Raltegravir combination therapy effective in untreated adults with HIV

New exploratory pre-specified analyses from the ongoing STARTMRK phase III study have compared the integrase inhibitor raltegravir (Isentress) tablets in combination therapy to efavirenz in combination therapy in previously untreated (treatment-naïve) adult HIV-1-infected patients.

The regimen containing raltegravir demonstrated better efficacy compared to the regimen containing efavirenz at 192 weeks of treatment, as measured by the percentage of patients maintaining undetectable virus levels (less than 50 copies/ml) (76.2% (*n*=214/281) *vs* 67.0% (*n*=189/282); 95% confidence interval 1.6–16.4).

The regimen containing raltegravir also showed a greater immunological effect as measured by mean increase from baseline in CD4 cell count at week 192 (361 *vs* 301 cells/mm^3; confidence interval 24–95) *vs* the efavirenz regimen.

'These results offer further insight into the virologic and immunologic response seen with raltegravir in combination therapy when compared to efavirenz at 192 weeks in treatment-naïve adult patients with HIV-1,' said Dr Jürgen Rockstroh, University of Bonn, Bonn-Venusberg, Germany, who presented the data at the 13th European AIDS Conference in Belgrade, Serbia.

Additionally, based on analyses of pre-specified demographics (age, gender, region, race and hepatitis co-infection) and baseline prognostic factors (viral load, CD4 cell count and HIV-1 subtypes), raltegravir in combination therapy demonstrated consistent virological and immunological efficacy relative to efavirenz in combination therapy at week 192.

Data also showed that using raltegravir in combination therapy resulted in fewer reported drug-related clinical adverse events than combination therapy with efavirenz (50.2% *vs* 80.1% respectively; *P*<0.001).

Anti-dementia drugs may delay care home admission

Prescribing anti-dementia drugs to patients could help delay their admission to care homes, according to a new study (Salib and Thompson, 2011).

A total of 339 people with dementia were studied, who were referred to psychiatric services in Peasley Cross Hospital in St Helens in 2006.

Of these, 127 (24%) had been prescribed cholinesterase inhibitors, which can help slow the progression of the disease by preventing acetylcholinesterase from breaking down acetylcholine in the brain.

Of the patients who were prescribed cholinesterase inhibitors, almost three-quarters (74%) were given donepezil (Aricept). A further 14% were given galantamine (Reminyl), 8% rivastigmine (Exelon), and 4% memantine (Ebixa). The remaining 212 patients in the study were not prescribed cholinesterase inhibitors.

After 4 years, the researchers followed up all 339 patients to see if they had been placed in care or remained in their own home.

The researchers found that, on average, patients who did not take anti-dementia drugs moved to care homes sooner than patients who did. There was a delay in admission to care homes by a median of 12 months for patients who took anti-dementia drugs, compared to those who did not, but after 3 years, an equal proportion of patients from both treatment groups had been admitted to care homes, indicating that the delay in admission was relatively short-lived.

Salib E, Thompson J (2011) Use of anti-dementia drugs and delayed care home placement: an observational study. *The Psychiatrist* **35**: 384–8

NHS Technology Adoption Centre key to increasing use of innovations

The NHS Technology Adoption Centre has re-launched. As part of this process NHS Technology Adoption Centre underwent a comprehensive review and has launched a new set of services to speed up the diffusion of proven technologies across the NHS. These services are based on the considerable expertise and knowledge which has been built up over the last 4 years and are better aligned with the changing NHS and the current medical technology landscape.

Led by CEO Sally Chisholm the NHS Technology Adoption Centre is building on this base of knowledge and experience with a new team of purposely selected individuals who have the skill and expertise to bring life-changing technologies to NHS patients. NHS Technology Adoption Centre is the only organization solely dedicated to the diffusion of proven innovation across the NHS.

NHS Technology Adoption Centre has worked on a number of projects which have enabled medically proven technologies be adopted by the NHS, thus ensuring patients are able to benefit from these innovations.

NHS Technology Adoption Centre believes that examples of innovation are not an issue in the UK but the lack of a 'pull' culture within the NHS often prevents these benefits from being realized.

The National Institute for Health and Clinical Excellence is recognized as the organization with the expertise to review the evidence linked to individual technologies but experience shows that NHS organizations also benefit from receiving practical support at the front line of care delivery to enable rapid uptake of this technology. The NHS Technology Adoption Centre is intended to encourage prompt use of appropriate technology to benefit patients.

