

### Immune-Related Adverse Event Guideline: Hepatoxicity

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 culprit 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 As per mild (grade 1) +

#### 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 autoantibodies

#### Treatment:

• Commence prednisolone 60mg/day+ gastric protection

#### Actions:

- Withhold 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. If improving check LFTs weekly.

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

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

## Clinical Admission As per moderate (Grade 2) + Consider admission of patient

#### Investigations:

- Daily LFTs, clotting profile and lactate. If deteriorating, consider venous gas.
- MRI of liver to exclude PD & thromboembolism and evaluate if evidence of inflammation or sclerosing cholangitis
- Exclude other causes (e.g. Heart failure/ PD)

#### Treatment:

- IV methylprednisolone 2mg/kg/day
- Increasing to 4mg/kg/day could be considered if clinical improvement is unsatisfactory.
- 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:

#### ctions:

- Referral to hepatologists for further advice
- Consider antibiotic prophylaxis with patients on high dose, prolonged steroids
- Establish escalation plan and ceiling of care

#### <u>Abbreviations</u>

LFTs = liver function tests

INR = international normalised ratio ULN = upper limit of normal PD = progressive disease Symptoms: Resolve or Improve to Mild See steroid tapering guidance

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

Symptoms: Resolve or Improve to Mild See steroid tapering quidance Assess response to treatment, if no improvement within 72 hours, consider additional immunosuppression.
Consider CCC
Subsequent Management quidelines

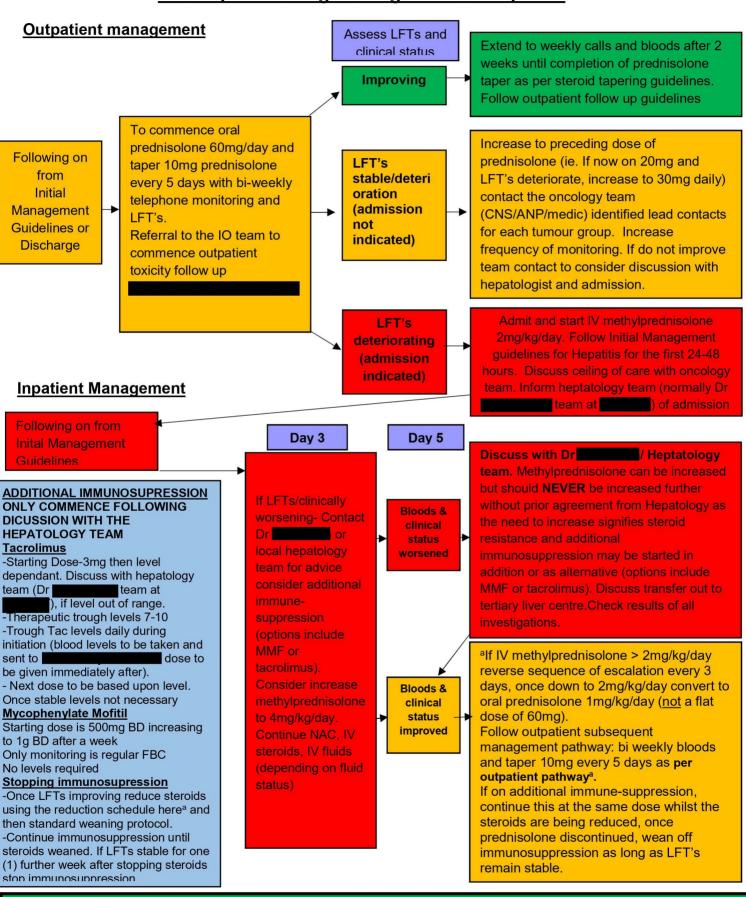
Interrupt SACT immunotherapy until discussed with Acute Oncology Team. Please contact on-call oncology/haematology team for advice. Ensure that the patient has monitoring/follow up planned with their oncology/immuno-oncology team.

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\*\* 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



is the regional hepatology advisor for CPI-induced hepatitis and may be contacted by local teams for

discussion/advice