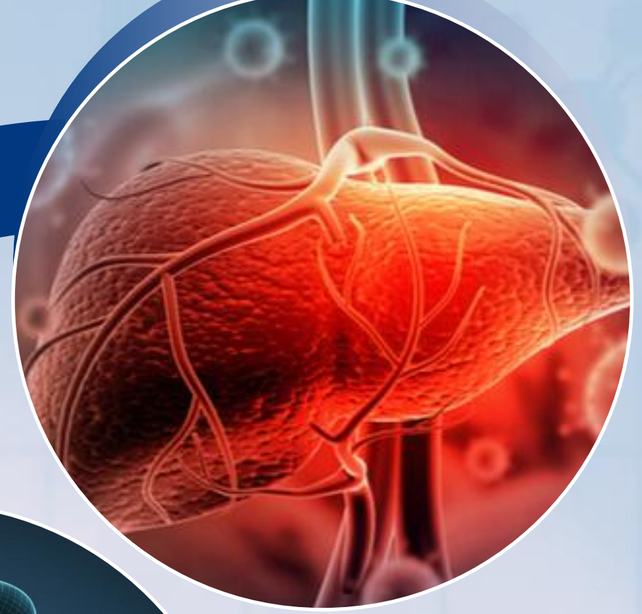
One patient , two Battles

the therapeutic puzzle of AIH with UC



Supervised by : Dr Sawsan Ali Deeb

Presented By : Dr Diana Alsaeed

Damascus Hospital

Clinical presentation:

A 16 year –old male presented to our clinic with complaints of fatigue and general malaise along with diarrhea occurring five times daily sometimes bloody and sometimes watery for three months . A complete review of systems yielded no relevant findings .

The patients medical history: was DM type 1 treated with insulin

clinical examination : jaundice was noted ,the rest of examination was within normal limits , BMI :18.3

Lab tests showed : ID Anemia, elevated of AST /ALT :4*UNL TB :3 DB :2 and ALP /GGT /Albumin /INR was normal

Abdominal ultrasound revealed splenomegaly 15cm with a liver heterogeneity

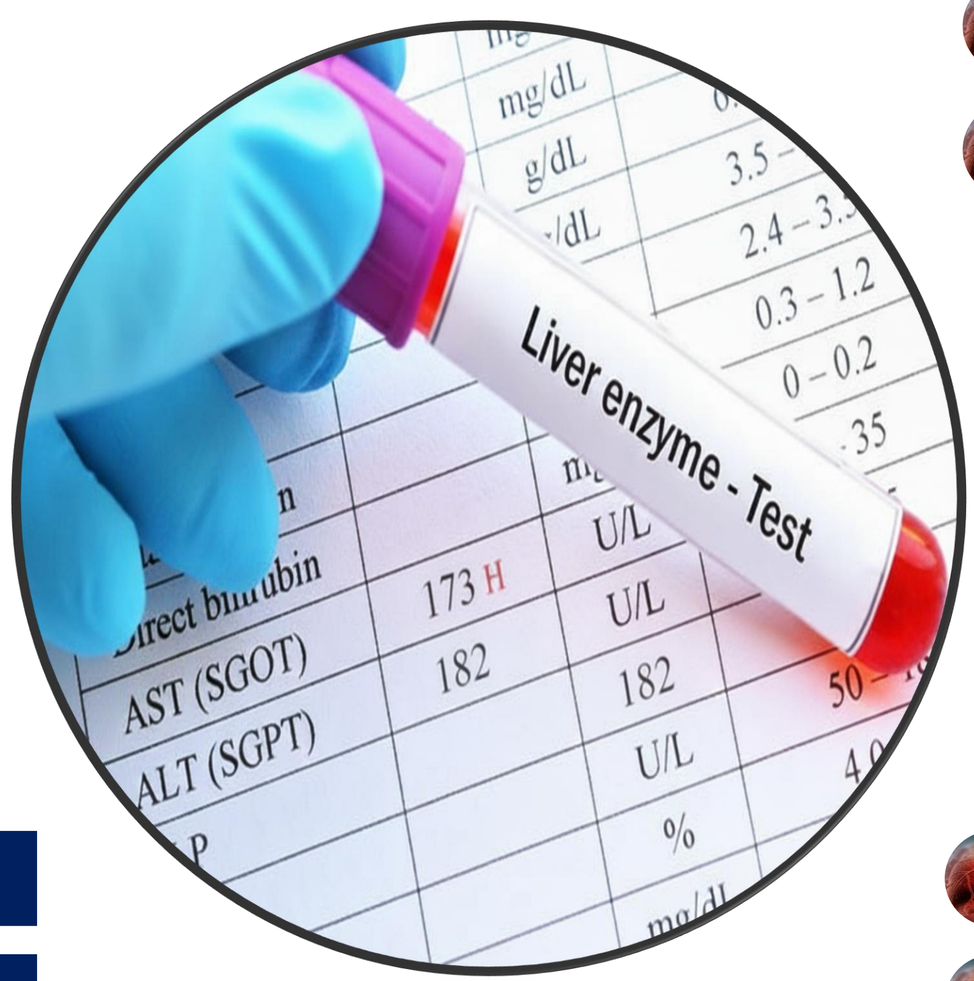
To investigate the cause of chronic diarrhea ,the following tests were performed :

