

Supplemental Online Content

Wang Z, Wang X, Wang Z, et al. Comparison of hepatotoxicity associated with new BCR-ABL tyrosine kinase inhibitors vs imatinib among patients with chronic myeloid leukemia: a systematic review and meta-analysis. *JAMA Netw Open*. 2021;4(7):e2120165. doi:10.1001/jamanetworkopen.2021.20165

eTable 1. Search Strategy

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eFigure 2. Evaluation of Publications Bias

This supplemental material has been provided by the authors to give readers additional information about their work.

		Leukemia) OR Philadelphia-Positive Myeloid Leukemias) OR Granulocytic Leukemia, Chronic) OR Chronic Granulocytic Leukemia) OR Chronic Granulocytic Leukemias) OR Granulocytic Leukemias, Chronic) OR Leukemia, Chronic Granulocytic) OR Leukemias, Chronic Granulocytic) Filters: Clinical Trial	
Cochrane Library	Bosutinib	<p>#1 (Bosutinib):ti,ab,kw OR (SKI606):ti,ab,kw OR (SKI-606):ti,ab,kw (Word variations have been searched)</p> <p>#2 (Leukemia, Myelogenous, Chronic, BCR-ABL Positive):ti,ab,kw OR (Philadelphia-Positive Myeloid Leukemia):ti,ab,kw OR (Myeloid Leukemias, Chronic):ti,ab,kw OR (Leukemia, Myelogenous, Ph1 Positive):ti,ab,kw OR (Leukemias, Chronic Granulocytic):ti,ab,kw (Word variations have been searched)</p> <p>#3 (Leukemia, Myelogenous, Chronic, BCR-ABL Positive):ti,ab,kw OR (Myelogenous Leukemias, Ph1 Positive):ti,ab,kw OR (Leukemia, Myeloid, Philadelphia Positive):ti,ab,kw OR (Myelocytic Leukemias, Chronic):ti,ab,kw OR (Granulocytic Leukemia, Chronic):ti,ab,kw (Word variations have been searched)</p> <p>#4 (Chronic Myelogenous Leukemia):ti,ab,kw OR (Leukemias, Ph1 Positive Myelogenous):ti,ab,kw OR (Myelogenous Leukemias, Chronic):ti,ab,kw OR (Chronic Granulocytic Leukemia):ti,ab,kw OR (Leukemia, Myelogenous, Ph1 Positive):ti,ab,kw (Word variations have been searched)</p> <p>#5 (Leukemia, Philadelphia-Positive Myeloid):ti,ab,kw OR (Ph1 Positive Myeloid Leukemia):ti,ab,kw OR (Myeloid Leukemia, Chronic):ti,ab,kw OR (Leukemia, Myeloid, Ph1 Positive):ti,ab,kw OR (Leukemia, Granulocytic, Chronic):ti,ab,kw (Word variations have been searched)</p> <p>#6 (Leukemia, Ph1 Positive Myeloid):ti,ab,kw OR (Chronic Myelocytic Leukemia):ti,ab,kw OR (Myeloid Leukemias, Ph1 Positive):ti,ab,kw OR (Granulocytic Leukemias, Chronic):ti,ab,kw OR (Myeloid Leukemia, Philadelphia Positive):ti,ab,kw (Word variations have been searched)</p> <p>#7 #2 or #3 or #4 or #5 or #6</p> <p>#8 #1 and #7</p>	82
	Dasatinib	<p>#1 (dasatinib):ti,ab,kw OR (Sprycel):ti,ab,kw OR (BMS-354825):ti,ab,kw OR (BMS354825):ti,ab,kw OR (354825, BMS):ti,ab,kw (Word variations have been searched)</p> <p>#2 (Leukemia, Myelogenous, Chronic, BCR-ABL Positive):ti,ab,kw OR (Philadelphia-Positive Myeloid</p>	244

