Emerging patterns in the clinical development of medicines in paediatric oncology

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INTRODUCTION

Understanding the patterns in clinical development of paediatric oncology medicinal products may facilitate the approval of safer and more effective medicines to treat children with cancer.

AIMS

To review clinical development programs (CDPs) of paediatric oncology medicinal products for acute lymphoblastic leukaemia (ALL) to identify emerging patterns.

METHOD

The methodology consisted of 2 phases (Fig 1)

• Phase 1: CDPs for authorised products and drugs in the development phase were retrieved from European public assessment reports, Paediatric Investigation Plans and clinical trials registered in the EU clinical trial register and the United States national library of medicine database of clinical trials. CDPs were analysed and compared based on the number, type and design of studies, and the endpoints used.

• Phase 2: Prospective treatment protocols for paediatric ALL were proposed to understand the potential impact that drugs in the development phase could have on clinical practice. The drug category and line of therapy was described for each authorised and prospective product.

RESULTS

• Nine centrally authorised products (7 small molecules and 2 biologicals) indicated to treat paediatric ALL were identified (Table 1).

• The CDPs supporting the authorisation of products varied from extensive (10 adult trials, 2 paediatric studies and 1 pharmacokinetic modelling study) for products applying for first line indications through full applications to minimal (1 adult and 1 paediatric trial) for products seeking third line indications under exceptional circumstances.

• Thirty-five prospective products are in phase II and phase III development: small molecules (17 products including 2 novel liposomal formulations), advanced therapy medicinal products (9 ATMPs), biologicals (7 products including 2 novel PEGylated or erythrocyte-encapsulated formulations) and antibody drug conjugates (2 products).

• Prospective products for de novo ALL will be used as add-on therapies to conventional chemotherapeutic backbone while monotherapy with ATMPs and antibody-drug conjugates is explored to improve cure rates in relapsed or refractory paediatric patients.

CONCLUSION

CDPs are based on the application method chosen by companies and the indication sought. Small molecules were observed to be the most frequent drug category in development and included new formulations of established products. Drugs presently in the development phase should not significantly alter first line ALL treatment protocols in children that were established in past large scale clinical trials.