- Celiac serology : Anti TTg IgA negative , total IgA was normal
- thyroid function tests: TSH ,FT3 ,FT4 was normal
- EGD : normal and the biopsies taken from the duodenum were normal
- fecal calprotectin : elevated
- Colonoscopy : revealed ulcerations throughout the colon
- Histopathology : colonic biopsies confirmed the diagnosis of ulcerative colitis

pancolitis

PUCAI : 40 moderate active UC

- Autoimmune hepatitis
- PSC
- PSC with autoimmune feature
- Viral hepatitis
- PBC
- Steatosis



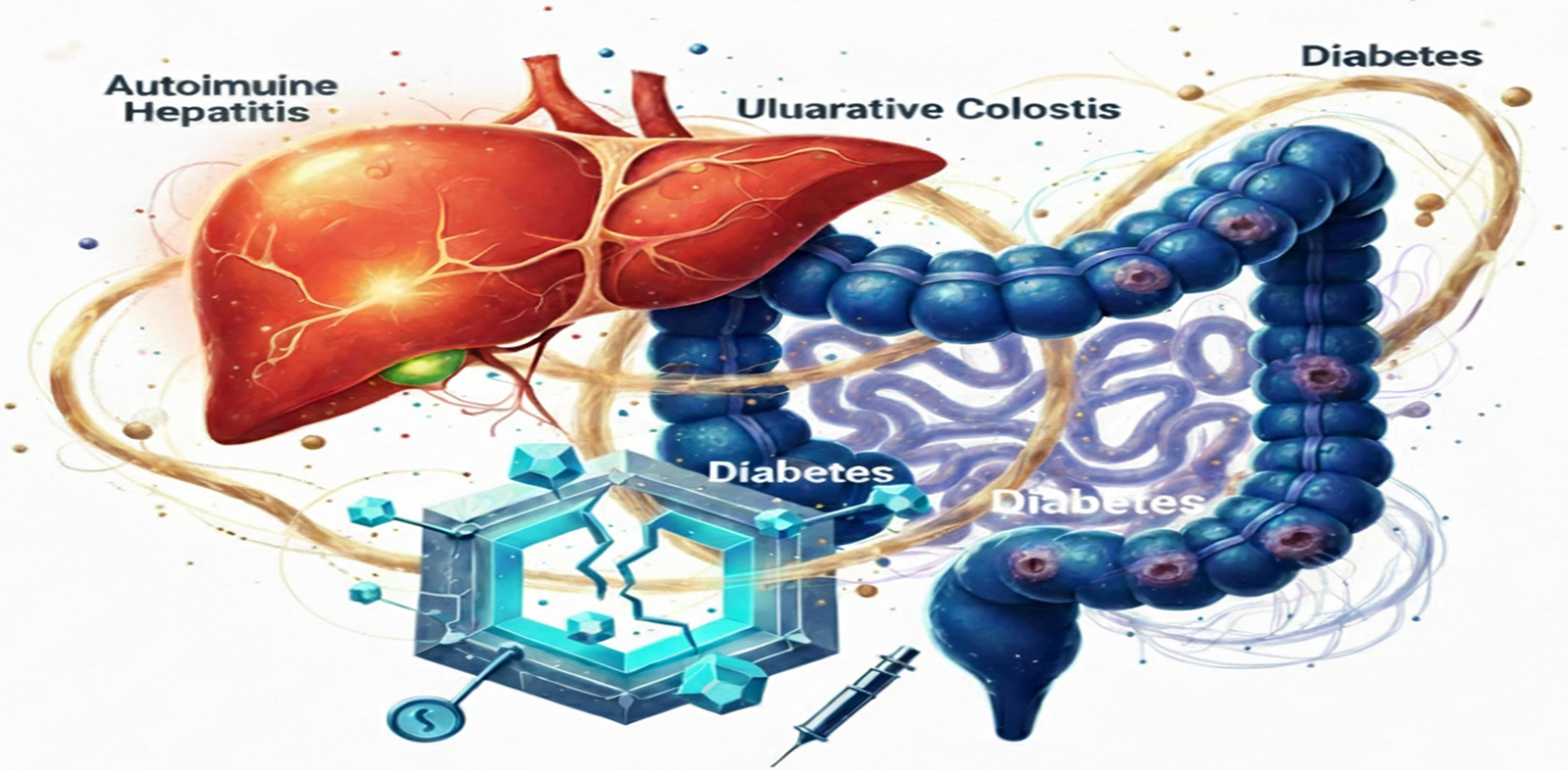
- Bile stones
- Choledocal malformation
- Portal or hepatic vein thrombosis
- Wilson disease
- Coeliac disease
- Hereditary haemochromatosis