Non-invasive positive-pressure ventilation linked to increased hospital mortality rates

Although increased use of non-invasive positive pressure ventilation nationwide has helped decrease mortality rates among patients hospitalized with chronic obstructive pulmonary disease, a small group of patients requiring subsequent treatment with invasive mechanical ventilation have a significantly higher risk of death than those placed directly on invasive mechanical ventilation, according to researchers in the United States who studied patterns of non-invasive positive pressure ventilation use (Chandra et al, 2011).

Researchers reviewed patient data gathered by the Healthcare Cost and Utilization Project Nationwide Inpatient Sample database between 1998 and 2008.

The researchers examined changes in the frequency of non-invasive positive pressure ventilation and invasive mechanical ventilation use, and compared patient demographics, income status, payer type, hospital region and hospital type among patients who initially received non-invasive positive pressure ventilation, invasive mechanical ventilation or no respiratory support after hospital admission. They also compared in-hospital mortality, length of stay and total hospitalization charges.

Although the annual number of hospitalizations for acute exacerbations was relatively constant, there was a progressive increase in the use of non-invasive positive pressure ventilation and a progressive decrease in use of invasive mechanical ventilation; during the entire study period, there was a fourfold increase in the use of non-invasive positive pressure ventilation.

The authors felt that the trend toward greater use of non-invasive positive pressure ventilation was likely the result of several factors, including clinical trial results, increased confidence in using non-invasive positive pressure ventilation and the ability to use non-invasive positive pressure ventilation outside the intensive care unit.

Chandra D, Stamm JA, Taylor B et al (2011) Outcomes of Non-invasive Ventilation for Acute Exacerbations of COPD in the United States, 1998-2008. *Am J Respir Crit Care Med* Oct 20 [Epub ahead of print]

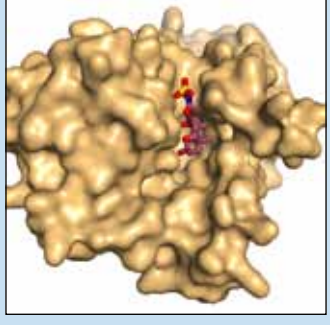
X-rays help advance battle against heart disease

Scientists from Imperial College London and Diamond Light Source have revealed the structure of a cholesterol-lowering drug target (Hu et al, 2011). This finding could lead to much more effective drugs to tackle high cholesterol levels.

The researchers from Imperial College London used intense X-rays, generated by the Diamond synchrotron and the European Synchrotron Radiation Facility, to determine for the first time the structure of bacterial homologue of the apical sodium-dependent bile acid transporter protein, a target for hypercholesterolaemia drugs since it can affect the level of cholesterol in the blood.

In the liver, cholesterol makes bile acids which are used in the intestine to absorb fat. These bile acids are then reabsorbed by apical sodium-dependent bile acid transporter to be transported to the liver and recycled. By blocking apical sodium-dependent bile acid transporter, bile acid levels returning to the liver are lowered, so the liver converts more cholesterol into bile acids, which lowers the level of cholesterol in the blood.

Surface representation of apical sodium-dependent bile acid transporter looking from the inside face of the membrane showing bile acid bound in a deep cavity.



Professor So Iwata, David Blow Chair of Biophysics at Imperial College London, BBSRC Fellow and Director of the Membrane Protein Laboratory at Diamond, said: 'There are currently a number of existing ASBT [apical sodium-dependent bile acid transporter] inhibitors effective in animal models, which were developed without structural knowledge of the protein. Now that we know the shape and size of the drug-binding site within a bacterial model of the protein, this detailed structural information should enable the design of improved drugs which are much more targeted and will "fit" much better.'

Hu NJ, Iwata S, Cameron AD, Drew D (2011) Crystal structure of a bacterial homologue of the bile acid sodium symporter ASBT. *Nature* **478**(7369): 408–11

Indacaterol improves clinical benefits for COPD patients

INTENSITY is the first blinded head-to-head study comparing once-daily Onbrez Breezhaler with Spiriva HandiHaler, an established chronic obstructive pulmonary disease (COPD) therapy. It found that indacaterol was more effective than tiotropium in reducing shortness of breath and use of reliever medication and in improving patients' capacity for day-to-day activities.

Osteoarthritis patients not given long-term options

In the UK 86% of osteoarthritis patients are told to take painkillers by their physicians, rather than being given information about treatment options that could alleviate their long-term pain, according to a new survey of 404 patients conducted by ICM Research and funded by Genzyme.

