007  
Sustained response following withdrawal of guselkumab treatment with reduced Th17 and Th22 effector cytokine levels

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Guselkumab (GUS) is a human therapeutic antibody targeting IL-23, a key driver of pathogenic Th17 and Th22 cytokines (PSO). VOYAGE 2 is a Phase 3 study that investigated the efficacy of GUS in moderate-to-severe PSO and included a randomized withdrawal experiment. We explored the potential association of serum biomarkers and clinical parameters with response following treatment withdrawal. Subjects initially randomized to GUS who achieved ≥ 20% improvement vs baseline in the PASI Area and Severity Index (PASI 90) response at WK 28 were re-randomized to either continue GUS (n = 193) or withdraw from GUS (n = 182). Serum biomarkers were evaluated at baseline, WK 28 and then every 4 WK through the completion of the 52 WK post-treatment period. Each diagnosis was confirmed by reviewing the medical records and 10 matched non-F1 control persons per FN1 patient were collected from Population Registry Centre of Finland. FN1 patients and controls were included in the Medical Birth Register and the Register of Congenital Abnormalities. Odds ratios (OR) and 95% confidence intervals (CI 95%) were calculated for having major or congenital malformations (major IFI = 0.08). In addition, the SIR of FN1-child was almost threefold (adjusted OR 2.92, CI 95% 1.80-4.72) compared to matched controls. Children with FN1 had significantly increased risk of congenital malformations of the central nervous system (adjusted OR 3.73, CI 95% 1.88-7.43), urinary (unadjusted OR 5.35, CI 95% 1.86-15.37) and musculoskeletal (adjusted OR 2.77, CI 95% 1.13-6.77) systems. In conclusion, abnormalities of the eye, ear, head and neck of FN1 children were more common than among controls (adjusted OR 4.66, CI 95% 1.42-13.11). Non-FN1 children of mothers with FN1 did not have more malformations than controls (adjusted OR 0.53, CI 95% 0.13-2.21). Children with FN1 have more congenital malformations than controls and close follow-up during the pregnancy and neonatal period is required if the parent has FN1. Healthy children of mother with FN1 do not have an increased risk for malformations.

008  
Congenital anomalies in neurofibromatosis 1: A retrospective register-based total population study

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Neurofibromatosis type 1 (NF1) is a dominantly inherited disorder caused by mutations in NF1 gene on chromosome 17. NF1 has been connected to congenital malformations, for example in the skeletal and cardiovascular systems, but overall incidence of the anomalies has been unknown. In this register-based, total population register study conducted in Finland, we evaluate congenital malformations in NF1. A total of 1,410 patients with NF1 was identified by searching inpatient and outpatient hospital visits of patients with associated diagnosis. Data were retrieved by reviewing the medical records and 10 matched non-F1 control persons per FN1 patient were collected from Population Registry Centre of Finland. FN1-patients and controls were included in the Medical Birth Register and the Register of Congenital Abnormalities. Odds ratios (OR) and 95% confidence intervals (CI 95%) were calculated for having major or congenital malformations (major IFI = 0.08). In addition, the SIR of FN1-child was almost threefold (adjusted OR 2.92, CI 95% 1.80-4.72) compared to matched controls. Children with FN1 had significantly increased risk of congenital malformations of the central nervous system (adjusted OR 3.73, CI 95% 1.88-7.43), urinary (unadjusted OR 5.35, CI 95% 1.86-15.37) and musculoskeletal (adjusted OR 2.77, CI 95% 1.13-6.77) systems. In conclusion, abnormalities of the eye, ear, head and neck of FN1 children were more common than among controls (adjusted OR 4.66, CI 95% 1.42-13.11). Non-FN1 children of mothers with FN1 did not have more malformations than controls (adjusted OR 0.53, CI 95% 0.13-2.21). Children with FN1 have more congenital malformations than controls and close follow-up during the pregnancy and neonatal period is required if the parent has FN1. Healthy children of mother with FN1 do not have an increased risk for malformations.