

## Summary Table of Statements

<p><b>Statement 1: Definition</b> The diagnosis of ASUC is defined by the modified Truelove and Witts criteria as ≥6 bloody stools per day plus at least one of the following:</p> <ol style="list-style-type: none"> <li>Temperature &gt;37.8 degree Celsius;</li> <li>Pulse rate &gt;90 beats per minute</li> <li>Haemoglobin &lt;105g/L</li> <li>Erythrocyte sedimentation rate &gt;30mm/h</li> </ol> <p>Hospital admission under a gastroenterologist is strongly recommended. Confirmation of the diagnosis requires exclusion of infective colitis. <b>EL:</b> III-2 <b>RG:</b> B <b>LA:</b> A: 47% B: 53% C: 0% D: 0% E: 0%</p>
<p><b>Statement 2: Aim</b> The immediate treatment aim in ASUC is to achieve clinical remission. The long term goal is to achieve clinical, endoscopic, and histological remission. <b>EL:</b> III-3 <b>RG:</b> B <b>LA:</b> A: 63% B: 37% C: 0% D: 0% E: 0%</p>
<p><b>Statement 3: First presentation investigations - laboratory</b> On presentation with ASUC, tests required include FBC, EUC, CRP, ESR, LFT, Mg<sup>2+</sup>, lipid profile, abdominal x-ray, stool microscopy/culture/sensitivities and <i>Clostridium difficile</i> testing. In addition, assessment for TB risk, hepatitis B serology (HBsAg, HBsAb, and HbCAb), TPMT testing, CMV IgG and IgM, EBV IgG and IgM, serology for HIV and VZV, and Streptococcus pneumoniae and influenza vaccination status should be considered. <b>EL:</b> III-2 <b>RG:</b> B <b>LA:</b> A: 32% B: 68% C: 0% D: 0% E: 0%</p>
<p><b>Statement 4: First presentation investigations – endoscopy</b> A flexible sigmoidoscopy without any preparation should be performed, preferably within 24 hours of admission. Biopsies collected should be tested for CMV colitis. <b>EL:</b> III-2 <b>RG:</b> B <b>LA:</b> A: 74% B: 26% C: 0% D: 0% E: 0%</p>
<p><b>Statement 5: Clinical pathway</b> The management of patients with ASUC, where available, should be guided by a clinical pathway to aid treatment, identify variance, and to audit outcomes. <b>EL:</b> IV <b>RG:</b> C <b>LA:</b> A: 68% B: 21% C: 11% D: 0% E: 0%</p>
<p><b>Statement 6: Ongoing review</b> Ongoing assessment should include at least once daily review of haemodynamic status and abdominal examination by a medical officer, stool charts (frequency, consistency, presence of blood and estimated stool volume), FBC, EUC, CRP, albumin, and serial abdominal x-ray. <b>EL:</b> III-2 <b>RG:</b> B <b>LA:</b> A: 63% B: 37% C: 0% D: 0% E: 0%</p>
<p><b>Statement 7: Management Team</b> Patients with ASUC are best managed by a multidisciplinary team comprising a gastroenterologist, colorectal surgeon, gastrointestinal nursing staff, dietitian, pharmacist, and stomal therapist on a specialised gastrointestinal ward. If the above are not available, discussion with a specialist centre should be considered. <b>EL:</b> IV <b>RG:</b> C <b>LA:</b> A: 55% B: 45% C: 0% D: 0% E: 0%</p>
<p><b>Statement 8: Nutrition</b> The nutritional status of the patient should be assessed by a dietitian. Enteral supplements should be introduced as required. There is no proven role for routine parenteral nutrition in ASUC. There is also no role for routine fasting. <b>EL:</b> II <b>RG:</b> B <b>LA:</b> A: 80% B: 20% C: 0% D: 0% E: 0%</p>
<p><b>Statement 9: Venous thromboembolism – inpatient</b> Venous thromboembolism prophylaxis should be administered to all hospitalised patients with ASUC, using subcutaneous heparin or low molecular weight heparin and graduated compression stockings, unless contraindicated. <b>EL:</b> III-2 <b>RG:</b> A <b>LA:</b> A: 84% B: 16% C: 0% D: 0% E: 0%</p>
<p><b>Statement 10: Venous thromboembolism – outpatient</b> Continuation of VTE prophylaxis for several days following discharge from hospital should be considered. <b>EL:</b> Nil <b>RG:</b> Not recommended <b>LA:</b> A: 0% B: 5% C: 5% <b>D: 58% E: 32%</b></p>
<p><b>Statement 11: Corticosteroids</b> Intravenous hydrocortisone 100mg three to four times daily or equivalent is the standard initial treatment of ASUC and should not be delayed pending screening tests for infectious colitis. <b>EL:</b> III-2 <b>RG:</b> A <b>LA:</b> A: 58% B: 37% C: 5% D: 0% E: 0%</p>
<p><b>Statement 12: Indicators for rescue therapy</b> A. Failure to achieve an adequate response to IV corticosteroids is defined by: i) on day 3, &gt;8 stools per day or 3-8 stools per day with a CRP&gt;45mg/L; ii) on day 7, &gt;3 stools per day or visible blood; or iii) a PUCAI &gt;65 (in patients &lt;18 years old) on day 5 An emphasis should be placed on formal assessment of severity at day 3 to identify these patients. B. Additional indicators of severity include mucosal islands and colonic dilatation on abdominal x-ray and deep ulceration on flexible sigmoidoscopy. <b>EL:</b> III-2 (A); III-3(B) <b>RG:</b> B <b>LA:</b> A: 42% B: 58% C: 0% D: 0% E: 0%</p>
<p><b>Statement 13: Optios of rescue therapy</b> Rescue therapies include infliximab, ciclosporin, or surgery, with the choice depending on the judgment of the treatment team, drug availability, and patient factors such as preference and prior thiopurine failure. <b>EL:</b> II <b>RG:</b> A <b>LA:</b> A: 53% B: 47% C: 0% D: 0% E: 0%</p>
<p><b>Statement 14: Rescue therapy in thiopurine-experienced patients</b> Patients who have previously had an inadequate response to thiopurine maintenance therapy (i.e. appropriately dosed with treatment adherence or have therapeutic levels of TGN for &gt;3 months) should preferably not receive ciclosporin. An alternative rescue therapy such as infliximab is recommended. <b>EL:</b> III-3 <b>RG:</b> B <b>LA:</b> A: 37% B: 63% C: 0% D: 0% E: 0%</p>
<p><b>Statement 15: Rescue therapy – other biologics</b> There are currently no data on the efficacy and safety of adalimumab, vedolizumab, and golimumab in ASUC. <b>EL:</b> Nil <b>RG:</b> B <b>LA:</b> A: 90% B: 5% C: 5% D: 0% E: 0%</p>

