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CLINICAL INVESTIGATION

NEWS

Highlights from the latest news and research in Clinical Investigation

Study suggests that socioeconomic status may affect clinical trial participation

US researchers publish their analysis of clinical trial participation patterns in lower-income patients.

"The current heightened awareness of socioeconomic disparities in access to resources provided the motivation to explore potential socioeconomic barriers to clinical trial participation..."

A group of researchers from the NCI-supported Southwest Oncology Group (SWOG) have recently published their findings into how socioeconomic status (SES) may affect oncological clinical trial participation. Their results were recently published in the *Journal of Clinical Oncology*, and suggest that lower-income patients are less likely to participate in clinical trials, irrespective of their age.

The group, headed by Joseph Unger (SWOG Statistical Center, Fred Hutchinson Cancer Research Center, WA, USA), surveyed 5499 patients between 2007 and 2011 and monitored how many discussions with physicians led to clinical trial participation. The survey was carried out via an internet-based treatment decision tool, and patterns were assessed according to 'important SES (income, education) and demographic factors'.

Using univariate models to analyze the data, the research indicated that older patients, and patients with lower income/education were less likely to participate in clinical trials ($p = 0.002$, 0.001 and 0.02, respectively). When applying a multivariate model this pattern remained statistically significant (odds ratio: 0.73; 95% CI: 0.57–0.94; $p = 0.01$).

Speaking exclusively to *Clinical Investigation,* Unger commented on what lead to their investigations into SES factors: "SWOG had previously shown that older patients were substantially underrepresented in cancer clinical trials. But the impact of socioeconomic status on participation had not been well studied." He continued in explaining their motivation: "The current heightened awareness of socioeconomic disparities in access to resources provided the motivation to explore potential socioeconomic barriers to clinical trial participation, which might also inform the age disparity."

Looking to expand the findings of this study, the group plan to assess: "whether the main income finding from this study can be independently confirmed using data from a prior SWOG study of barriers to clinical trials." Unger explained that this previous study presents advantages such as following a homogenous group of patients over an expanded timeframe in a set of SWOG institutions.

Unger stated how he hoped their findings will impact future trial design: "Specific interventions to increase lower income participation still need to be determined. But some possibilities might include better clarity about how the study will be paid for in patient informed consents. Patients may still be concerned about co-pays and co-insurance, even if they're not necessarily higher in a clinical trial than for non-trial care. Also, considerations to help relieve the indirect costs of participation – things like free bus passes or paid parking to help with transportation, or flexible work schedules – could also be a step toward lessening the burden on patients."

– Written by Alice O'Hare

Source: Unger JM, Hershman DL, Albain KS *et al.* Patient income level and cancer clinical trial participation. *J. Clin. Oncol.* doi: 10.1200/JCO.2012.45.4553 (2013) (Epub ahead of print).

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Tetravalent vaccine for dengue fever shows promise

"Other vaccines in development require two or three injections at higher doses to achieve similar results."

A new study conducted by a team of scientists from the National Institutes of Health has shown that a prospective dengue fever vaccine is safe and elicits a strong immune response in the majority of people vaccinated. The results published in *The Journal of Infectious Diseases* have sparked hope for a new vaccine, after this early-phase clinical trial sponsored by National Institute of Allergy and Infectious Diseases.

Dengue fever can be caused by any of the four related virus subtypes DENV-1, DENV-2, DENV-3 and DENV-4 carried by the *Aedes aegypti* mosquito, mainly affecting people living in tropical and subtropical climates. It continues to cause a significant health burden around the world, causing millions of infections and is also now more frequently seen in world travelers.

The team conducted the Phase I study in Baltimore, testing the TetraVax-DV vaccine on healthy men and women not previously exposed to the dengue virus. They were split into four groups, testing four versions of the vaccine containing different measures of the components to protect against all four virus subtypes.

The vaccine was found to be safe after vaccinating subjects; "there was no significant difference in the incidence of adverse events between vaccinees and placebo-recipients other than rash" stated the team. No participants experienced any fever or other dengue fever symptoms.

Whilst measuring the antibody response of individuals to the dengue virus after vaccination, the team found that one particular combination of TetraVax-DV known as TV003 stood out. "What is promising about TV003 is that it elicited solid antibody responses after just one dose," explained Stephen Whitehead, lead investigator of the trial from the National Institute of Allergy and Infectious Diseases. "Other vaccines in development require two or three injections at higher doses to achieve similar results."

