

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Arndt Vogel, 2018	+	+	-	-	+	+	+
A Santoro, 2015	+	+	+	+	+	+	+
David Malka, 2014	+	+	-	-	+	+	+
Francesco Leone, 2016	+	+	-	-	+	+	+
Jeeyun Lee, 2012	+	+	-	-	+	+	+
J S Chen, 2015	+	+	-	-	+	+	+
Juan W Valle, 2015	+	+	+	+	+	+	+
Juan W Valle, 2021	+	+	+	-	+	+	+
M Moehler, 2014	+	+	+	-	+	+	+

Supplementary Figure 1 Quality assessment of included studies.

Supplement Table 1 Search strategy

Databases (n)	Search strategy
Pubmed (449)	<p>((((((((((((("Biliary Tract Neoplasms"[Mesh]) OR (Biliary Tract Neoplasm)) OR (Neoplasm, Biliary Tract)) OR (Neoplasms, Biliary Tract)) OR (Biliary Tract Cancer)) OR (Biliary Tract Cancers)) OR (Cancer, Biliary Tract)) OR (Cancers, Biliary Tract)) OR (Cancer of the Biliary Tract)) OR (Cancer of Biliary Tract)) OR (((((((((((((((("Cholangiocarcinoma" [Mesh]) OR (Cholangiocarcinomas)) OR (Cholangiocellular Carcinoma)) OR (Carcinoma, Cholangiocellular)) OR (Carcinomas, Cholangiocellular)) OR (Cholangiocellular Carcinomas)) OR (Extrahepatic Cholangiocarcinoma)) OR (Cholangiocarcinoma, Extrahepatic)) OR (Cholangiocarcinomas, Extrahepatic)) OR (Extrahepatic Cholangiocarcinomas)) OR (Intrahepatic Cholangiocarcinoma)) OR (Cholangiocarcinoma, Intrahepatic)) OR (Cholangiocarcinomas, Intrahepatic)) OR (Intrahepatic Cholangiocarcinomas))) OR (((((((((((((((("Gallbladder Neoplasms"[Mesh]) OR (Gallbladder Neoplasm)) OR (Neoplasm, Gallbladder)) OR (Neoplasms, Gallbladder)) OR (Cancer of Gallbladder)) OR (Gallbladder Cancers)) OR (Gallbladder Cancer)) OR (Cancer, Gallbladder)) OR (Cancers, Gallbladder)) OR (Gall Bladder Cancer)) OR (Bladder Cancer, Gall)) OR (Bladder Cancers, Gall)) OR (Cancer, Gall Bladder)) OR (Cancers, Gall Bladder)) OR (Gall Bladder Cancers)) OR (Cancer of the Gallbladder))) AND (((("Antineoplastic Agents"[Mesh]) OR ("Drug Therapy"[Mesh])) OR ("Molecular Targeted Therapy"[Mesh])) OR ("Drug Therapy, Combination"[Mesh])) OR ("Protein Kinase Inhibitors"[Mesh]))) AND (((advanced [tiab]) OR (unresectable [tiab])) OR (metastatic [tiab])) AND (((("randomized controlled trial"[pt]) OR ("controlled clinical trial"[pt])) OR ("randomized"[tiab])) OR ("trial"[tiab])) OR ("randomly"[tiab]))</p>
Embase (420)	<p>('biliary tract tumor'/exp OR 'bile duct carcinoma'/exp OR 'gallbladder tumor'/exp) AND ('molecular therapy'/exp OR 'molecularly targeted therapy'/exp OR 'antineoplastic agent'/exp OR 'drug therapy'/exp) AND 'article'/it AND 'controlled clinical trial'/de</p>
Socpus (499)	<p>TITLE-ABS-KEY (" Biliary Tract Neoplasms" OR " Cholangiocarcinoma" OR</p>

" Gallbladder Neoplasms") AND (TITLE-ABS-KEY ("antineoplastic" OR "protein Kinase inhibitors" OR "molecular target therapy")) AND (TITLE-ABS-KEY ("survival rate" OR mortality OR "progression-free survival" OR "treatment outcome")) AND (TITLE-ABS-KEY ("randomized controlled trial" OR "controlled clinical trial" OR "randomized" OR "trial" OR "randomly")) AND (LIMIT-TO (DOCTYPE,"ar")) AND (LIMIT-TO (LANGUAGE,"English"))

Cochrane Library #1 MeSH descriptor: [Biliary Tract Neoplasms] explode all trees 482
#2 MeSH descriptor: [Cholangiocarcinoma] explode all trees 240
#3 MeSH descriptor: [Gallbladder Neoplasms] explode all trees 88
#4 MeSH descriptor: [Drug Therapy] explode all trees 146535
#5 MeSH descriptor: [Molecular Targeted Therapy] explode all trees 156
#6 MeSH descriptor: [Immunotherapy] explode all trees 8506
#7 MeSH descriptor: [Antineoplastic Agents] explode all trees 12970
#8 #1 OR #2 OR #3 598
#9 #4 OR #5 OR #6 OR #7 158337
#10 #8 AND #9 120

ClinicalTrials (166) Completed Studies | Biliary Tract Neoplasms OR Cholangiocarcinoma OR Gallbladder Neoplasms | antineoplastic OR Molecular Targeted Therapy OR protein kinase inhibitor*
