Announcement of top-line results

The TUDCA-ALS consortium announces top-line results from the European phase 3 clinical trial of TUDCA in patients with amyotrophic lateral sclerosis (ALS).

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Summary of outcomes:

The TUDCA-ALS study did not meet the primary endpoint, measured by ALSFRS-R scores (a measure of functional and motor changes in ALS). There were also no significant differences observed across secondary endpoints.

Treatment with TUDCA was well tolerated and generally safe, with predominantly mild gastrointestinal adverse effects occurring both in the placebo and treatment arms.

The COVID-19 pandemic contributed to a reduced patient recruitment, which negatively impacted the statistical analysis due to low participant numbers at the later timepoints.

Aspects of the data are being pursued further to explore additional differences between placebo and treatment arms, including different time points and analysis in slow versus fast progressing groups. Full results will be presented at a later stage.

The TUDCA-ALS consortium is announcing headline results from the randomised placebo-controlled phase 3 clinical trial of tauroursodeoxycholic acid (TUDCA) in people living with amyotrophic lateral sclerosis (ALS), also known as Motor Neurone Disease (MND). The study ran over 18 months, with 25 European sites participating in the study across seven European countries.

The study failed to meet its primary endpoint, defined as a difference in responding and non-responding patients in month 18 as measured by Revised

Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) scores. Furthermore, no statistically significant difference was found between TUDCA and placebo in secondary outcomes including time of survival and changes in biomarkers such as neurofilament light protein.

The study leader, Professor Alberto Albanese, Neurology Unit Director at Humanitas Research Hospital (Italy) comments:

"We are very disappointed to see there was no overall benefit demonstrated. Given the heterogeneity of ALS, it is important to explore whether the lack of effect was uniform across the whole trial population. Therefore, thorough analysis of subgroups based at intermediate time points is ongoing.

We would like to express our deep gratitude to the people with ALS who so generously participated in the trial."

– Professor Alberto Albanese, Trial Lead

The trial took place during the COVID-19 pandemic and faced numerous challenges posed by repeated pandemic waves. This included a drop from the projected 440 to 336 participants, equally distributed between treatment arms at the start of the trial. Markedly more placebo participants dropped out of the trial during the first 9 months than from the TUDCA arm, with about half of patients reaching the 18-month mark in each treatment arm.

The consortium is undertaking additional tasks, including further statistical analysis of data and biomarkers at various timepoints, to gain a clearer understanding of the effects of TUDCA in slow progressing patients compared to fast progressors. These analyses will be presented at the meeting of the European Network for the Cure of ALS (ENCALS) in Stockholm, June 2024.

About the TUDCA-ALS consortium

Studies have previously shown that TUDCA has neuroprotective properties, preventing motor neurons from dying. A phase 2b clinical trial showed that patients who received TUDCA in addition to riluzole for 54 weeks had a

prolonged median survival of 4-5 months. The TUDCA-ALS trial was developed to determine the clinical efficacy of TUDCA in ALS.

The TUDCA-ALS consortium was organised by Humanitas Research Hospital (Italy), the study sponsor. The consortium included experts from Universitaet Ulm (Germany), The University of Sheffield (United Kingdom), Centre Hospitalier Regional Universitaire de Tours (France), Katholieke Universiteit Leuven (Belgium), Universitaire Medisch Centrum Utrecht (Netherlands), Trinity College Dublin (Ireland), Bruschettini s.r.l. (Italy), Istituto Superiore di Sanita (Italy), and Motor Neurone Disease Association (United Kingdom).

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