The Clatterbridge Cancer Centre NHS Foundation Trust

Immune-Related Adverse Event: Diarrhoea & Colitis

Gastrointestinal (GI) irAEs are among the most common and although they are typically mild to moderate in severity, if they are left unrecognised or untreated, they can become life-threatening. These toxicities can be managed effectively in almost all patients by using established guidelines that stress vigilance and the use of corticosteroids and other immunosuppressive agents when necessary.

Mild (Grade 1)

- < 4 stools/day over baseline
- *or* mild increase in ostomy output

in the absence of abdominal pain, mucous/blood in stools

Investigations:
- Baseline bloods (FBC, U&E, LFTs, TFTs, cortisol & CRP)
- Stool microscopy and culture
- C. difficile toxin
- Faecal calprotectin

Treatment:
- Encourage fluids
- Avoid high fibre and lactose

Actions:
- Regular monitoring
- Consider holding immunotherapy (if on combination anti-PD1/CTLA4 withhold immunotherapy)
- Refer to IO Toxicity Service.

Symptoms: PERSIST (≥5 days) or WORSEN or are associated with deranged U & E's

Moderate (Grade 2)

If **any** of the following symptoms are present:

- 4-6 stools/day over baseline *or* moderate increase in ostomy output
- Moderate abdominal pain/cramps/discomfort
- Mucous in stool

Clinical Assessment
- As per mild (grade 1) +

Investigations:
- CMV viral load + PCR (red top blood sample)
- Faeces CMV
- Faecal calprotectin
- Abdominal X-Ray (consider CT abdo/pelvis if AXR abnormal or in presence of abdominal pain)
- Consider Infliximab screen as per Grade **3&4**
- If recurrent, send for faecal elastase.
- Flexi sigmoidoscopy/Endoscopy*

Treatment:
- Prednisolone 60mg/day + gastric protection
- Fluid balance and replacement as appropriate (inc. diarolyte sachets)

Actions:
- Omit next dose of immunotherapy
- Taper per steroid weaning guidance
- Regular telephone monitoring
- Consider Gastroenterology advice/review
- Refer to IO Toxicity Service

Assess response to treatment within 72 hours

Symptoms: Resolve or Improve to Mild
See steroid tapering guidance

PERSIST or WORSEN or RELAPSE

Severe or Life-Threatening (Grade 3 + 4)

If any of the following symptoms are present:

- **≥7 stools/day over baseline *or* significant increase in osotomy output**
- **Severe abdominal pain**
- **Fever**
- **Dehydration**
- **Blood in stool**
- **Incontinence**
- **Limiting ADL's**

As per moderate (grade 2) +
Consider Admission of patient

- **Investigations on day 1:**Screen for Infliximab administration suitability on admission (to include- TB Quantiferon test, hepatitis screen, HIV, varicella zoster anti-bodies (IGG antibody), chest X-Ray (if chest CT not already performed)
- Refer for endoscopy with biopsies on day 1 of admission (request form on Meditech under documents)*
- Daily bloods (FBC, U&E, LFTs & CRP)
- CT Abdomen/pelvis

Treatment:
- IV hydration and fluid balance
- IV Methylprednisolone 2 mg/kg/day + gastric protection cover and continue for a minimum of 3 days
- Antibiotics are not required as standard

Use analgesia with CAUTION

Actions:
- Daily stool chart
- Consider referral & potential transfer to gastroenterology
- Dietician review
- Consider discontinuation of immunotherapy
- Taper per steroid weaning guidance.
- Refer to IO Toxicity Service

Assess response to treatment within 72 hours, if no improvement consider infliximab treatment.
See CCC subsequent management guidelines

***If endoscopy findings in keeping with collagenous/microscopic colitis, switch from prednisolone/methylprednisolone to budesonide. Budesonide 9mg OD should be given for 10 weeks and then reduced to 6mg OD for 1 week and then to 3mg OD for 1 week then stop. The systemic dose of budesonide is equivalent to less than 10mg prednisolone.**

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.