European Crohn's and Colitis Organisation

Toolkits for therapies in IBD

Project Description:

- Gratefully acknowledging the unrestricted educational grant from Shire
- Toolkits are meant to serve as a checklist for daily use by clinicians
- Can be applied at a local level to improve patient care with IBD
- Acts as a framework and explains mechanisms by which auditable standards can be translated into practice
- Practice varies not just per country, but according to centers so that the checklist suggests ranges instead of one fixed value
- Due to the lack of data for many points of practice, a Consensus procedure (including two online voting rounds) was used to quantify expert opinion
- Available as a download at www.ecco-ibd.eu/toolkits in exchange for registering the email address in order to allow a follow-up survey later on
- Open to amendment and revision to make them useful in practice in response to feedback from clinicians

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Important Note Disclaimer

- This checklist consists of recommendations designed to inform every day practice.
- Many recommendations are not supported by controlled trials and practice may differ between countries. The Toolkits for Therapies in IBD Checklist is based on an international Consensus process and relates to ECCO Consensus Guidelines (www.ecco-ibd.eu/publications). Treatment decisions remain a matter for the individual clinician, their patient and the clinical context: they should not be based exclusively on the content of this Toolkit.
- The IBDIM-IBD in Motion Ltd (as Research Unit of the European Crohn´s and Colitis Organisation) and/or any of its staff members and/or any project contributor cannot be held liable for any information published in good faith in the Toolkits for therapies in IBD Checklist.

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Medication	Before treatment	Dosing	Follow-up	Red flag interactions	Comments
General Comments: - "Consider" means that the checklist suggestion should not automatically be followed but carefully contemplated. - Treatment start and follow up: Assess disease activity by one or other of the combined measures: ileocolonoscopy/endoscopy, C-reactive protein, faecal calprotectin, magnetic resonance enterography and/or Ultrasound, as available. - Infection Control: Please see attached Checklist to be completed preferably at first visit, but always before immunosuppression treatment. This is in accordance with the ECCO Consensus on Opportunistic Infections.					
5-ASA DERIVATIVES					
5-ASA	- Complete blood count, liver enzymes, creatinine	- Remission induction 3-5 gram once daily - Maintenance (after 6-12 months remission) ≥2g once daily - Rectal 5-ASA for remission induction 1g daily - Rectal 5-ASA for maintenance 1g three times weekly	- Patients with pre-existing renal impairment, or those taking additional potentially nephrotoxic drugs should have renal function monitored during 5-ASA therapy - Creatinine and complete blood count are best monitored every 3-12 months	- Rarely exacerbates colitis - Headaches or nausea can be due to 5-ASA - Rarely a rash, pancreatitis, hepatitis, or thrombocytopenia can occur - If coughing or shortness of breath occurs, pneumonitis should be excluded	- Combine oral and topical 5-ASA for inducing remission - Choice of proprietary mesalazine matters less than adherence to therapy - If people take <80% of the prescribed dose, the risk of relapse is increased >5-fold - Caution should be exercised in pre-existing renal impairment - No additional benefit of dose >1g for rectal therapy - Once daily dosing is at least as good and may be better than divided dosing
Sulfasalazine	- Complete blood count, liver enzymes, creatinine		- Patients with pre-existing renal impairment, or those taking additional potentially nephrotoxic drugs should have renal function monitored during 5-ASA therapy - Creatinine and complete blood count are best monitored every 3-12 months	- Intolerance (commonly headaches, nausea, diarrhoea, rash, neutropenia) is more common than with mesalazine - Leukopenia	- Men who wish to have children should be informed about potential reduction in sperm count and quality - When contemplating pregnancy extra folic acid 5mg/d is best given. Some advise switching to mesalazine in pregnancy - Caution is required when combining with other sulfonamides (owing to potential cross-reaction)
ANTIBIOTICS					
Ciprofloxacin	- For CD antibiotics are only considered appropriate for septic complications, symptoms attributable to bacterial overgrowth, or perianal disease - The role of antibiotics for the treatment of UC flare-ups or for maintenance of remission alone or in combination is not well established - For acute and chronic pouchitis ciprofloxacin may be effective	- For symptomatic perianal fistula: 1000 mg/day (in 2 divided doses)		- Avoid in first trimester of pregnancy unless absolutely necessary. Avoid during lactation - Stop if pain in Achillles tendon develops	- Consider reduced renal tubular transport of methotrexate when co-administered
Metronidazole	- For CD antibiotics are only considered appropriate for septic complications, symptoms attributable to bacterial overgrowth, or perineal disease - In UC the main role of antibiotics in patients with active UC is the treatment of co-existing enteric infection with C. difficile. The role of antibiotics for the treatment of UC flare ups or for maintenance of remission alone or in combination is not well established - For acute and chronic pouchitis metronidazole may be effective - Metronidazole is clearly effective for the prevention of post-operative recurrence	- For post-operative prophylaxis in CD: 20 mg/kg for 3 months - For symptomatic perianal fistula: 750-1500 mg/day (in 2-3 divided doses)		- May cause peripheral neuropathy - Avoid in first trimester of pregnancy unless absolutely necessary. Avoid during lactation	- Warn about alcohol consumption while on metronidazole due to potential disulfiram-like reaction - Monitor serum ciclosporin level if administered as concomitant therapy - Monitor lithium levels when lithium is prescribed concomitantly - Can induce nausea

