

AIH Therapie – neue Konzepte in Sicht?

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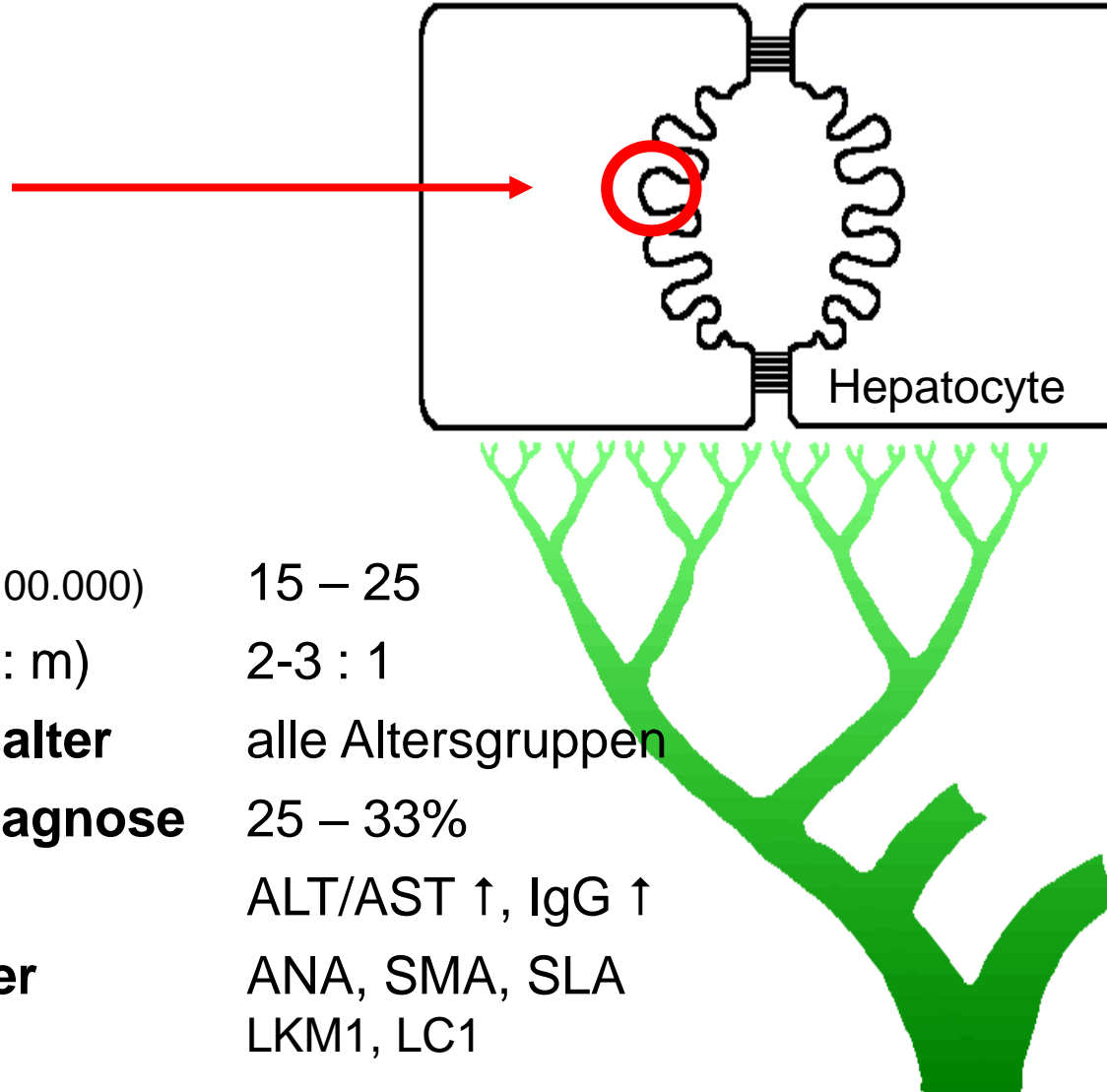
Weiterbildungszentrum Gastroenterologie 2025, Zürich – 04. Juli 2025



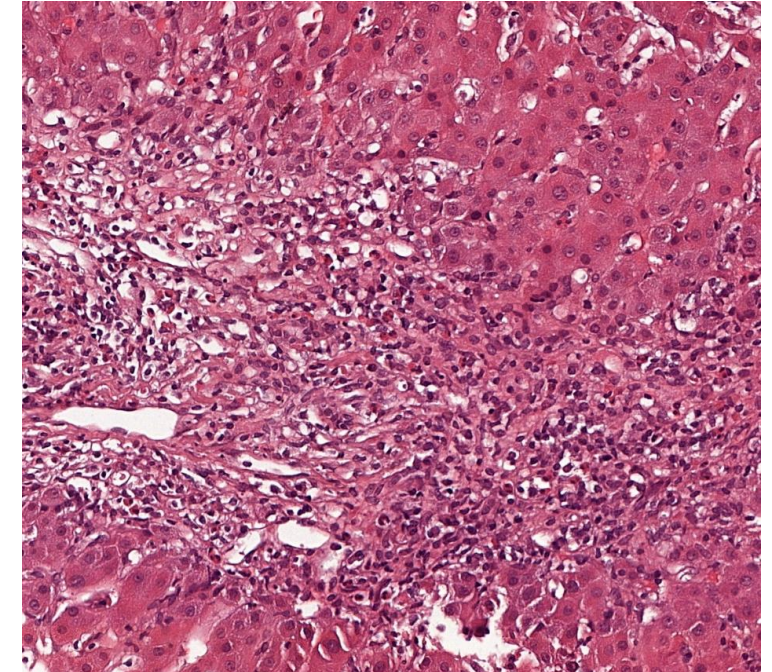
Autoimmunhepatitis (AIH)

- Klinische Aspekte -

AIH



Prävalenz (pro 100.000)	15 – 25
Geschlecht (w : m)	2-3 : 1
Manifestationsalter	alle Altersgruppen
Zirrhose bei Diagnose	25 – 33%
Hepatitis	ALT/AST ↑, IgG ↑
Auto-Antikörper	ANA, SMA, SLA LKM1, LC1



Symptome

- Fatigue
- Malaise
- Gelenkbeschwerden
- Amenorrhoe
- ...

