

Highlights from

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Long-term use of topical calcineurin inhibitors is safe in children with atopic dermatitis

An observational study including more than 44,000 patient-years of follow up showed that there is no increased cancer risk in children with atopic dermatitis (AD) that use topical calcineurin inhibitors.

“AD is a chronic disease requiring long term treatment. Therefore, we need prospective safety studies to evaluate cancer risk”, said Prof. Regina Fölster-Holst (University Clinic Schleswig-Holstein, Germany). APPLES™ (A Prospective Pediatric Longitudinal Evaluation to Assess the Long-Term Safety of Tacrolimus Ointment for the Treatment of Atopic Dermatitis) is an international observational study designed to address the possibility of increased lymphoma or other cancer risk in patients treated long-term with topical calcineurin inhibitors. Children with AD were eligible if they had exposure to topical tacrolimus for at least 6 weeks, and the first exposure was before the age of 16. Patients were observed over 10 years under actual-use conditions, with regular clinic visits and completion of questionnaires by the patients or their parents/caregivers. “Data were collected regularly, but it was still an observational study”, emphasised Prof. Fölster-Holt. The primary outcome was occurrence of any malignancy. In addition, incidence of lymphoma or cutaneous malignant melanoma were assessed. Standardised incidence ratios for cancer events were compared to sex-, age-, and race-matched background population data from national cancer registries.

Between May 2005 and August 2012, APPLES enrolled 7,954 eligible patients at 314 sites in 9 North American or European countries. After this time, the FDA endorsed an early stop in 2019 due to futility of continuation: They thought it unlikely that continued observations could alter the study findings.

Most patients suffered from moderate to severe AD, the majority also had other atopic diseases. Median study persistence was 6.4 years, with 14.7% of patients remaining on-study for ≥ 10.0 years. During this time, 6 cases of cancer occurred, but not lymphoma. There was no difference in cancer incidence to the matched background population data. “Even if we higher the hypothetical incidence to 2.5, the cancer incidence would remain non-significantly elevated over the expected background population rate”, said Prof. Fölster-Holt.

1. Fölster-Holst R. No increased risk of cancer in children using topical tacrolimus for atopic dermatitis: A 10-year prospective cohort study. Late-breaking abstract D3T01.1J. EADV 2019. Oct. 9-13, Madrid, Spain.