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STEROIDS					
Budesonide	- Assess disease activity by appropriate tests before start of treatment	- Recommended dose: 9 mg/day for 8 weeks - Then taper gradually to zero within 8-10 weeks depending on response	- Systemic steroid side effects may still occur but these are significantly less frequent than with prednisolone	- Mood changes may occasionally occur and may necessitate therapy cessation	
Oral Prednisolone or Prednisone	- Assess disease activity by appropriate tests before start of treatment - Measure blood pressure, and serum glucose, creatinine, and electrolytes before start of treatment - Consider a Dual Emission X-ray Absorptiometry (DEXA), if risk factors for osteoporosis are identified and a baseline DEXA is not available	- Start 40-60mg/day depending on the severity of the clinical condition and the body weight. Upon response taper weekly to zero within 8-16 weeks. - Add calcium and vitamin D (1500-2000 International Unit /day) supplementation	- Avoid prolonged and/or repeated exposure to systemic steroids and consider switching to conventional immune-modulators (thiopurines or methotrexate) or biologic therapies, if necessary, in case of steroid-dependency or refractoriness - Consider annual or biennial DEXA if in prolonged or repeated exposure to steroids is unavoidable - Check vitamin D status	- Mood changes, serious cosmetic adverse events, eye lens cataract, glaucoma, and osteonecrosis may necessitate therapy cessation	- Rule out: infectious disease, hypertension, diabetes, severe mental disorder, glaucoma, osteopenia/osteoporosis - Avoid or use with caution in patients with diabetes mellitus, hypertension, and osteopenia/osteoporosis
CALCINEURIN INHIBITORS					
Ciclosporin	- Evaluation for opportunistic infections according to ECCO Checklist - Complete blood count, liver enzymes, urea, creatinine, magnesium, cholesterol, blood pressure	- Intravenous: start 2 mg/kg - 24h after start measuring blood levels daily - Adjust blood levels to 150–250 ng/ml - Check response within 5-7 days - Upon response switch to 5-8 mg/kg orally (the total daily dose is divided in two doses every 12 h) upon response - Aim for whole-blood trough levels of 150–300 ng/ml	- Monitor according to the drug indication and co-medication. Emphasise: blood pressure, peripheral paraesthesiae, creatinine, magnesium, potassium - For oral ciclosporin users assess monthly for clinical status, potential adverse events, blood pressure, creatinine, electrolytes, and ciclosporin levels - The duration of oral ciclosporin treatment should be approximately 3-4 months - After a flare of severe UC, transition of oral ciclosporin to thiopurines (in thiopurine-naïve patients) should be better done after cessation of steroids and one month before stopping	- Monitor blood pressure and creatinine (reduce dosage if there is a >20% change compared with baseline) - Monitor blood levels of ciclosporin	- Avoid live vaccines and follow Guidelines for Opportunistic Infections - Caution is required in hypertensive patients, those receiving potassium-sparing diuretics and patients with malignancies - Do not take within an hour of grapefruit juice consumption - Co-trimoxazole for Pneumocystis jiroveci (carini) pneumonia prophylaxis should be given in patients on triple immunosuppression. It should also be considered when double immunosuppression is used, especially if one of the immune-modulators is a calcineurin inhibitor
Tacrolimus	- Evaluation for opportunistic infections according to ECCO Checklist - Complete blood count, creatinine, serum glucose, liver enzymes, lipid profile - Consider an electrocardiogram before start of treatment	- Intravenous: 0.05 mg/kg/day - A daily oral dose of 0.1 mg.kg is divided in two doses (every 12h, Prograf®) or is given once daily (Advagraf®), increase according to the trough level after 24 h, a trough concentration of 10-15ng/mL is desired - Proprietary forms of tacrolimus are NOT interchangeable, since bioavailability varies	- Every 2 weeks for 6-8 weeks after start levels, complete blood count, creatinine, glucose - Follow-up every 3-4 months - Monitor according to the drug indication and co-medication emphasise: blood pressure, creatinine; magnesium; potassium lipid profile	- Monitor closely to prevent hypertension, hyperglycaemia, and impairment of renal function	- Avoid live vaccines and follow Guidelines for Opportunistic Infections - Caution is required in hypertensive patients, those receiving potassium-sparing diuretics and patients with malignancies - Do not take within an hour of grapefruit juice consumption - Co-trimoxazole for Pneumocystis Jiroveci (Carini) Pneumonia (PCP) prophylaxis should be given in patients on triple immunosuppression. It should also be considered when double immunosuppression is used, especially if one of the immune-modulators is a calcineurin inhibitor