New emphysema treatment approved

InterVapor System has received CE Mark approval for marketing in Europe. The first endoscopic lung volume reduction system for the treatment of severe emphysema, it uses the body's natural healing processes without leaving foreign materials behind.

European Multidisciplinary Cancer Congress
Stockholm, Sweden, 23–27 September

Survey reveals education gaps in head and neck cancer

People with head and neck cancers want more information on treatment options to help them make informed decisions and improved support networks to help them cope with the impact of the disease, reveals a survey of European patients, which also shows the need for improved education of health-care professionals on this type of cancer.

The survey, About Face 2, interviewed 104 patients with head and neck cancers (aged 50–70 years) representative of patient populations in six European countries. They were interviewed about their experiences and feelings before and at diagnosis. The findings showed most of the patients' needs – at every stage of their disease journey – were related to information and education, in addition to support from health-care professionals. There was also a need for improved education on head and neck cancer for both the public and health professionals so that people with symptoms present earlier and can benefit from earlier diagnosis and treatment.

Once diagnosed, patients wanted more information to help them to make appropriate choices of treatment. They wanted information that explained potential outcomes and was tailored to their needs.

'The public and GPs need to be better informed about the symptoms of head and neck cancers because they can be quite non-specific, including sore throat, hoarse voice and earache. This will help to achieve earlier diagnosis,' suggested lead author Professor Jean-Louis Lefebvre, from the Centre Oscar Lambret Northern France Comprehensive Centre, Lille Cedex, France, and President of the European Head and Neck Society.

Cancers of the oral cavity, pharynx and larynx account for almost 5% of all cancers, and the vast majority are currently diagnosed at a late stage. He added: 'We also need to improve communication with patients at the time of diagnosis and when explaining treatment options.'

Key findings from the survey were presented as a theatrical performance during a unique 'Senseless' symposium, hosted by the European Head and Neck Society and Merck Serono. It told the story of a head and neck cancer patient's journey from initial symptoms, through the devastating moment of diagnosis, and coping with the side effects of treatment.

Professor Jean-Louis Lefebvre, from the Centre Oscar Lambret Northern France Comprehensive Centre, Lille Cedex, France

Professor Lefebvre explained that a group of experts from national head and neck cancer societies will develop a report recommending practical measures to improve education, awareness and support for head and neck cancers patients. He concluded: 'We hope our efforts will reduce the senseless number of lives being lost to head and neck cancer.' Delegates signed a 'wall' supporting the call to action for better education and information in head and neck cancer.

Sue Mayor

Cetuximab increases resection rate for colorectal liver metastases

One-third of colorectal cancer patients with initially non-resectable liver disease can undergo complete resection of their liver metastases after treatment with cetuximab plus chemotherapy, and this is associated with improved survival, according to results from the Cetuximab in Neoadjuvant Treatment of Non-resectable Colorectal Liver Metastases (CELIM) study.

The independently conducted study randomized 110 patients with colorectal cancer and non-resectable liver metastases to first-line treatment with cetuximab, a monoclonal antibody targeting the epidermal growth factor receptor, plus FOLFOX6 (oxaliplatin, fluorouracil and folinic acid) or FOLFIRI (irinotecan, fluorouracil and folinic acid). Patients' responses were assessed every 8 weeks using computed tomography or magnetic resonance imaging. A multidisciplinary team reassessed resectability after 16 weeks and then every 2 months for up to 2 years.

Nearly two-thirds of patients (62%) responded to treatment and 34% were able to undergo complete (R0) resection. Patients undergoing R0 resection of liver metastases showed significantly longer overall survival (median 46.7 months) than those who did not (median 27.3 months; P=0.002). Three-year overall survival in patients with R0 resection was 64%, and overall survival was 49% at 4 years compared to only 16% in those not resected (P=0.002).

'The median overall survival of almost 4 years for patients in CELIM who underwent complete resection of liver metastases is remarkable,' said lead author Professor Gunnar Folprecht, Senior Consultant in Medical Oncology at University Carl Gustav Carus, Dresden, Germany. He noted that potentially curative surgical resection is a major treatment goal for metastatic colorectal cancer: 'This trial helps to support the common belief that complete resection improves overall survival... we can improve overall survival by increasing patients' chances of undergoing liver resection.'

Around 25% of colorectal cancer patients present with metastatic disease at diagnosis and the majority are considered unresectable, said Professor Folprecht. 'Medical treatment to shrink metastases to a point where they can be removed by surgery offers the only possibility of cure for these patients,' he said.

