Supplementary 1. PRISMA Checklist

Section/Topic	#	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7
	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9-10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9-11

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Section/Topic	#	Checklist Item	Reported on Page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9-11
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9-10
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	12
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	12
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	13-14
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	13-15
Synthesis of results	21	Present the main results of the review. If meta-analyses done, include for each, confidence intervals and measures of consistency.	13-15
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	14
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	16
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17-18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	21
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

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For more information, visit: **www.prisma-statement.org**.

Supplementary 2. 2820 articles exclusion

1. Oral contraceptives and the liver. *IPPF medical bulletin* 1966;1:3.
2. Cytotoxic drugs in treatment of nonmalignant diseases. *Annals of internal medicine* 1972;76:619-42.
3. [Round-table discussion: problems of the surgical treatment of intrahepatic block]. *Langenbecks Archiv fur Chirurgie* 1976;342:195-8.
4. Bile acid therapy in the 1990s. *Lancet* 1992;340:1260-1.
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6. Ursodeoxycholic acid for primary biliary cirrhosis. *Drug and therapeutics bulletin* 1999;37:30-2.
7. Ursodeoxycholic acid: a second look. Primary biliary cirrhosis: dashed hopes. *Prescrire international* 2002;11:67-9.
8. Deaths from intravenous colchicine resulting from a compounding pharmacy error--Oregon and Washington, 2007. *MMWR Morbidity and mortality weekly report* 2007;56:1050-2.
9. [Infrequent but serious: autoimmune hepatitis and primary biliary cirrhosis. Early therapy improves long-term prognosis]. *MMW Fortschritte der Medizin* 2008;150:45.
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11. Abbas G, Jorgensen RA, Lindor KD. Fatigue in primary biliary cirrhosis. *Nature reviews Gastroenterology & hepatology* 2010;7:313-9.
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14. Abe K, Ohira H, Kobayashi H, Saito H, Takahashi A, Rai T, et al. Breakthrough of immune self-tolerance to calreticulin induced by CpG-oligodeoxynucleotides as adjuvant. *Fukushima journal of medical science* 2007;53:95-108.
15. Abe M, Onji M. Natural history of primary biliary cirrhosis. *Hepatology research : the official journal of the Japan Society of Hepatology* 2008;38:639-45.
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Supplementary 3. 162 articles exclusion