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IMMUNOMODULATORS					
Azathioprine	- Evaluation for opportunistic infections according to ECCO Checklist - Complete blood count, kidney function test, liver enzymes - Check thiopurine methyltransferase genetic testing or enzyme phenotype if available - Homozygous: consider alternative therapy - Heterozygous: start with 50% of the recommended dose - Consider baseline liver ultrasound	- Target dose: 2–2.5 mg/kg/day - Consider increasing the dose gradually	- Complete blood count: within 2 weeks of starting; then at least every 4 weeks for 2 months; then every 2-3 months - Liver enzymes: consider checking regularly	- White blood cells decrease to <3000 - Neutrophils <2000 - Liver enzymes 3× normal range - Pancreatitis (always suspect in case of abdominal pain and vomiting) and confirm with laboratory and imaging	- Avoid live vaccines - Advise caution with sun exposure and advise sunscreen use, perform periodic skin cancer screening - Reduce dose to 25% of normal dose in patients taking allopurinol - Female patients are advised to undergo Pap smear test annually
Mercaptopurine (6-MP)	- Evaluation for opportunistic infections according to ECCO Checklist - Complete blood count, kidney function test, liver enzymes - Check thiopurine methyltransferase genetic testing or enzyme phenotype if available - Homozygous: consider alternative therapy - Heterozygous: start with 50% of the recommended dose - Consider baseline liver ultrasound	- Target dose: 1.0-1.5 mg/kg/day - Consider increasing the dose gradually - Meeting target dose within 6 weeks is recommended	- Complete blood count: within 2 weeks of starting; then at least every 4 weeks for 2 months; then every 2–3 months - Liver enzymes: consider checking regularly	- White blood cells decrease to <3000 - Neutrophils <2000 - Liver enzymes 3× normal range - Pancreatitis (always suspect in case of abdominal pain and vomiting) and confirm with laboratory and imaging	- Avoid live vaccines - Advise caution with sun exposure and advise sunscreen use, perform periodic skin cancer screening - Reduce dose to 25% of normal dose in patients taking allopurinol - Female patients are advised to undergo Pap smear test annually
Methotrexate (MTX)	- Evaluation for opportunistic infections according to ECCO Checklist - Complete blood count, kidney function test, liver enzymes - Baseline liver ultrasound is recommended - Optional baseline Fibroscan	- Dose: subcutaneous (preferred) 25 mg/week (oral or IM if unavailable) for 16 weeks. Then reduce to 15 mg/week. If required, the higher dose for longer time periods or oral therapy may be attempted - Combine with folic acid 5mg/week, on the day after MTX	- Complete blood count, liver enzymes within 4 weeks of starting; then at least every 4 weeks for 2 months; then every 2-3 months - Creatinine every 2 weeks during the first 3 months - Note: blood should be obtained PRIOR to MTX administration	- New onset of cough or dyspnoea and no obvious cause: stop medication and perform pulmonary evaluation - 3-fold elevation in liver enzymes: consider liver biopsy if no return to normal after cessation	- Exercise caution with co-administration of anti-folate medications (e.g. Trimethoprim) - Consider pre-treatment anti-emetic therapy if necessary if side-effect - Pregnancy absolutely contraindicated (reliable form of contraception essential during and 3-6 months after treatment) - Exercise caution in patients with third space (ascites, oedema) - Caution in patients with diabetes mellitus, fatty liver or alcohol abuse - Caution regarding drug interactions with drugs eliminated by renal excretion

