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Enalapril orodispersible minitablets (ODMTs) for children with heart failure – a successful EU-funded drug development program for children

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Introduction: Until today, European and American children with chronic heart failure do virtually not benefit from approved drugs despite the major successes of the US paediatric legislation initiative in 1997 and the European paediatric regulation in 2007. The EU-funded LENA consortium (FP7 Grant agreement no 602295) has bridged this gap by generating all data necessary for a paediatric-use marketing authorization (PUMA) application for the angiotensin-converting enzyme (ACE) inhibitor enalapril to treat paediatric heart failure patients.

Methods and Results: On the bases of good manufacturing, as well as good clinical and laboratory practices, investigator-driven clinical trials in 24 healthy volunteers, and in 102 children aged from birth to 12 years (72% below 1 year of age) demonstrated substantial bioavailability of the enalapril orodispersible minitablets (ODMT) as well as safe, simple and reliable use. The ODMTs were highly accepted by patients, parents and medical staff. The ODMTs remove the need for off-label enalapril use in extemporaneous formulations, including liquids, capsules or crushed tablets in children below the age of 6 years or 20 kg and age-appropriate safe dosages of enalapril are now established.
The LENA consortium has successfully developed a risk-adapted quality management system for an academic consortium. In addition, they developed an innovative active learning tool for particularly critical processes in these trials. This enabled the LENA team to fulfil all applicable ethical and regulatory standards for study performance and reliable data generation in their pharmacokinetic and pharmacodynamic investigations.

Conclusions: As ACE-inhibitors are regarded as first line treatment and enalapril was prioritized by the EMA to be developed for paediatric heart failure treatment, the LENA enalapril ODMTs provide a substantial step towards the safe and reliable treatment of children with heart failure.

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