# Oral Abstracts

## 7A-06

### IV SILIBININ (LEGALON ® SIL) FOR THE TREATMENT OF AMATOXIN MUSHROOM POISONING (AMP) INDUCED LIVER INJURY AND FULMINANT HEPATIC FAILURE (FHF): AN OPEN LABEL PROSPECTIVE UNCONTROLLED CLINICAL TRIAL

ST Mitchell[1], A Buchwald[1], M D'Amato[2], DA Spyker[3]

*[1]Dominican Hospital; Santa Cruz, CA USA, [2]Rottapharm Biotech, Monza, Italy, [3]Oregon Health Sciences University*

**Objectives:** IV SilibininLegalon® SIL ( *SIL*), registered in Europe since 1980s for AMP hepatotoxicity based on dog studies and retrospective human data, never investigated prospectively. SIL treatment failures, resulting in deaths/liver transplants, recently reported in Turkey, Australia, Germany, France. Sil stimulates RNA Polymerase I, inhibits apoptosis, antioxidant. Diverts amatoxin into general circulation by inhibiting enterohepatic reuptake, occupying bile salt intended hepatocyte sinusoidal membrane transporters OATP1B3 and NTCP.

**Methods:** Prospective Uncontrolled Open Label USA Clinical Study; 80 enrollees since 2007. SIL provided free; delivery takes ~ 24 hours. Bolus 5 mg/kg over 1 hour; 20mg/kg/day continuous infusion of 2496hours. Protocol includes rapid ED volume replacement, sustained aggressive IV hydration, multilumen central IV catheter, Foley catheter, npo status, Octreotide infusion (*s ince2013* ). Requirements: 1) Daily telephone contact between PI, treating physicians; 2) Complete inpatient chart copy to PI following discharge.

**Results:** 44 males, 36 females; ages 694. Peak ALT >2000, 62/79. Peak INR > 1.5, 53/80 (35 > 2.0). Nine poor outcomes. One death: late presentation; pH 6.8, irreversible oliguric Acute Kidney Injury (*AKI* ), rapidly progressing FHF. Two transplants, 1 death: SIL initiated > 108 hours postingestion. Four deaths, 1 transplant: IV hydration interruption/restriction, usually upon arrival to transplant unit from community hospital (*4 /5* ). Triggered precipitous serum lactate elevation, oliguric AKI acquisition; then severe rapidly progressing FHF. Protocol IV hydration recommendations not followed in 7. SIL infusion < 24 hours in 2. SIL begun < 108 hours, hydrated per protocol and avoided oliguric AKI: **6 9/69** full recovery with INR correction beginning by ~ infusion hour 30. Median ED presentation to hospital discharge ~ 5 days.Occasional warmth/flushing during SIL bolus. ICU care rarely required. No sequelae or complications.

**Conclusions**: Oliguric AKI precedes/precipitates full blown FHF in most poor outcome AMPs, not vice versa. Uncorrected lactate elevation sensitively portends impending oliguric AKI leading to severe FHF, transplant indication and poor prognosis. Sustained lactate correction likewise augurs recovery. SIL treatment failure inevitable after oliguric AKI; amatoxin diverted into general circulation cannot be cleared. AMP treatment success or failure largely determined by IV fluid management. Oliguric AKI easily prevented with rapid ED volume replacement and sustained aggressive IV hydration. SIL safe and well tolerated; effective initiation window ~ 108 hours. Combined with rapid ED volume replacement and sustained aggressive IV hydration, SIL reliably reverses severe AMP induced FHF with INR reduction by ~ 30th infusion hour unfailingly heralding recovery.