Viral study	Anti HCV	Anti HBC	HBS Ag	Anti HAV Igm
	Negative	Negative	Negative	Negative
Metabolic	Ceruloplasmin	Copper in urine 24h	LDH ,reticulocytes	Coombs test
	24	46.2	Normal	negative
Serum lipids	Cholesterol	HDL	LDL	transferrin saturation
	normal	Normal	Normal	20 %
Immunology	ANA	ASMA	Anti LKM1	AMAM2
	1/320	1/160	Negative	Negative
P . Electrophoresis	IgG			
	elevated			
Histology	Chronic hepatitis grade 2 stage 2			

MRCP :
was performed as part of the evaluation for possible overlap syndrome and showed normal intrahepatic and extrahepatic bile ducts

Doppler ultrasound showed no evidence thrombosis in the portal vein or hepatic veins

Findings were consistent with AIH


Autoimuine
Hepatitis
Uluarative Colostis
Diabetes
Diabetes
Diabetes

ECCO Guidelines on Extraintestinal Manifestations in Inflammatory Bowel Disease

Hannah Gordon,[a] Johan Burisch,[b] Pierre Ellul,[c] Konstantinos Karmiris,[d] Konstantinos Katsanos,[e] Mariangela Allocca,[f] Giorgos Bamias,[g] Manuel Barreiro-de Acosta,[h] Tasanee Braithwaite,[i] Thomas Greuter,[j] Catherine Harwood,[k] Pascal Juillerat,[l] Triana Lobaton,[m] Ulf Müller-Ladner,[n] Nurulamin Noor,[o] Gianluca Pellino,[p] Edoardo Savarino,[q] Christoph Schramm,[r] Alessandra Soriano,[s] Jürgen Michael Stein,[t] Mathieu Uzzan,[u] Patrick F. van Rheenen,[v] Stephan R. Vavricka,[w] Maurizio Vecchi,[x] Stephane Zuily,[y] Torsten Kucharzik[z]

ECCO guidelines 2024

3.3 Autoimmune hepatitis and overlap syndrome

Statement 12

The prevalence of AIH in adult patients with IBD is less than 0.5%, with higher rates in children and adolescents [EL2] [consensus: 100%]

Therapeutic challenges

Patient Age < 18

Whether AIH is an EIM of UC or if its merely co-morbidity

Limited data in the literature on similar cases

Type 1 diabetes mellitus

All of these challenges together made it difficult to choice the appropriate treatment .