Sue Mayor

European Multidisciplinary Cancer Congress
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Denosumab delays metastasis in prostate cancer patients

The monoclonal antibody denosumab (XGEVA) can impede the onset of bone metastases in men with hormone-refractory prostate cancer by just over 4 months, found a phase III study presented at the congress. These results held across all demographic and disease-related subgroups.

Up to 90% of men with prostate cancer resistant to hormone treatment will have their primary tumour metastasize to the bone, placing the patient at risk of serious skeletal-related events. Denosumab is a fully human monoclonal antibody that inhibits RANKL, a protein key to formation of osteoclasts. If formation of osteoclasts can be impeded, the bone can continue to resist development of metastases, explained study presenter Professor Stéphane Oudard, from Georges Pompidou Hospital, Paris, France.

In the study, 1432 men with castrate-resistant prostate cancer considered at high risk for bone metastasis were randomized to denosumab 120 mg subcutaneously every 4 weeks (n=716) or placebo subcutaneously every 4 weeks (n=716). The primary end point was time to first bone metastasis (symptomatic or asymptomatic) or death on study. Exclusion criteria included bone metastasis detected radiographically, metastatic involvement of distant organs and intravenous bisphosphonates.

Bone metastasis-free survival was 29.5 months in those randomized to denosumab *vs* 25.2 months in those receiving placebo (hazard ratio 0.85, 95% confidence interval 0.73–0.98; P=0.028). The results held across all subgroups, with hazard ratios ranging from 0.58 to 0.87. 'Subgroup analysis showed that whatever the patient's age, race, histology, or patient characteristics they all benefitted from denosumab,' said Professor Oudard.

Adverse effects were relatively similar between patients randomized to denosumab and placebo, although low blood calcium levels and jaw osteonecrosis were slightly more frequent among the denosumab group.

Janet Fricker

Ipilimumab improves survival from melanoma metastases

Ipilimumab shows similar antitumour activity in patients with malignant melanoma and brain metastases as in those without brain disease, show 2-year results from prospective studies.

Dr Kim Margolin, from the University of Washington, Seattle, USA, reported results for the prospective CA184-042 study, including patients with malignant melanoma and active, measurable brain metastasis that was stable without steroid therapy or required steroids for CNS symptoms. They were treated with ipilimumab 10 mg/kg every 3 weeks for four doses. She also reported on the expanded access programme CA184-045 with ipilimumab 3 or 10 mg/kg every 3 weeks for four doses.

Ipilimumab augments T-cell-mediated antitumour responses. Activated T-cells cross the blood–brain barrier, supporting a trial of ipilimumab in patients with brain metastases. One in three metastatic melanoma patients (30%) have brain metastases at diagnosis, and a further 30% develop these within 1–2 years of diagnosis. Only 10% of patients respond to current therapy (radiation) and median survival is 3–6 months.

Patients with brain metastases not requiring steroids had 12-month overall survival of 31% after treatment with ipilimumab, sustained at 26% out to 2 years. The 12-month overall survival in patients with symptomatic brain metastases was 10%, but they had more advanced disease.

Dr Margolin concluded: 'Ipilimumab prolonged survival and achieved durable responses in patients with malignant melanoma and brain metastases.'

Sue Mayor

Synchronous chemoradiation reduces breast cancer recurrence

Giving radiotherapy between or during chemotherapy cycles significantly reduces the risk of recurrence in women with early breast cancer, according to a major UK study.

The Sequencing of Chemotherapy and Radiotherapy in Adjuvant Breast cancer study randomized 2296 women who had undergone breast-conserving surgery or mastectomy to sequential chemotherapy and radiotherapy or synchronous treatment, where radiotherapy was given in the gaps between chemotherapy cycles. More than 60% of patients received 40 Gy in 15 fractions over 3 weeks.

'Synchronous chemoradiation reduces the risk of local cancer recurrence by 35%,' reported Dr Indrajit Fernando, consultant clinical oncologist at University Hospitals Birmingham NHS Foundation Trust, UK.

The 5-year local recurrence rates were 2.8% in the synchronous chemoradiation group and 5.1% in the sequential group. The 2.3% difference between groups was statistically significant.

Dr Fernando suggested that the reduction in recurrence would significantly improve survival: 'even a 2.3% reduction in local recurrence rates will have an impact because this is such a common cancer.' He said his clinic has switched to giving synchronous chemoradiation based on the findings.

More patients undergoing synchronous chemoradiation showed acute skin toxicity with radiotherapy treatment, but only 4% had a severe reaction, which took several weeks to heal.

Sue Mayor