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BIOLOGICS					
Adalimumab	- Evaluation for opportunistic infections according to ECCO Checklist - Complete blood count, creatinine, liver enzymes, cardiac failure or a history of demyelinating disease are relative contraindications to therapy	- Subcutaneous loading dose for UC or CD with 160 mg, then 80mg after 2 weeks, and 40 mg every 2 weeks thereafter - Dose escalation (40 mg every week) may be warranted if there is objective evidence of active disease and/or low trough drug levels during treatment	- Monitor complete blood count and liver enzymes every 3-4 months - Monitor drug and anti-drug antibody levels when available	- New elevation of liver enzymes should lead to consideration of therapy discontinuation if no other cause can be detected - Respiratory symptoms may indicate opportunistic infection and should be investigated - Psoriasiform dermatitis can occur, as with infliximab	- Avoid live vaccines - Consider repeat test for tuberculosis after a trip to endemic areas - Prophylaxis against *P. jiroveci* when triple immunosuppression is used - Starting treatment during active infection is not advisable
Golimumab	- Evaluation for opportunistic infections according to ECCO Checklist - Complete blood count, creatinine, liver enzymes, cardiac failure or a history of demyelinating disease are relative contraindications to therapy	- Subcutaneous, only for UC. If body weight <80 kg then an initial dose of 200 mg, followed by 100 mg at week 2, then 50 mg every 4 weeks, thereafter - If body weight >80 kg then an initial dose of 200 mg, followed by 100 mg at week 2, then 100 mg every 4 weeks thereafter - Dose escalation may be warranted if there is objective evidence of active disease during treatment	Similar to adalimumab	Similar to adalimumab	Similar to Adalimumab - Drug monitoring is not widely available
Infliximab	- Evaluation for opportunistic infections according to ECCO Checklist - Complete blood count, creatinine, liver enzymes, cardiac failure or a history of demyelinating disease are relative contraindications to therapy	- Intravenous 5 mg/kg at weeks 0, 2 and 6 and then every 8 weeks for UC or CD - Dose escalation may be warranted depending on clinical considerations	- Complete blood count, liver enzymes every 4-6 months - Monitor drug and anti-drug antibody levels when available and if applicable	- Anaphylaxis during infusion is a contraindication to further infusions - New elevation of liver enzymes should lead to consideration of therapy discontinuation if no other potential cause can be detected - Respiratory symptoms may indicate opportunistic infection - Be aware of dermatologic complications such as palmar-plantar psoriasis and consider discontinuation	- Recommendation: combined therapy with thiopurines - Infused over 2 hours for the first 5 doses, then infusion duration may be shortened according to local protocol - Avoid live vaccines - Consider repeated test for tuberculosis after a trip to endemic areas - Consider pre-dose intravenous hydrocortisone if the patient is not already on steroids or thiopurines - Prophylaxis against *P. jiroveci* when triple immunosuppression is used - Starting treatment during active infection is not advisable
Vedolizumab	- Evaluation for opportunistic infections according to ECCO Checklist	- Intravenous infusion for UC or CD - IV 300 mg at weeks 0, 2, 6 and every 8 weeks thereafter - Dose escalation (by shortening treatment interval) may be warranted if there is objective evidence of active disease during treatment		- Neurological symptoms or signs should be investigated, although side-effect profile from published trials show no material differences to placebo	- Infused over 30mins - Offers gut-specific immunosuppression