	<p>Leukemia):ti,ab,kw OR (Myeloid Leukemias, Chronic):ti,ab,kw OR (Leukemia, Myelogenous, Ph1 Positive):ti,ab,kw OR (Leukemias, Chronic Granulocytic):ti,ab,kw (Word variations have been searched)</p> <p>#3 (Leukemia, Myelogenous, Chronic, BCR-ABL Positive):ti,ab,kw OR (Myelogenous Leukemias, Ph1 Positive):ti,ab,kw OR (Leukemia, Myeloid, Philadelphia Positive):ti,ab,kw OR (Myelocytic Leukemias, Chronic):ti,ab,kw OR (Granulocytic Leukemia, Chronic):ti,ab,kw (Word variations have been searched)</p> <p>#4 (Chronic Myelogenous Leukemia):ti,ab,kw OR (Leukemias, Ph1 Positive Myelogenous):ti,ab,kw OR (Myelogenous Leukemias, Chronic):ti,ab,kw OR (Chronic Granulocytic Leukemia):ti,ab,kw OR (Leukemia, Myelogenous, Ph1 Positive):ti,ab,kw (Word variations have been searched)</p> <p>#5 (Leukemia, Philadelphia-Positive Myeloid):ti,ab,kw OR (Ph1 Positive Myeloid Leukemia):ti,ab,kw OR (Myeloid Leukemia, Chronic):ti,ab,kw OR (Leukemia, Myeloid, Ph1 Positive):ti,ab,kw OR (Leukemia, Granulocytic, Chronic):ti,ab,kw (Word variations have been searched)</p> <p>#6 (Leukemia, Ph1 Positive Myeloid):ti,ab,kw OR (Chronic Myelocytic Leukemia):ti,ab,kw OR (Myeloid Leukemias, Ph1 Positive):ti,ab,kw OR (Granulocytic Leukemias, Chronic):ti,ab,kw OR (Myeloid Leukemia, Philadelphia Positive):ti,ab,kw (Word variations have been searched)</p> <p>#7 #2 or #3 or #4 or #5 or #6</p> <p>#8 #1 and #7</p>	
Nilotinib	<p>#1 (nilotinib):ti,ab,kw OR (Tasigna):ti,ab,kw OR (AMN107):ti,ab,kw (Word variations have been searched)</p> <p>#2 (Leukemia, Myelogenous, Chronic, BCR-ABL Positive):ti,ab,kw OR (Philadelphia-Positive Myeloid Leukemia):ti,ab,kw OR (Myeloid Leukemias, Chronic):ti,ab,kw OR (Leukemia, Myelogenous, Ph1 Positive):ti,ab,kw OR (Leukemias, Chronic Granulocytic):ti,ab,kw (Word variations have been searched)</p> <p>#3 (Leukemia, Myelogenous, Chronic, BCR-ABL Positive):ti,ab,kw OR (Myelogenous Leukemias, Ph1 Positive):ti,ab,kw OR (Leukemia, Myeloid, Philadelphia Positive):ti,ab,kw OR (Myelocytic Leukemias, Chronic):ti,ab,kw OR (Granulocytic Leukemia, Chronic):ti,ab,kw (Word variations have been searched)</p>	265

