Table 81: Clinical evidence profile: Comparison 1. UDCA versus placebo or control

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	UDCA	Placebo/control	Relative (95% CI)	Absolute		
Lack of normalisation of AST (follow-up 6 months)												
2 (Merli 1994, O'Brien	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	6/6 (100 %)	5/8 (62.5%)	RR 1.51 (0.83 to 2.78)	319 more per 1000 (from 106 fewer to	MODERATE	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	UDCA	Placebo/control	Relative (95% CI)	Absolute		
1992)										1000 more)		
								75%		382 more per 1000 (from 128 fewer to 1000 more)		
Lack of normalisation of ALT (follow-up 6 months)												
2 (Merli 1994, O'Brien 1992)	randomised trials[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	4/8 (50%)	3/4 (75%)	RR 0.69 (0.27 to 1.74)	233 fewer per 1000 (from 548 fewer to 555 more)	MODERATE	CRITICAL
								83.3%		258 fewer per 1000 (from 608 fewer to 616 more)		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	UDCA	Placebo/control	Relative (95% CI)	Absolute		
Lack of normalisation of GGT (follow-up 6 months)												
2 (Merli 1994, O'Brien 1992)	randomised trials1	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	2/6 (33.3 %)	2/4 (50%)	RR 0.6 (0.16 to 2.29)	200 fewer per 1000 (from 420 fewer to 645 more)	LOW	CRITICAL
								33.3%		133 fewer per 1000 (from 280 fewer to 430 more)		
Final bilirubin value (umol/l) (follow-up 6 months; Better indicated by lower values)												
1 (O'Brien 1992)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	6	6	-	MD 4 higher (3.72 lower to 11.72 higher)	LOW	CRITICAL
Percentage change in AST (follow-up 12 months; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	UDCA	Placebo/control	Relative (95% CI)	Absolute		
1 (Colombo 1996)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	serious[2]	none	15	12	-	MD -14 (-39.93 to 11.93)	LOW	CRITICAL
Percentage change in ALT (follow-up 12 months; Better indicated by lower values)												
1 (Colombo 1996)	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	serious[2]	none	15	12	-	MD -13 (-29.35 to 3.35)	LOW	CRITICAL
Percentage change in GGT (follow-up 12 months; Better indicated by lower values)												
1 (Colombo 1996)	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	serious[2]	none	15	12	-	MD -11.00 (-36.74 to 14.74)	LOW	
No development of liver disease (follow-up 6 months)												
1 (Merli 1994)	randomised trials1	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	11/11 (100%)	11/11 (100%)	Not calculable[5]	-	HIGH	CRITICAL
Liver failure (jaundice) (follow-up 12 months)												
1 (Colombo 1996)	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1/15	0/13	RR 2.62 (0.12 to 59.40)	Not calculable[6]	MODERATE	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	UDCA	Placebo/control	Relative (95% CI)	Absolute		
Liver transplantation (follow-up 12 months)												
1 (Colombo 1996)	randomised trials	serious[4]	no serious inconsistency	no serious indirectness	Not applicable		15 1 patient in the treatment group was withdrawn to receive transplantation	13	Not applicable	Not applicable	MODERATE	CRITICAL

Abbreviations: CFLD: ALT: alanine aminotransferase; AST: aminotransferase; cystic fibrosis liver disease; CI: confidence interval; GGT: gamma glutamyltransferase; MD: mean difference; RR: risk ratio

1 Merli (1994) used a cross-over study design

2 The quality of the evidence was downgraded by 1 because the 95% CI crossed 1 default MID.

3 The quality of the evidence was downgraded by 2 because the 95% CI crossed 2 default MIDs.

4 The quality of the evidence was downgraded by 1 due to lack of allocation concealment reporting.

5 RR not calculable - no development of liver disease in 11/11 participants who did not have CF related liver disease at entry in this cross-over trial.

6 Not calculable - 0 events in placebo arm.