Autoimmunhepatitis

- Leitlinien -

HEPA
PRACTICE
Clinical Practice Guidelines

publiziert bei:  AWMF online
Portal der wissenschaftlichen Medizin

 1913 DGVS
Deutsche Gesellschaft für
Gastroenterologie,
Verdauungs- und
Stoffwechselkrankheiten

Diag
Auto
Child
and
Asso

EASL

European Association

Summary

Autoimmune hepatitis
or ethnicity. At base
massive hepatocyte
agement of AIH both
AIH is also provided
hypertension and he

Cara L. Mack,¹
Mouaz Alsawas

WHAT'S
GUIDE

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AI training, and similar

USZ
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S3-Leitlinie „Seltene Lebererkrankungen (LeiSe LebEr) – autoimmune Lebererkrankungen von der Pädiatrie bis zum Erwachsenenalter“ der Deutschen Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten (DGVS)

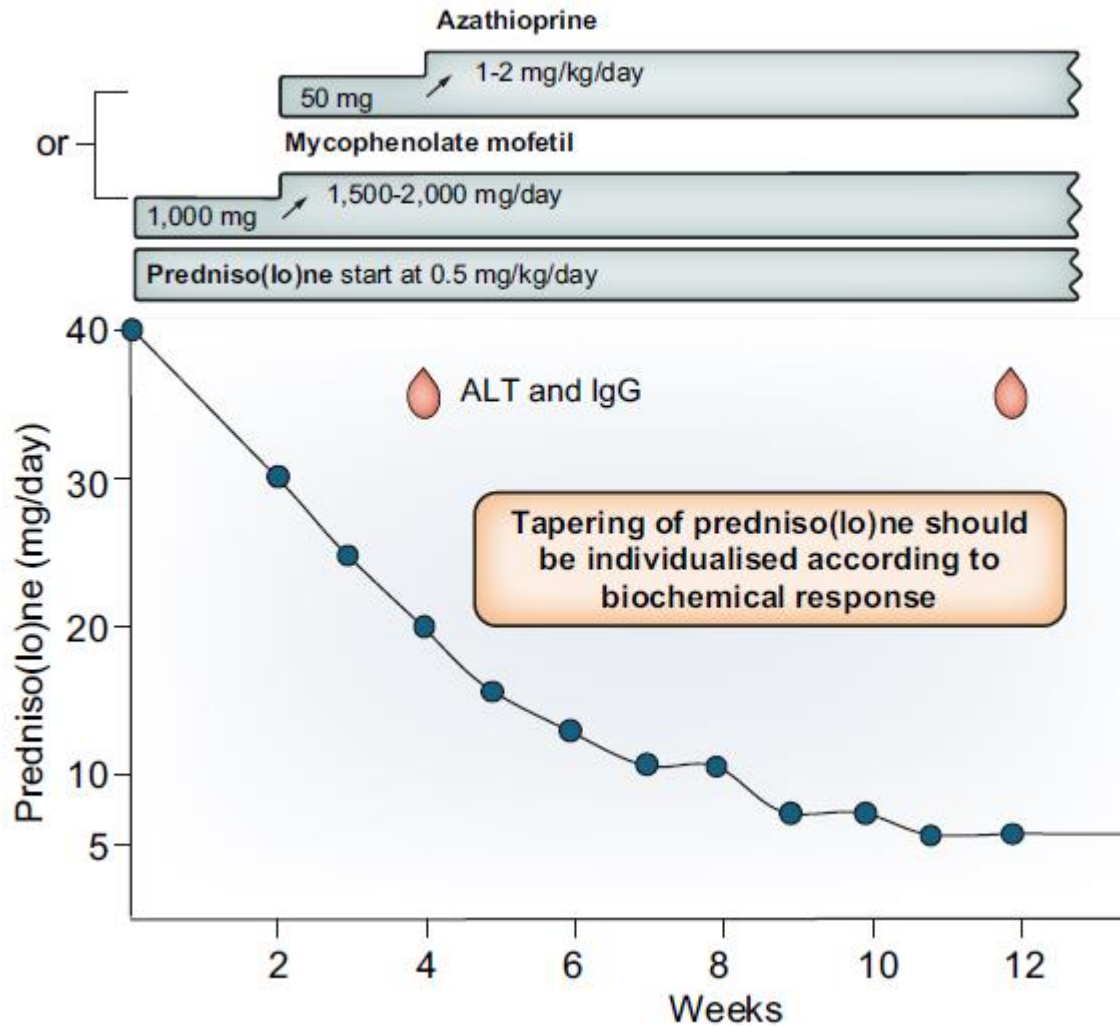
Februar 2025 – AWMF-Registernummer: 021 - 027