Treatment

Induction of remission:

5 ASA + **Oral corticosteroid**

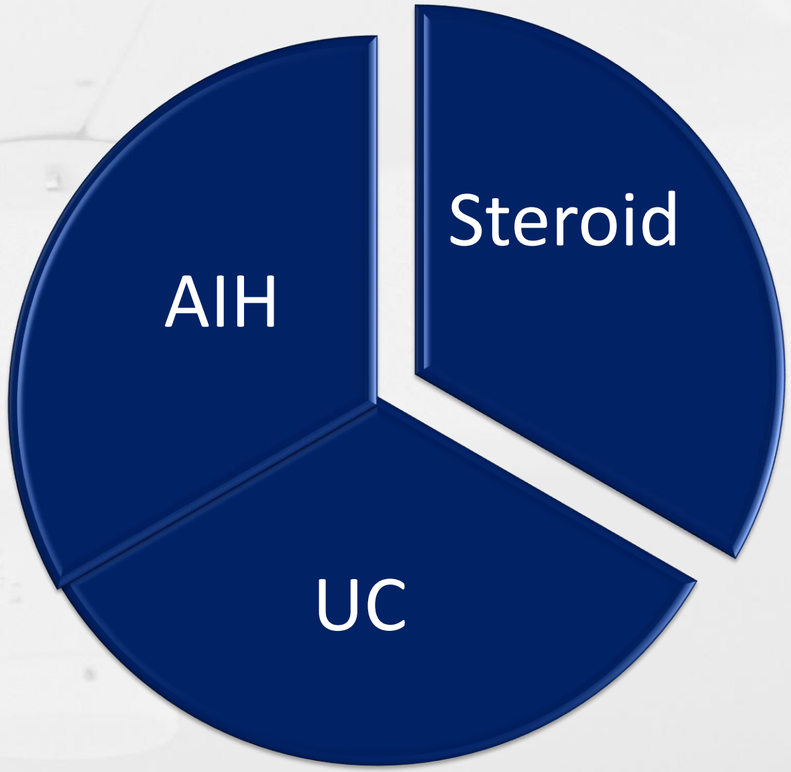
Oral mesalamine 80 mg/kg day

Treatment

Induction of remission:

