Treatment of Alkaptonuria and Tyrosinemia type 1

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PATENT STATUS: granted in Italy

PRIORITY NUMBER: 102016000018748

PUBLICATION: 19/09/2019

PUBLISHED AS: IT, WO, EP, US

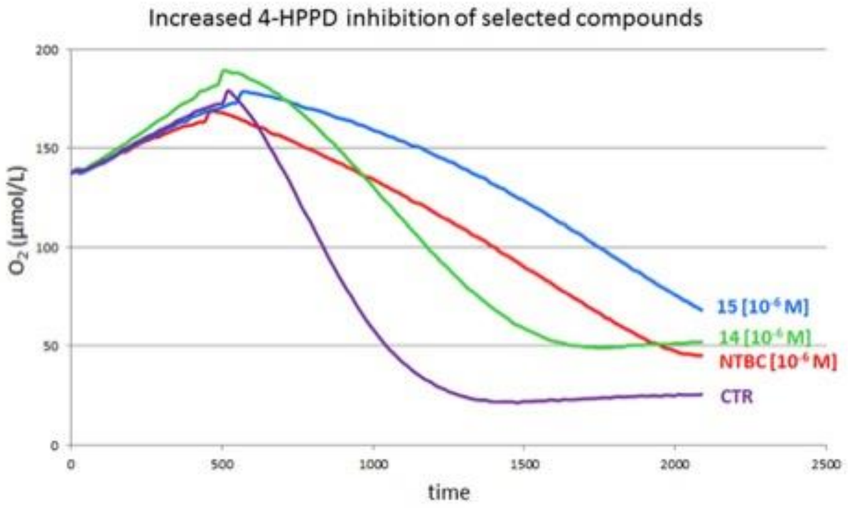
Invention

Alkaptonuria (AKU) is a rare genetic disorder characterised by accumulation and oxidation of homogentisic acid (HGA), derived from the insufficient activity of the enzyme homogentisate 1,2-dioxygenase (HGD) involved in tyrosine catabolism.

The herbicide nitisinone is a human and rat inhibitor of 4-hydroxyphenylpyruvate dioxygenase (4-HPPD), which converts 4-hydroxyphenylpyruvate (HPP) into HGA. The use of nitisinone, while approved by the FDA 'in exceptional circumstances' as a life-saving remedy in the hereditary paediatric disease tyrosinaemia type 1 (HT1), comes with heavy side effects. Recent clinical studies have confirmed that nitisinone consistently reduces plasma and urinary levels of HGA, while leading to tyrosine accumulation.

The invention therefore consists of alternative compounds to nitisinone, having a trichetonic structure, as 4-HPPD inhibitors with lower cytotoxicity, for the treatment of both AKU and HT1, which reduce HGA accumulation while minimising tyrosinemia.

Drawings
& pictures



Industrial applications

The technology may interest chemical and/or pharmaceutical companies having (or wishing to expand to) orphan drugs in their pipeline, to be distributed to all requesting alkaptonuria treatment centres.

In particular, the invention can be formulated as a pharmaceutical composition that can be taken topically, orally, parenterally or inhaled, and includes multiple isotopic variants that can be used as a starting point for the development of new drugs for the treatment of AKU and HT-1.

Possible developments

Initially evaluated at a TRL of 3, the technology is still being developed through specific technology maturation projects aimed at demonstrating its efficacy and safety, possibly applying for orphan drug designation (ODD). The maturation project ends in late August 2022.

The group is looking for industrial partners operating in the pharmaceutical field who are interested in collaborating in order to conduct follow-up and pre-marketing studies of the drug.

The University of Siena is open to negotiating specific agreements for the exploitation, licensing or option of the patented invention.

For more information:

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