Autoren

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Autoimmunhepatitis

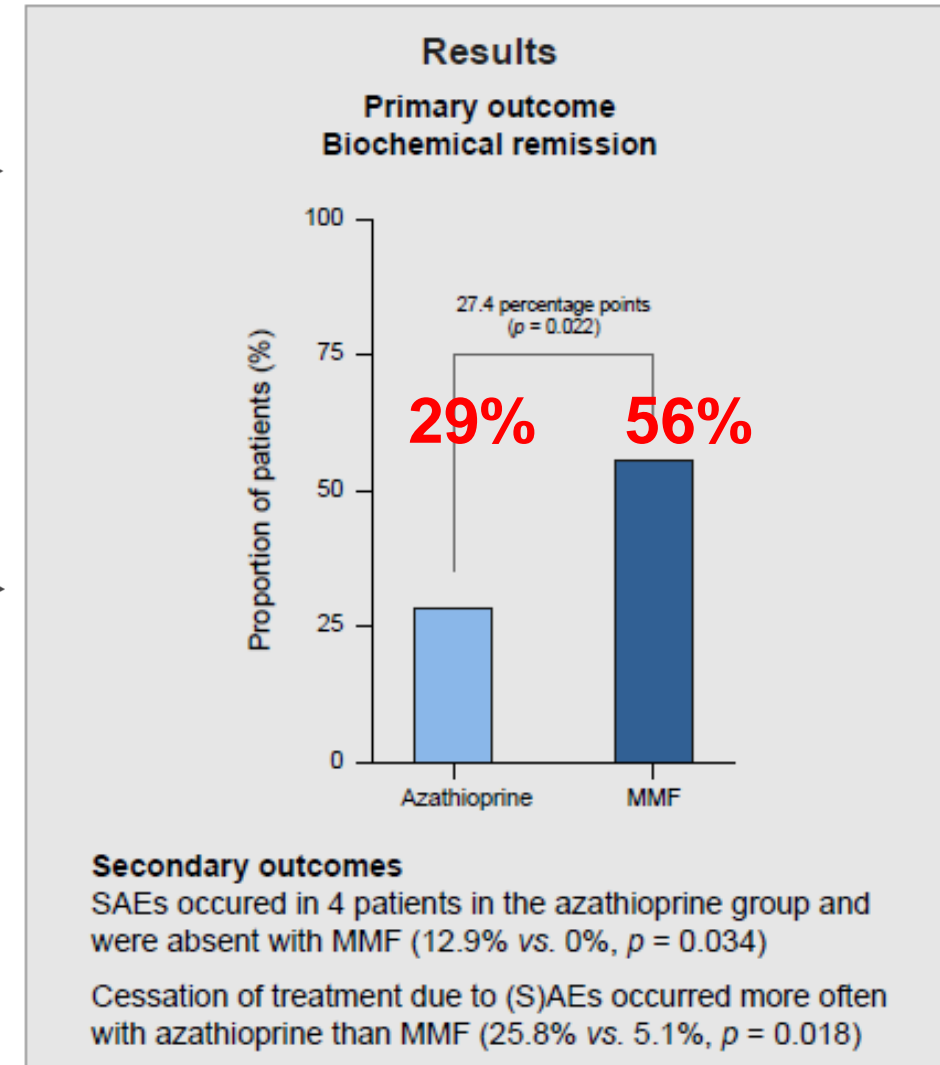
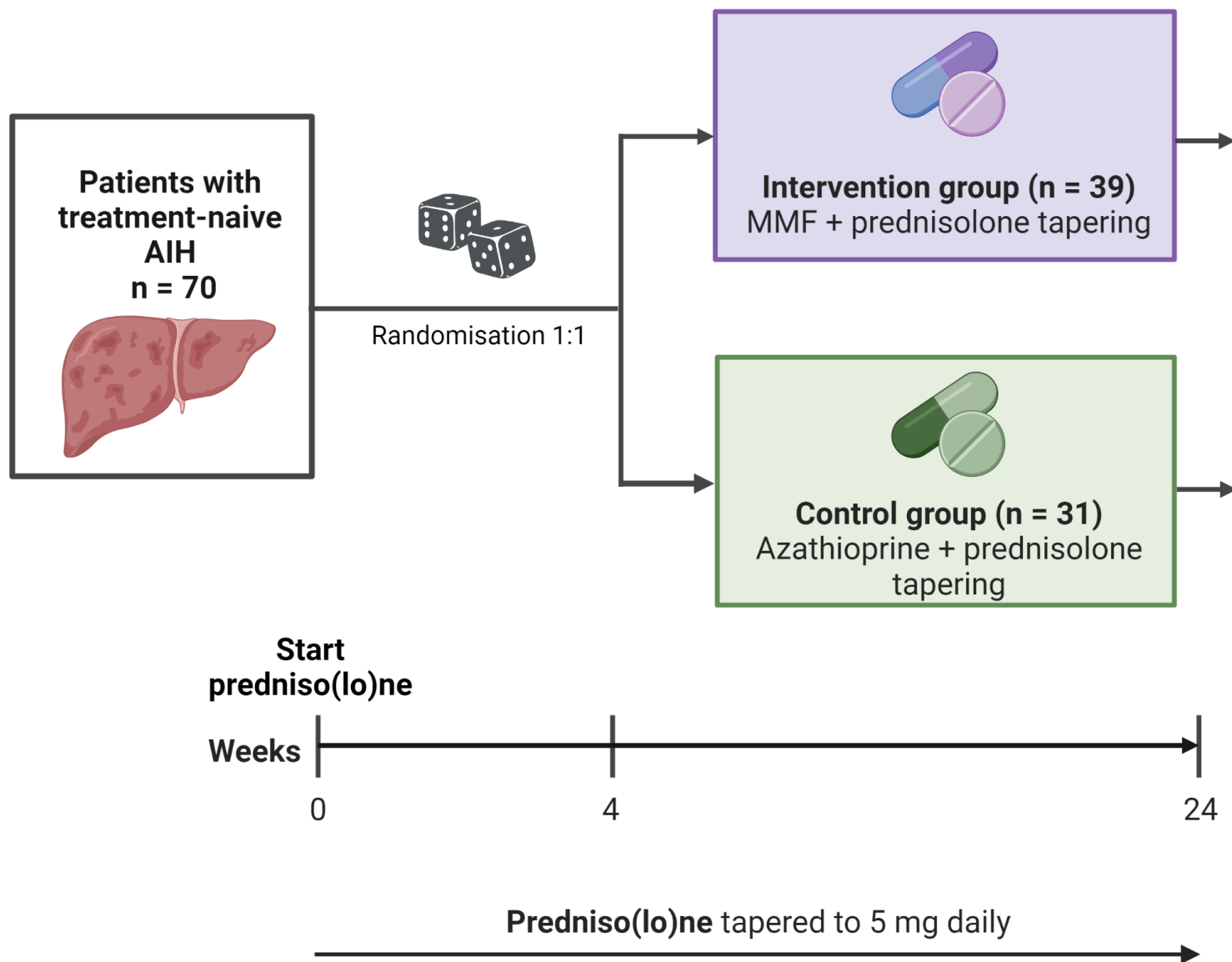
- Erstlinien-Therapie -