	<p>#4 (Chronic Myelogenous Leukemia):ti,ab,kw OR (Leukemias, Ph1 Positive Myelogenous):ti,ab,kw OR (Myelogenous Leukemias, Chronic):ti,ab,kw OR (Chronic Granulocytic Leukemia):ti,ab,kw OR (Leukemia, Myelogenous, Ph1 Positive):ti,ab,kw (Word variations have been searched)</p> <p>#5 (Leukemia, Philadelphia-Positive Myeloid):ti,ab,kw OR (Ph1 Positive Myeloid Leukemia):ti,ab,kw OR (Myeloid Leukemia, Chronic):ti,ab,kw OR (Leukemia, Myeloid, Ph1 Positive):ti,ab,kw OR (Leukemia, Granulocytic, Chronic):ti,ab,kw (Word variations have been searched)</p> <p>#6 (Leukemia, Ph1 Positive Myeloid):ti,ab,kw OR (Chronic Myelocytic Leukemia):ti,ab,kw OR (Myeloid Leukemias, Ph1 Positive):ti,ab,kw OR (Granulocytic Leukemias, Chronic):ti,ab,kw OR (Myeloid Leukemia, Philadelphia Positive):ti,ab,kw (Word variations have been searched)</p> <p>#7 #2 or #3 or #4 or #5 or #6</p> <p>#8 #1 and #7</p>	
Ponatinib	<p>#1 (Ponatinib):ti,ab,kw OR (ponatinib hydrochloride):ti,ab,kw OR (AP24534):ti,ab,kw OR (AP-24534):ti,ab,kw OR (Iclusig):ti,ab,kw (Word variations have been searched)</p> <p>#2 (Leukemia, Myelogenous, Chronic, BCR-ABL Positive):ti,ab,kw OR (Philadelphia-Positive Myeloid Leukemia):ti,ab,kw OR (Myeloid Leukemias, Chronic):ti,ab,kw OR (Leukemia, Myelogenous, Ph1 Positive):ti,ab,kw OR (Leukemias, Chronic Granulocytic):ti,ab,kw (Word variations have been searched)</p> <p>#3 (Leukemia, Myelogenous, Chronic, BCR-ABL Positive):ti,ab,kw OR (Myelogenous Leukemias, Ph1 Positive):ti,ab,kw OR (Leukemia, Myeloid, Philadelphia Positive):ti,ab,kw OR (Myelocytic Leukemias, Chronic):ti,ab,kw OR (Granulocytic Leukemia, Chronic):ti,ab,kw (Word variations have been searched)</p> <p>#4 (Chronic Myelogenous Leukemia):ti,ab,kw OR (Leukemias, Ph1 Positive Myelogenous):ti,ab,kw OR (Myelogenous Leukemias, Chronic):ti,ab,kw OR (Chronic Granulocytic Leukemia):ti,ab,kw OR (Leukemia, Myelogenous, Ph1 Positive):ti,ab,kw (Word variations have been searched)</p> <p>#5 (Leukemia, Philadelphia-Positive Myeloid):ti,ab,kw OR (Ph1 Positive Myeloid Leukemia):ti,ab,kw OR (Myeloid Leukemia, Chronic):ti,ab,kw OR (Leukemia, Myeloid, Ph1 Positive):ti,ab,kw</p>	39

	<p>OR (Leukemia, Granulocytic, Chronic):ti,ab,kw (Word variations have been searched)</p> <p>#6 (Leukemia, Ph1 Positive Myeloid):ti,ab,kw OR (Chronic Myelocytic Leukemia):ti,ab,kw OR (Myeloid Leukemias, Ph1 Positive):ti,ab,kw OR (Granulocytic Leukemias, Chronic):ti,ab,kw OR (Myeloid Leukemia, Philadelphia Positive):ti,ab,kw (Word variations have been searched)</p> <p>#7 #2 or #3 or #4 or #5 or #6</p> <p>#8 #1 and #7</p>	
Imatinib	<p>#1 (Imatinib Mesylate):ti,ab,kw OR (Gleevec):ti,ab,kw OR (Glivec):ti,ab,kw OR (Methanesulfonate, Imatinib):ti,ab,kw OR (Mesylate, Imatinib):ti,ab,kw (Word variations have been searched)</p> <p>#2 (Imatinib Methanesulfonate):ti,ab,kw OR (ST 1571):ti,ab,kw OR (ST1571):ti,ab,kw OR (STI571):ti,ab,kw OR (STI-571):ti,ab,kw (Word variations have been searched)</p> <p>#3 (STI 571):ti,ab,kw OR (CGP57148B):ti,ab,kw OR (CGP 57148):ti,ab,kw OR (CGP57148):ti,ab,kw OR (CGP-57148):ti,ab,kw (Word variations have been searched)</p> <p>#4 #1 or #2 or #3</p> <p>#5 (Leukemia, Myelogenous, Chronic, BCR-ABL Positive):ti,ab,kw OR (Philadelphia-Positive Myeloid Leukemia):ti,ab,kw OR (Myeloid Leukemias, Chronic):ti,ab,kw OR (Leukemia, Myelogenous, Ph1 Positive):ti,ab,kw OR (Leukemias, Chronic Granulocytic):ti,ab,kw (Word variations have been searched)</p> <p>#6 (Leukemia, Myelogenous, Chronic, BCR-ABL Positive):ti,ab,kw OR (Myelogenous Leukemias, Ph1 Positive):ti,ab,kw OR (Leukemia, Myeloid, Philadelphia Positive):ti,ab,kw OR (Myelocytic Leukemias, Chronic):ti,ab,kw OR (Granulocytic Leukemia, Chronic):ti,ab,kw (Word variations have been searched)</p> <p>#7 (Chronic Myelogenous Leukemia):ti,ab,kw OR (Leukemias, Ph1 Positive Myelogenous):ti,ab,kw OR (Myelogenous Leukemias, Chronic):ti,ab,kw OR (Chronic Granulocytic Leukemia):ti,ab,kw OR (Leukemia, Myelogenous, Ph1 Positive):ti,ab,kw (Word variations have been searched)</p> <p>#8 (Leukemia, Philadelphia-Positive Myeloid):ti,ab,kw OR (Ph1 Positive Myeloid Leukemia):ti,ab,kw OR (Myeloid Leukemia, Chronic):ti,ab,kw OR (Leukemia, Myeloid, Ph1 Positive):ti,ab,kw OR (Leukemia, Granulocytic, Chronic):ti,ab,kw (Word variations have been searched)</p>	329