Further investigation into TetraVax-DV will soon begin in Phase II clinical trials taking place in Thailand and Brazil. These promising results so far may be an early indicator of a new dengue virus vaccine on the horizon.

– Written by Georgina Askeland

Source: Durbin AP, Kirkpatrick BD, Pierce KK *et al.* A single dose of any of four different live attenuated tetravalent dengue vaccines is safe and immunogenic in flavivirus-naive adults: a randomized, double blind clinical trial. *J. Infect. Dis.* doi: 10.1093/infdis/jis936 (2013) (Epub ahead of print).

Novel once-daily tablet against HIV

Jannsen Therapeutics has recently announced the US FDA approval of its novel darunavir (PREZISTA®) 800 mg once-daily tablet for the treatment of HIV. This will allow HIV sufferers without darunavir resistance-associated mutations currently taking darunavir 400 mg to reduce the number of tablets they take by half.

Darunavir is a protease inhibitor recommended by the Office of AIDS Research Advisory Council for both treatment-naive and treatment-experienced adults and adolescents. This new 800 mg tablet is twice as potent as the previous darunavir 400 mg tablet, which required two tablets to be taken in combination with ritonavir and other HIV medications.

HIV treatment currently involves a complicated dosing regime; often many drugs are taken at different times of the day with and without food. A strict adherence is required to help avoid the development of resistance. Being able to reduce the number of pills to be taken could help patients comply with their treatment. "The single 800 mg tablet provides an option for a reduced pill burden and reflects our ongoing commitment to offer more treatment options for the diverse population of people living with HIV," stated Bryan Baugh, Medical Director at Janssen Therapeutics.

Jannsen plans to discontinue the production of darunavir 400 mg, as the introduction of this new strength version will render it obsolete. The darunavir 800 mg tablet is expected to be made available shortly.

This new approval brings the endeavor for more simple dosing regimes closer to realization and may inspire more research to achieve effective and less complicated treatments for HIV sufferers.

– Written by Georgina Askeland

Source: Janssen Therapeutics Press Release: www.janssentherapeutics.com/news-center/fda-approves-new-800mg-prezista-darunavir-tablet

US FDA approves three new drugs for Type 2 diabetes

The US FDA has recently approved three new drugs to assist with controlling blood sugar levels in individuals with Type 2 diabetes (T2D): Nesina, Kazano and Oseni.

T2D affects approximately 24 million individuals and accounts for more than 90% of diabetes cases in the USA. As the number of individuals suffering from T2D is increasing, continuous research is being carried out to identify new agents and drugs to help treat diabetics.

These newly approved drugs, which have all been developed by Takeda Pharmaceuticals America, Inc. (IL, USA), contain a new DPP-4 inhibiting compound called alogliptin, which was found to be superior to other DPP-4 inhibitors, such as Voglib, in a Japanese clinical trial in 2011.

Mary Parks, director of the Division of Metabolism and Endocrinology Products in the FDA's Center for Drug Evaluation and Research (MD, USA), said "controlling blood sugar levels is very important in the overall treatment and care of diabetes." She continued "Alogliptin helps stimulate the release of insulin after a meal, which leads to better blood sugar control."

One of the drugs, Nesina, is composed purely of alogliptin and was found to be effective and safe in 8500 patients with T2D across 14 clinical trials. These trials showed a reduction in glycosylated hemoglobin (HbA1C) of 0.4–0.6% compared with a placebo after 26 weeks of use.

Kazano is composed of alogliptin and metformin hydrochloride, a biguanide class antidiabetic drug, and performed significantly better in clinical trials than when the two drugs were administered separately. Kazano resulted in the reduction of 1.1 and 0.5% HbA1C more than Nesina and metformin, respectively.