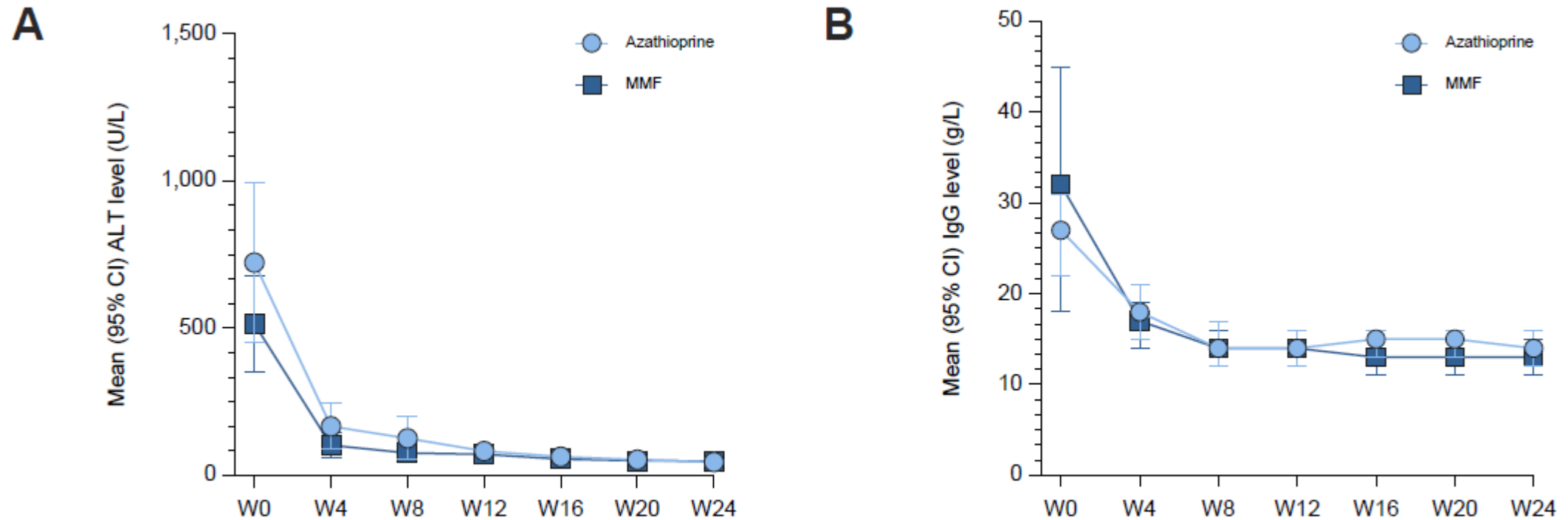
Recommendations

- In adults with AIH, predniso(lo)ne of at least 0.5 mg/kg/day, and potentially up to 1 mg/kg/day in more severe and advanced disease, in combination with azathioprine (whenever bilirubin is <6 mg/dl and ideally 2 weeks apart from corticosteroid start at an initial dose of 50 mg/day up to a final dose of 1-2 mg/kg/day) or mycophenolate mofetil (MMF, 1.5-2 g/day) should be the first-line treatments (**LoE 2, strong recommendation, consensus**).

CAMARO-Trial: Azathioprin vs MMF in AIH



CAMARO-Trial: Azathioprin vs MMF in AIH



- Similar mean cumulative predniso(lo)ne dose
- At 24 weeks: mean Aza 1.16 mg/kg, mean MMF 1853 mg/d
- TRSAE: 3 in Aza, 0 in MMF, group
- Cessation of treatment due to (S)AE Aza (25.8%) vs. MMF (5.1%; $p=0.018$)

Autoimmunhepatitis

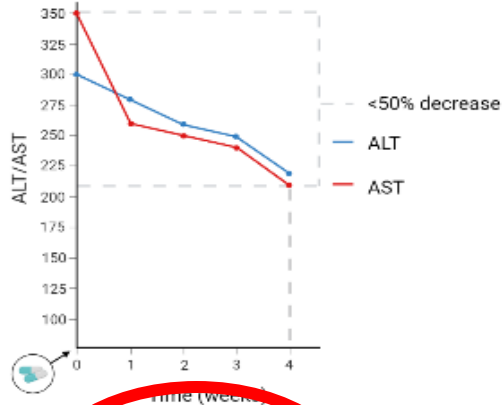
- Beurteilung des Therapieansprechen -

Intolerance to treatment

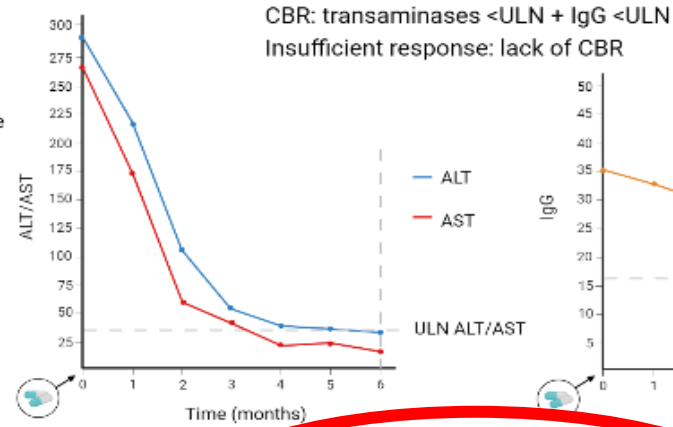
Any adverse event possibly related to treatment as assessed by the treating physician leading to potential discontinuation of the drug



