CAN LANGERHAN'S CELL HISTIOCYTOSIS PATIENTS IN EUROPE HAVE UNINTERRUPTED LONG-TERM ACCESS TO MAPK-INHIBITORS? RESULTS OF THE EUROPEAN CONSORTIUM FOR HISTIOCYTOSES (ECHO) GROUP SURVEY

V. Tsinopoulos[1], V. Tzotsola[1], E. Sieni[2], T. Nguyen[3], A. Raciborska[4], J. Donadieu[5], M. Minkov[6], V. Papadakis[1]

[1]Department of Pediatric Hematology-Oncology, Agia Sofia Children's Hospital, Marianna V Vardinoyanni-ELPIDA Children's Oncology Hospital, Athens, Greece
[2]Pediatric Hematology-Oncology Department, Meyer Children's Hospital IRCCS, Florence, Italy
[3]Department of Pediatric Hemato Oncology, Great Ormond Street Hospital London, UK
[4]Mother and Child Institute, Department of Oncology and Surgical Oncology for Children and Youth, Warszawa, Poland
[5]French Reference Center for Langerhans Cell Histiocytosis, Trousseau Hospital, Paris, France
[6]St Anna Kinderspital, Department of Pediatrics, Medical University of Vienna, Austria

Introduction: Langerhans cell histiocytosis (LCH) is driven by alterations in the MAPK pathway in most patients, and MAPK inhibitors (MAPKi) have become an important treatment option, particularly for relapsed or refractory disease. Despite this, access of MAPKi for LCH patients may vary considerably among countries. We aimed to investigate access and availability of MAPKi for LCH across ECHO countries.

Methods: A structured questionnaire was built and delivered for completion by selected country leading physicians, involved in LCH management. Questions covered physician and country characteristics, access to MAPKi, clinical indications, available medications, clinical trials, off-label approval and reimbursement pathways, previous treatment experience, long-term feasibility, reporting requirements and registries. Responses were analyzed descriptively.

Material: Twenty-four physicians from 20 countries were included. The respondents were predominantly pediatric LCH physicians, and most had extensive experience in LCH management.

Results: MAPKi use for LCH patients was reported feasible by 23/24 respondents (95.8%). The most frequently reported indication was refractory disease (23/24), followed by relapsed disease (16/24), neurodegenerative LCH (16/24) and poor response to first-line therapy (15/24). Severe disease at initial diagnosis was reported as an indication by 9/24 respondents. Two active MAPKi clinical trial was reported by 2/24 respondents. Vemurafenib, dabrafenib and trametinib were most commonly available through routine practice and/or

off-label use. The most frequent routes for off-label access were national insurance approval and local hospital approval (9/24 each). State insurance was the main funding source (15/24). The vast majority of the families do not pay for MAPKi out of pocket. Previous MAPKi treatment experience was reported by 22/24 respondents. Long-term treatment was indeed considered highly feasible, with 20/24 respondents rating feasibility at 9–10/10. However, renewal procedures, reporting requirements and registry availability varied greatly among countries.

Conclusions: Despite previous negative perceptions, MAPKi can be available for use in most participating ECHO countries for LCH patients. Access depends on off-label approval local or national and there are different reimbursement arrangements, covering most patients. Greater consistency in approval and funding pathways, together with better coordination of treatment protocols, registries and reporting, could make access more predictable and equitable for the benefit of children with LCH.