



US FDA approves denosumab for the prevention of cancer-related fractures

The US FDA has approved the first and only RANK ligand inhibitor, denosumab for the prevention of skeletal-related events (SREs) in cancer patients with bone metastasis. The approval was based on three Phase III trials involving a total of 5723 patients and followed a 6-month priority review by the FDA based on denosumab's ability to fulfil an unmet need in current therapy.

The three head-to-head trials compared denosumab with zoledronic acid in patients with breast cancer, prostate cancer and in a range of other cancers. The investigators measured the time until the occurrence of a fracture or spinal cord compression, or until control of bone pain via radiation or surgery was necessary, and found denosumab to be superior to zoledronic acid in delaying SREs in patients with prostate or breast cancer. In patients with prostate cancer, the median time to a SRE was 17 months in the zoledronic acid group compared with 21 months in the denosumab group, while in the breast cancer trial, median time to a SRE was 26 months in the zoledronic acid group and has not yet been reached in the denosumab group. Comparable median times

to a SRE were seen between the two groups in solid tumors, but the FDA decided against approving denosumab for this indication in multiple myeloma patients.

David Henry from Pennsylvania Hospital (PA, USA) welcomed the approval, commenting that "as many as three out of four patients with advanced prostate, lung and breast cancer will experience spread to their bones. Despite the availability of current treatments, a significant proportion of these patients still experience bone complications or are not candidates for existing treatment."

Bone metastasis is a common occurrence in cancer patients and, prior to denosumab's latest approval, there has been limited treatment options available to help control or prevent it. "Based on the compelling science and robust clinical evidence, I expect this new option to quickly become a mainstay of cancer care," concluded Henry.

Source: Amgen Press Release: www.amgen.com/media/media_pr_detail.jsp?releaseID=1498709

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CYT107 (IL-7) in combination with raltegravir and maraviroc enters Phase II trial in HIV patients

An international, multicenter, randomized, noncomparative controlled Phase II study of therapeutic intensification plus immunomodulation in HIV-infected patients with long-term viral suppression (ERAMUNE 01) has been launched and is being conducted at clinical sites in France, Spain, Italy and the UK.

The therapeutic components include the investigative immunomodulatory agent CYT107 (recombinant human IL-7, Cytheris SA, Paris, France) in combination with two potent antiretroviral drugs,

raltegravir (ISENTRESS®, integrase inhibitor, Merck & Co., NJ, USA) and maraviroc (SELZENTRY™, CCR5 inhibitor, ViiV Healthcare, Uxbridge, UK).

The ERAMUNE 01 study was designed, and is being sponsored and conducted by Objectif Recherche Vaccins SIDA (ORVACS) to test the hypothesis that combination therapy with potent antiviral agents and immunomodulator may result in a decrease in HIV reservoirs and, in the best case scenario, eradication of the virus may be feasible. Created in 2001, ORVACS is a nonprofit organization



based in Paris, France, that is funded by the Bettencourt Schueller Foundation. ORVACS's mission is to promote and conduct research on therapeutic vaccines and immunotherapeutic approaches in the field of AIDS.

Christine Katlama of Groupe Hospitalier Pitié-Salpêtrière (Paris, France) is the study's Principal Investigator. Other participants include Bonaventura Clotet (co-Principal Investigator, University Hospital Germans Trias i Pujol, Barcelona, Spain), Brigitte Autran, Vincent Calvez and Dominique Costagliola (Université Pierre et Marie Curie, Paris, France).

"The novelty of the approach in this study is three-fold," commented Katlama. "First, the use of highly potent

antiretroviral therapy combining drugs with different HIV enzyme targets or receptors and different penetrations in cells, to suppress the virus to truly undetectable levels; secondly, the addition of immunomodulatory therapy that specifically targets viral reservoirs; and lastly, the rigorous selection of patients already having a low HIV reservoir as measured by peripheral blood HIV DNA content."

An estimated 28 HIV patients between 18 and 60 years of age are expected to be enrolled in ERAMUNE 01. The patients will be divided into two arms. Arm A will receive the current regimen of antiretroviral therapy plus a combination of raltegravir and maraviroc for 56 weeks (HAART intensification). Arm B will receive

HAART intensification (as in Arm A) plus two cycles of CYT107 at a 20 µg/kg dose. The first cycle is at week 8 and the second is at week 28. Each cycle consists of three weekly injections.

Participants are being recruited at Groupe Hospitalier Pitié-Salpêtrière (Paris, France), San Raffaele Scientific Institute (Milan, Italy); Fundacio Irsicaixa (Badalona, Spain); University Hospital Clinic of Barcelona (Barcelona, Spain), and Royal Free Hospital (London, UK). The study is expected to be completed in June 2012.

Source: *Cyntheris SA, France: www.cyntheris.com; Clinical Trials: www.clinicaltrials.gov/ct2/show/NCT01019551?term=NCT01019551&rank=1*

US FDA approves testosterone topical solution CIII

The US FSA has approved Axiron® (Eli Lilly, IN, USA), a testosterone topical solution CIII replacement therapy in men for the treatment of certain conditions associated with an absence or deficiency of testosterone, including primary hypogonadism and hypogonadotropic hypogonadism.

