	1.62 (0.83,3.18)	3.13 (1.78,5.49)			
0.97 (0.65,1.45)	1.57 (0.86,2.89)	1.13 (0.57,2.25)	1.35 (0.69,2.63)	FLT3 600mg QD	0.79 (0.40,1.56)	0.65 (0.37,1.15)	0.91 (0.46,1.82)	1.13 (0.59,2.16)	2.18 (1.28,3.71)			
0.41 (0.22,0.75)	0.67 (0.31,1.42)	0.48 (0.21,1.09)	0.57 (0.25,1.28)	0.42 (0.20,0.88)	BOS 400mg QD	0.82 (0.41,1.64)	1.15 (0.52,2.54)	1.42 (0.67,3.03)	2.74 (1.42,5.32)			
1.02 (0.63,1.63)	1.65 (0.86,3.17)	1.19 (0.57,2.47)	1.41 (0.69,2.88)	1.05 (0.56,1.95)	2.48 (1.15,5.35)	BOS 500mg QD	1.41 (0.70,2.84)	1.74 (0.89,3.38)	3.35 (1.92,5.84)			
1.20 (0.60,2.40)	1.95 (0.85,4.45)	1.41 (0.58,3.41)	1.67 (0.70,4.00)	1.24 (0.56,2.76)	2.93 (1.17,7.34)	RAD 300mg BID	1.24 (0.68,2.26)	2.38 (1.21,4.67)	2.38 (1.21,4.67)			
1.45 (0.70,3.02)	2.36 (1.00,5.57)	1.70 (0.68,4.26)	2.02 (0.82,5.00)	1.50 (0.65,3.46)	3.55 (1.37,9.17)	1.43 (0.60,3.41)	1.21 (0.56,2.61)	RAD 400mg BID	1.93 (1.02,3.63)			
0.57 (0.35,0.93)	0.92 (0.47,1.81)	0.67 (0.32,1.40)	0.79 (0.38,1.64)	0.59 (0.31,1.11)	1.39 (0.63,3.03)	0.56 (0.28,1.11)	0.47 (0.20,1.11)	0.39 (0.16,0.94)	IM 800mg QD			
D												
IM 400mg QD	/	2.22 (1.54,3.20)	3.10 (2.15,4.46)	1.77 (0.99,3.17)	4.53 (3.05,6.73)	/	/	3.49 (2.40,5.07)	7.82 (3.82,16.04)	13.26 (6.26,28.08)		
7.07 (1.20,41.60)	DAS 100mg QD	/	/	/	/	/	/	/	/	/		
0.13 (0.09,0.19)	0.02 (0.00,0.11)	NIL 300mg BID	1.40 (1.00,1.96)	0.80 (0.40,1.59)	2.04 (1.19,3.50)	/	/	1.57 (0.93,2.66)	3.53 (1.58,7.90)	5.98 (2.59,13.78)		
0.09 (0.06,0.14)	0.01 (0.00,0.08)	0.71 (0.49,1.02)	NIL 400mg BID	0.57 (0.29,1.14)	1.46 (0.85,2.50)	/	/	1.13 (0.67,1.90)	2.52 (1.13,5.65)	4.28 (1.86,9.85)		
0.53 (0.32,0.87)	0.07 (0.01,0.47)	4.00 (2.13,7.50)	5.66 (3.00,10.70)	FLT3 600mg QD	2.56 (1.26,5.19)	/	/	1.97 (0.99,3.95)	4.42 (1.75,11.16)	7.49 (2.89,19.40)		
0.89 (0.03,28.42)	0.13 (0.01,2.47)	6.74 (0.21,219.93)	9.55 (0.29,311.92)	1.69 (0.05,55.81)	DAS 70mg QD	/	/	/	/	/		
0.13 (0.09,0.20)	0.02 (0.00,0.11)	1.00 (0.57,1.74)	1.41 (0.80,2.48)	0.25 (0.13,0.47)	0.15 (0.00,4.83)	BOS 400mg QD	/	/	/	/		
0.19 (0.13,0.28)	0.03 (0.00,0.17)	1.45 (0.85,2.49)	2.06 (1.19,3.56)	0.36 (0.19,0.68)	0.22 (0.01,7.03)	1.46 (0.84,2.55)	BOS 500mg QD	0.77 (0.45,1.33)	1.73 (0.76,3.92)	2.93 (1.25,6.84)		
0.07 (0.03,0.16)	0.01 (0.00,0.07)	0.55 (0.24,1.29)	0.78 (0.33,1.84)	0.14 (0.06,0.34)	0.08 (0.00,2.84)	0.55 (0.23,1.31)	0.38 (0.16,0.89)	RAD 300mg BID	2.24 (1.00,5.04)	3.80 (1.64,8.79)		
0.06 (0.03,0.13)	0.01 (0.00,0.06)	0.46 (0.19,1.09)	0.65 (0.27,1.55)	0.11 (0.05,0.29)	0.07 (0.00,2.36)	0.46 (0.19,1.10)	0.31 (0.13,0.75)	0.83 (0.38,1.80)	RAD 400mg BID	1.69 (0.85,3.39)		
/	/	/	/	/	/	/	/	/	/	IM 800mg QD		