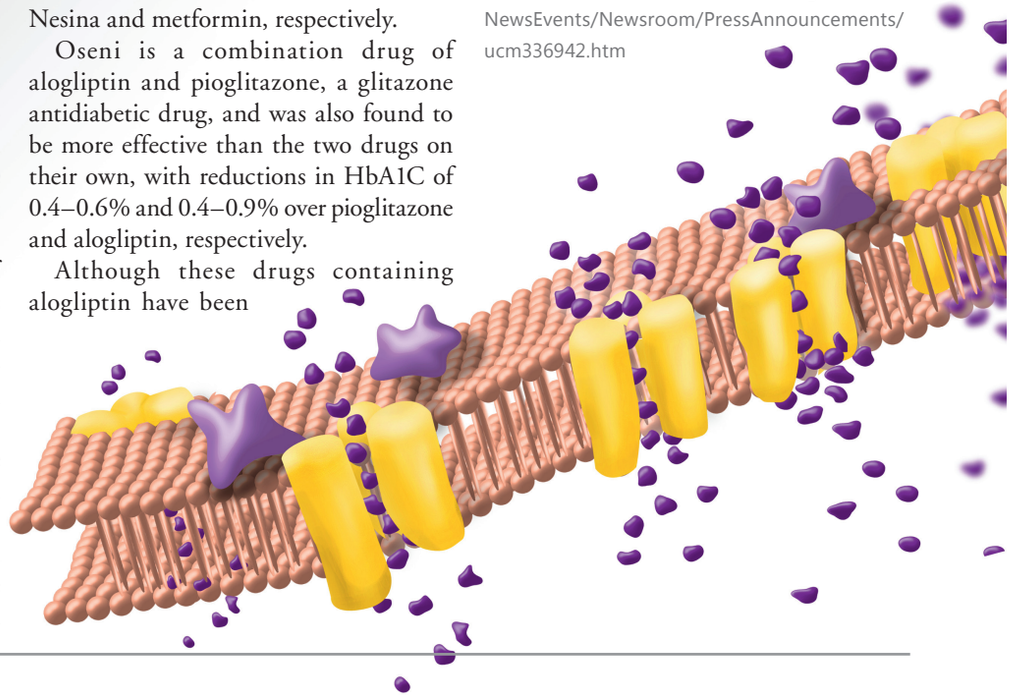
Oseni is a combination drug of alogliptin and pioglitazone, a glitazone antidiabetic drug, and was also found to be more effective than the two drugs on their own, with reductions in HbA1C of 0.4–0.6% and 0.4–0.9% over pioglitazone and alogliptin, respectively.

Although these drugs containing alogliptin have been shown to be more effective than the current available treatments for diabetes, side effects have also been observed. With the most common being headaches, upper respiratory tract infection and back pain.

The FDA's approval of these drugs represents the introduction of alogliptin, a new antidiabetic compound, to the USA.

– Written by Theo Bond

Source: FDA Press Release: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm336942.htm



Ravicti™ approved by US FDA

The US FDA has recently approved Ravicti™ in the management of some urea cycle disorders (UCDs) in patients over 2 years in age. Ravicti (glycerol phenylbutyrate), a liquid marketed by Hyperion Therapeutics (CA, USA), is taken orally three times a day with food.

UCDs are genetic disorders of the urea cycle, leading to disrupted removal of nitrogen from the body. Due to deficiencies in specific urea cycle enzymes, nitrogen is not converted to urea (which would usually be removed from the body in urine). Thus nitrogen is converted to ammonia, which, if left to accumulate, can cause brain damage, coma, or death.

Hyperion's therapeutic, aimed for UCD patients who cannot control their condition purely with diet or supplements, aids in the disposal of ammonia from the body when used with a protein-restricted diet. Its safety and effectiveness in adults and children over 2 years was indicated in four clinical studies. One of these, a non-inferiority clinical trial involving 44 adults, compared Ravicti with the current UCD therapeutic Buphenyl. Ravicti was shown to be "as effective as Buphenyl in controlling ammonia levels."

> "Ravicti provides another treatment for chronic management of urea cycle disorders, a group of life-threatening conditions..."

Ravicti was reviewed under the FDA's 'fast track program' – an initiative to ensure the expedition of particularly important therapeutic developments. In addition, since Ravicti is implicated in a rare condition, it was granted 'orphan product' designation.

Director of the Division of Gastrointestinal and Inborn Errors Products in the FDA's Center for Drug Evaluation and Research (MD, USA), Donna Griebel, said of the approval: "Ravicti provides another treatment for chronic management of urea cycle disorders, a group of life-threatening conditions. The approval of this new therapeutic option demonstrates FDA's commitment to providing treatments for patients suffering from rare diseases."

– Written by Alice O'Hare

Source: FDA Press Release: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm337639.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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