Summary of the results of the clinical trial for laypersons

Protocol number:
CRO-PK-24-372 - Sponsor code ACEBIO/11

Title of the study:
Clinical study to evaluate the bioequivalence of a new Aceclofenac 100 mg film-coated tablets formulation compared with the marketed Gladio® 100 mg film-coated tablets formulation, after administration to healthy volunteers.

Sponsor name and contact details:
Abiogen Pharma S.p.A.,Via Meucci, 36, 56121 Loc. Ospedaletto, Pisa, Italy
Phone: +39.05.03.15.41.01
E-mail: marina.accoto@abiogen.it

General information about the study:
Non-steroidal anti-inflammatory drugs (NSAIDs) represent one of the most common classes of medications used worldwide to reduce inflammation, fever and pain. The main signs and symptoms of inflammation are related to the synthesis and physiological action of prostaglandins in damaged tissue, which cause vasodilation (with consequent redness, heat and swelling), inflammation and pain. NSAIDs act by inhibiting the enzymes responsible for prostaglandin production and, in this way, exert anti-inflammatory, analgesic and antipyretic actions.
Aceclofenac is a NSAID approved in 69 countries worldwide and widely prescribed for musculoskeletal disorders, such as osteoarthritis and rheumatoid arthritis, or other inflammatory and painful conditions, such as back pain and toothache.
The Sponsor, Abiogen Pharma S.p.A., has developed a new formulation of aceclofenac (Aceclofenac 100 mg film-coated tablets), which contains the same active substance, at the same dose and in the same pharmaceutical form, as the authorised product Gladio® 100 mg film-coated tablets.
Since the new formulation is manufactured in a different facility and using a different manufacturing method from Gladio®, it was necessary to conduct a clinical study to evaluate the bioequivalence (i.e., to determine whether the amount of active substance that reaches the bloodstream and the rate at which it is absorbed, distributed, metabolised and eliminated by the body are equivalent) between the two products. In addition, safety and tolerability data were collected for both pharmaceutical products.
The clinical study was conducted at the CROSS Research S.A. Phase I Unit clinical centre, located in Arzo, Switzerland.
All participants received a single dose of each of the two formulations during two separate study periods, separated by an interval of at least 7 days. The study was open label (i.e., both the Investigator and the participants knew which product had been assigned) and randomised (i.e., the order in which each participant received the two formulations was decided by chance).

Population of participants:
Twenty (20) healthy volunteers, men and women, aged between 18 and 55 years, took part in this clinical trial. All participants completed the study according to the protocol and were included in the analyses of the results.
The main criteria for the participant's inclusion in the clinical study were the following: 1) Informed consent signed by each participant; 2) Ability to comprehend the full nature and purpose of the study and to comply with the study requirements, visit schedule and planned procedures; 3) Body mass index between 18.5 and 30 kg/m^2, blood pressure and heart rate within normal limits, and no clinically significant abnormalities on physical examination, laboratory tests and electrocardiogram (ECG); 4) Absence of diseases or allergies that could affect the study results; 5) If woman, sterile or post-menopausal for at least one year or, if of childbearing potential, not breastfeeding, with a negative result of pregnancy tests and available to abstain from sexual intercourse or to use an acceptable contraceptive method until completion of the study; 6) If male, sterile or, if fertile, available to abstain from sexual intercourse or to use an acceptable contraceptive method until completion of the study.

Investigational product used:
Prior taking part in the clinical study, participants underwent a preliminary visit. This visit included a physical examination, an ECG, an assessment of vital signs (blood pressure and heart rate), an alcohol saliva test, a pregnancy test for women, a drug screening test, and blood and urine laboratory analyses. Following this initial evaluation, the Investigator assessed participants' eligibility: only participants meeting all required criteria were included in the clinical trial and received a progressive number that determined the sequence in which they were to receive the two study products.
In each study period, participants took the product by mouth, in the morning, at about 8:00, after a fasting of at least 10 hours. Blood samples were collected before taking each product and at several time points during the 12 h following its intake, to determine the concentration of aceclofenac in the blood. Additionally, vital signs were measured.

Investigational product used (cont.):
At the final visit, participants underwent a complete physical examination, an ECG, and blood and urine tests, to check if any changes occurred in comparison with the preliminary visit.
Throughout the entire study, participants were asked to report any change in their health status. The Investigator continuously checked the occurrence of any adverse effect, with particular attention to those potentially related to the intake of the study products.

Description of adverse reactions and their frequency:
During the clinical study, one side effect was experienced by one participant (5.0%). The event, an episode of dizziness of mild intensity, occurred after administration of Aceclofenac 100 mg film-coated tablets, was evaluated by the Investigator as unlikely related to the pharmaceutical product, and resolved spontaneously by the study end.
No participants withdrew from the study due to an adverse event, and no serious or severe adverse events were reported. No clinically significant effects of the study products on laboratory analyses results, vital signs, ECG or physical examination were observed throughout the study.

Overall results of the clinical trial:
The two study products, Aceclofenac 100 mg film-coated tablets and Gladio® 100 mg film-coated tablets, were found to be bioequivalent. Therefore, the primary objective of the clinical study was achieved, demonstrating that the amount of the active substance aceclofenac that reaches the bloodstream and the rate at which it is absorbed, distributed, metabolised and eliminated by the body are equivalent after administration of the two study products.
In detail, no significant differences emerged in the maximum concentration of aceclofenac in the blood, nor in the time taken to reach it, nor in the overall amount of active substance present in the body up to 12 hours after administration. Similarly, the total amount of aceclofenac present in the body from absorption until its complete elimination (an amount estimated using statistical calculations) was also equivalent.

Comments on the outcome of the clinical trial:
In compliance with European regulations, the new Aceclofenac 100 mg film-coated tablets formulation is bioequivalent to the already authorised Gladio® 100 mg film-coated tablets formulation available on the market.
The safety of the two pharmaceutical products was excellent: no adverse effects related to the study products occurred during the clinical trial.

Indication where additional information could be found:
Further information can be obtained by contacting the study sponsor, as indicated above.