P-228 - NEWBORN SCREENING FOR SIX LYSOSOMAL DISEASES: PILOT STUDY IN BRAZIL

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INTRODUCTION: Lysosomal storage disorders (LSDs) are inborn errors of metabolism caused by excessive accumulation of undegraded metabolites due to the deficiency of soluble lysosomal hydrolases, membrane proteins or accessory proteins that lead to an impaired turnover of complex macromolecules, including glycosaminoglycans, proteins and lipids. Many LSDs already have specific therapies, and in most cases the earlier introduction of therapy provides better outcomes. However, patients are usually diagnosed only after a long “diagnostic odyssey”, with therapies introduced when irreversible manifestations are already present. OBJECTIVE: This project aims to evaluate the feasibility of newborn screening (NBS) for selected LSDs in Brazil, using a tandem mass spectrometry (MS/MS) platform with a 6-Plex kit (supplied by PerkinElmer). MATERIALS AND METHODS: The study includes the screening for Gaucher, Fabry, Pompe, Krabbe, Niemann-Pick A/B and Mucopolysaccharidosis I. This is a prospective study in 20,000 unselected newborns from the state of Bahia, Brazil. The newborns with low enzyme activity are further evaluated by biochemical and molecular genetics methods until the diagnosis is confirmed and are referred for treatment as appropriate. All lysosomal enzymes were analyzed with NeoLSD MS/MS kit (PerkinElmer) on a Waters Xevo TQ-S Micro. RESULTS: Validation of the method was conducted in dried blood spots provided by the supplier and from unselected newborns. Instrument optimization was conducted in order to increase the signal and to decrease the in source fragmentation. Initial cutoffs were established as percentage of median in nmol/h/mL, as 0.8 (Gaucher), 1 (Fabry), 1.6 (Pompe), 0.8 (MPS I), 0.46 (Krabbe) and 0.9 (Niemann-Pick A/B). CONCLUSIONS: Further positive samples will be included in order to confirm the cutoffs. This validation of the MS/MS method enabled the beginning of a pilot study, which, when completed, will include 20,000 newborns and will provide important information about the feasibility of a NBS for LSDs in Brazil.