Vemurafenib provides a rapid and robust clinical response in paediatric Langerhans cell histiocytosis with the BRAF V600E mutation but does not eliminate low-level minimal residual disease based on ddPCR using cell-free circulating DNA

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Abstract

Background Langerhans cell histiocytosis (LCH) involves abnormal proliferation of Langerhans cells (LC), which is typically driven by the BRAF V600E mutation. High-risk LCH has a poor prognosis. Procedure Fifteen children (5 girls, 10 boys) with BRAF V600E+ LCH received vemurafenib (initial dose median 40 mg/kg/day, range: 11–51.6 mg/kg/day) between March 2016 and February 2020. All patients had previous received LCH-directed chemotherapy. The median age at LCH onset was 2 months (range: 1–28 months) and the median age at the start of vemurafenib treatment was 22 months (range: 13–62 months). The median disease activity score (DAS) at the start of vemurafenib treatment was 12 points (range: 2–22 points). Results The median duration of vemurafenib therapy was 29 months (range: 2.4–45 months). All patients responded to treatment, with median DAS values of 4 points (range: 0–14 points) at week 4 and 1 point (range: 0–3 points) at week 26. Toxicities included skin/hair changes (93%) and non-significant QT prolongation (73%). Two patients died, including 1 patient who experienced hepatic failure after NSAID overdose and 1 patient who developed neutropenic sepsis. Electively stopping vemurafenib treatment resulted in relapse in 5 patients, and complete cessation was only possible for 1 patient. Digital droplet PCR for BRAF V600E using cell-free circulating DNA revealed that 7 patients had mutation statuses that fluctuated over time. Conclusion Our study confirms that vemurafenib treatment is safe and effective for young children with BRAF V600E+ multisystem LCH. However, treatment using vemurafenib does not completely eliminate the disease.

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