Prednisone : dose 40 mg daily in combination with AZA 1-2 mg/d

type 1 diabetes mellitus



k

Steroids

hyperglycemia

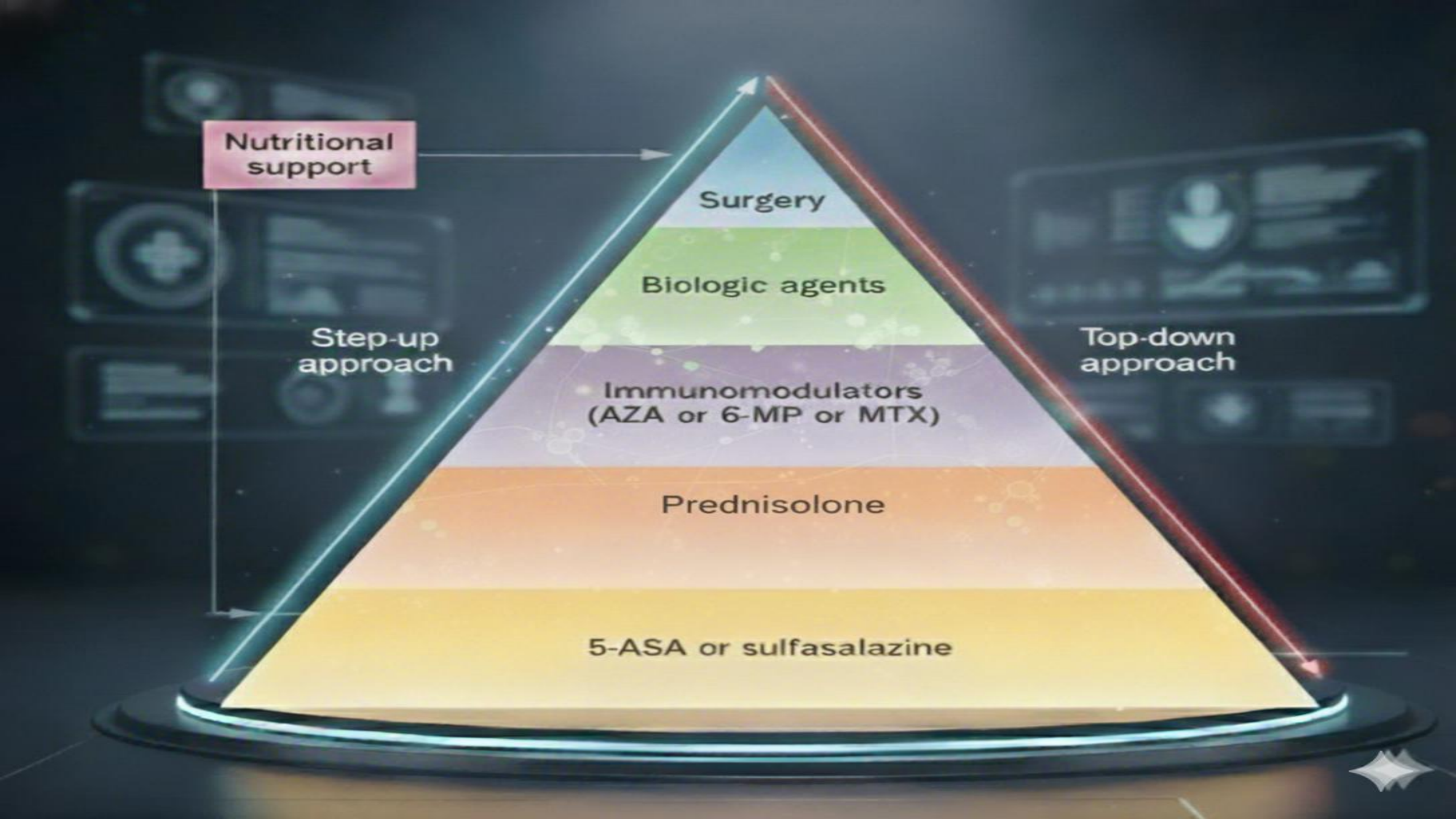
DKA

Discontinued prednisone

GLU > 400 in first week with Prednisolone 40 mg

in second week with Prednisolone 30 mg

20 mg prednisolone ,GLU >200 , AST/ALT elevated ,no clinical response for UC


Nutritional support
Surgery
Biologic agents
Immunomodulators (AZA or 6-MP or MTX)
Prednisolone
5-ASA or sulfasalazine
Step-up approach
Top-down approach

Biology

- **Age**

Infliximab

Adalimumab

Approved for the treatment of pediatric UC

- **Treatment of AIH**

EASL 2015

42. In patients requiring high dose, long-term (>20 mg/day) steroid therapy, conventional treatment should be optimized (high doses of predniso(lo)ne combined with 2 mg/kg/day azathioprine). Alternatively, a trial of CNIs (ciclosporine or tacrolimus), infliximab, methotrexate, or cyclophosphamide can be initiated. The relative effectiveness of second line treatments has not been examined in clinical trials. Therefore, these drugs should be used after consultation with a specialist centre only **(II-3)**

ESPGHAN 2018

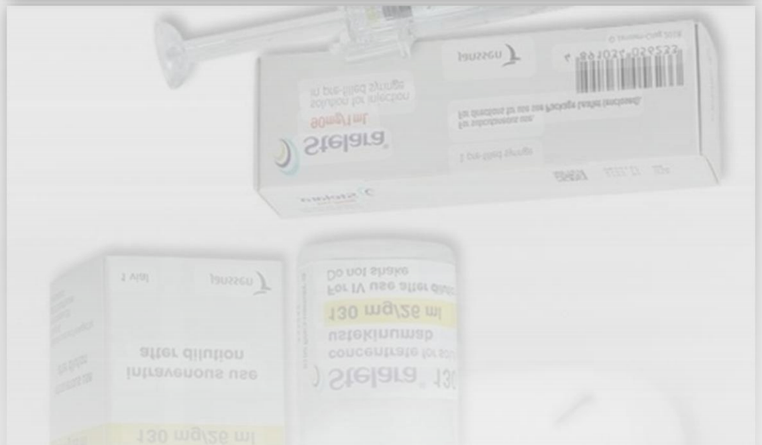
- The minority of patients who do not respond to standard treatment, and those who relapse frequently, should be offered alternative immunosuppression, the efficacy of which is still anecdotal (including in order of priority MMF, calcineurin inhibitors, rituximab, anti-TNF-α).

