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Study shows once-yearly Aclasta® better than risedronate at increasing bone mass in patients with osteoporosis caused by glucocorticoids

- *Glucocorticoids, commonly known as steroids, widely used to treat inflammatory conditions but can increase risk of osteoporotic fractures with up to 50% of patients on long-term therapy at risk^{1,2}*
- *Study of more than 800 men and women shows higher bone mineral density with Aclasta than risedronate, a current established therapy³*
- *Regulatory approval sought for treatment and prevention of glucocorticoid-induced osteoporosis in EU and US*

Basel, April 11, 2008 – New data show that a once-yearly infusion of Aclasta® (zoledronic acid 5 mg)* was significantly better than risedronate at increasing bone mass in patients with osteoporosis caused by glucocorticoids, commonly known as steroids³. These medications are widely used to treat inflammatory conditions but can cause bone loss and osteoporosis^{1,2}.

Up to 50% of patients receiving long-term glucocorticoid therapy are at increased risk of fracture due to osteoporosis², and approximately nine million people worldwide are affected by glucocorticoid-induced osteoporosis (GIO)^{4,5}.

Results of a clinical study in 833 men and women were presented today at the European Congress on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ECCEO) in Istanbul, Turkey³.

“Recognizing and treating GIO is an important need, as glucocorticoid therapy is so widely used and presents an ongoing challenge for physicians,” said Professor David M. Reid, Head of the Division of Applied Medicine at the University of Aberdeen, UK. “The significant efficacy of this once-yearly treatment, offering year-long bone protection, will provide a very valuable treatment option for healthcare professionals treating and managing osteoporosis induced by glucocorticoids.”

The trial investigated both prevention (288 patients) and treatment (545 patients) of GIO³. Results demonstrated that a single yearly infusion of Aclasta significantly increased bone mineral density (BMD) in the lumbar spine at 12 months compared to risedronate in both the treatment group (Aclasta 4.1%, risedronate 2.7%; P=0.0001) and prevention group (Aclasta 2.6%, risedronate 0.6%; P<0.0001)³.

Risedronate is one of the established treatments for GIO⁶ and, like Aclasta, is a member of the bisphosphonate class of drugs⁶. Risedronate is taken in the form of a daily pill⁶, whereas

* The tradename in the US is Reclast®

Aclasta is given as a once-yearly 15-minute infusion^{7,8}, promoting compliance with bisphosphonate treatment and providing annual protection against the consequences of osteoporosis.

Novartis is applying for an indication with the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) for the treatment and prevention of GIO.

Aclasta is already approved in more than 50 countries for the treatment of postmenopausal osteoporosis and in more than 70 countries for the treatment of Paget's disease of bone, the second most common metabolic bone disorder. Additional indications for Aclasta are being pursued worldwide for the prevention of clinical fractures after hip fracture and the treatment of osteoporosis in men.

A growing body of clinical evidence supports Aclasta as the only treatment for postmenopausal osteoporosis approved in the US and EU to reduce the risk of fractures in all key sites typically affected by osteoporosis, including the hip, spine and non-spine (e.g. wrist and rib)⁷.

“These new data reinforce the efficacy of this novel once-yearly treatment and confirm Aclasta's ability to increase bone mineral density significantly in different populations,” said Trevor Mundel, MD, Head of Global Development Functions at Novartis Pharma AG. “We already know from previous osteoporosis studies that patients prefer a single yearly dose versus oral weekly treatment^{9,10}, confirming that Aclasta should provide a real benefit for patients affected by osteoporosis.”

The primary objective of the GIO study was to demonstrate non-inferiority of Aclasta to risedronate in percentage change in lumbar spine BMD from baseline at 12 months³. Secondary endpoints included change in lumbar spine BMD at six months, and in the BMD of femoral neck and total hip at six and 12 months³.

Results from the study confirm that Aclasta is generally safe and well-tolerated. The most common adverse events associated with Aclasta were transient post-dose symptoms such as fever and muscle pain. The majority of these symptoms occurred in the first three days after Aclasta administration and resolved within three days. Post-dose symptoms can be reduced by taking paracetamol or ibuprofen shortly after the Aclasta infusion^{7,8,11}.

Analysis of key safety parameters, including osteonecrosis of the jaw, atrial fibrillation, renal impairment and delayed fracture healing, found Aclasta was comparable to risedronate¹¹.

The active ingredient in Aclasta is zoledronic acid, which is also available in a different dosage under the brand name Zometa® (zoledronic acid 4 mg) for use in certain oncology indications.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as “can”, “will”, “should”, or similar expressions, or by express or implied discussions regarding potential new indications or labelling for Aclasta or regarding potential future revenues from Aclasta. Such forward-looking statements reflect the current views of the Company regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with Aclasta to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Aclasta will be approved for any additional indications or labelling in any market. Nor can there be any guarantee that Aclasta will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Aclasta could be

affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry and general public pricing pressures, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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