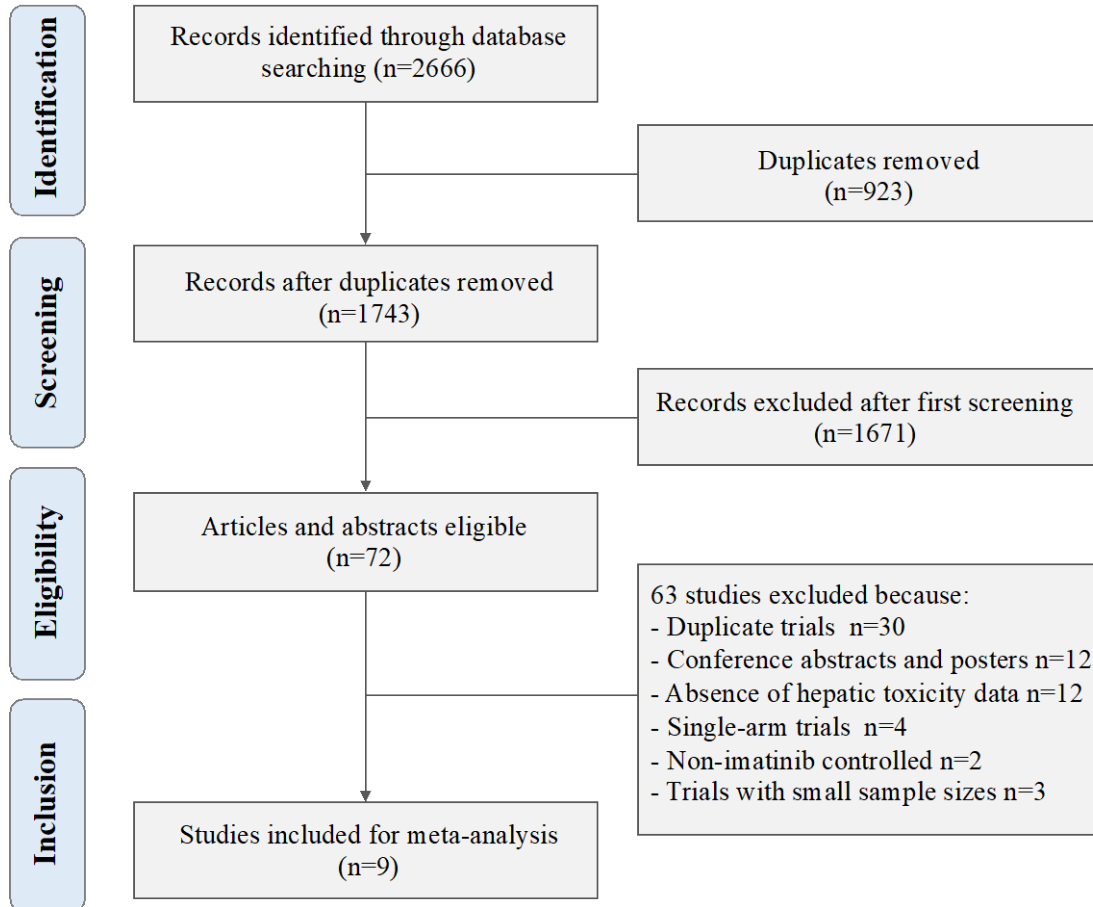
		<p>#9 (Leukemia, Ph1 Positive Myeloid):ti,ab,kw OR (Chronic Myelocytic Leukemia):ti,ab,kw OR (Myeloid Leukemias, Ph1 Positive):ti,ab,kw OR (Granulocytic Leukemias, Chronic):ti,ab,kw OR (Myeloid Leukemia, Philadelphia Positive):ti,ab,kw (Word variations have been searched)</p> <p>#10 #5 or #6 or #7 or #8 or #9</p> <p>#11 #4 and #10</p>	
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Table 2: Characteristics of included studies and quality assessment.

