US FDA approves denosumab for 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 an 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 an 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

in the news...

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 is designed, 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, and is funded by

part of future medicine fsg

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 18–60 years of age are expected to be enrolled to ERAMUNE 01. The patients will be divided into two arms. Arm A will receive current regimen of antiretroviral therapy plus a combination of raltegravir and maraviroc for 56 weeks (HAART intensification). Arm B will receive HAART intensification (same as Arm A) plus two cycles of CYT107 at a 20 µg/kg dose. First cycle is at week 8 and second cycle 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: Cytheris SA, France: www.cytheris.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 number 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).*