<p><b>Statement 16: Surgical rescue therapy</b> Following failure of one rescue medical treatment, surgery is recommended. Sequential rescue medical therapy risks sepsis and a delay in surgery. <b>EL:</b> III-3 <b>RG:</b> B <b>LA:</b> A: 37% B: 63% C: 0% D: 0% E: 0%</p>
<p><b>Statement 17: Efficacy of rescue therapy</b> The efficacy of the rescue therapy should be assessed daily. In the event of deterioration or failure to improve patients should proceed to surgery. <b>EL:</b> III-3 <b>RG:</b> B <b>LA:</b> A: 89% B: 11% C: 0% D: 0% E: 0%</p>
<p><b>Statement 18: Failure of rescue therapy</b> Colectomy in ASUC should be performed by a surgeon experienced in emergency colectomy, who will discuss with the patient regarding surgical options, outcomes and possible complications. Patients should be reviewed by a stomal therapist where available. <b>EL:</b> Nil <b>RG:</b> Expert Opinion <b>LA:</b> A: 89% B: 11% C: 0% D: 0% E: 0%</p>
<p><b>Statement 19: Rescue therapy – Infliximab dosage</b> The product information of infliximab recommends infusions at week 0, 2, and 6 at a dose of 5mg/kg. The value of shorter dosing intervals and/or higher doses of infliximab remains to be determined. <b>EL:</b> IV <b>RG:</b> B <b>LA:</b> A: 68% B: 26% C: 6% D: 0% E: 0%</p>
<p><b>Statement 20: Combination of Infliximab and thiopurine</b> If infliximab is used for maintenance therapy, combination of thiopurine and infliximab is more efficacious than infliximab alone. <b>EL:</b> III-1 <b>RG:</b> B <b>LA:</b> A: 68% B: 32% C: 0% D: 0% E: 0%</p>
<p><b>Statement 21: Infliximab trough level</b> The maintenance dose of infliximab should be guided by the trough infliximab level. <b>EL:</b> III-2 <b>RG:</b> Not Recommended <b>LA:</b> A: 0% B: 0% C: 20% <b>D: 48% E: 32%</b></p>
<p><b>Statement 22: Ciclosporin as rescue therapy</b> Ciclosporin should be administered as a continuous IV infusion at the initial dose of 2 mg/kg/day adjusted to blood levels (target 150-250ng/ml). Thereafter dosing is converted to oral ciclosporin at a dose of 4mg/kg/daily, and continued for approximately three months. The target trough level for oral ciclosporin is 150-250 ng/ml. <b>EL:</b> II <b>RG:</b> A <b>LA:</b> A: 52% B: 48% C: 0% D: 0% E: 0%</p>
<p><b>Statement 23: Pharmacy</b> All rescue medical therapies should be readily available into hospital pharmacies that manage ASUC, and have a mechanism for prompt dispensing. <b>EL:</b> Nil <b>RG:</b> Expert Opinion <b>LA:</b> A: 100% B: 0% C: 0% D: 0% E: 0%</p>
<p><b>Statement 24: Pharmacy</b> There is no evidence of occupational health and safety risks relating to occupational exposure to anti-TNF agents. Standard precautions are sufficient for drug preparation and administration. <b>EL:</b> IV <b>RG:</b> B <b>LA:</b> A: 84% B: 16% C: 0% D: 0% E: 0%</p>
<p><b>Statement 25: Maintenance therapy - thiopurines</b> Patients who respond to rescue medical therapy but have not yet failed thiopurine maintenance therapy (such as thiopurine-naïve patients) should be commenced on a thiopurine as a maintenance medication. <b>EL:</b> I <b>RG:</b> A <b>LA:</b> A: 100% B: 0% C: 0% D: 0% E: 0%</p>
<p><b>Statement 26: Maintenance therapy - thiopurines</b> TPMT genotype/ phenotype can guide the starting dose if available. However, thiopurine therapy can be commenced without TPMT results. FBC and LFTs should be measured weekly for 4 weeks after commencement of thiopurine, then fortnightly for next 4 weeks, and then 3-monthly. <b>EL:</b> III-3 <b>RG:</b> B <b>LA:</b> A: 48% B: 48% C: 4% D: 0% E: 0%</p>
