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CLINICAL INVESTIGATION

NEWS

Highlights from the latest news and research in clinical investigation

Investigation into the assessment of tobacco use in clinical trials

The assessment of tobacco use in oncology clinical trials has been investigated by a group of scientists, leading to their recommendations for heightened tobacco assessment and tobacco cessation support

In a collaboration between numerous US cancer research sites, a group of scientists have investigated the assessment of tobacco use in oncology clinical trials. Their results, published in the *Journal of Clinical Oncology*, suggest more could be done in the assessment of tobacco use by patients enrolled on clinical trials.

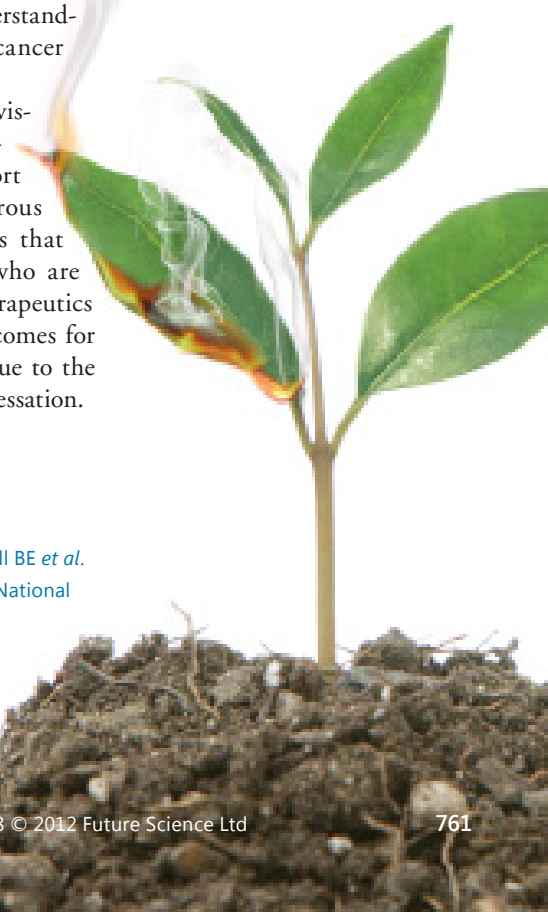
The research team, led by Graham Warren (Roswell Park Cancer Institute, NY, USA) evaluated the protocols and forms from 155 active trials in the National Cancer Institute's Clinical Trials Cooperative Group Program. This program aims to promote and support oncology clinical trials, offering help to trials across the USA, Canada and Europe. The group noted how tobacco use was assessed during clinical trials – from enrollment, to post-trial follow-up.

> "...standardized tobacco assessments and smoking cessation support for participants could have numerous beneficial effects ... could help identify patients who are best suited to certain oncology therapeutics and also generally improve the outcomes for patients enrolled in clinical trials..."

The team found that 29.4% of trials had any form of tobacco use assessment and only 4.5% trials assessed use during follow-up. In comparison, second-hand smoke was monitored to a lesser amount – with only 2.6 and 0.6% trials assessing at enrollment and follow-up, respectively. The researchers discovered that this tobacco status assessment was higher in head and neck or lung cancer trials and in Phase III clinical trials; however, none of the trials they studied provided structured guidance for tobacco cessation or evaluation of patients who were trying to stop smoking.

Warren explains the significance of their findings: "Most people don't realize that continued tobacco use by cancer patients decreases the effectiveness of cancer treatment. Several studies demonstrate that smoking increases cancer treatment toxicity, decreases cancer treatment compliance, decreases quality of life, and decreases survival in cancer patients. Unfortunately, tobacco assessments and cessation are not well incorporated into federally funded research." The team urges clinical trial investigators to incorporate standardized tobacco assessments into their oncology trial designs, since as Warren explains, the current limitations "significantly decrease our understanding of the effects of smoking on cancer treatment."

