EMERGENT THERAPIES

New prostate drug heralds 'golden age'

Enzalutamide (Xtandi), the novel and promising new treatment for prostate cancer, has been recommended by NICE for treatment of metastatic disease that has progressed following hormone therapy and docetaxel chemotherapy.

Formerly known as MDV3100, enzalutamide is an oral, once-daily androgen receptor signaling inhibitor with a triple mode of action. Currently licensed throughout the EU in the second line castration-resistant setting, it is the latest in a procession of new agents to come onto the market for advanced prostate cancer.

Responding to new NICE draft guidance Professor Alan Ashworth, Chief Executive of The Institute of Cancer Research, London, said:

"Advanced prostate cancer is very difficult to treat, and it's taken a coordinated effort to finally bring new drugs into the pipeline after decades where there were no options once old-style hormone treatment stopped working.

"What we're seeing now is an unprecedented period of success for prostate cancer research, with four new drugs shown to extend life in major clinical trials in just two years, and several others showing promise. It truly is a golden age for prostate cancer drug discovery and development."

Meanwhile, new Phase 3 data on enzalutamide provides substantial support for extending its use to patients who have not received chemotherapy.

The PREVAIL trial investigated the efficacy and safety of enzalutamide in 1,700 chemo-naïve men with metastatic castration-resistant prostate cancer (mCRPC). Early results showed significant benefit for enzalutamide over placebo in terms of overall and progression-free survival. The study was therefore stopped and patients treated with placebo were offered enzalutamide. Additional data from the Phase 3 PREVAIL results, including safety data, will be submitted for presentation at an upcoming medical conference.

Promising data emerge for lipid-reducing antibody

Data from the ODYSSEY MONO Phase 3 trial of the novel lipid-lowering drug alirocumab demonstrate that it met its primary efficacy endpoint. In patients with primary hypercholesterolemia and moderate cardiovascular risk, mean LDL-C reduction from baseline to week 24 was significantly greater in patients randomised to alirocumab compared with patients randomised to cholesterol-absorption inhibitor ezetimibe.

Alirocumab is an investigational monoclonal antibody targeting the specific protein PCSK9. Most trials of the drug have been designed to evaluate its efficacy in combination with different background therapies. These are the first Phase 3 data to emerge for alirocumab monotherapy.

The trial employed a dose increase for patients who did not achieve an LDL-C level of 70mg/dL; however the majority of patients achieved the reduction on the initial low dose of alirocumab of 75mg.

The percentage of patients who reported treatment emergent adverse events was 78.4% in the ezetimibe group and 69.2% in the alirocumab group. The most common class of adverse events was infections, which included nasopharyngitis, influenza, and upper respiratory tract infection.

Detailed results from the ODYSSEY MONO study will be presented at an upcoming medical conference in 2014.

● Meanwhile, a retrospective analysis of over 7000 patients in whom previous treatment with ezetimibe was discontinued following advice from the National Prescribing Centre has found that approximately one third did not receive a cholesterol measurement in the six months prior to the treatment being stopped.

The findings were gleaned from a retrospective analysis of the Health Improvement Network primary care database, which also showed that 42% of patients discontinued on ezetimibe were offered no further lipid modifying treatment for six months.

Specialists have voiced concern that patients were being removed from a treatment in the absence of cholesterol levels being known.

Fast-acting LABA approved for COPD maintenance

The new highly selective inhaled long-acting ß2-agonist (LABA) olodaterol (Striverdi Respimat) has received marketing approval in the UK for patients with COPD.

The approval is based on data from the Phase 3 clinical trial program involving more than 3,500 patients with moderate to very severe COPD (GOLD spirometric level 2-4), which has shown that once-daily olodaterol provided rapid and sustained improvements in lung function when given in addition to usual care.

Long-lasting anticholinergic bronchodilators are established as baseline maintenance therapy in the treatment of COPD. Olodaterol is both a fast-acting and long-lasting bronchodilator, delivering significant bronchodilator effects within five minutes after the first dose and providing sustained improvement in FEV1 over 24 hours.

Phase 3 trial data have shown that, compared to usual care alone, lung function improvements with once-daily olodaterol translated into significant improvements in patients' quality of life, as measured by the reduction in their St. George's Respiratory Questionnaire (SGRQ) total score.

Novel psoriasis treatment nears registration

An interim analysis of Phase 3 data for apremilast, a novel treatment for psoriasis, has shown promising results, according to the manufacturer Celgene.

The trial, ESTEEM 1, is the largest of two registration studies evaluating apremilast, an oral small-molecule specific inhibitor of phosphodiesterase 4 (PDE4), in more than 1,200 patients with moderate-to-severe plaque psoriasis.

Previously reported findings from ESTEEM 1 showed that apremilast significantly improved general signs and symptoms of psoriasis across a wide-range of patient types.