Authors (year)	Trial register	Trial design	Country	Treatment arm	Number of	Population	Median age	Male, n (%)	Jadad
Gambacorti-Passerini et al, ²³	NCT00574873	Phase III; RCT	30 countries	bosutinib	250	chronic	48(19-	149(59.	2
				imatinib	252	phase CML	47(18-89)	135(53.6)	
Cortes et al, ²⁴ 2018	NCT02130557	Phase III;	country	bosutinib	268	chronic	53(18-	156(58.	2
				imatinib	268	phase	53(19-	155(57.	
Hjorth-Hansen et al, ²⁵ 2014	NCT00852566	Phase II; RCT	Finland, Norway	dasatinib	22	chronic	53(29-	7(31.8)	2
				imatinib	24	phase CML	58(38-78)	15(62.5)	
Kantarjian et al, ²⁶	NCT00481247	Phase III;	country	dasatinib	259	chronic	46(18-	144(56)	3
				imatinib	260	phase	49(18-	163(63)	
Radich et al, ²⁷ 2012	NCT00070499	Phase II;	Canada, United	dasatinib	123	chronic	47(18-	75(61)	3
				imatinib	123	phase	50(19-	72(58.5)	
Hughes et al, ²⁸ 2014	NCT00760877	Phase III;	country	nilotinib	104	chronic	46 (23-	71(68.3)	2
				imatinib	103	phase	52 (19-	65(63.1)	
Saglio et al, ²⁹ 2010	NCT00471497	Phase III;	country	nilotinib	563	chronic	47(18-	333(59.	3
				imatinib	283	phase	46(18-	158(56)	
Wang et al, ³⁰ 2015	NCT01275196	Phase III;	China	nilotinib	134	chronic	41(18-	91(67.9)	3
				imatinib	133	phase	39(19-	81(60.9)	
Lipton et al, ³¹ 2016	NCT01650805	Phase III;	country	ponatinib	154	chronic	55 (18-	97(63)	3
				imatinib	152	phase	52 (18-	92(61)	

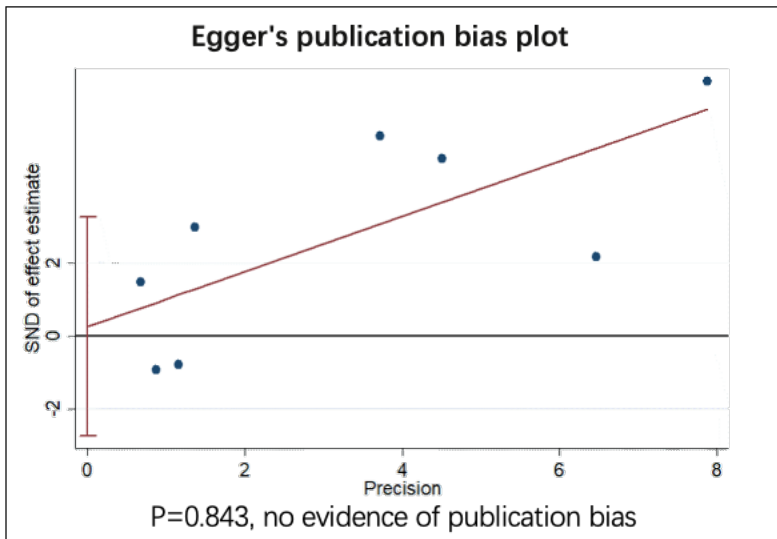
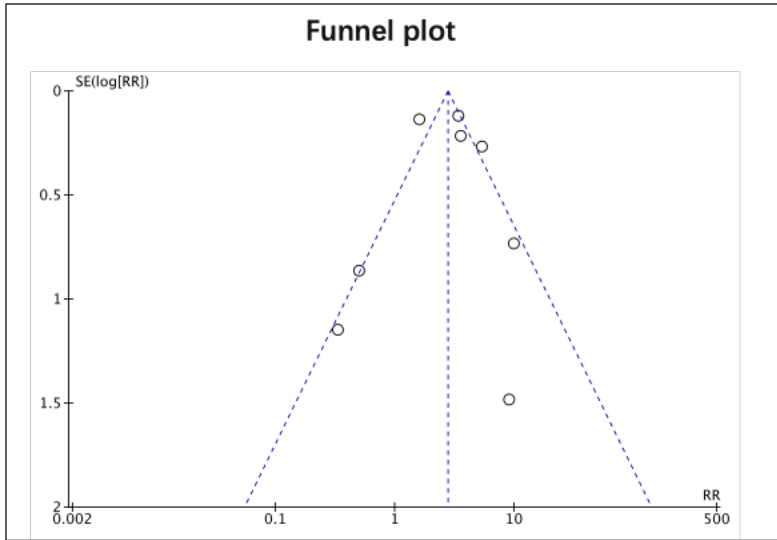
Abbreviation: CML = Chronic myeloid leukemia.

