Background and Aim
An international disease registry was started in September 2009 to evaluate the long-term disease course of NP-C in clinical settings.

Methods
Descriptive data from enrolment are presented for all patients with available data who were included in the Registry as of 19th August 2011.

Results
121 patients have been enrolled. The median (range) age at enrolment was 16.9 (0.9–56.6) years, age at onset of neurological manifestations was 8.2 (1–48.0) years (n=100), and age at diagnosis was 11.8 (0.1–53.9) years (n=110). A history of neonatal jaundice was recorded in 4/14 evaluable patients with early-infantile (EI) onset of neurological manifestations (at age <2 years; n=9), 6/21 (29%) with late-infantile (LI) onset (at 2 to <6 years; n=31), 6/21 (29%) with juvenile (JUV) onset (at 6 to <15 years; n=51), and 3/20 (15%) with adolescent/adult (AA) onset (at ≥15 years; n=29).

Mgltustat therapy at enrolment was recorded in 88/121 (73%) patients; mean (SD) exposure 1.69 (1.85) years (n=86). Neurological manifestations were observed in 71/84 (85%) patients: ataxia (71%), vertical gaze palsy (68%) and dystarthria (62%) were most frequent. Median (range) disability scores (0=normal; 1=worst) were: 0.0 (0.0–0.94) in EI (n=7), 0.29 (0.0–1.0) in LI (n=28), 0.41 (0.15–0.88) in JUV (n=28), and 0.29 (0.06–0.81) in AA-onset patients (n=26). A low proportion of patients had normal language, manipulation, ambulation, and/or swallowing.

Conclusions
Over two-thirds of this NP-C cohort had infantile or juvenile onset of neurological manifestations; neonatal jaundice was observed more frequently in these patients versus adolescent/adult-onset patients.

1036 GRACLE SYNDROME IN A TURKISH NEWBORN INFANT CAUSED BY A HOMOZYGOUS MUTATION (P99L) IN COMPLEX III ASSEMBLY FACTOR BCS1L

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Background and Aim
GRACLE syndrome, a neonatal, autosomal recessive disorder found in Finland, featuring growth retardation, aminoaciduria, cholestasis, iron overload, lactic acidosis and early death, is caused by a homozygous mutation (S78C) in BCS1L, the assembly factor for respiratory chain complex III. We investigated a newborn Turkish girl with similar symptoms. Her two sisters with low birth weight, metabolic acidosis, cholestasis and renal Fanconi syndrome, had died at 18 and 105 days age, respectively.

Methods and results
The girl was born to healthy nonconsanguineous parents. She was growth retarded (1789 g at term), developed tachypnea and metabolic acidosis on day one. Lactic acidosis, jaundice with direct hyperbilirubinemia, non-specific aminoaciduria, high phosphaturia, proteinuria and glucosuria were detected. Serum iron (190 mcg/dl), ferritin (2819 ng/ml) and transferrin saturation (99.4%) were increased. Metabolic, cardiologic and sonographic workup were otherwise normal. Because of similarities with GRACLE syndrome, the BCS1L gene was investigated. The Finnish SNP was not found, but gene sequencing revealed a homozygous mutation resulting in an amino acid exchange (P99L) in the protein.

Conclusions
The studied infant had a GRACLE-like disorder caused by a different mutation than that in newborns of Finnish ancestry. Most likely the two deceased siblings had the same homozygous BCS1L mutation that previously has been published in three other newborns or Turkish origin. We proposed that P99L-mutation in BCS1L is a Turkish genotype resulting in GRACLE syndrome phenotype, and should be investigated in Turkish newborns with the typical clinical features.