This latest analysis assessed the effects of apremilast on patients in ESTEEM 1 with nail and scalp psoriasis. After 16 weeks of treatment, patients in the apremilast group had significantly greater improvements in the nail psoriasis severity index (NAPSI) scores compared with patients treated with placebo, showing an improvement of 22.5% vs. a worsening of 6.5%, respectively (p<0.0001). Improvements continued through 32 weeks of treatment for those patients on apremilast 30mg BID (an improvement of 43.6%).

Psoriasis of the scalp was also significantly improved by treatment with apremilast vs placebo after 16 weeks of therapy, with significantly more patients in the active arm becoming clear or almost clear compared with those in the placebo group (46.5% vs. 17.5%, respectively(p<0.0001).

Apremilast was generally well tolerated. Adverse events (AEs) were generally mild to moderate in severity and the discontinuation rate due to AEs was low.

Marketing application in Europe is planned this year.

TECHNOLOGY APPRAISALS

SMC approves Botox for neurogenic incontinence

The Scottish Medicines Cornsortium (SMC) has followed NICE in recommending Botox (botulinum toxin type A) for the management of neurogenic detrusor overactivity with urinary incontinence (leakage) due to subcervical spinal cord injury (SCI) (traumatic or non-traumatic) or multiple sclerosis (MS) in adult patients who are not adequately managed with anticholinergic.

Current treatment options include oral medications that need to be taken daily. However, fewer than 30% of patients stay on oral medication for longer than 12 months.

Targeted injections with Botox into the bladder muscle have been shown to reduce involuntary contractions of the muscle and increase bladder capacity, reducing the number of urinary leakage episodes or even stopping leakage altogether in some patients.

Green light for Hep C combination treatment

In final draft guidance, NICE has confirmed its recommendation of the use of peginterferon alfa in combination with ribavirin as an option for treating chronic hepatitis C in children and young people.

Although hepatitis C rarely causes serous liver damage in children, if left untreated chronic hepatitis C infection increases the risk of scarring of liver fibrosis and cirrhosis, liver failure and liver cancer in the future.

Peginterferon alfa-2a (Pegasys, Roche Products) and peginterferon alfa-2b (ViraferonPeg, MSD), in combination with ribavirin are the only treatments currently licensed in the UK for the treatment of chronic hepatitis C in children and adolescents. They are also licensed for the treatment of chronic hepatitis C in adults.

REGULATORY NEWS

EMA advises on NovoMix recall

The European Medicines Agency (EMA) has issued advice relating to a recall of some batches of the diabetes medicine NovoMix 30 FlexPen and Penfill. The affected batches (below) are being recalled because of a manufacturing problem during the filling of the cartridges, which resulted in a small percentage of batches of NovoMix 30 containing too high or too low amounts of insulin units per millilitre, which could lead to hypoglycaemia or hyperglycaemia.

The European Medicines Agency therefore recommends that patients using NovoMix 30 FlexPen/Penfill from the affected batches be switched to products from unaffected batches or, if such batches are not available, to alternative treatment.

The numbers of the affected NovoMix 30 FlexPen batches are: CP50912, CP50750, CP50639, CP51706, CP50940, CP50928, CP50903, CP50914, CP50640, CP51095, CP50904, CP50650, CP51098, CP50915, CP50412, CFG0003, CFG0002, CFG0001, CP50902, CP50749, CP50393, CP50950, CP51025, CP50751, CP50375, CP50420, CP51097, CP50641, CP51096 and CP50392. The numbers of the affected NovoMix 30 Penfill batches are: CS6D422, CS6C628 and CS6C411.

The batch numbers are printed on the pen for NovoMix 30 FlexPen and on the cartridge for NovoMix 30 Penfill.

EMA advises against obstetric SABA use

The European Medicines Agency has published new recommendations that short-acting beta agonists (SABAs) should no longer be used in oral or suppository forms in obstetric indications, such as for suppressing premature labour or excessive labour contractions. However, injectable forms of these medicines can still be given for short-term obstetric use under specific conditions.

These recommendations follow a review by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC), which looked into the known risk of cardiovascular side effects with high doses of short-acting beta-agonists when used in this indication.

The PRAC concluded that there was a risk of serious cardiovascular side effects to both the mother and unborn baby when high-dose short-acting beta-agonists are used, with the data suggesting these mostly occur with prolonged use. The PRAC add that very limited data exists on the effectiveness of the oral and suppository forms of these medicines.

Benefits of CHCs 'continue to outweigh risks'

Following a review of the risk of venous thromboembolism (VTE) associated with combined hormonal contraceptives (CHCs), The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has concluded that the benefits of CHCs at preventing unwanted pregnancies continue to outweigh their risks.

The recommendations state that there is no reason for women who have been using CHCs without any problem to stop taking the medicines. However, the PRAC stresses the importance of women being made aware of the risk of VTE and its signs and symptoms, and of doctors takeing into consideration a woman's individual risk factors when prescribing a contraceptive.