eFigure 1: Flow diagram of study selection according to PRISMA statement.

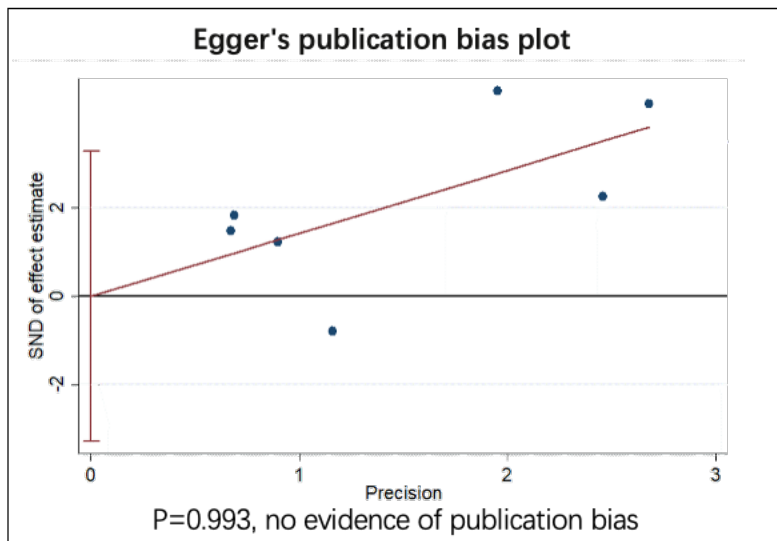
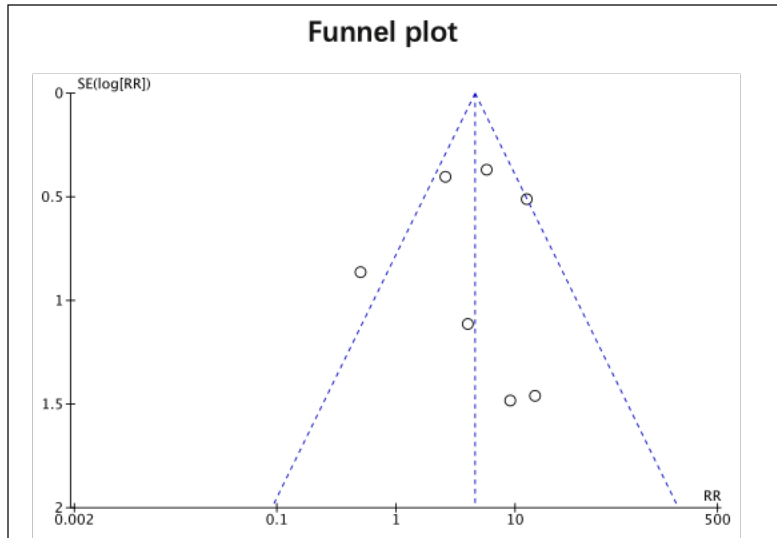


eFigure 2: Evaluation of publications bias.

