ICR The Institute of Cancer Research

Early-stage clinical trials of cancer drugs for children

Position Statement from

The Institute of Cancer Research, London

Summary

The Institute of Cancer Research (ICR) believes the way in which the EU Paediatric Regulation is implemented is denying children access to the latest cancer drugs. We believe the EU's system of paediatric investigational plans (PIPs) needs to be revised to ensure cancer drugs developed for adults are also tested in children whenever their mechanism of action suggests they could be effective. The ICR also believes there need to be improved financial incentives for developing drugs specifically for children, and new collaborative models of funding involving Government, academic, charities and industry. Where clinically appropriate, adult cancer trials should be much more open to accepting adolescent cancer patients.

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Background information

There is a shortage of early-stage clinical trials testing new cancer drugs in children, and this acts as a major barrier to efforts to improve survival rates from paediatric cancers. Few cancer drugs are developed specifically for children, and when drugs are developed for adults, they are often either not tested in children at all, or not for some years afterwards. The lack of paediatric cancer trials restricts or delays access for children to the latest drugs, some of which could be of significant benefit to them.

International clinical trials have significantly improved patient survival in childhood cancers. The EU Paediatric Regulation, which came into force in 2007, has been a step forward in getting more drugs into paediatric early-stage clinical trials. As part of the legislation, if the drug may be suitable for children, pharmaceutical companies are obliged to develop a paediatric investigational plan (PIP) describing how the drug will be studied for potential paediatric use, before they can gain a marketing authorisation for the drug in adults. It is a significant commitment for companies to prepare these documents, particularly if the drug is only suitable for a very small patient population, and so as an incentive companies are given an additional six-month market exclusivity for submitting a new marketing authorisation application based on data from a completed PIP. However, companies are able to gain a waiver from having to prepare and carry out a PIP, if the product is unlikely to be effective or safe, if it does not represent a significant therapeutic benefit over existing treatments or if the disease the drug targets does not occur in children. In practice, many adult cancers do not have direct equivalents in children, and as a result companies have often been granted waivers exempting them from testing their drugs in children – even though many have mechanisms of action that could be effective against other types of children's cancer.

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Key ICR positions on early-stage clinical trials of cancer drugs for children

- The ICR would like to see an expansion of early-stage paediatric clinical trials in order to accelerate development of safe, effective, innovative treatments for children. Paediatric cancer medicine needs to incorporate advances seen in adult cancer treatments such as molecularly targeted drugs and the use of biomarkers, and this can only occur through more trials.

- The ICR believes the way in which EU Paediatric Regulation, is implemented is delaying and in many instances denying children access to the latest cancer drugs. The ICR is supportive of the Paediatric Regulation, which has been a significant step forward in increasing numbers of clinical trials for children, but believes the PIP process now needs to be revised to deliver further benefits. Pharmaceutical companies are currently given class waivers from testing potentially important cancer drugs in children because the drugs are being registered for adult cancers that do not occur in children – even though the drugs may work in a way that could be effective against paediatric cancers. We support replacing the class waiver system with one that looks at the mechanism of action of the drug and feel this single change would have the greatest impact on increasing access to clinical trials for children and adolescents.

- The ICR believes that orphan drug designation has not proved effective at providing financial incentives for companies to develop drugs solely for paediatric cancers. No cancer drugs have gone through this process purely for childhood cancers, indicating that companies do not regard it as financially attractive. Instead, we believe that an improved PIP process should be the main route for developing paediatric medicines.

- We believe pharmaceutical companies need stronger financial incentives to develop and trial drugs which are purely for paediatric use. Developing drugs for small patient populations is financially challenging and there is currently little commercial incentive for companies to develop drugs designed only for paediatric cancers. Incentives such as extra protection of market exclusivity or R&D tax credits might help to persuade companies to complete evaluation in children. Developing a drug purely for paediatric use would enhance a company's attractiveness to the ICR as a potential partner in drug development.

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- We would like to see a cultural change to phase I trial design to lower the age limit of eligibility for adult trials where appropriate. Adult phase I trials have a fixed lower age limit of 18 years and the ICR believes that this age limit should be lowered to safely include adolescents in a staggered fashion. Once an adult phase I study has shown an appropriate safety profile in adults, if the target is appropriate and if the drug has a relevant mechanism of action, adolescents should have the option of being included in the adult trial without waiting for a subsequent paediatric phase I trial. In certain cases this could be as low as 12 years old, if cared for by medical professionals experienced in running early phase studies in this age group. The Paediatric and Adolescent Drug Development Unit at the ICR and The Royal Marsden is well placed to facilitate this as it has properly structured support and expertise in looking after teenagers and children on trials.

- The ICR feels strongly that early clinical evaluation of drugs in children should not be stopped just because a company is unable to gain market authorisation for a drug in adults. We believe that novel financial models including partnerships between Government, academia, charities and industry are needed to help to take new cancer drugs into early-stage paediatric trials. Here at the ICR, we are developing unique and non-traditional funding models for running paediatric trials of promising drugs when neither the Government nor industry can pursue them. In the US, the Creating Hope Act 2011 has established collaborations with sponsors to develop drugs for possible paediatric use where companies are not taking trials forward. We feel that novel approaches like this could be explored further in Europe.

- We would like to see additional measures to support the basic scientific research which feeds the delivery of novel drugs and treatments for children to the clinic as early research into paediatric drug targets is currently underfunded. In addition, we strongly encourage pharmaceutical and biotechnology companies to provide academic researchers with easier access to their drugs to support early-stage pre-clinical paediatric studies.