

## 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 for mild hepatic impairment 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. Prior to commencement of immunotherapy all patients should have LFTs checked

### Mild (Grade 1)

AST or ALT < 3 x ULN but increasing from baseline

#### Investigations:

- Weekly LFT (including ALT) check between cycles of immunotherapy and ensure remain stable prior to next cycle. Inform oncology team
- Consider concomitant medications

#### Actions:

- Continue immunotherapy treatment

**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, direct and indirect bilirubin and clotting profile
- MRI/USS of liver to exclude PD & thromboembolism and evaluate if evidence of inflammation
- Hepatitis viral panel (hepatitis A, B, C, E)
- CMV, EBV and HIV and auto-antibodies

##### Treatment:

- Commence prednisolone 60mg/day+ PPI

##### Actions:

- Withdraw dose until the adverse reaction resolves to Grade 0-1 (or returns to baseline).
- Review medications (e.g. statins, antibiotics)
- Re-check LFTs and INR every 3 days and review patient by phone twice weekly

**Symptoms: Resolve or Improve to Mild See steroid tapering guidance**

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

**Symptoms: Resolve or Improve to Mild See steroid tapering**

**Review patient daily, if no improvement within 24 hours, seek further hepatologist advice. Follow Subsequent Management guideline**

### Severe or Life-Threatening (Grade 3/4)

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

#### Clinical Admission

##### Investigations:

- Daily LFTs, clotting profile and daily venous gas
- MRI of liver to exclude PD & thromboembolism and evaluate if evidence of inflammation
- Hepatitis viral panel (hepatitis A, B, C, E)
- CMV, EBV and HIV and auto-antibodies
- Exclude other causes (e.g. Heart failure/ PD)

##### Treatment:

- IV methylprednisolone 2mg/kg/day
- IV 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)  
If albumin low, discuss with hepatologist and consider administration of human albumin solution (HAS) **Actions:**
- Referral to 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
- Consider antibiotic prophylaxis with patients on high dose, prolonged steroids
- Establish escalation plan and ceiling of care

#### Abbreviations

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

Interrupt SACT immunotherapy until discussed with Acute Oncology Team. Please contact [on-call oncology/haematology team](#) for advice. Ensure that Acute Oncology/Haematology team are informed of admission.