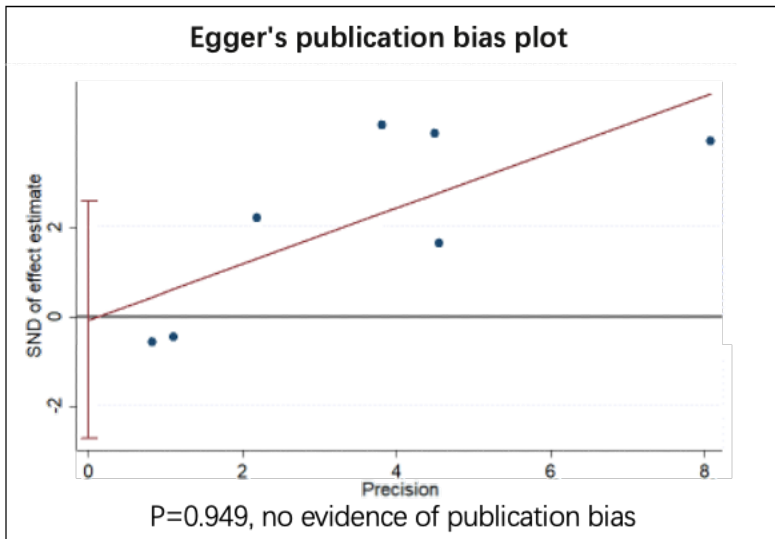
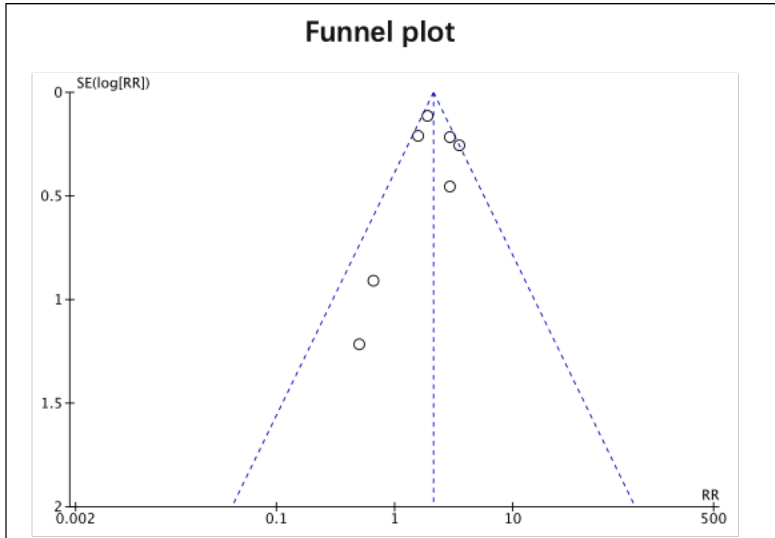
A. All grades alanine aminotransferase (ALT) elevation



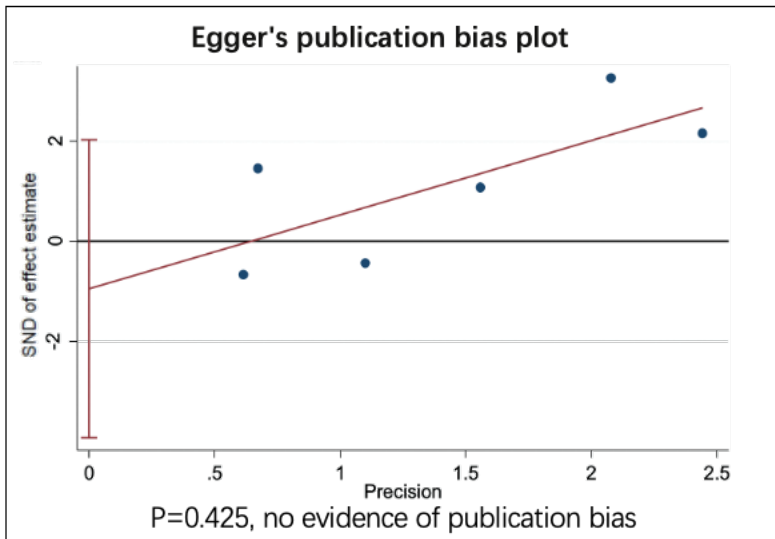
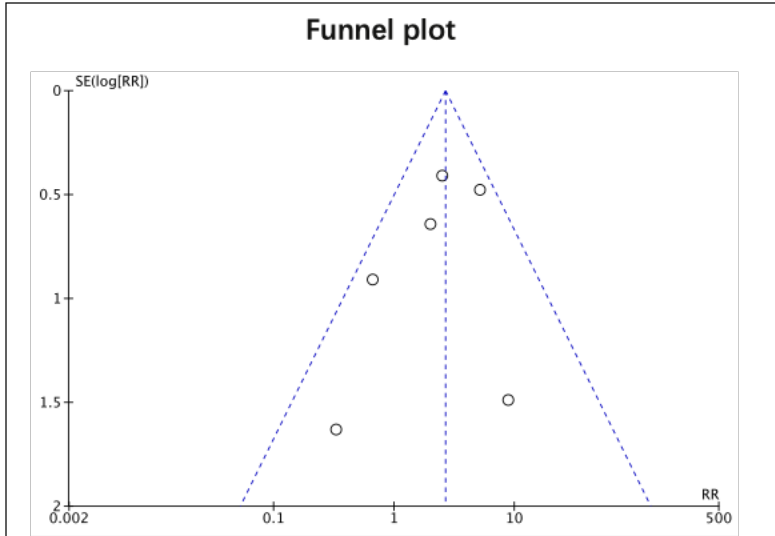
B. Grade 3-4 ALT elevation



