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Creating a unique, multi-stakeholder Paediatric Oncology Platform to improve drug development for children and adolescents with cancer

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Abstract Seven years after the launch of the European Paediatric Medicine Regulation, limited progress in paediatric oncology drug development remains a major concern amongst stakeholders – academics, industry, regulatory authorities, parents, patients and caregivers. Restricted increases in early phase paediatric oncology trials, legal requirements and

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Paediatric Investigation Plan
Precompetitive development
Long-term follow up

regulatory pressure to propose early Paediatric Investigation Plans (PIPs), missed opportunities to explore new drugs potentially relevant for paediatric malignancies, lack of innovative trial designs and no new incentives to develop drugs against specific paediatric targets are some unmet needs. Better access to new anti-cancer drugs for paediatric clinical studies and improved collaboration between stakeholders are essential. The Cancer Drug Development Forum (CDDF), previously Biotherapy Development Association (BDA), with Innovative Therapy for Children with Cancer Consortium (ITCC), European Society for Paediatric Oncology (SIOPE) and European Network for Cancer Research in Children and Adolescents (ENCCA) has created a unique Paediatric Oncology Platform, involving multiple stakeholders and the European Union (EU) Commission, with an urgent remit to improve paediatric oncology drug development. The Paediatric Oncology Platform proposes to recommend immediate changes in the implementation of the Regulation and set the framework for its 2017 revision; initiatives to incentivise drug development against specific paediatric oncology targets, and repositioning of drugs not developed in adults. Underpinning these changes is a strategy for mechanism of action and biology driven selection and prioritisation of potential paediatric indications rather than the current process based on adult cancer indications. Pre-competitive research and drug prioritisation, early portfolio evaluation, cross-industry cooperation and multi-compound/sponsor trials are being explored, from which guidance for innovative trial designs will be provided.

1. Introduction

Childhood and adolescent cancers remain a major cause of morbidity, mortality and social concern in Europe [1–3] with 3000 children and adolescents dying of cancer each year [4]. In the developed world, although 80% of children survive cancer, they may suffer long-term effects from their treatment [5] and approximately 20% of patients will die of their disease or of disease-related causes; as such paediatric cancer remains the number one non-accidental cause of death in children and adolescents [6]. Improvements to all standards of paediatric cancer care and a focus on incurable diseases are urgently needed, entailing fresh approaches to the many complex aspects of treating childhood cancers, including faster introduction of new medicines for children into front-line care, innovations in study design and drug development and collaboration between stakeholders. Additionally, as new drugs are introduced, it is imperative for childhood cancer survivors to have long-term follow up (LTFU) into adulthood to collect data on the later effects of childhood treatment for cancer [2].

The European Paediatric Regulation [7] provides the regulatory framework for drug development for children and adolescents with cancer. It aims to increase availability of authorised medicines for children through generation of safety and efficacy data and high-quality ethical paediatric clinical research, and to produce better information on paediatric medicines, in general. Overcoming off-label use by developing and making available new, age-appropriate paediatric medicines is also within the Regulation's remit.

The Paediatric Regulation stipulates that pharmaceutical companies propose and comply with a Paediatric Investigation Plan (PIP) before seeking marketing authorisation (MA) for a new medicine (or variation of an existing MA). Completed PIPs are rewarded with a six-month extension of the medicine's Supplementary Protection Certificate (SPC) or, in the case of orphan-designated medicines, a 2-year extension of the 10-year market exclusivity for the authorised indication.

Despite significant changes in paediatric oncology drug development in the years after the Regulation came into force in 2007 and an increase in the total number of PIPs filed, frustration remains amongst all stakeholders at the seemingly slow speed of progress [8]. The lack of a unified driving force to facilitate coherent actions for further change and progress has become apparent. A lack of increase in early phase paediatric oncology trials in Europe compared with the United States (US), growing regulatory requirement to propose PIPs early in drug development, missed opportunities to explore efficient drugs in development for adults that may be relevant for paediatric malignancies, lack of innovation in trial designs and limited incentives to develop drugs against specific paediatric targets continue to be areas of significant concern for paediatric drug developers across academia, industry, regulatory authorities, and importantly, amongst patients, parents and caregivers.

To address these concerns and promote progress, two-yearly Paediatric Oncology Workshops were initiated in 2011 by the Cancer Drug Development Forum (CDDF, previously the Biotherapy Development Association (BDA)) along with the European consortium for Innovative Therapies for Children with Cancer (ITCC), and the European Society for Paediatric Oncology (SIOP Europe) [1], within the framework of the European Network for Cancer Research in Children and Adolescents (ENCCA). The ITCC consortium was created in 2003 to develop early evaluation of new