<p><b>Statement 27: Maintenance therapy – thiopurines metabolites</b> Metabolite levels may be used to determine the management in patients with failure of response, toxicity or to assess medication adherence. <b>EL:</b> III-2 <b>RG:</b> B <b>LA:</b> A: 84% B: 16% C: 0% D: 0% E: 0%</p>
<p><b>Statement 28: Maintenance therapy – thiopurines with allopurinol</b> Thiopurine shunters (those with inadequate TGN levels and MMP:TGN ratio &gt;11) or patients who are intolerant of an effective dose of thiopurine, can try allopurinol with dose-reduced azathioprine or mercaptopurine to a third/ quarter of original dose in conjunction with close monitoring of FBC and LFT, as outlined in Statement 14b, and thiopurine metabolites. <b>EL:</b> III-3 <b>RG:</b> B <b>LA:</b> A: 74% B: 21% C: 5% D: 0% E: 0%</p>
<p><b>Statement 29: Pregnancy</b> The management of ASUC in pregnant patients should be no different from the management of the non-pregnant patients. Corticosteroids, ciclosporin, thiopurines, infliximab, and colectomy should be used as needed in all stages of pregnant and during breast feeding. <b>EL:</b> III-2 to IV <b>RG:</b> B <b>LA:</b> A: 89% B: 11% C: 0% D: 0% E: 0%</p>
<p><b>Statement 30: Opportunistic infections – pneumocystis jiroveci pneumonia (PJP)</b> Patients on corticosteroids, thiopurine, and either a calcineurin inhibitor or infliximab require prophylaxis against PJP using cotrimoxazole 800mg/160mg three times per week. Dapsone 100mg daily or atovaquone 1500mg daily are options for patients with sulphur allergy. <b>EL:</b> III-2 <b>RG:</b> A <b>LA:</b> A: 89% B: 11% C: 0% D: 0% E: 0%</p>
<p><b>Statement 31: Opportunistic infections – Cytomegalovirus (CMV) diagnosis</b> CMV colitis should be considered in all patients with ASUC. The diagnosis of CMV colitis should be made on the basis of colonic biopsy, histology, and immunohistochemistry. Additional supportive information is provided by colonic biopsy PCR and plasma PCR. <b>EL:</b> III-2 <b>RG:</b> B <b>LA:</b> A: 100% B: 0% C: 0% D: 0% E: 0%</p>
<p><b>Statement 32: Opportunistic infections – CMV treatment</b> Treatment of CMV colitis is intravenous ganciclovir 5mg/kg twice daily for 3-5 days followed by oral valganciclovir 900mg PO twice daily for 2-3 weeks. Early infectious disease physician consultation is recommended. Temporary withdrawal of immunosuppressive therapy should be considered on a case-by-case basis. <b>EL:</b> III-3 <b>RG:</b> B <b>LA:</b> A: 28% B: 72% C: 0% D: 0% E: 0%</p>
<p><b>Statement 33: Opportunistic infections – EBV</b> Seronegative-status adolescents and young adults should avoid thiopurines and use alternative immunomodulators. <b>EL:</b> Nil <b>RG:</b> Not Recommended <b>LA:</b> A: 0% B: 0% C: 39% <b>D: 44% E: 17%</b></p>

## Abbreviations in the Summary Table

ASUC: Acute severe ulcerative colitis; EL: level of Evidence; RG: Grade of Recommendation; LA: Level of Agreement; FBC: Full blood count; EUC: Electrolyte / urea / creatinine; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; LFT: Liver function test; TB: Tuberculosis; HBsAg: hepatitis B surface antigen; HBsAb: hepatitis B surface antibody; HbCAb: hepatitis B core antibody; TMPT: Thiopurine methyltransferase; CMV: Cytomegalovirus; EBV: Epstein-Barr virus; HIV: Human immunodeficiency virus; VZV: Varicella zoster virus; VTE: Venous thromboembolism; PUCAI: Paediatric ulcerative colitis activity index; TGN: Thioguanine nucleotide; MMP: Methylmercaptopurine; PCR: Polymerase chain reaction