

## Symptom Grade

### GRADE 1

ALT or AST > ULN - 3x ULN

### GRADE 2

ALT or AST 3 - 5x ULN

### GRADE 3

ALT or AST 5 - 20x ULN

### GRADE 4

ALT or AST > 20x ULN

## Management escalation pathway

Continue treatment

If both ALT & AST are Grade 1:  
postpone 1 week

Withhold ICPI treatment

If rising ALT/AST when re-checked  
start oral prednisolone 1 mg/kg

Cease treatment

ALT/AST < 10 x ULN and normal bilirubin/INR/albumin: oral prednisolone 1 mg/kg

ALT/AST > 10 x ULN or raised bilirubin/INR/low albumin: i.v. (methyl)prednisolone 2 mg/kg

i.v. (methyl)prednisolone 2 mg/kg

Permanently discontinue treatment

## Assessment and Investigations

If > ULN - 3x ULN repeat in 1 week

Control until normalisation

Re-check LFTs/INR/albumin every 3 days

Review medications, e.g. statins, antibiotics and alcohol history

Perform liver screen:  
- Hepatitis A/B/C serology  
- Hepatitis E PCR  
- Anti-ANA/SMA/LKM/SLA/LP/LCI  
- Iron studie

Consider imaging for metastases/portal trombosis

As above; daily LFTs/INR/albumin

Perform US with Doppler

Low threshold to admit if clinical concern

If refractory after 3 days consult hepatologist

As above; hepatology consult  
Consider liver biopsy

+

Review medications:  
e.g. statins, antibiotics, alcohol history and alternative medicines (herbs)

Perform liver screen:  
- Hepatitis A/B/C serology  
- Hepatitis E PCR  
- Anti-ANA/SMA/LKM/SLA/LP/LCI - Iron studies

Consider imaging for metastases/portal trombosis

### Abbreviations:

ICPI = immune checkpoint inhibitor  
ALT = Alanine transaminase  
AST = Aspartate transaminase  
ANA = anti nuclear antibodies  
ULN = Upper limit of normal  
LFT = liver function test  
SMA = smooth muscle antibody  
LKM = liver/kidney microsome type 1  
SLA = soluble liver antigen  
LP = liver/pancreas  
LCI = liver cytosolic antigen  
US = ultrasound

### Steroid wean:

-G2: once G1, wean over 2 weeks; re-escalate if worsening; treatment may be resumed once prednisolone < 10 mg  
-G3/4: once improved to G2, can change to oral prednisolone and wean over 4 weeks; for G3, rechallenge only at consultant discretion

### Worsening despite steroids:

- If on oral change to i.v. (methyl)prednisolone  
- If on i.v. add MMF 500-1000 mg b.d.  
- If worse on MMF, consider addition of tacrolimus  
- A case report has described the use of anti-thymocyte globulin in steroid + MMF-refractory fulminant hepatitis

