Idiosyncratic Drug-Induced Liver Injury

Diagnostic workup by injury pattern, biopsy indications, prognosis, rechallenge, treatment, herbal/supplement hepatotoxicity, and DILI in chronic liver disease.

2021 ACG Clinical Guideline
Diagnosis and Management of Idiosyncratic Drug-Induced Liver Injury
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STRENGTH Strong Conditional

1 Hepatocellular/Mixed DILI Workup

REC	STATEMENT	STR.
1a	Exclude acute viral hepatitis A/B/C + AIH via standard serologies + HCV RNA	Strong
1b	Consider anti-HEV IgM in selected patients (endemic travel, atypical phenotype, no culprit agent) — test performance unclear	Conditional
1c	Test for acute CMV/EBV/HSV if viral hepatitis excluded or atypical lymphocytosis/lymphadenopathy present	Strong
1d	Evaluate for Wilson disease and Budd-Chiari syndrome when clinically appropriate	Strong

2 Cholestatic DILI Workup

REC	STATEMENT	STR.
2a	Abdominal imaging (US/CT/MRI) in all cases to exclude biliary pathology/infiltrative process	Strong
2b	Limit PBC serology to those without obvious biliary pathology on imaging	Strong
2c	Limit ERCP to cases where MRI/EUS cannot exclude CBD stones, PSC, or pancreaticobiliary malignancy	Conditional

3 When to Biopsy

REC	STATEMENT	STR.
3a	AIH remains a competing diagnosis and immunosuppression is contemplated	Strong
3b	Unrelenting LFT rise or worsening liver function despite stopping agent	Conditional
3c	Peak ALT hasn't fallen >50% by 30–60d (hepatocellular) or peak Alk P hasn't fallen >50% by 180d (cholestatic)	Conditional
3d	Continued use/re-exposure to implicated agent is contemplated	Conditional
3e	LFT abnormalities persist beyond 180d, especially with symptoms/signs — assess for chronic liver disease/chronic DILI	Conditional

4 Prognosis & Drug Management

REC	STATEMENT	STR.
4	Use MELD + Charlson comorbidity index + albumin prognostic model for 6-month mortality (DILI-CAM calculator: gihep.com/calculators)	Conditional
5	Strongly against re-exposure to suspected causative drug, especially with significant transaminase elevation (>5×ULN, Hy's law, jaundice); exception: life-threatening situations with no alternative	Strong
6	Promptly stop suspected agent, especially with rapidly rising LFTs or liver dysfunction	Strong

5 Treatment

REC	STATEMENT	STR.
7	Consider NAC in adults with early-stage ALF (good safety; some efficacy evidence in early coma-stage patients)	Conditional
8	Against NAC in children with severe DILI leading to ALF	Conditional
9	No definitive evidence for/against corticosteroids; may consider in DILI with AIH-like features	Conditional

6 Herbal & Dietary Supplement (HDS) Hepatotoxicity

REC	STATEMENT	STR.
10	Encourage patients to report HDS use; remind that HDS aren't subject to the same rigorous safety/efficacy testing as prescription drugs	Strong
11	Apply the same diagnostic approach as DILI to suspected HDS-hepatotoxicity — exclude other causes via history/labs/imaging; confident diagnosis with recent HDS use	Strong
12	Stop all HDS in suspected HDS-hepatotoxicity; monitor for resolution	Strong
13	Consider LT evaluation in ALF/severe cholestatic injury from HDS-DILI	Strong

7 DILI in Chronic Liver Disease (CLD)

REC	STATEMENT	STR.
14	High index of suspicion required; exclude more common causes including a flare of underlying liver disease	Strong
15	Case-by-case risk-vs-benefit assessment for potentially hepatotoxic drugs in CLD	Conditional
16	No specific monitoring-plan data; advise prompt symptom reporting; reasonable to monitor LFTs q4–6wk, especially in first 6 months of hepatotoxic therapy	Conditional

Chalasani NP, Maddur H, Russo MW, Wong RJ, Reddy KR. ACG Clinical Guideline: Diagnosis and Management of Idiosyncratic Drug-Induced Liver Injury. *Am J Gastroenterol.* 2021;116(5):878–898.