

PROJECT REVIEW

"Detection of Sotatercept (ACE-011, ActRIIA-IgGI) in human urine and blood – Protocols for initial and confirmatory doping testing"

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Aside from human endogenous erythropoietin (EPO), its recombinant analogues (e.g. Epoetins alfa/beta/delta/omega, Darbepoetin alfa) and EPO-mimetics (e.g. Peginesatide), which stimulate erythropoiesis through the EPO-receptor pathway, formation of erythrocytes can also be stimulated via the so called "activin-receptor type IIA signal transduction pathway": as soon as ligands, which interact with activin-receptor type IIA ("ActRIIA ligands") are removed by so-called ActRIIA ligand traps in a targeted way, erythropoiesis is also stimulated. ActRIIA ligands belong in particular to the transforming growth factor-beta (TGF- β) superfamily (e.g. activin).

Sotatercept (ACE-011, ActRIIA-IgGI), a fusion protein consisting of the extracellular domain of ActRIIA receptor and the Fc-part of human immunoglobulin G1 (IgG1), is capable of acting as ActRIIA ligand trap, and was primarily developed as pharmaceutical for enhancing bone mineralisation in order to revert osteoporosis. However, aside from increasing bone mineral density, it was discovered that Sotatercept also stimulates erythropoiesis in a dose dependant manner leading to an increase in red blood cell counts. Sotatercept is currently intensely investigated in several phase II clinical trials.