

Additional file 2: Table S2. Summary of published screening studies based primarily on biomarker analysis

| Reference | Study population | Design / observation period | Centres / countries | Screening method(s) | Patients identified, n/N (%)* |
|----------------------------|---|--|-------------------------------|---|--|
| Zhang et al. 2014 [46] | Children and adults with cholestasis/HSL or psychomotor regression/retardation N = 302 | Prospective observational / 2 years | Single centre / China | Oxysterol level (7-KC) NPC1/NPC2 sequencing [†] | Patients: 12 (4.0%) |
| Sheth et al. 2014 [48] | Patients with clinical features suggesting LSDs N = 1,110 | Prospective observational / 10 years | Multicentre/ International | Urine/plasma metabolic screen Filipin staining | Patients: 4 (0.4%) |
| Cebolla et al. 2015 [49] | Patients with NP-C N = 97 | Retrospective observational / NA | Single centre / Spain | Oxysterol level (7-KC) ChT, CCL18/PARC NP-C SI | Patients: NA |
| Reunert et al. 2016 [44] | Patients with suspected NP-C N = 1,800 | Prospective observational / 3 years | Single-centre / Germany | Oxysterol level (C-triol) NPC1/NPC2 sequencing [†] | Patients: 72 (4.0%) Carriers: 24 (1.3%) |
| Ribas et al. 2016 [45] | Patients with suspected NP-C N = 122 | Prospective observational / No period specified | Multicentre/ Brazil | Oxysterol level (C-triol) ChT Filipin staining | Patients: 12 (9.8%) |
| Polo et al. 2016 [56] | Neonates with cholestasis N = 7 | Prospective observational / No period specified | Multicentre / Italy | Oxysterol levels (7-KC, C-triol) | Patients: 1 (14.0%) |
| De Castro et al. 2017 [47] | Patients with ≥2 symptoms typically seen in NP-C N = 236 | Prospective observational / 2 years | Multicentre / Spain | ChT, CCL18/PARC NP-C SI NPC1/NPC2 sequencing [†] | Patients: 10 (4.2%) |

*n/N (%), number of cases detected per cohort or study over the total number of subjects in cohort/study (% based on n/N); [†]Sanger sequencing; HSL, hepatosplenomegaly; LSD, lysosomal storage disease; NA, not applicable; NR, not reported; SI, suspicion index.