Although other forms of testosterone replacement therapy exist, such as oral tablets and injections, this new approval is the first to utilize an underarm applicator for the topical solution.

The approval of the testosterone topical solution was based on a multicenter, open-label Phase III study, which

demonstrated that 84% of men who completed the 120-day clinical study achieved average serum testosterone concentration within the normal range of 300–1050 ng/dl. Furthermore, 75% of patients who responded to treatment finished the study on the recommended starting dose of 60 mg once daily.

Adverse events included application site skin reactions, nausea, diarrhea, headache, increased red blood cell count and an increase in prostate specific antigen in the blood, which is a test used in prostate cancer screening. The replacement therapy's safety and efficacy in males

under the age of 18 years has not yet been established.

While the precise number of men with testosterone deficiency has not been determined, it is estimated that conditions associated with an absence or deficiency in testosterone affect up to 13 million men over the age of 45 years in the USA alone. This latest approval of the testosterone topical solution enhances the treatment options available for a range of conditions affecting millions of men.

Source: <http://newsroom.lilly.com/releasedetail.cfm?ReleaseID=532924>

New clinical trial results for severe malaria

Study results from the largest ever clinical trial investigating hospitalized patients with severe malaria suggest that artesunate should be the preferred treatment worldwide for all age groups.

The African Quinine versus Artesunate Malaria Trial (AQUAMAT) was carried out in ten centers across nine African countries over a 5-year period. It found that the percentage of deaths caused by severe malaria was reduced by 22.5% when treated with artesunate as compared with quinine. A total of 8.5% of patients

admitted to hospital with severe malaria died when treated with artesunate compared with 10.9% of those treated with quinine. Results from this open-label randomized trial have led experts to recommend a change to the treatment guidelines for severe malaria, which currently advise quinine as the first-choice treatment.

"For over a century, quinine administered by injection has been the best treatment available for treating severe malaria, but thanks to the development of the artemisinin compounds, we now have a

safer and much more effective treatment. We recommend that artesunate should now replace quinine for the treatment of severe malaria in both children and adults everywhere in the world." Commented Nick White (Bangkok, Thailand) the lead author of the study.

Source: *Dondorp AM, Fanello CI, Hendriksen IC et al.: Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. Lancet 376(9753), 1647–1657 (2010).*

Drug Approvals October to December 2010

Trade name	Generic name	Indication	Region	Manufacturer	Date approved
Cardiology					
Pradaxa®	Dabigatran etexilate mesylate	To reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation	USA	Boehringer Ingelheim	October 2010
Brilique™	Ticagrelor	For the prevention of atherothrombotic events in adult patients with acute coronary syndromes	EU	AstraZeneca	December 2010
Endocrinology and metabolism					
Axiron®	Testosterone	Replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone	USA	Acrux Pharma	November 2010
Egrifta™	Tesamorelin	For the reduction of excess abdominal fat in HIV-infected patients with lipodystrophy	USA	Theratechnologies	November 2010
Kombiglyze™ XR	Saxagliptin/metformin HCl extended-release	An adjunct to diet and exercise to improve glycemic control in adults with Type 2 diabetes mellitus when treatment with both saxagliptin and metformin is appropriate	USA	Bristol-Myers Squibb	November 2010
LO LOESTRIN™ FE	Norethindrone acetate and ethinyl estradiol tablets, ethinyl estradiol tablets, and ferrous fumarate tablets	Prevention of pregnancy	USA	Warner Chilcott	October 2010
VPRIV®	Velaglucerase alfa	For long-term use in pediatric and adult type 1 Gaucher disease	Canada	Shire	December 2010
Infectious disease					
Teflaro™	Ceftaroline fosamil	For the treatment of acute bacterial skin and skin structure infections and community-acquired bacterial pneumonia	USA	Cerexa	October 2010
Neurology					
Gablofen®	Baclofen	Management of severe spasticity of cerebral or spinal origin in adult and pediatric patients aged 4 years or more	USA	CNS Therapeutics	November 2010
Latuda®	Lurasidone	Schizophrenia	USA	Sunovion	October 2010
Lyrica®	Pregabalin	Peripheral neuropathic pain	Japan	Pfizer	October 2010
Nuedexta™	Dextromethorphan hydrobromide and quinidine sulfate	Pseudobulbar affect	USA	Avanir	October 2010
Oncology					
Halaven™	Eribulin mesylate	Treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting	USA	Eisai	November 2010
XGEVA™	Denosumab	Prevention of skeletal-related events in patients with bone metastases from solid tumors	USA	Amgen	November 2010
Respiratory					
Aridol™	Mannitol inhalation powder	For the assessment of bronchial hyperresponsiveness in patients older than 6 years who do not have clinically apparent asthma	USA	Pharmaxis	October 2010
Rheumatology					
Atelvia™	Risedronate sodium delayed release	Postmenopausal osteoporosis	USA	Warner Chilcott	October 2010