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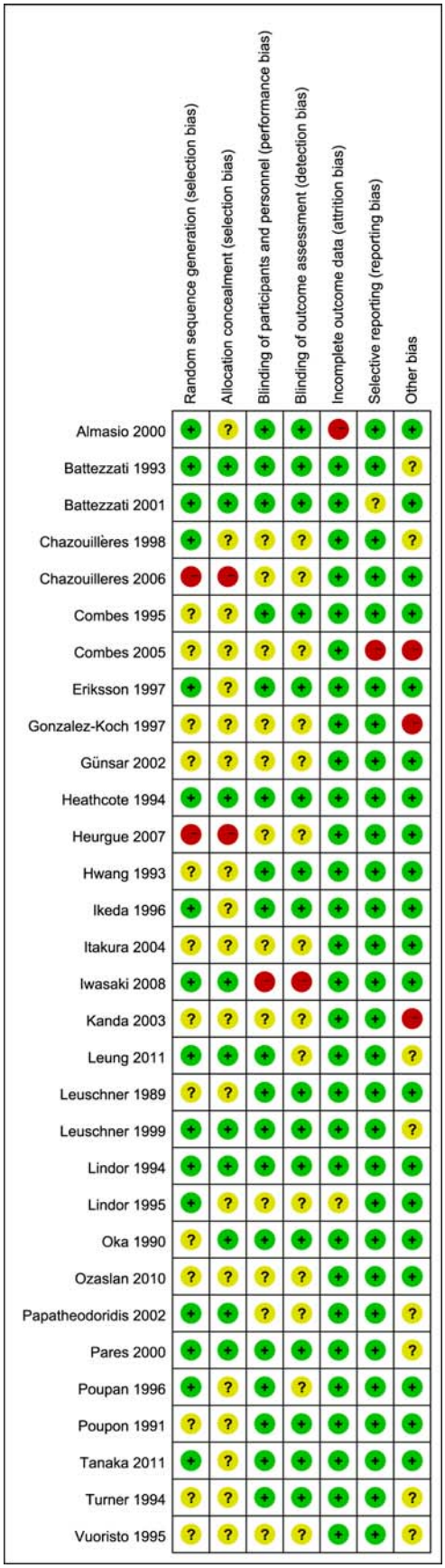
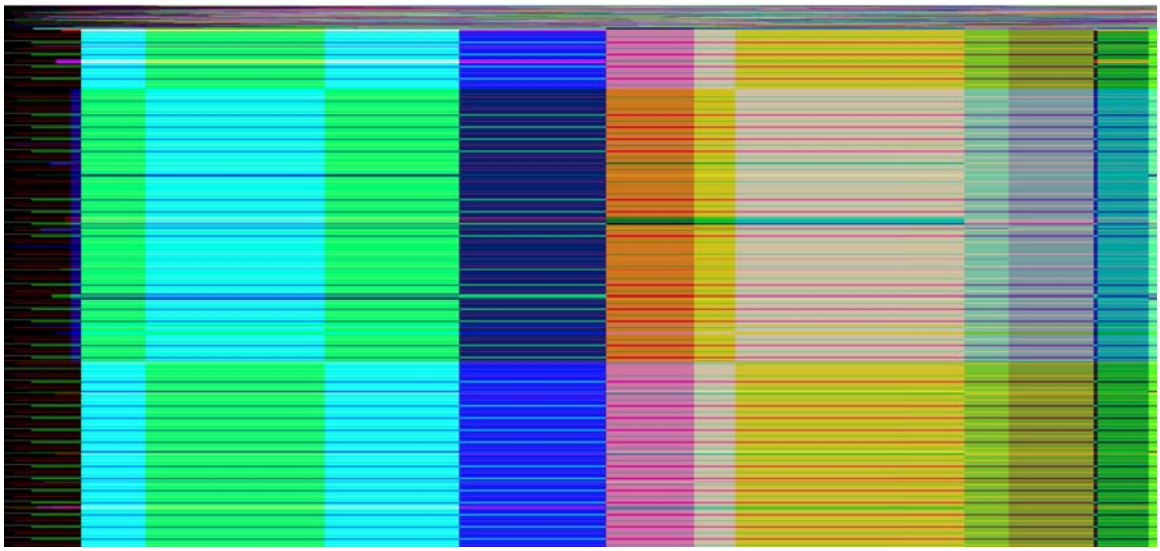
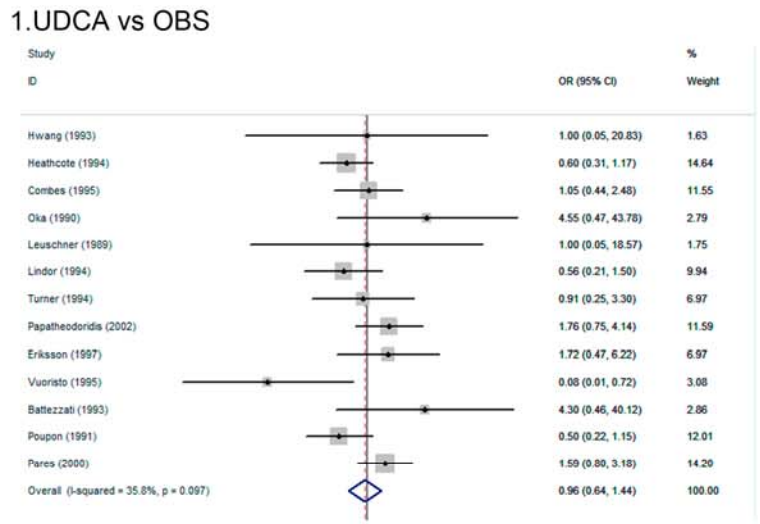
Supplementary 4. Summary for risk of bias of included randomized controlled trials. The green symbols represent low risk of bias, the yellow symbols represent unclear risk of bias, and the red symbols represent high risk of bias. The figure was generated using Review Manager Version 5.

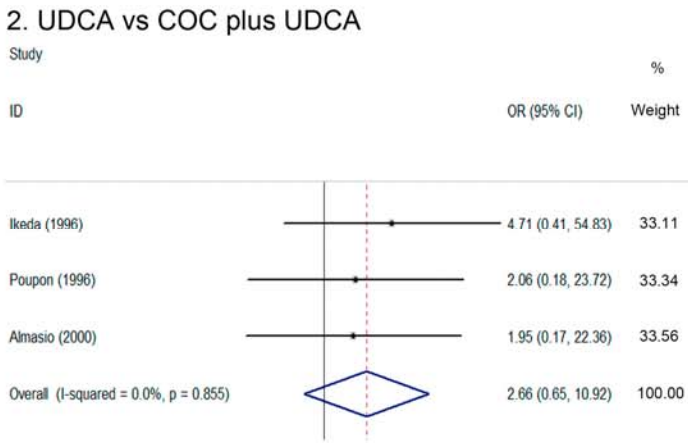

Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Almasio 2000
Battezzati 1993
Battezzati 2001
Chazouillères 1998
Chazouilleres 2006
Combes 1995
Combes 2005
Eriksson 1997
Gonzalez-Koch 1997
Günsar 2002
Heathcote 1994
Heurgue 2007
Hwang 1993
Ikeda 1996
Itakura 2004
Iwasaki 2008
Kanda 2003
Leung 2011
Leuschner 1989
Leuschner 1999
Lindor 1994
Lindor 1995
Oka 1990
Ozaslan 2010
Papatheodoridis 2002
Pares 2000
Poupan 1996
Poupon 1991
Tanaka 2011
Turner 1994
Vuoristo 1995

