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

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Guselkumab (GUS) is a human therapeutic antibody targeting IL-23, a key driver of patho-
genic T cells in chronic plaque psoriasis (PSO). VOYAGE 2 is a Phase 3 study that evaluated
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 pa-
rameters with response following treatment withdrawal. Subjects initially randomized to
GUS who achieved >20% improvement from baseline to week 48 were randomized to
receive GUS or placebo for 24 weeks. Clinical parameters evaluated at each diagnosis
and treatment were disease duration, body mass index (BMI), baseline body surface area
and PASI score, and GUS pharmacokinetic parameters. PASI 90 response was better maintained at WK 48 in the continuous
maintenance group compared to the withdrawal group (p < 0.001). However, sustained ef-
ficacy through 24 weeks after the last dose of GUS was observed (p < 0.001). Clinical outcomes
were treated with at least one dose of secukinumab and FAE and week 24 assessments
were responders if they were responders at the time of drop-out. Moderate psoriasis was
under consideration as a new treatment goal. As an alternative for long-term management,
we evaluate congenital malformations in NF1. A total of 1,410 patients with NF1 was ac-
quired by searching inpatient and outpatient hospital visits of patients with associated
diagnoses, confirmed by reviewing medical records. Excluding 10 and 10 matched non-NF1 control patients per NF1-patient were collected from Population Regis-
ter Centre of Finland. NF1-patients and controls were included to the Medical Birth Regis-
ter and the Register of Congenital Anomalies. Odds ratios (OR) and 95% confidence intervals (CI 95%) for having major congenital malformations were calculated. The SIR of NF1-
child was almost threefold (adjusted OR 2.92, CI 95% 1.80-4.72) compared to matched
controls. Children with NF1 had significantly increased risk of congenital malformations
(circulatory (adjusted OR 3.73, CI 95% 1.88-7.43), urinary (unadjusted OR 5.35, CI 95% 1.86-15.73) and muscoskeletal (adjusted OR 2.77, CI 95% 1.13-6.77) systems). In addition,
the anomalies of the eye, ear, head and neck of NF1-children were more common than
among control persons (adjusted OR 4.66, CI 95% 1.42-15.31). Non-NF1 children of mothers
with NF1 did not have more malformations than controls (adjusted OR 0.53, CI 95% 0.13-
2.21). Children with NF1 have more congenital malformation than controls and close follow-
up during the pregnancy and neonatal period is required if the parent has NF1. However,
healthy children of mother with NF1 do not have an increased risk for malformations.