

## Oxford University Hospitals

**Hepatic Immune-Related Adverse Event Management Algorithm**

Grade of Liver Test Elevation (NCI CTCAE v4.03)	Management	Follow-up
<p><b>Grade 1</b> AST or ALT greater than ULN – 3 x ULN and/or Bilirubin greater than ULN – 1.5 x ULN</p>	<ul style="list-style-type: none"> <li>Continue I-O therapy</li> </ul>	<ul style="list-style-type: none"> <li>Continue routine LFT monitoring</li> <li><b>If worsens:</b> <ul style="list-style-type: none"> <li>Treat as G2 or 3-4</li> </ul> </li> </ul>
<p><b>Grade 2</b> AST or ALT greater than 3 to less than or equal to 5 x ULN and/or Bilirubin greater than 1.5 to less than or equal to 3 x ULN</p>	<ul style="list-style-type: none"> <li>Delay I-O therapy</li> <li>Increase frequency of monitoring to every 3 days</li> <li>Investigations               <ul style="list-style-type: none"> <li>US liver</li> <li>Viral screen:                   <ul style="list-style-type: none"> <li>Hep A IgM</li> <li>Hep B surface antigen and cAb</li> <li>Hep E IgM</li> <li>CMV IgM</li> <li>EBV IgM</li> </ul> </li> </ul> </li> <li>Exclude:               <ul style="list-style-type: none"> <li>Other drug causes</li> <li>Metastases</li> <li>Biliary Obstruction/ Gallstones</li> <li>Pre-existing liver disease.</li> </ul> </li> </ul>	<p><b>If returns to baseline:</b></p> <ul style="list-style-type: none"> <li>Resume routine monitoring and I-O therapy.</li> </ul> <p><b>If elevations persist more than 5-7 days or worsen:</b></p> <ul style="list-style-type: none"> <li>1mg/kg oral prednisolone (maximum 60mg OD) for 1 week then taper as per tapering regimen below</li> <li>Resume I-O therapy after course of steroids completed and liver biochemistry has returned to baseline</li> </ul> <p><b>If flare on steroid wean or no improvement</b></p> <ul style="list-style-type: none"> <li><b>Refer to hepatology</b></li> <li>Increase prednisolone dose by 10mg then slowly taper (maximum 60mg OD)</li> </ul>
<p><b>Grade 3-4</b> AST or ALT greater than 5 x ULN and/or Bilirubin greater than 3 x ULN</p> <p>Or evidence of decompensated liver disease e.g. Jaundice Prolonged PT greater than 15 Encephalopathy</p>	<ul style="list-style-type: none"> <li>Investigations as above</li> <li>Discontinue I-O therapy</li> <li><b>Urgent hepatologist referral (on call available out of hours)</b></li> <li>Increase frequency of monitoring to every 1-2 days</li> <li>1mg/kg methylprednisolone sodium succinate IV</li> <li>Daily bloods</li> <li>Admit to hospital</li> </ul>	<p><b>If improvement after 72 hours intravenous steroids:</b></p> <ul style="list-style-type: none"> <li>prednisolone 1mg/kg (max 60mg OD) and taper steroids (as described below and with guidance from hepatologist)</li> </ul> <p><b>If not improving after 3-5 days, worsens or rebounds:</b></p> <ul style="list-style-type: none"> <li>Continued discussion with hepatologist</li> <li>Add mycophenolate mofetil 1g BD PO (if side effects reduce to 500mg BD) – under guidance of hepatology only</li> <li>If no response within 3-5 days, consider tacrolimus (as per current recommended brand) 0.1-0.15mg/kg daily – under guidance of hepatology only</li> <li>Consider prophylactic antibiotics</li> </ul>