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Application of a non-invasive integrated screening approach to facilitate enrollment of clinical trials with investigational NAFLD/NASH therapeutics

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Introduction: Despite NAFLD/NASH being a prevalent co-morbidity in obesity and type 2 diabetes, clinical development of NAFLD/NASH therapeutics is currently hindered by significant challenges in clinical trial enrollment. Traditional study screening is commonly associated with screen failure rates of up to 80%. Given the cost and timeline implications of subjects failing to meet MRI- or biopsy-based inclusion criteria, there is a clear need for optimized screening strategies in NAFLD/NASH clinical studies.

Aims: Our goal was to assess the potential utility of an integrated screening approach aimed at pre-identifying individuals who have a high probability of being eligible for NAFLD/NASH clinical studies.

Material and Methods: Our integrated screening approach consists of: 1) a scoring system based on specific equation matrixes from 2 validated published NAFLD screening algorithms; and 2) a validated lipidomic testing panel for NAFLD and NASH, developed by One Way Liver (OWL) Metabolomics. OWL assays include profiling of 28 triglycerides. Testing validated against liver biopsy. We applied this scoring system (score of 0 to 5, with 5 having the highest probability of NAFLD) to two cohorts of subjects (Cohort 1: 204 obese type 2 diabetic subjects; Cohort 2: 55 obese nondiabetic subjects). Cohort 1 subjects with a score of 5 underwent MRI-PDFF-based quantitation of liver fat (%), whereas cohort 2 subjects with a score of 5 underwent additional lipidomic testing to further characterize the probability of NAFLD and NASH.

Results: Of the 18 subjects from cohort 1 with a score of 5, 15 (83%) had >10% liver fat by MRI-PDFF (range: 12.5 - 27.8%). Algorithm's detection profiling of >10% liver fat had a Se of 88.24% (95%CI 0.63-0.98), Sp of 62.50% (95%CI 0.24-0.91), PPV of 83.33% (95%CI 0.66-0.92) and NPV of 71.43% (95%CI 0.37-0.91). Of the 13 subjects from cohort 2 with a score of 5, all (100%) tested positive for NAFLD lipidomic index and of those, 5 (38%) also tested positive for NASH lipidomic index. MRI-PDFF data will be presented at the meeting.

Conclusions: These preliminary results point to the potential utility of optimized, non-invasive screening algorithms for NAFLD/NASH studies. Pre-screening strategies to identify individuals who are most likely to have significant steatosis or steatohepatitis on MRI or biopsy, may be a scalable, efficient means of reducing screen failure rates in NAFLD/NASH clinical trials. Refinement and validation in larger cohorts is currently underway.

Disclosure of Interest: G. Rodriguez-Araujo: Employee: ProSciento, Inc, M. Hernandez: Employee: ProSciento, Inc, C. Weyer: Employee: ProSciento, Inc, L. Morrow: Employee: ProSciento, Inc, L. Millán: Employee: OWL Metabolomics, I. Martínez-Arranz: Employee: OWL Metabolomics, M. Hompesch: Employee: ProSciento, Inc

ABSTRACTS

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