A specific active immunotherapy to control cholesterol levels in blood

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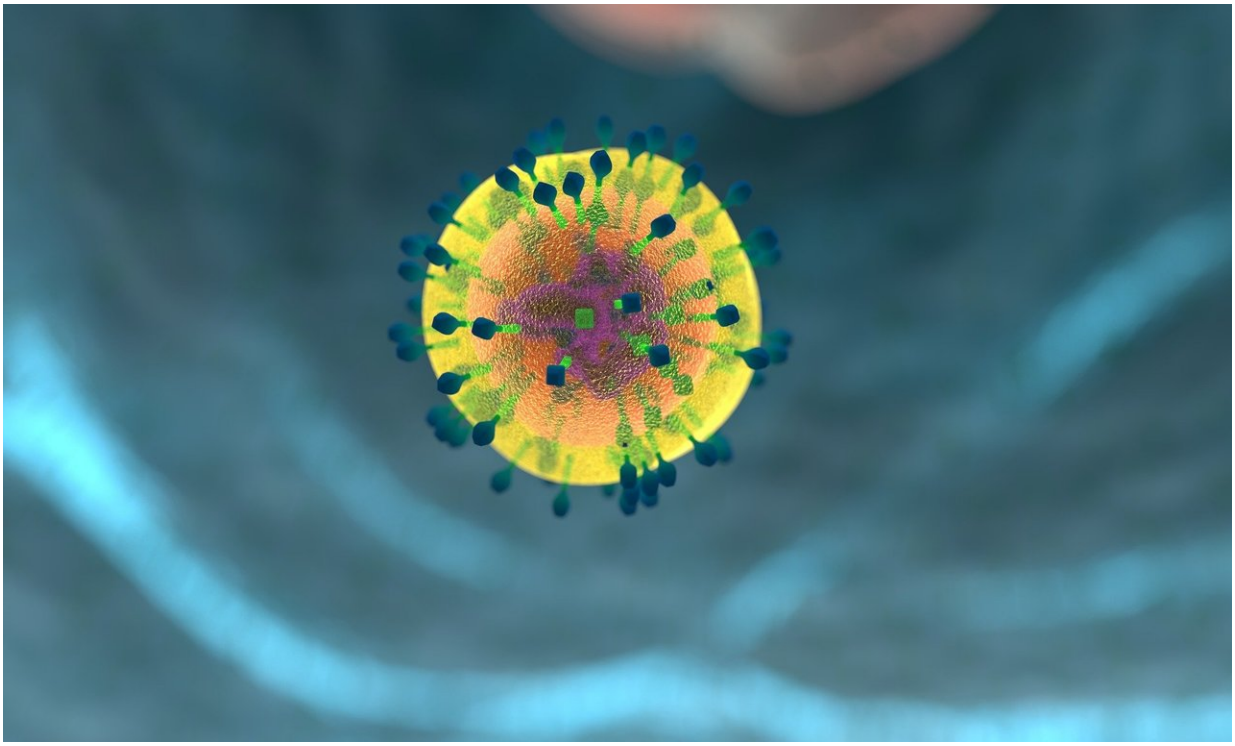

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Cardiovascular disease still accounts for the greatest number of deaths worldwide. PCSK9-inhibition reduces the risk of cardiovascular events by regulation of the LDL (low density lipoprotein) receptor, one of the transporters of cholesterol in blood. The protein PCSK9 binds to the LDL-cholesterol receptor and enhances its degradation, which leads to

the reduced clearance of LDL-cholesterol and a higher risk of atherosclerosis.

So far, blocking PCSK9 was clinically limited by the need for frequent injections with therapeutic antibodies and economically restricted by their high cost. As a promising novel strategy, active immunotherapy that induces a long-lasting PCSK9-specific antibody response may overcome these disadvantages to reduce the burden of cardiovascular disease as the major cause of death in the developed world. On the basis of this innovative concept AFFiRiS AG (Vienna, Austria) developed two products, AT04A and AT06A, which were tested at the Medical University of Vienna (Dept. of Clinical Pharmacology). Results of the first in-human study of this immunotherapy actively targeting PCSK9 are now available.

72 healthy individuals with slightly elevated LDL-cholesterol (75 to 200 mg/dl) were enrolled in three parallel treatment groups. Participants were randomized to receive AT04A, AT06A or placebo. Immunizations were administered as three priming immunizations at four-weekly intervals. In a second part of the study, 50 participants received a booster immunization at week 60 with a follow-up until week 90, including an interim analysis at week 70. The primary study objective was safety and tolerability of AT04A and AT06A with immunogenicity and efficacy as secondary, exploratory study objectives.

Both immunotherapies, AT04A and AT06A, were safe and well tolerated. No significant difference in the safety profile was observed between active and placebo treatment groups with the exception of injection site reactions. These local reactions – typical for vaccinations – were the most frequently reported adverse events (63.3%) and were more common in the active treatment groups. Injection site reactions were usually of mild to moderate severity, transient and not interfering with activities of daily living. More than 90% of individuals who

received AT04A or AT06A developed a PCSK9-specific antibody response, which was readily reactivated after booster immunization at week 60. The mean LDL-cholesterol reduction after the booster was 13.3% at week 70 when comparing AT04A with placebo. Over the entire study period of 90 weeks, the difference in LDL-cholesterol reduction between AT04A and placebo was statistically highly significant (p

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