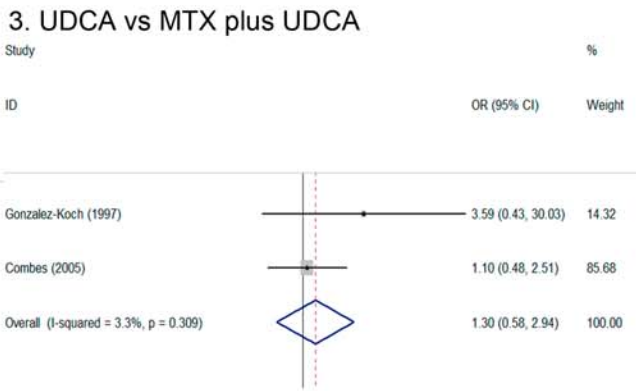
Supplementary 5. Forest plot of mortality or liver transplantation in traditional meta-analysis

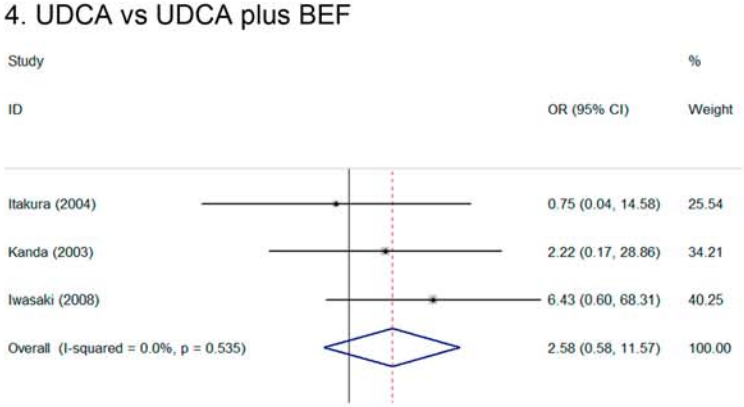


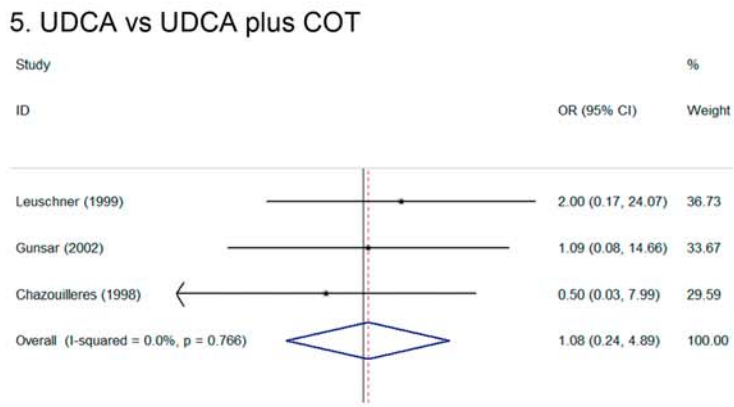
Supplementary 6. Forest plot of adverse events in traditional meta-analysis











Supplementary 7. Clinical efficacy and safety of all treatments according to network meta-analysis in the sensitivity analysis

A. Mortality or liver transplantation

COC plus UDCA	3.65 (0.17, 75.99)	1.02 (0.09, 11.13)	1.72 (0.10, 29.52)	1.36 (0.08, 22.83)
0.27 (0.01, 5.84)	COT plus UDCA	0.28 (0.04, 1.85)	0.48 (0.11, 1.87)	0.38 (0.10, 1.31)
0.98 (0.09, 11.23)	3.59 (0.54, 23.96)	MTX plus UDCA	1.69 (0.39, 7.39)	1.34 (0.34, 5.49)
0.58 (0.03, 9.79)	2.09 (0.54, 8.80)	0.59 (0.14, 2.55)	OBS	0.80 (0.46, 1.30)
0.74 (0.04, 11.83)	2.66 (0.76, 10.20)	0.75 (0.18, 2.94)	1.26 (0.77, 2.16)	UDCA

B. Adverse events

COC plus UDCA	0.59 (0.01, 25.27)	0.47 (0.01, 13.52)	0.55 (0.01, 12.89)	0.43 (0.01, 9.49)
1.70 (0.04, 159.17)	COT plus UDCA	0.80 (0.05, 11.86)	0.93 (0.11, 8.82)	0.71 (0.09, 6.14)
2.13 (0.07, 167.25)	1.26 (0.08, 18.79)	MTX plus UDCA	1.17 (0.21, 6.90)	0.91 (0.17, 4.85)
1.82 (0.08, 102.61)	1.08 (0.11, 9.37)	0.85 (0.14, 4.77)	OBS	0.78 (0.41, 1.38)
2.33 (0.11, 126.79)	1.41 (0.16, 11.39)	1.10 (0.21, 5.87)	1.28 (0.72, 2.46)	UDCA