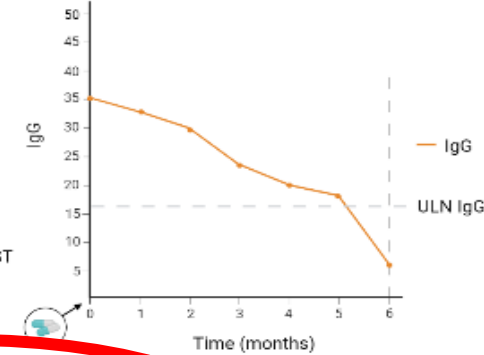
Diagnosis of AIH and initiation of treatment



Non-response

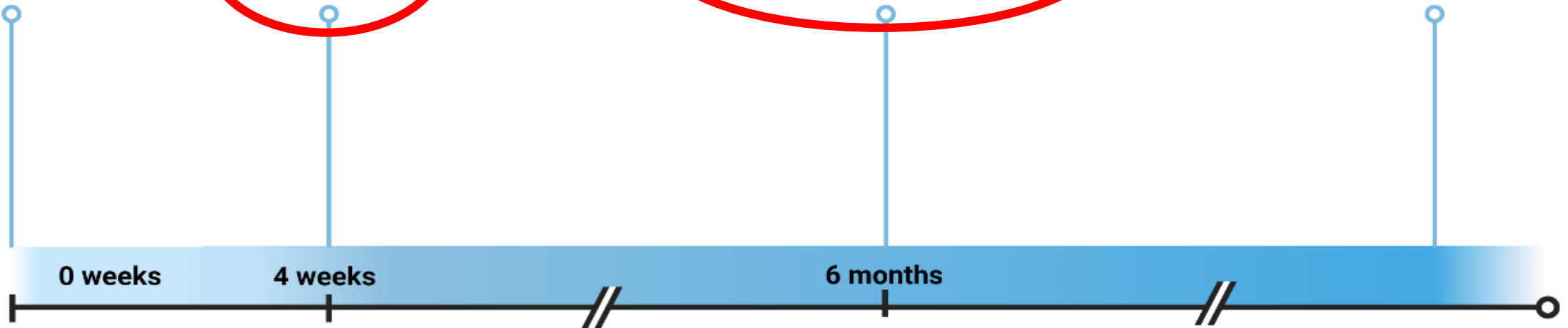


Complete biochemical response (CBR) / insufficient response

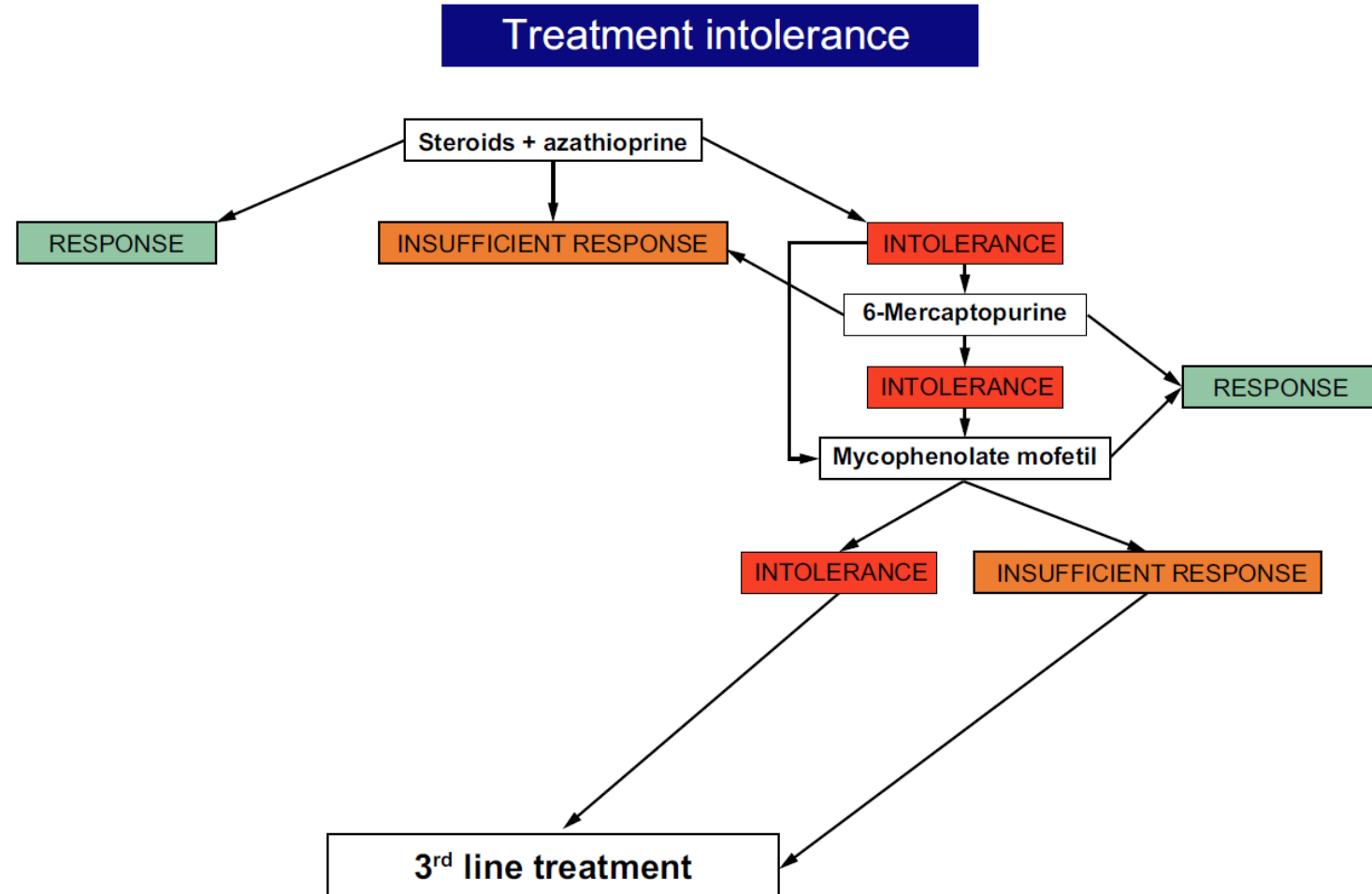
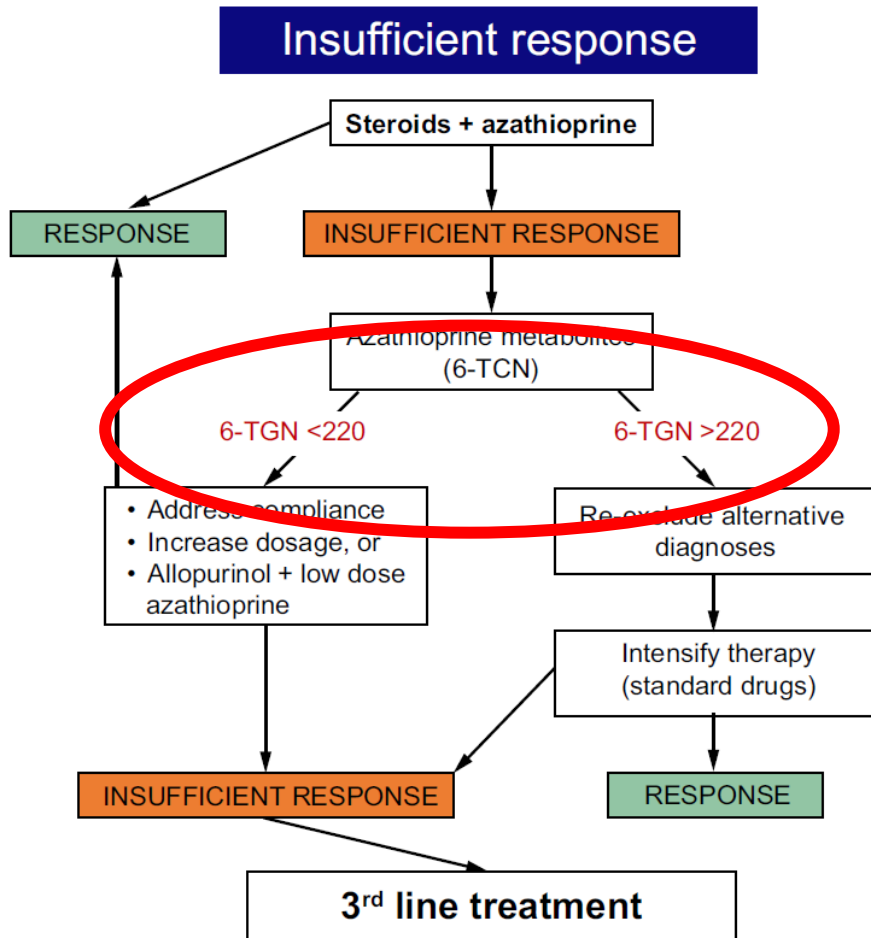


