Background

The MAPK pathway, is a signal transduction pathway involved in the oncogenesis of a variety of pediatric tumors. The clinical use of BRAF inhibitors and MEK inhibitors is increasingly used in oncology practice. The toxicity profile of these drugs in the pediatric population, particularly in relation to development, growth and sexual maturation remains insufficiently studied.

Procedure

This study includes 22 pediatric patients with molecularly confirmed MAPK pathway driven tumors treated with MEK or BRAF between August 2014 and March 2020. Throughout treatment they underwent regular laboratory, endocrine, cardiac, ophthalmic and dermatologic evaluation. Toxicity was recorded and evaluated according to CTCA v4.

Results

Overall an adverse event frequency of 86% was encountered. Dermatological disorders accounted for 68% of the adverse events. Overall 8 patients suffered from severe adverse events including Erythema Nodosum, PLEVA-like rash, osteoporosis, Sarcoid-like massive lymphadenopathy, retinal toxicity and elevated liver enzymes & CPK. Four patients discontinued treatment as a result of adverse events. In this cohort we did not encounter any treatment-related abnormalities of sexual maturation or gonadal function nor statistically significant growth retardation, however a slower than expected growth rate was observed in one patient. In addition dose-dependent, non-symptomatic and within normal range for age decreased cardiac SF% was noted in two patients treated with MEK inhibitor.

Conclusion

Treatment with BRAF and MEK inhibitors was shown to be generally safe, we report drug tolerability of 82%. However, further prospective studies should be preformed to are characterize the full scope of side effects in the pediatric population.