Poster Number: 113

Hyperuricemia May Be a Suitable Cost-containing Screening Gateway for Determining Nonalcoholic Fatty Liver Disease/Nonalcoholic Steatohepatitis Clinical Trial Eligibility Requiring Hepatic Steatosis and/or Fibrosis

C. A. Dehn[1], N. McDonald[1], M. Fein[1], M. Pearson[1], L. Galitz[1], L. Rusch[1]

[1]High Point Clinical Trials Ctr, High Point, NC, USA

Statement of Purpose, Innovation or Hypothesis: Nonalcoholic fatty-liver disease (NAFLD) is an epidemic condition that may slowly advance to nonalcoholic steatohepatitis (NASH). First described in 1980, NASH may lead to the development of hepatocellular carcinoma and is expected to overtake all other causes as the leading indication for liver transplant by 2020. Recent developments in the industry, including the 2015 suggestion from the US Food & Drug Administration and American Association for the Study of Liver Diseases that surrogate endpoints may be allowed to substitute for an outcomes trial have stimulated investment and innovation in the NAFLD/NASH space. This has created an unmet need for clinical trial participants with these conditions, but in whom a pre-existing diagnosis is highly unlikely. As such, we investigated the suitability of hyperuricemia as a cost-containing screening gateway to more conclusive eligibility determining procedures by correlating it to positive findings of hepatic steatosis and fibrosis with a FibroScan® device. Elevated FibroScan results and uric acid levels are known to have independent relationships with fatty-liver disease, but to our knowledge, these have never been correlated with each other. All participants signed informed consent prior to any procedures being performed.

Description of Methods and Materials: The FibroScan device operates similar to an ultrasound and is a rapid, non-invasive, painless test which can report parameters estimating steatosis (controlled attenuation parameter [CAP] [dB/m]) and fibrosis (E[kPa]). Participant profiles with complete data for FibroScan results and uric acid level were selected. Based on evidence in the literature, for the purposes of this investigation, cutoff values for positive findings of steatosis were defined at CAP scores ≥260 dB/m and elastographic measures of fibrosis >7 E[kPa] and (Pearson) correlated to serum uric acid levels. In an alternate approach, selection for hyperuricemia ≥ upper quartile of the normal range (≥6.0 females, ≥7.4 males) and retrospectively evaluated for the ability to predict that FibroScan CAP and elastography measures would meet the defined acceptable ranges.

Data and Results: 236 participants profiles with complete data sets were reviewed. Of those, 182 had CAP scores ≥260 dB/m, while 70 had elastography scores above >7 E[kPa]. Selecting first for FibroScan scores resulted in a very weak and statistically-insignificant correlation to uric acid levels (CAP [dB/m] $r = 0.07$, $p>0.05$; E[kPa] $r = 0.05$, $p>0.05$). However, selecting instead for hyperuricemia ≥ the upper quartile of the normal range (≥6.0 females, ≥7.4 males) resulted in 54 participant profiles. 87% of these had CAP scores ≥260 dB/m and 22% had E[kPa] values >7.

Interpretation, Conclusion or Significance: The causal or casual role of hyperuricemia relative to the metabolic constellation of disorders including NAFLD/NASH is controversial. It may, however, prove to be an adequate selection tool for determining which study participants to submit for more conclusive testing of steatosis and/or fibrosis eligibility requirements. This may be especially valuable in the absence of more sophisticated alternatives such as FibroScan.