

Supplemental Table 1: Cause of death categories for cases where DILI had only a contributory role or no role in the death or need for liver transplant.

Cause of death
Cardiovascular disease
Cerebrovascular disease
Malignant neoplasm
Chronic respiratory disease
Acute respiratory disease
Influenza & pneumonia
Neurologic disorders
Alzheimer's disease/Dementia
Accidental (unintentional injuries)
Intentional self-harm (suicide)
Diabetes, complications of
Renal disease
Septicemia
Multi-organ failure (MOF)/Systemic inflammatory response syndrome (SIRS)
Non-DILI liver related death
DRESS/Stevens Johnson
Unknown or indeterminate
Other (details specified by committee)

Supplemental Tables 2-5: Primary implicated agents and frequencies for primary role cases categorized by course of liver failure.

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**Supplemental Table 2: Primary role**

<b><u>Acute liver failure</u></b>	<b>#</b>	<b>%</b>
Herbal/Dietary Supplement	9	18
ISONIAZID	9	18
NITROFURANTOIN	4	8
AMOXICILLIN W/CLAVULANIC ACID	2	4
AZITHROMYCIN	2	4
ATRIPLA	1	2
BUPROPION	1	2
CARBOPLATIN	1	2
CIPROFLOXACIN	1	2
EPHEDRINE	1	2
ERYTHROMYCIN W/SULFISOXAZOLE	1	2
HYDRALAZINE	1	2
INTERFERON BETA-1A	1	2
IPILIMUMAB	1	2
LEFLUNOMIDE	1	2
LENALIDOMIDE	1	2
LEVOFLOXACIN	1	2
LISINAPRIL/HYDROCHLOROTHIAZIDE	1	2
MOXIFLOXACIN	1	2
OXALIPLATIN	1	2
PHENTERMINE	1	2
PHENYTOIN	1	2
PROMETHAZINE	1	2
PROPYLTHIOURACIL	1	2
SULFAMETHOXAZOLE	1	2
TRIMETHOPRIM	1	2
TELITHROMYCIN	1	2
TERBINAFINE	1	2
TOPIRAMATE	1	2
VALPROIC ACID	1	2
<b>Total</b>	<b>50</b>	<b>100</b>

**Supplemental Table 3: Primary role**

<b><u>Acute on chronic liver failure</u></b>	<b>#</b>	<b>%</b>
HERBAL/DIETARY SUPPLEMENT	2	40
CEFOTAXIME	1	20
EZETIMIBE W/SIMVASTATIN	1	20
NICOTINIC ACID	1	20
<b>Total</b>	<b>5</b>	<b>100</b>

**Supplemental Table 4: Primary role**

<b>Chronic liver failure</b>	<b>#</b>	<b>%</b>
HERBAL/DIETARY SUPPLEMENT	3	33
AMIODARONE	1	11
ATAZANAVIR	1	11
CIPROFLOXACIN	1	11
FENOFIBRATE	1	11
METHOTREXATE	1	11
MOXIFLOXACIN	1	11
<b>Total</b>	<b>9</b>	<b>100</b>

**Supplemental Table 5: Primary role**

<b>Rapid cholestatic liver failure</b>	<b>#</b>	<b>%</b>
CEFALEXIN	1	25
DOXYCYCLINE	1	25
LEVOFLOXACIN	1	25
NITROFURANTOIN	1	25
<b>Total</b>	<b>4</b>	<b>100</b>

Supplemental Table 6: Cox regression analysis for associations between Hy's Law, nR Hy's Law, MELD at DILI onset with early DILI fatalities (<26 weeks) by acute liver failure or acute on chronic liver failure.

Variable	Hazard ratio	95% CI	p-value	C-statistic	95% CI
Hy's Law <sup>Δ</sup>	2.2	1.3, 3.7	<0.01	0.60	0.53, 0.67
nR Hy's Law <sup>◊</sup>	6.2	3.4, 11.1	<0.01	0.73	0.67, 0.78
MELD score	1.2	1.1, 1.2	<0.01	0.87	0.82, 0.92
MELD > 14	12.1	2.9, 49.9	<0.01	0.66	0.62, 0.69
MELD > 19	35.8	11.1, 115.2	<0.01	0.83	0.79, 0.86
MELD > 24	10.6	5.9, 18.9	<0.01	0.74	0.67, 0.80
MELD > 29	13.9	7.7, 25.1	<0.01	0.67	0.61, 0.74

<sup>Δ</sup> bilirubin  $\geq$  2.5 mg/dL, ALT > 3x ULN and Alk P < 2x ULN at presentation

<sup>◊</sup> bilirubin  $\geq$  2.5 mg/dL, and R-ratio > 5 at presentation. (AST is substituted for ALT if AST yields greater R-ratio)

CI = Confidence interval

