Supplementary Table 1- Main Initial Study inclusion and exclusion criteria

Inclusion criteria

1. Adult men or women 18 to 70 years of age *
2. Severe acute liver injury **
3. INR > 1.5
4. Presence of any degree of hepatic encephalopathy
5. Duration of illness < 26 weeks
6. Enrolled into the ALFSG registry study
7. Written informed consent from the patient or their legal next of kin

Exclusion criteria

1. Evidence of pre-existing chronic liver disease
2. Pre-existing New York Heart Association stage ¾ heart failure
3. Evidence of pre-existing chronic renal failure requiring hemodialysis including chronic hemodialysis prior to ALI/ ALF hospital admission
4. Evidence of cirrhosis unless clinically acute Wilson's disease or autoimmune ALF.
5. ALF due to Budd-Chiari, malignancy or suspected HSV
6. Severe shock requiring 2 or more vasopressor agents
7. Evidence of upper GI bleeding at enrollment
8. Pregnancy/ breastfeeding
9. Subjects who have received amiodarone or an HMG-CoA reductase inhibitor (Stains ***) in the 30 days prior to enrollment
10. Consumption of any alcohol or caffeine containing beverage or food within 24 hours of enrollment.
11. Use of contraindicated medications within 48 hours of enrollment including: acyclovir ***, allopurinol, carbamazepine, cimetidine, ciprofloxacin, daidzen, disulfiram, echinacea, enoxacin, famotidine ***, fluvoxamine, methoxsalen, mexiliten, montelukast, norfloxacin, phenylpropanolamine, phenytoin, propafenone, rifampin, terbinafine, ticlodipine, thiabendazole, verapamil, zileuton or oral contraceptives

* Changed to 80 years with protocol amendment

** Eligibility criteria were expanded with protocol amendment to include patients with severe non-APAP ALI

*** Criteria changed with protocol amendment to allow for use of famotidine or acyclovir within 48 hours of enrollment as well as use of statins in 30 days prior to enrollment.