Biology

- **Available drugs :**

Golimumab

Ustekinumab



Biology

- **Age :**

Golimumab

2. Adalimumab [EL4, adults EL4] or golimumab [EL4, adults EL3] could be considered in those who initially respond but then lose response or are intolerant to IFX, based on serum levels and antibodies (Fig. 4). **(95% agreement)**

5. Golimumab recommended doses for induction are 200 mg at week 0 followed by 100 mg at week 2 for those weighing ≥45 kg. Children with lower weight should be dosed based on body surface area (115 and 60 mg/m^2 at weeks 0 and 2). Maintenance doses q4w are 60 mg/m^2 if weight <45 kg and 100 mg if weight ≥45 kg. Target trough levels during maintenance are >2 μg/mL. **(100% agreement)**

- **Use in AIH :**

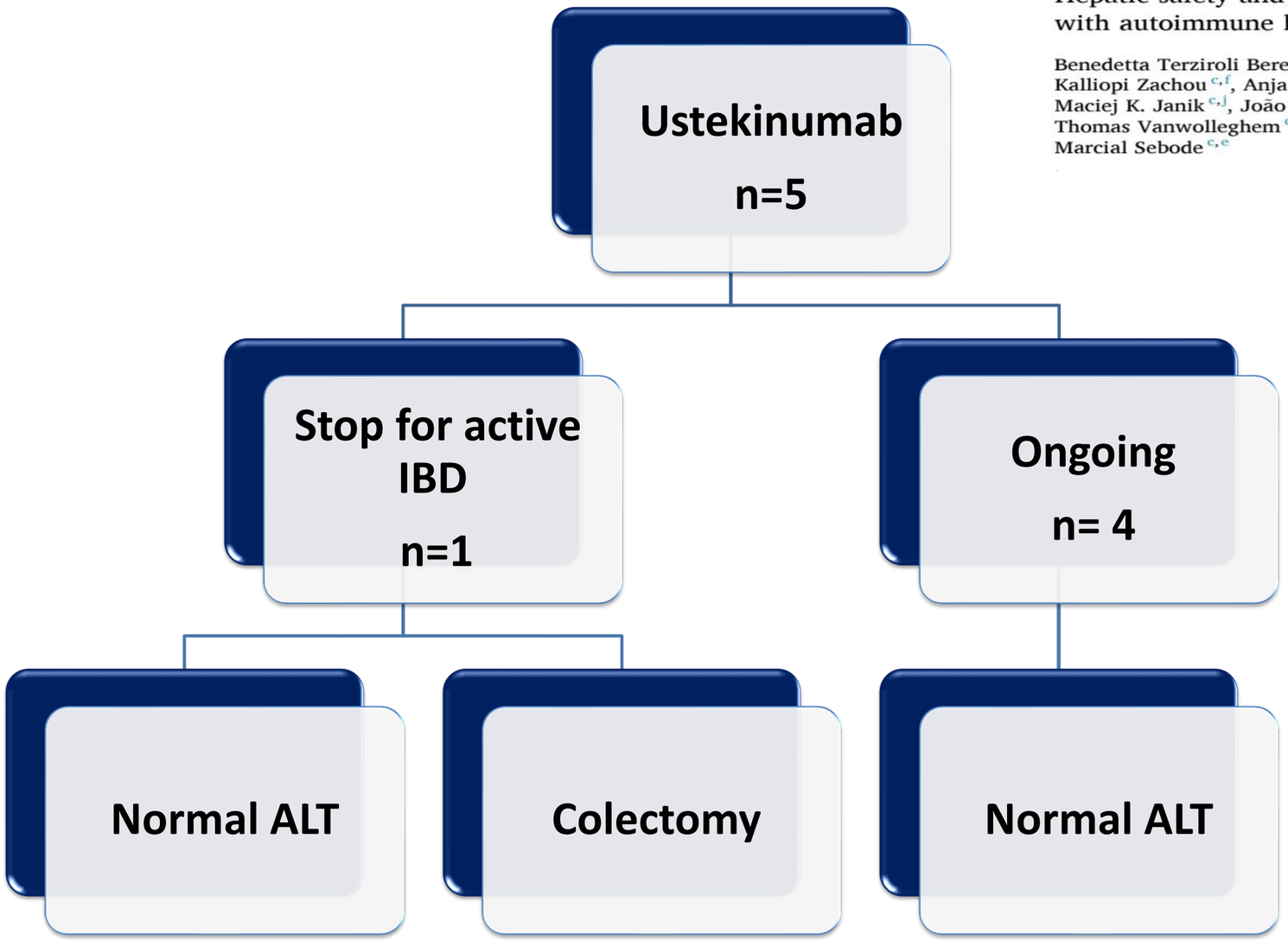
There is no evidence supporting the use of Golimumab in patient with AIH

