**Supplemental Digital Content 1**

## Table. Overview of Publications Identified Evaluating PEBD Clinical Outcomes in PFIC Patients

| **Publication** | **Na** | **Liver Biochemistry Parameters Reportedb** | **Outcomes Reported** | **Responder Rate/Description** |
| --- | --- | --- | --- | --- |
| **Aggregate data, early response** |
| Ismail,19991 | 16 | ALT, BA, bilirubin  | Growth, histology, pruritus | * 12/16 responders (complete clinical and biochemical improvement)
* 2/16 partial responders
* 2/16 non-responders
* Biochemical improvement creates a bias toward liver biochemistry parameters
* Difficult to match bile acid levels to individuals; the group as such is regarded as “partial responders”
* Bilirubin levels are defined for 12 responders vs the rest; in the bilirubin analysis, data are therefore tabulated as responders and partial/non-responders
 |
| Melter,20002 | 6c | ALT, AST, BA, bilirubin, GGT  | Growth, liver function, pruritus, QoL | * 6/6 responders (complete responses within 1 week with respect to pruritus and jaundice)
 |
| Kalicinski,20033 | 20 | BA | Growth, pruritus | * 15/20 responders (pruritus and jaundice resolved)
* 3/20 partial responders
* 2/20 non-responders (required liver transplant)
* As a group, this was considered as a partial-responding group
 |
| Yang,20094 | 11 | ALT, ALP, AST, BA, bilirubin, GGT | Growth, pruritus, sleep, QoL | * 5/11 responders (no pruritus)
* 3/11 partial responders (mild pruritus)
* 3/11 non-responders (severe pruritus)
 |
| Halaweish,20105 | 7 | ALT, ALP, AST, bilirubin | Pruritus | * 6/7 responders (i.e. complete or near-complete resolution of pruritus and jaundice during the initial 6 months)
* Pruritus re-occurred later in some patients
* Defined as a partial-responding group
 |
| Schukfeh,20126 | 21c | ALT, AST, BA, bilirubin, GGT | Liver function, pruritus | * 13/21 responders (relief of pruritus and bile acid normalization)
* 8/21 non-responders
* Bias toward BA
* Defined as a partial-responding group
 |
| Jankowska,20167 | 26 | BA, bilirubin | Pruritus | * 18/26 responders (complete relief from pruritus and normalization of total bilirubin and BA)
* 8/26 non-responders
 |
| **Individual patient data, early response** |
| Whitington,19888  | 4 | ALT, ALP, BA, bilirubin | Growth, histology, pruritus, QoL  | * 4/4 responders (complete clinical remission from pruritus within 48 hours)
 |
| Ng,20009 | 3 | ALT, BA, bilirubin | Histology, pruritus | * 3/3 responders (resolution of pruritus)
 |
| Kurbegov,200310 | 3 | ALT, ALP, AST, bBA, bilirubin, GGT | Histology, pruritus, growth | * 3/3 responders (resolution of jaundice, pruritus, improved growth, morphological improvement)
 |
| Ekinci,200811 | 2 | ALP, BA, bilirubin, GGT | Pruritus | * 2/2 responders (pruritus ceased within 2 weeks, appetite and sleep improved)
 |
| Arnell, 200812,d | 12 | ALT, BA, bilirubin | Growth, histology, pruritus | * 7/12 responders (pruritus resolved)
* 2/12 partial responders
* 3/12 non-responders
 |
| Schukfeh,201413 | 2 | BA, bilirubin  | Pruritus | * 2/2 responders (total relief of pruritus within 6 weeks)
 |
| **Individual patient data, early response and/or long-term outcomes**  |
| Arnell,201014,d,e  | 12 | Data from Arnell, 2008 | Histology, LTX, death | * Used only for long-term outcomesd
* 11 patients followed for >5 years; 2 needed LTX or died
 |
| Emerick,200815 | 7 | ALT, BA, bilirubin | Histology, pruritus, LTX, death | * 4/7 responders (reduction in pruritus by 2 units or BA <40 µmol/L); 3/7 non-responders (pruritus change <1 unit or BA >40 µmol/L)
* 5 needed LTX or died
 |
| Davit-Spraul,201016 | 15 | BA | Histology, pruritus, LTX, death | * 4/15 responders (disappearance of jaundice and pruritus)
* 4/15 partial responders (disappearance of pruritus only)
* 7/15 non-responders (no effect on pruritus or jaundice)
* 6/15 had LTX and 2 were planned
 |

aN=number of PFIC patients for whom liver biochemistry data could be extracted; total N may be higher.

bNot all reported parameters could be included in this analysis due to limitations such as inability extract values or to link specific values to specific patients and/or outcomes.

c6/21 patients in Schukfeh 2012 were also reported in Melter 2000.

dArnell 2008 and Arnell 2010 report short- and long-term outcomes, respectively, for the same 12 individuals. Individual liver biochemistry parameter data were provided and used in the current analysis in agreement with the authors and with ethical approval.

eFor early outcomes and liver biochemistry parameters, see Arnell et al, 2008.12

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; BA, bile acids; bBA, biliary bile acids (not included in analysis of bile acids); GGT, gamma-glutamyl transferase; LTX, liver transplant; PEBD, partial external biliary diversion; PFIC, progressive familial intrahepatic cholestasis; QoL, quality of life.

**Supplemental Digital Content 2**

**Figure. Pre-PEBD Levels of Liver Biochemistry Parameters. A)** Individual pre-BEBD serum bile acid levels in 42 patients from 7 studies.8,9,11-13,15,16 **B)** Individual pre-PEBD serum bilirubin levels in 31 patients from 7 studies.8-13,15 **C)** Individual pre-PEBD ALT levels in 28 patients from 5 studies.8-10,12,15 Solid horizontal bars indicate the median value for each group; dotted horizontal lines indicate upper limit of normal. ALT, alanine transaminase; PEBD, partial external biliary diversion.



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