ID 145749: OPTIMISING MANAGEMENT AND OUTCOMES OF ACTIVATED PHOSPHOINOSITIDE 3-KINASE DELTA SYNDROME (APDS) IN SPAIN: BEWAYAPDS PROJECT

BACKGROUND AND OBJECTIVES

- Activated phosphoinositide 3-kinase delta syndrome (APDS) is a hereditary ultra-rare disease resulting from pathogenic genetic variants that cause hyperactivity of the PI3Kδ enzyme, leading to a heterogeneous primary immune regulatory disorder characterised by both immunodeficiency and immune dysregulation (1-5)
- There is currently no approved pharmacological treatment for APDS in Europe, and the management of the disease relies on symptomatic treatment without standardised clinical practice guidelines or protocols in Spain, culminating in variability in patient care across different regions and healthcare settings that can impact on patient health status and quality of life (QoL). Leniolisib has been recently approved in the UK.
- The objectives of this study are to ascertain the current care pathway identifying unmet needs, challenges and opportunities in the management of APDS in Spain and to propose an actionable patient care roadmap to improve patients' care and health outcomes.

METHODOLOGY

Literature review to identify and synthesize current pathway, challenges, and unmet needs in the management of APDS patients in Spain, Constitution of a multidisciplinary expert panel of 12 Spanish experts (including clinicians, hospital pharmacists, primary care physicians, hospital managers, nurses and patients' representatives) from 10 different centres spread across 6 regions. Design of the patient pathway proposal identification of challenges and proposed solutions based on individual interviews, group discussion and consensus.

RESULTS

APDS PATIENT PATHWAY PROPOSAL

An APDS Patient pathway proposal was designed and structured into 3 main sections and 9 sub-sections (Figure 1). The first section corresponds to diagnosis, including diagnostic suspicion, referral to specialist and definitive diagnosis. The second section refers to short-term management, including initial treatment, short-term follow-up and treatment discontinuation/change. Finally, the last section relates to long-term management including complications management, HSCT and long-term follow-up.

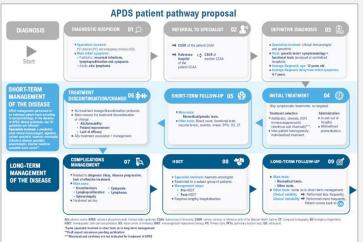


Figure 1: APDS patient pathway proposal

CHALLENGES IDENTIFIED AND SOLUTIONS PROPOSED

- Along the APDS patient pathway, key challenges affecting patient outcomes and impacting quality of life were identified by the experts, including lack of neonatal screening programs, limited awareness/training of primary care resulting in delayed diagnosis, lack of guidelines/protocols resulting in heterogenicity of approaches across centres, lack of a disease modifying treatment (Figure 2).
- Recommendations from the experts included disease training and development artificial intelligence tools for primary care could contribute to earlier suspicion and referral for final diagnosis. Generation of protocols/guidelines derived from the proposed pathway could help standardise management, from diagnosis to long-term, ensuring best evidence-based practices improving clinical outcomes. Experts recommended implementation of multidisciplinary teams, and the inclusion of patient perspective as key elements to improve clinical management. Early diagnosis in the symptomatic phase at national level to prevent disease progression would be also recommended, as well as improving patient support at time of diagnosis (since the diagnosis of this chronic disease with a high impact on patient lifestyle represents an important psychological burden for the patient) (Figure 2).

- DIAGNOSIS. The suspicion of diagnosis typically begins in Primary Care or Emergency Departments. Normally, main initial symptoms for paediatric patients include recurrent respiratory infections, lymphoproliferation and cytopenia. For adults, main indicators for suspicion also includes lymphoma. Following suspicion, patients are referred to hospital specialists at regional reference hospitals or, if available, designated CSUR (reference centre, service or unit) hospitals. Diagnosis of APDS is generally confirmed by an immunologist, in collaboration with a geneticist, through genetic and occasionally functional testing. The average diagnostic age is 12 years old with an average diagnosis delay from initial symptoms of 4-7 years.
- SHORT-TERM MANAGEMENT. The specialties involved include a paediatric/adult clinical immunologist. digestive system specialist, haemato-oncologist, infectious disease specialist, pneumologist, internal medicine specialist and a nurse. Initial treatment focuses on symptom management, administered either at home or in hospital depending on the treatment method. During the first months of treatment, the shortterm follow-up includes the performance of a range of biomedical tests based on general IEI recommendations (blood count, enzyme level, immunoglobulins, among other) to evaluate disease control. If safety issues arise or there is insufficient improvement, treatment may be adjusted or discontinued.
- LONG-TERM MANAGEMENT. Same healthcare specialties as in the short-term management are involved at this stage. As treatment progresses, complications from diagnostic delays or disease progression may necessitate tailored interventions. In specific cases, haemato-oncologists might consider haematopoietic stem cell transplantation (HSCT), the only potentially curative option for APDS, acknowledging its associated risks and long-term hospitalisation requirements. Routine controls with biomedical tests ensure monitoring for complications, guiding necessary treatment adjustments.



Figure 2: Challenges identified and solutions proposed

CONCLUSIONS

APDS is an ultra-rare complex disease. This project represents the first APDS patient pathway proposal in Spain, identifying key challenges linked to patient management across the healthcare system defining the patient pathway and making recommendations for its practical implementation. Execution of proposed actions within Spanish hospitals could effectively contribute to the achievement of key clinical objectives and positively impact health outcomes for APDS patients in Spain.

REFERENCES

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