

Oxford University Hospitals

Hepatic Immune-Related Adverse Event Management Algorithm

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