

Immune-Related Adverse Event Guideline: Hepatotoxicity

Hepatic transaminases (ALT/AST) and bilirubin must be evaluated before each dose of immunotherapy, as early laboratory changes may indicate emerging immune-related hepatitis. Elevations in LFTs may develop in the absence of clinical symptoms.

This guidance should be used in context of baseline LFTs and presence of known liver metastases. No dose adjustment is required but data is limited for use of these drugs in moderate/severe hepatic impairment and patients should be closely monitored for elevation in LFTs from baseline.

Mild (Grade 1)

AST or ALT < 3 x ULN but increasing from baseline

Investigations:

- Weekly LFTs inc ALT and AST
- Ensure stable or improving prior to next cycle of treatment
- Consider USS/CT if suspicion of disease progression

Actions:

- Review medications and exclude other causes of abnormal LFTS
- Continue IO with monitoring of LFTs

Biochemical Abnormality WORSENS or RELAPSE see moderate/severe strand (LFT dependant)

Moderate (Grade 2)

AST or ALT >3 to ≤5 x ULN

Clinical Assessment

Investigations:

- Regular LFTs inc ALT and AST, direct and indirect bilirubin and clotting profile
- Consider liver imaging to exclude PD & VTE
- Hepatitis viral panel (hepatitis A, B, C, E)
- CMV, EBV and HIV and auto-antibodies

Treatment:

- Commence prednisolone 60mg/day+ PPI

Actions:

- Withhold dose until the adverse reaction resolves to Grade 0-1 (or returns to baseline).
- Review medications and exclude other causes of abnormal LFTS
- **Re-check LFTs 3days and review patient by phone with results**

Symptoms: Resolve or Improve to Mild See steroid tapering guidance

Biochemical Abnormality PERSISTS (≥3 days), WORSEN or RELAPSE see severe strand

Severe or Life-Threatening (Grade 3/4)

AST or ALT >5 x ULN (Grade 4 >20x ULN)

Clinical Assessment

Investigations:

- **Daily LFTs inc AST** and clotting profile
- As per Moderate grade 2.

Treatment:

- Consider admission for monitoring
- Commence IV methylprednisolone 1mg/kg/day for 3 days
- Hydration (patients need to be well hydrated to promote hepatic perfusion with fluid balance)
- Vitamin K 10mg IV daily x 3 days if INR deranged
- **Grade 4 (loss of synthetic function or hyperbilirubinemia) commence N-acetylcystine (NAC as per paracetamol overdose protocol in BNF)**

Actions:

- IP referral to gastroenterology/ hepatologists for further advice
- If Grade 3 on combination therapy reduce to monotherapy; if monotherapy continue discontinuation of treatment
- If Grade 4 discontinue treatment permanently
- Establish escalation plan and ceiling of care

Symptoms: Resolve or Improve to Moderate/ Mild Switch to oral steroids and follow subsequent management guidance

Review patient daily, if no improvement within 72 hours- follow Subsequent Management guideline

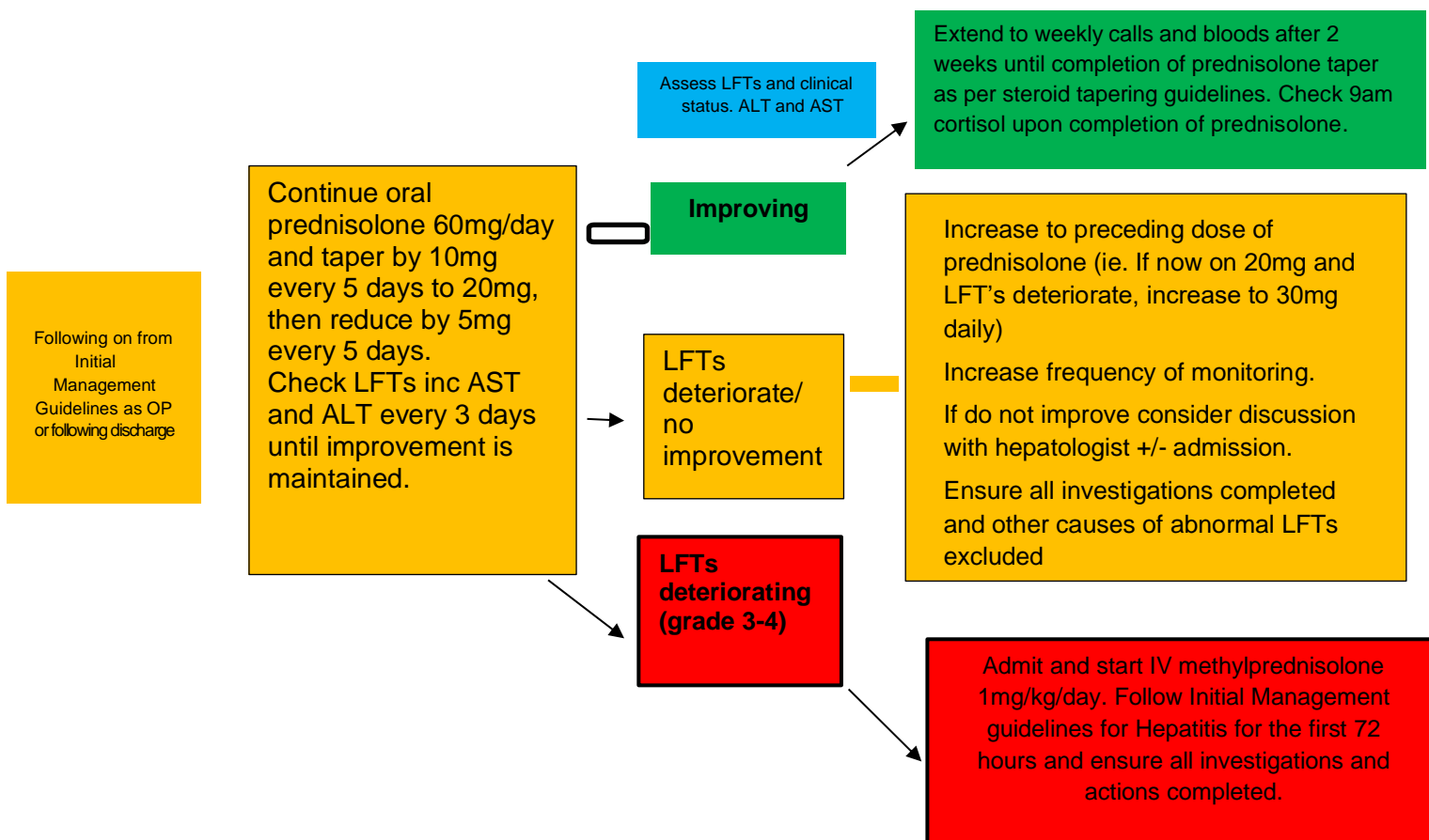
Abbreviations

LFTs = liver function tests
 INR = international normalised ratio
 ULN = upper limit of normal
 PD = progressive disease

**** IMPORTANT ****Subsequent management of patients with hepatitis that is either not improving or worsening should always be discussed with a gastroenterologist and the patient's oncologist

Subsequent management guideline– Hepatitis

Outpatient management



Inpatient Management