HAI <4/18

Remission

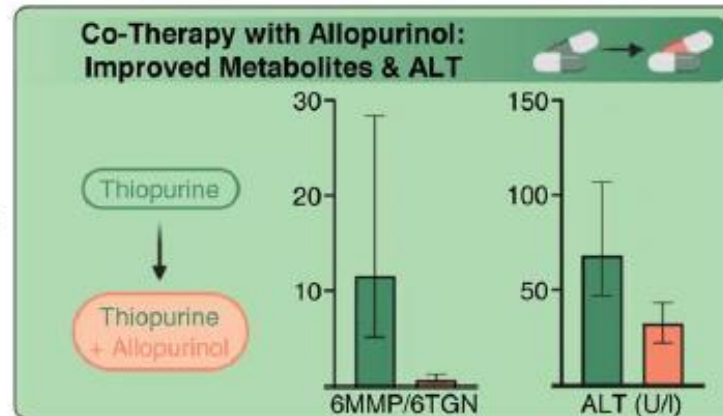
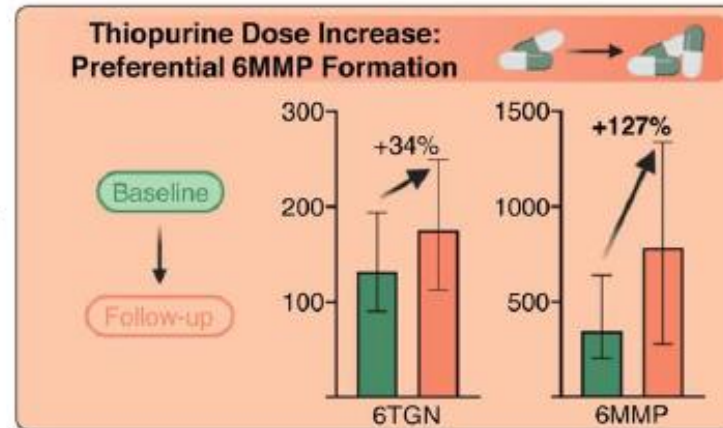
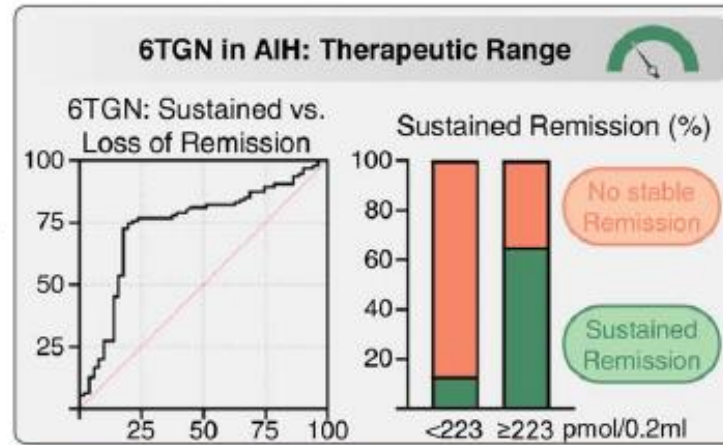
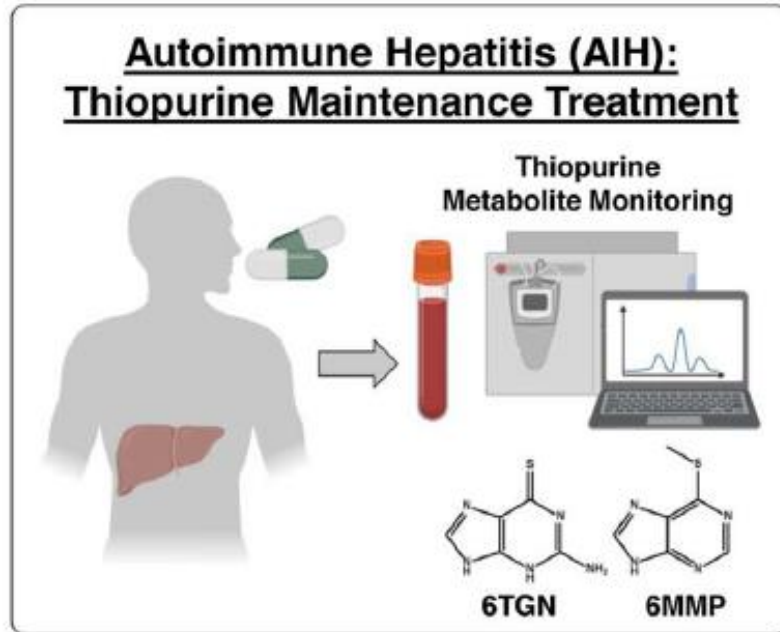