Looking to the future, the team envisage that standardized tobacco assessments and smoking cessation support for participants could have numerous beneficial effects. Warren explains that this could help identify patients who are best suited to certain oncology therapeutics and also generally improve the outcomes for patients enrolled in clinical trials due to the inherent health benefits of tobacco cessation.



Written by Alice O'Hare

Sources: NCI Fact Sheet: www.cancer.gov/cancertopics/factsheet/NCI/clinical-trials-cooperative-group; Peters EN, Torres E, Toll BE *et al.* Tobacco Assessment in Actively Accruing National Cancer Institute Cooperative Group Program Clinical Trials. *J. Clin. Oncol.* doi:10.1200/JCO.2011.40.8815 (2012) (Epub ahead of print).

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Dabrafenib to treat BRAF-positive melanoma: results from a recent Phase III trial

A novel inhibitor of mutated B-Raf shows its potential in a multicenter, randomized-controlled trial involving patients suffering from metastatic melanoma

In a recent report, researchers have shown the potential of dabrafenib for treating BRAF-positive metastatic melanoma. Their results are published 'online first' in *The Lancet*. The research was led by Axel Hauschild (Kiel University Hospital, Germany) and involved 250 trial participants.

BRAF-positive melanoma occurs in a subset of melanoma patients (~50%) who contain a mutated *BRAF* gene, which leads to an altered B-Raf protein. The majority of *BRAF* mutations fall under *BRAFV600E*. These mutations affect the role B-Raf plays in cell growth control. The pharmaceutical tested in this Phase III clinical trial, dabrafenib, is an inhibitor of mutated B-Raf, thus targeting this aspect of some metastatic melanomas.

Dabrafenib was compared with dacarbazine, the present conventional chemotherapeutic treatment for the disease. In addition to the two drugs different mechanisms of action, they are also administred differently – with dabrafenib and dacarbazine taken orally and intravenously, respectively.

The multicenter, randomized-controlled trial contained 250 patients, all of whom had stage III BRAFV600E mutation-positive melanoma. These patients either had untreated, stage IV or unresectable forms of melanoma. The patients were given either dabrafenib or dacarbazine, and progression-free survival was measured. The researchers found that progression-free survival for dabrafenib was 5.1 months compared with 2.7 months for dacarbazine. They conclude in their paper that "dabrafenib significantly improved progression-free survival."

Written by Alice O'Hare

Source: Hauschild A, Grob JJ, Demidov LV *et al.* Dabrafenib in BRAF-mutated metastatic melanoma: a multicentre, open-label, Phase 3 randomised controlled trial. *The Lancet* doi:10.1016/S0140–6736(12)60868-X (2012) (Epub ahead of print).

Perjeta™ approved by US FDA for treatment of HER2-positive breast cancer

The US FDA has recently approved Perjeta™ for the treatment of HER2-positive breast cancer. Perjeta is a humanized monoclonal antibody that targets HER2, a protein upregulated in certain HER2-positive breast cancer tumors. The drug was tested for its efficacy and safety in combination with another anti-HER2 therapy, trastuzumab and docetaxel (a targeted and chemotherapeutic agent, respectively).

Perjeta, produced by Genentech (CA, USA), is believed to work differently to trastuzumab – potentially targeting a different portion of HER2 – thus offering a two-pronged attack against HER2-positive breast cancer cells. This new targeted therapy was tested in 808 patients who had previously been diagnosed with HER2-positive metastatic cancer. The patients were randomly assigned to receive the trastuzumab–docetaxel combination with either a placebo or Perjeta, and progression-free survival was monitored. It was found that progression-free survival with Perjeta was 18.5 months, compared with 12.4 months for those given a placebo.

> "The therapeutic was given priority status by the FDA, due to the potential advances in melanoma treatment that it could offer, allowing fast-track assessment in 6 months."