Anti IL 12/23

Ustekinumab

- **Ustekinumab approved in adults only**

IBD + AIH
N=4 with normal ALT
N=1 elevated ALT



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Hepatic safety and efficacy of immunomodulatory drugs used in patients with autoimmune hepatitis

Benedetta Terziroli Beretta-Piccoli [a,b,c,d,*], Gustav Buescher [c,e], George Dalekos [c,f], Kalliopi Zachou [c,f], Anja Geerts [c,g], Nasser Semmo [h], Mirjam Kolev [h], Eleonora De Martin [c,i], Maciej K. Janik [c,j], João Madaleno [c,k], Milica Lalosevic Stojkovic [c,l], Jérôme Dumortier [c,m], Thomas Vanwolleghem [c,n,o], Ida Schregel [c,e], Silja Steinmann [c,e], Florence Lacaille [c,p], Marcial Sebode [c,e]

Authors	Report type	AIH With IBD
Terzioli beretta-piccoli et al 2023	Case series ,multicenter	N = 5

Authors	Report type	IBD	Age	Prior biologic	Induction	Maintenance	Following time	Response /outcome mentioned
Dhaliwal et al 2021	Cohort	UC N=25	12.3-16.2 years	IFX ADA Vedo	6mg/kg IV	90mg SC 45 mg q 8 week	52 week	Remission 44%
Dayan et al 2019	Cohort	CD n= 42 UC n=4 IBDU n=6	14-18 years	44 anti-tnf 10 biologic naïve	6mg/kg IV	90 mg SC q 8week	52 week	Remission Prior biologic 50% Naïve 90%
Kim et al 2021	Cohort	CD N=40	Median age 17.2 years	IFX/ADA /VEDO	6mg/kg IV	90 mg SC q 8week Some q 6 week Or q 4 week	62 week	Ongoing UST 84%
Kakiuchi and yoshiura 2022	Case report	UC	16 years	IFX	260 mg IV	90 mg SC q 8week	60 week	Clinical and endoscopic remission
Alhalabi et al 2023	Case report	UC	10 years	Biologic naïve	6mg/kg IV	90 mg SC q 8week	52 week	Clinical and endoscopic remission
Rodrigues – mauris et al 2021	Case report	CD	16 years	ADA	390 mg IV	90 mg SC q 8week Then q 6	6 months	Clinical remission

Ustekinumab dose ?

Original Article

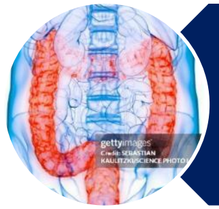
Ustekinumab in Paediatric Patients with Moderately to Severely Active Crohn's Disease: Pharmacokinetics, Safety, and Efficacy Results from UniStar, a Phase 1 Study

Joel R. Rosh,[a] Dan Turner,[b] Anne Griffiths,[c] Stanley A. Cohen,[d] Douglas Jacobstein,[e] Omoniyi J. Adedokun,[f] Lakshmi Padgett,[f] Natalie A. Terry,[f] Christopher O'Brien,[f] Jeffrey S. Hyams[g]