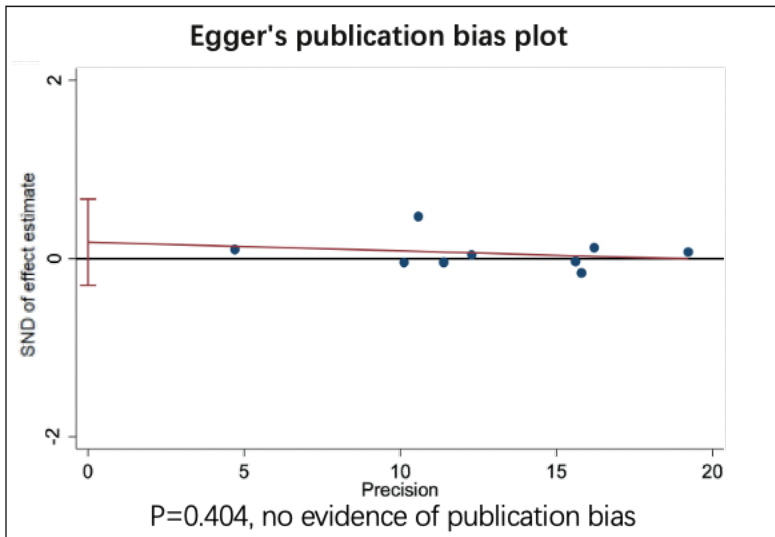
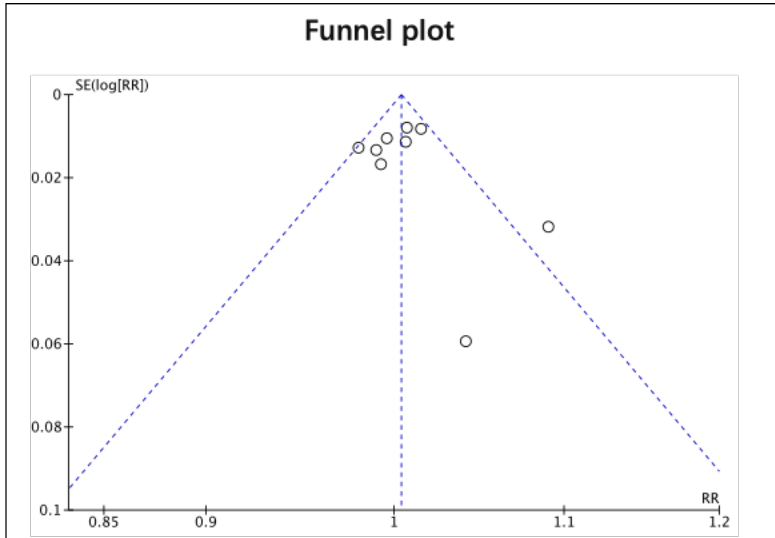
C. All grades AST elevation



D. Grade 3-4 aspartate aminotransferase (AST) elevation



E. Overall survival (OS)



F. Major molecular response (MMR)