Figure S2 Pooled estimates of the network meta-analysis. (A) Pooled risk ratio (95% confidence intervals) for MMR 3. (B) Pooled risk ratio (95% confidence intervals) for CCyR 6 (upper triangle) and MMR 6 (lower triangle). (C) Pooled risk ratio (95% confidence intervals) for neutropenia of grade 3 or 4 (upper triangle) and thrombocytopenia of grade 3 or 4 (lower triangle). (D) Pooled risk ratio (95% confidence intervals) for AST elevation of all grade (upper triangle) and ALT elevation of all grade (lower triangle). Data in each cell are risk ratio (95% confidence intervals) for the comparison of column-defining treatment versus row-defining treatment. Results were considered statistically significant if the relative risk value's 95% confidence interval did not include 1.0. IM, imatinib; DAS, dasatinib; NIL, nilotinib; FLU, flumatinib; BOS, bosutinib; RAD, radotinib; MMR, major molecular response; CCyR, complete cytogenetic response; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

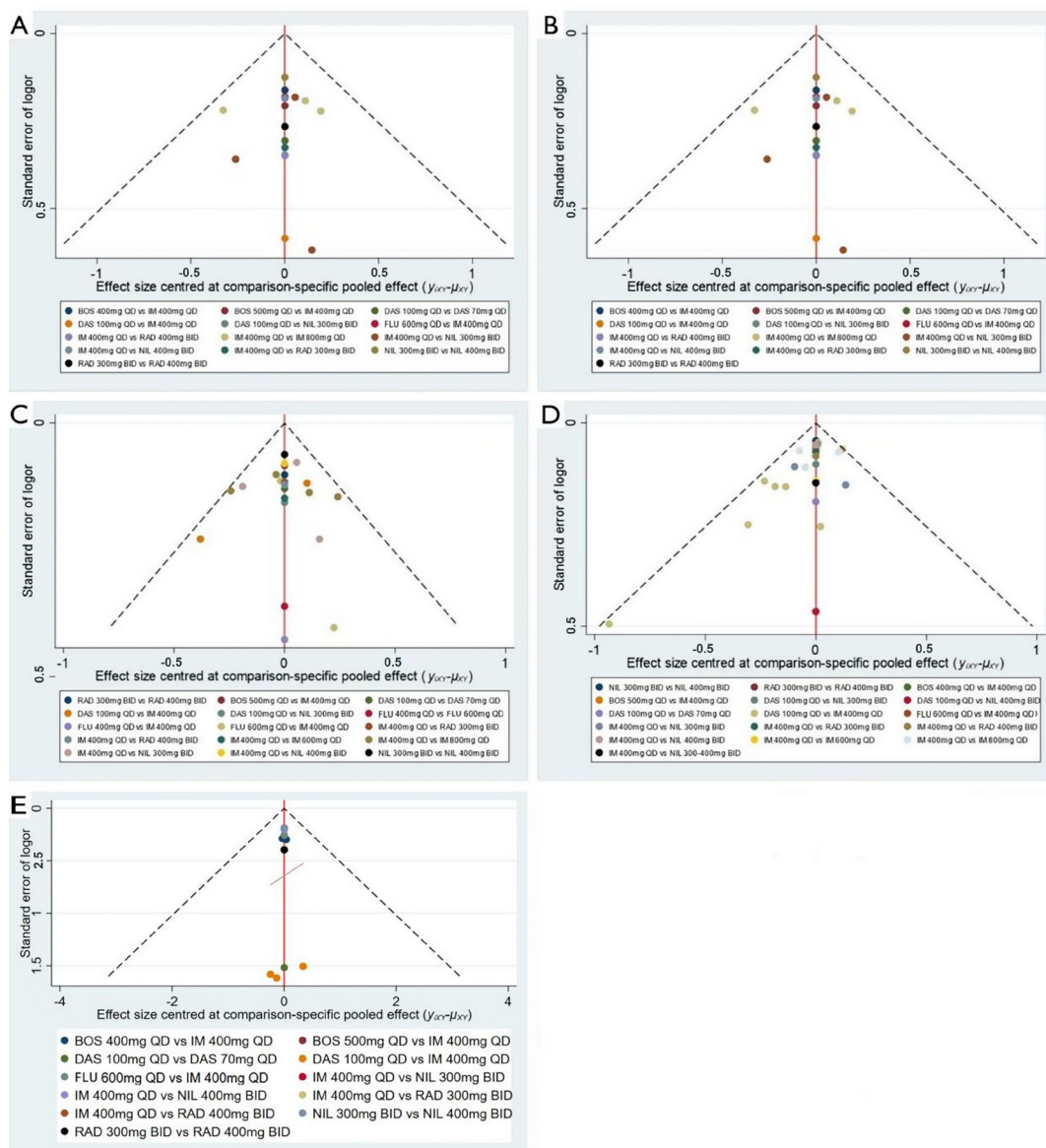


Figure S3 Funnel plots for publication bias. (A) MMR 6; (B) MMR 12; (C) CCyR 6; (D) CCyR 12; (E) ALT elevation of all grade. IM, imatinib; DAS, dasatinib; NIL, nilotinib; FLU, flumatinib; BOS, bosutinib; RAD, radotinib; MMR, major molecular response; CCyR, complete cytogenic response; ALT, Alanine Aminotransferase; QD, quaque die.