International cooperation necessary to speed up clinical trial results in cancer research

A new study emphasizes the critical need for regulatory authorities, pharmaceutical clinical trial sponsors, collaborative research groups and other interests to work together to expedite study approval for clinical trials in cancer research on a global scale (Metzger-Filho et al, 2013).

Dr Otto Metzger-Filho of the Dana-Farber Cancer Institute, Boston, Massachusetts, and a team of international colleagues reviewed the time taken to set up the Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization (ALTTO) trial, a phase III clinical breast cancer trial covering more than 8300 patients in 44 participating countries.

The research team evaluated different aspects of ALTTO activation across different geographical and economic regions, measuring time intervals for regulatory approval, ethics approval, protocol amendments, and times for patient enrollment. Although some of these time periods did vary in different regions, the study's primary finding was that significant delays and bottlenecks occurred across all regions.

'Improving the efficiency of the activation process would speed up the ability to gather scientific knowledge and evaluate its applicability,' said Dr Metzger-Filho. 'Most importantly, it would ultimately benefit the many patients who volunteer to participate in clinical trials. This is the only way to improve treatments for patients with cancer.'

'While the study's focus on ALTTO means its findings cannot be generalized to make definitive statements about a region's clinical trial proficiency, its main finding of consistently lengthy timetables should spark a global discussion about the need to improve the efficiency of all cancer trials,' Dr. Metzger-Filho concluded.

Commenting on the study's findings, Professor Christoph Zielinski, Chair of the Clinical Division of Oncology, Medical University Vienna, Austria, explained: 'As ALTTO is an almost global trial, it allowed researchers to undertake a differential analysis of how long the various approval stages took in different geographic and economic regions.'

'Unnecessary delays in the approval of clinical trials mean patients can miss the advantages of a new active drug, a new combination of drugs or a novel therapeutic strategy, because oncologists will be compelled to use traditional and potentially sub-optimal treatments,' added Professor Roberto Labianca, Director of the Department of Oncology and Haematology, Ospedali Riuniti di Bergamo, Italy.

Metzger-Filho O, de Azambuha E, Bradbury I et al (2013) Analysis of Regional Timelines To SetUpa Global Phase III Clinical Trial in Breast Cancer: The Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization Experience. *Oncologist* January 28 (Epub ahead of print)

Possible treatment target for obstetric cholestasis

Intrahepatic cholestasis of pregnancy is the most prevalent pregnancy-specific liver disease. It is associated with increased risk of adverse fetal outcomes, including preterm labour and intrauterine death.

Levels of 3β-sulfated progesterone metabolites are elevated in intrahepatic cholestasis of pregnancy, leading to a study of the impact of sulfated progesterone metabolites on farnesoid X receptor-mediated bile acid homeostasis pathways (Abu-Hayyeh et al, 2013). The 3β-sulfated progesterone metabolite epiallopregnanolone sulfate was found to be supraphysiologically raised in the serum of patients with intrahepatic cholestasis of pregnancy.

Levels of epiallopregnanolone sulfate found in intrahepatic cholestasis of pregnancy can act as a partial agonist for farnesoid X receptor, causing aberrant expression of bile acid homeostasis genes in hepatoma cell lines and primary human hepatocytes.

These results reveal a novel molecular interaction between intrahepatic cholestasis of pregnancy-associated levels of epiallopregnanolone sulfate and the farnesoid X receptor that couples the endocrine component of pregnancy in intrahepatic cholestasis of pregnancy to abnormal bile acid homeostasis.

Abu-Hayyeh S, Papacleovoulou G, Lövgren-Sandblom A et al (2013) Intrahepatic cholestasis of pregnancy levels of sulfated progesterone metabolites inhibit farnesoid X receptor resulting in a cholestatic phenotype. *Hepatology* 8 January (Epub before print)

Home monitoring reduces inappropriate ICD shocks by 52%

ECOST (Effectiveness and Cost Of ICD Follow-Up Schedule with Telecardiology) was a randomized controlled multicentre trial evaluating the safety and efficacy of Biotronik home monitoring compared with standard in-office follow-up visits for patients with implantable cardioverter-defibrillators (ICDs) (Guédon-Moreau et al, 2012).

ECOST prospectively analysed 433 patients from 43 sites throughout France who were randomly assigned to home monitoring follow up (221 patients, seen once per year unless a hospital visit was needed) or standard in-office care (212 patients seen every 6 months).

Over a 24.2-month follow up, 38.5% of patients in the active and 41.5% in the control group experienced ≥1 major adverse event ($P<0.05$ for non-inferiority). The overall number of shocks delivered was significantly lower in the active ($n = 193$) than in the control ($n = 657$) group ($P<0.05$) and 52% fewer patients received inappropriate shocks in the active ($n = 11$) than in the control ($n = 22$) group ($P<0.05$).

Guédon-Moreau L, Lacroix D, Sadoul N et al for the ECOST trial Investigators (2012) A randomized study of remote follow-up of implantable cardioverter defibrillators: safety and efficacy report of the ECOST trial. *Eur Heart J* 13 December (Epub ahead of print)