Therapie-Algorithmus bei AIH



Autoimmunhepatitis

- Thiopurine plus Allopurinol -



Praktische Anwendung:

1/3 der Aza / 6-MP-Dosis

+ 100 mg Allopurinol

Autoimmunhepatitis

- Zweit- und Drittlinien-Therapie -

Table 9. Studies evaluating treatment options in patients with insufficient response to azathioprine.

Author	Study	n	Aim	Efficacy in patients with insufficient response	Side effects to second-line agent
Mycophenolate					
Efe <i>et al.</i> ²⁹⁰	Retrospective	47*	Complete response: AST, ALT, and IgG normalisation	34% (16/47)**	Leukopenia (n = 6), gastrointestinal (n = 3), headache (n = 1)
Roberts <i>et al.</i> ²⁹¹	Retrospective	42	Complete response: AST, ALT, and IgG normalisation	57% (24/42)	Gastrointestinal (n = 11), cytopenia (n = 3), infections (n = 4), neuropsychiatric (n = 3), skin cancer (n = 3)
Dalekos <i>et al.</i> ²²⁹	Propensity matching trial	9	Complete response: AST, ALT, and IgG normalisation	100% (9/9)	NA
Dalekos <i>et al.</i> ²³⁰	Retrospective	16	Complete response: AST, ALT, and IgG normalisation	68% (11/16)	NA
Kolev <i>et al.</i> ²⁸⁷	Retrospective	10	Complete response: ALT and IgG normalisation	50% (5/10)	
Santiago <i>et al.</i> ²⁸⁶	Systematic review/ meta-analysis	124		32% (95% CI: 24-39%)	
Tacrolimus					
Efe <i>et al.</i> ²⁹⁰	Retrospective	46*	Complete response: AST, ALT, and IgG normalisation	56.5% (26/46)**	Neurological (n = 4), hypertension (n = 2), gastrointestinal (n = 2), renal failure (n = 1)
Aqel <i>et al.</i> ³¹³	Retrospective	11	Complete response: AST and ALT normalisation	91% (10/11)	Headache (n = 4), neurological (n = 1), hypertension (n = 1)
Than <i>et al.</i> ³¹¹	Retrospective	17	Not defined	29% normalisation of ALT and 50% normalisation of IgG	Headache (n = 2), abdominal pain (n = 1), psychosis (n = 1)
Ferre-Aracil <i>et al.</i> ²⁹⁹	Retrospective	20	Complete response: AST, ALT, and IgG normalisation	Not reported for patients with insufficient response; 78% (18/23) in the whole population	Diabetes (n = 1), tremor (n = 1), headache (n = 1), diarrhoea (n = 1), ototoxicity (n = 1)
Cyclosporine					
Sherman <i>et al.</i> ³⁰⁵	Case series	6	Decrease in ALT >1.5x ULN	67% (4/6)	Gingival hyperplasia (n = 6)
Fernandes <i>et al.</i> ³⁰⁶	Case series	5	AST/ALT normalisation	80% (4/5)	Hirsutism (n = 2), gingival hyperplasia (n = 2)
Malekzadeh <i>et al.</i> ³⁰⁷	Retrospective	19	Complete response: AST, ALT, and IgG normalisation	5% (1/19)	Paraesthesia (n = 4), gingival hyperplasia (n = 3), tremor (n = 1), hypertension (n = 1), diarrhoea (n = 1), hirsutism (n = 1)