Authors	Report type	IBD	Age	Prior biologic	Induction	Maintenance
Roush et al 2021	Phase 1 ,multicenter double blind Study	CD N=44	2-18 years	Anti-tnf	Patients 40 ≥ kg were randomized to 130 mg vs 390 mg or in patients < 40 kg 3mg/kg vs 9mg/kg	At week 8 ,patients 40 ≥ kg single dose SC 90mg Patients < 40 kg 2mg/kg SC

- Its findings supported a 6 mg/kg induction dose of Ustekinumab for children weighing more than 40 kg, but recommended a 9mg/kg induction for children weighing < 40 kg
- The PK and safety profiles resembled those in adults

Ustekinumab → 6 mg /kg → **Maintenance 90 mg SC q 8 week**



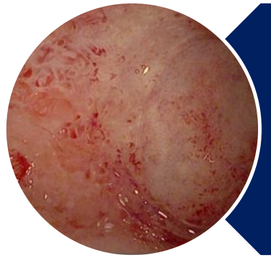
PUCAI

FC

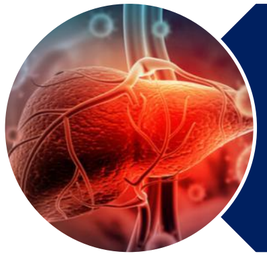
523 Before Ustekinumab

150 After 6 • months

55 After 12 • months



Colonoscopy



Transaminase

IgG

IgG		ALT / AST
1.5 g/dl	Before Ustekinumab	175/153
1.3 g\dl	After 6 months	100/66
1.1 g/dl	After 12 months	53/40

Received: 27 December 2024 | Accepted: 26 March 2025
DOI: 10.1002/jpn3.70097

JPGN

PRACTICE GUIDELINE

Management of paediatric ulcerative colitis, part 1: Ambulatory care—An updated evidence-based consensus guideline from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition and the European Crohn's and Colitis Organisation

✓CME

Eytan Wine[1,2,3] | Marina Aloi[4] | Stephanie Van Biervliet[5] | Jiri Bronsky[6] | Javier Martín di Carpi[7] | Marco Gasparetto[8] | Laura Gianolio[9] | Hannah Gordon[10] | Iva Hojsak[11] | Alexandra S. Hudson[3] | Séamus Hussey[12] | Johan van Limbergen[13] | Erasmo Miele[14] | Lorenzo Norsa[8] | Ola Olén[15] | Gianluca Pellino[16,17] | Patrick van Rheenen[18] | Lissy de Ridder[19] | Richard K. Russell[20] | Dror S. Shouval[21,22] | Eunice Trindade[23] | Dan Turner[24] | David C. Wilson[25] | Anat Yerushalmy Feler[26,27] | Amit Assa[24]

2. Anti-p40 (IL12/23; e.g., ustekinumab), anti-p19 (IL23; e.g., risankizumab, mirikizumab, guselkumab), Janus kinase (JAK) inhibitors (e.g., tofacitinib, upadacitinib, filgotinib), golimumab and sphingosine-1-phosphate (S1P) receptor agonists (e.g., Ozanimod, Etrasimod) may be also considered following failure of approved anti-TNF [EL4, adults EL2] (Agreement 100%).

Clinical Practice Guidelines

JOURNAL OF HEPATOLOGY

EASL Clinical Practice Guidelines on the management of autoimmune hepatitis☆

European Association for the Study of the Liver*

			and IgG normalisation		
Ustekinumab					
Terziroli Beretta-Piccoli *et al.*[317]	Case series in patients with concomitant IBD	5	AST and ALT normalisation	80% (4/5)	None

AST, aspartate aminotransferase; ALT, alanine aminotransferase; IgG, immunoglobulin G.

ELSEVIER

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EASL The Home of Hepatology

- **Regular review of the medical literature is essential to guide management and stay updated on evolving evidence in such rare presentation .**

Action	Manuscript Number	Title	Initial Date Submitted	Status Date	Current Status
View Submission Author Status View Publication Charges Send E-mail	MD-D-25-13668	Challenges in managing autoimmune hepatitis and ulcerative colitis with ustekinumab in an adolescent from a resource-constrained conflict-affected setting: a case report and literature review	Oct 17 2025 12:48AM	Oct 20 2025 9:37AM	Under Review