The therapeutic was given priority status by the FDA, due to the potential advances in melanoma treatment that it could offer, allowing fast-track assessment in 6 months. Richard Pazdur, Director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research (MD, USA), explains: "Since trastuzumab was first approved more than a decade ago, continued research has allowed us to better understand the role HER2 plays in breast cancer. This research provided the background to combine two targeted drugs – trastuzumab and Perjeta with docetaxel to slow disease progression in breast cancer."

Written by Alice O'Hare

Source: US FDA press release: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm307549.htm

The editorial team welcomes suggestions for timely, relevant items for inclusion in the news. If you have newsworthy information, please contact:

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A multimedia 'psychoeducational' intervention: better than a brochure for trial recruitment?

A group of scientists at the Moffitt Cancer Center and Research Institute (FL, USA) have investigated whether a multimedia presentation would create better attitudes to clinical trial involvement than traditional printed information. The team, led by Paul Jacobsen, found that the 'pyscho-educational' intervention may be more effective at recruitment than traditional resources.

The team tested their hypothesis on 472 adults who had not been previously asked to participate in an oncology clinical trial. The participants were randomly assigned to receive either the traditional printed information on the trial, or an 18-min multimedia presentation that explained the trial but additionally addressed 'misperceptions and concerns about clinical trials.' The participant's attitudes were tested before and after the information was given by patient self-report.

> "The group suggest that by informing patients about the trial and common misperceptions and concerns using pyschoeducational interventions, more patients will be interested in taking part in trials."

The group found that patients who watched the film were more willing to be involved in the clinical trial than the participants who had received the printed material, and although the results were modest, they have implications in trial design. The group suggest that by informing patients about the trial and common misperceptions and concerns using pyschoeducational interventions, more patients will be interested in taking part in trials. The team plan to continue their work by investigating whether this kind of intervention could improve the quality of decision making among such patients.

Written by Alice O'Hare

Source: Jacobsen PB, Wells KJ, Meade CD *et al.* Effects of a brief multimedia psychoeducational intervention on the attitudes and interest of patients with cancer regarding clinical trial participation: a multicenter randomized controlled trial. *J. Clin. Oncol.* doi:10.1200/JCO.2011.39.5186 (2012) (Epub ahead of print).

Combination vaccine against meningococcal and *Haemophilus influenzae* serotype b diseases approved by US FDA

Menhibrix™, a novel combination vaccine against the main causes of bacterial meningitis in young children, has recently been approved by the US FDA. The vaccine, marketed by GlaxoSmithKline (Rixensart, Belgium), has been tested in international clinical trials for efficacy and safety.

Menhibrix acts to prevent disease caused by the pathogens *Neisseria meningitidis* and *Haemophilus influenzae*, which can lead to meningococcal and *Haemophilus influenzae* serotype b (Hib) disease, repectively. Both diseases can be life threatening, and are the most common causes of bacterial meningitis in young children. The vaccine has been approved for children aged between 6 weeks to 18 months. As Karen Midthun, the Director of the FDA's Center for Biologics Evaluation and Research (MD, USA), explains: "With approval of Menhibrix, there is now a combination vaccine that can be used to prevent potentially life-threatening Hib disease and two types of meningococcal disease in children."

The safety and efficacy of the combination vaccine were tested in trials across the USA, Canada and Australia. The safety of the vaccine was demonstrated in a trial involving 7500 children across these three countries. The effectiveness of the vaccine was tested in several hundred children in the USA. The Hib component of the vaccine could be compared with a previously FDA-approved Hib vaccine. However the efficacy of the meningococcal component was assessed by measuring the immune response to the vaccine, with the researchers looking for a sufficient level of antibodies being produced to fight off a meningococcal infection.

Menhibrix is given as a four-dose series and as Midthun explains: "It is the first meningococcal vaccine that can be given starting as young as six weeks of age." This could offer heightened protection for young children against these diseases.

Written by Alice O'Hare

Source: US FDA press release: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm308350.htm