**Appendix: Randomized Controlled Drug Trials in Intrahepatic Cholestasis in Pregnancy**

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| Author  | Year | Double-Blind | Number of Patients in Treatment Group (Number of Controls) | Dose of Drug (mg / day) | Duration of Treatment | Significant Symptomatic Improvement | Significant Biochemical Improvement | Reference |
| ***UDCA vs placebo***  |
| Diaferia | 1996 | √ | 8 (8) | 600 | 20 days | Yes | SBA, ALT, BR | 81 |
| Nicastri | 1998 | X | 8 (8) | 600 | 20 days | Yes | LFT, SBA | 85 |
| Palma | 1997 | √ | 8 (7) | 1000 | Until delivery | Yes | ALT, AST, BR | 86 |
| Glantz  | 2005 | √ | 47 (47) | 1000 | 21 days | **Yes**\* | ALT, BR, **SBA** | 88 |
| Liu  | 2006 | X | 34 (34) | 900 | 14 days | Yes\* | ALT, SBA | 84 |
| Chappell  | 2012 | √ | 56 (55) | 2000† | Until delivery | Yes\* | ALT, GGT, BR | 80 |
| Joutsiniemi  | 2013 | √ | 10 (10) | 450 | 14 days | Yes\* | ALT, SBA | 89 |
| ***SAMe vs placebo***  |
| Frezza  | 1984 | X | 6, 6 (6) | 200800 | Until delivery | Yes\* ‡ | ALT, BR, SBA‡ | 98 |
| Frezza  | 1990 | X | 15 (15) | 800 | Until delivery | Yes | ALT, BR, SBA | 97 |
| Ribalta | 1991 | √ | 9 (9) | 800 | 20 days | No\* | No | 99 |
| Nicastri | 1998 | X | 8 (8) | 800 | 20 days | Yes | LFT, SBA | 85 |
| ***Guar gum vs placebo*** |
| Riikonen | 2000 | √ | 24 (24) | 1500† | Until delivery§ | Equivocal | Equivocal | 103 |
| ***Dexamethasone vs placebo*** |
| Glantz | 2005 | √ | 36 (47) | 12 | 7 days | No\* | SBA, BR | 88 |
| ***UDCA vs SAMe***  |
| Floreani | 1996 | X | 10 (12) | UDCA – 450SAMe - 1000 | Until delivery | UDCA - Yes | UDCA - SBA | 82 |
| Nicastri | 1998 | X | 8 (8) | UDCA – 600SAMe - 800 | 20 days | UDCA = SAMe‖ | LFT, SBA | 85 |
| Roncaglia | 2004 | X | 24 (22) | UDCA – 600SAMe - 1000 | Until delivery | UDCA = SAMe\* ‖ | UDCA > SAMe – SBA, ALT, AST, BR¶ | 87 |
| Binder | 2006 | X | 26 (25) | UDCA – 750SAMe - 1000 | Until delivery | UDCA = SAMe‖ | UDCA > SAMe – ALT, AST, SBA¶ | 79 |
| ***UDCA vs dexamethasone*** |
| Glantz | 2005 | √ | 47 (36) | UDCA – 1000Dex - 12 | 21 days7 days | UDCA - Yes\*Dex - No | UDCA > Dex¶ | 88 |
| ***UDCA vs cholestyramine***  |
| Kondrackiene | 2005 | X | 48 (48) | UDCA – 8-10 mg/kgChol - 8000 | 14 days | UDCA > Chol\* ¶ | UDCA > Chol – ALT, AST, SBA¶ | 83 |
| ***UDCA & SAMe vs SAMe***  |
| Nicastri | 1998 | X | 8 (8) | UDCA – 600SAMe - 800 | 20 days | UDCA + SAMe > SAMe¶ | LFT, SBA | 85 |
| Binder | 2006 | X | 27 (25) | UDCA – 750SAMe - 1000 | 14 days | Yes | UDCA + SAMe > SAMe¶ | 79 |
| ***UDCA and SAMe vs UDCA (level of evidence)*** |
| Nicastri | 1998 | X | 8 (8) | UDCA – 600SAMe - 800 | 20 days | Yes | LFT, SBA | 85 |
| Binder  | 2006 | X | 27 (26) | UDCA – 750SAMe - 1000 | Until delivery | Yes | UDCA + SAMe > UDCA¶ | 79 |

UDCA, ursodeoxycholic acid; SBA, serum bile acids; ALT, alanine transaminase; BR, bilirubin; LFT, liver function tests; AST, aspartate transaminase; GGT, gamma glutamyl transfarase; SAMe, S-Adenosyl methionine; dex, dexamethasone; chol, cholestyramine.

Boldface type indicates effect only observed in women with severe ICP, ie serum bile acids > 40 μmol/L at inclusion to the study. Only articles in written in the English language and available on PubMed are shown in this table.

\*Studies that used visual analog charts to assess maternal pruritus.

†Maximum dose recorded in study.

‡Effect only observed with high dose SAMe treatment.

§Minimum duration of treatment was 10 days.

‖Equivalent effect in both of the drugs studied.

¶Greater effect in the first than the second drug.