Autoimmunhepatitis

- Zweit- und Drittlinien-Therapie -

Author	Study	n	Aim	Efficacy in patients with insufficient response	Side effects to second-line agent
Tacrolimus					
Aqel <i>et al.</i> ³¹³	Retrospective	11	Complete response: AST and ALT normalisation	91% (10/11)	Headache (n = 4), neurological (n = 1), hypertension (n = 1)
Infliximab					
Weiler-Normann <i>et al.</i> ³¹⁴	Case series	11	Complete response: AST, ALT, and IgG normalisation	54% (6/11)	Urinary tract infection (n = 2), ocular herpes (n = 2), recurrent herpes zoster infection (n = 2), pneumonia (n = 2)
Rituximab					
Burak <i>et al.</i> ³¹⁸	Case series	11	Decrease in ALT/AST and IgG.	Significant decrease	Dental abscess (n = 1)
Than <i>et al.</i> ³¹²	Case series	22	Not defined	Significant decrease in ALT, AST, and IgG at 24 months; 59% (13/22) → corticosteroid dose reduction; 23% (5/22) → flare	Infections (n = 2), tongue cancer (n = 1)
Riveiro-Barciela <i>et al.</i> ³¹⁵	Retrospective	35	Complete response: AST, ALT, and IgG normalisation	88.6% (31/35); Flare-free rate at 1st, 2nd and 3rd year: 86%, 73% and 62%, respectively	Infections (n = 5), anaphylaxis (n = 1), flu-like symptoms (n = 2)
Belimumab					
Arvaniti <i>et al.</i> ³¹⁰	Case series	2	Complete response: AST, ALT, and IgG normalisation	100% (2/2)	Rectal fistula (n = 1)
Kolev <i>et al.</i> ³⁰⁹	Case series	3	Complete response: AST, ALT, and IgG normalisation	66.7% (2/3)	Headache episodes (n = 1)
Ustekinumab					
Terziroli Beretta-Piccoli <i>et al.</i> 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.

Autoimmunhepatitis

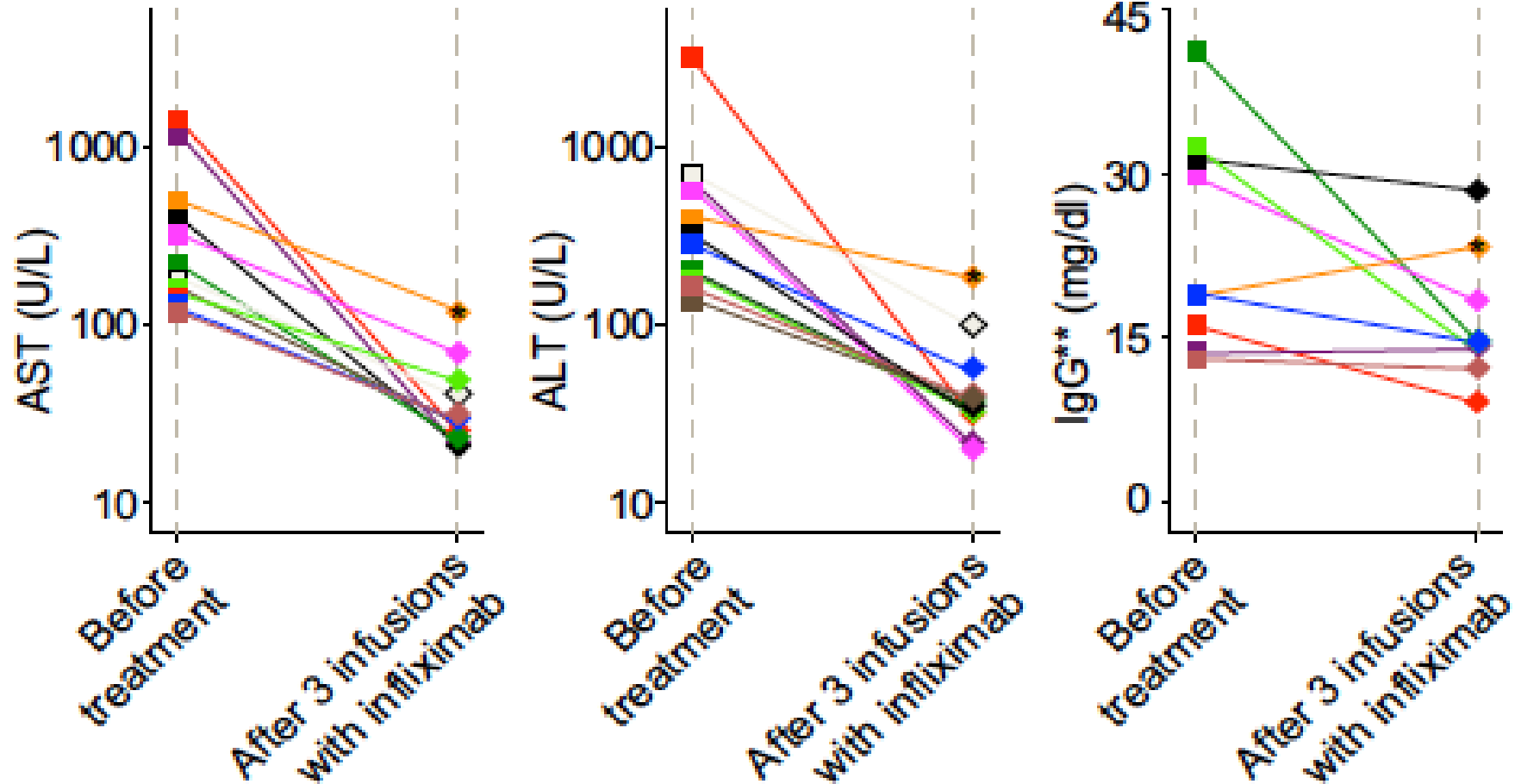
- Zweit- und Drittlinien-Therapie – Dosierungsempfehlung laut Leitlinie-

Table 11. Dose recommendation for third-line treatment options.

Drug	Dose
Tacrolimus	0.1 mg/kg/12h (or equivalent on extended-release formulation). Recommended trough levels: 6 ng/ml
Rituximab	1,000 mg i.v. week 0 and 2. Readminister every 6 months if needed
Infliximab	Induction: 5 mg/kg weeks 0, 2, 6 and 10 Maintenance: 5 mg/kg every 4–8 weeks
Belimumab	10 mg/kg day 0, 14, 28 and then every 1-2 months.

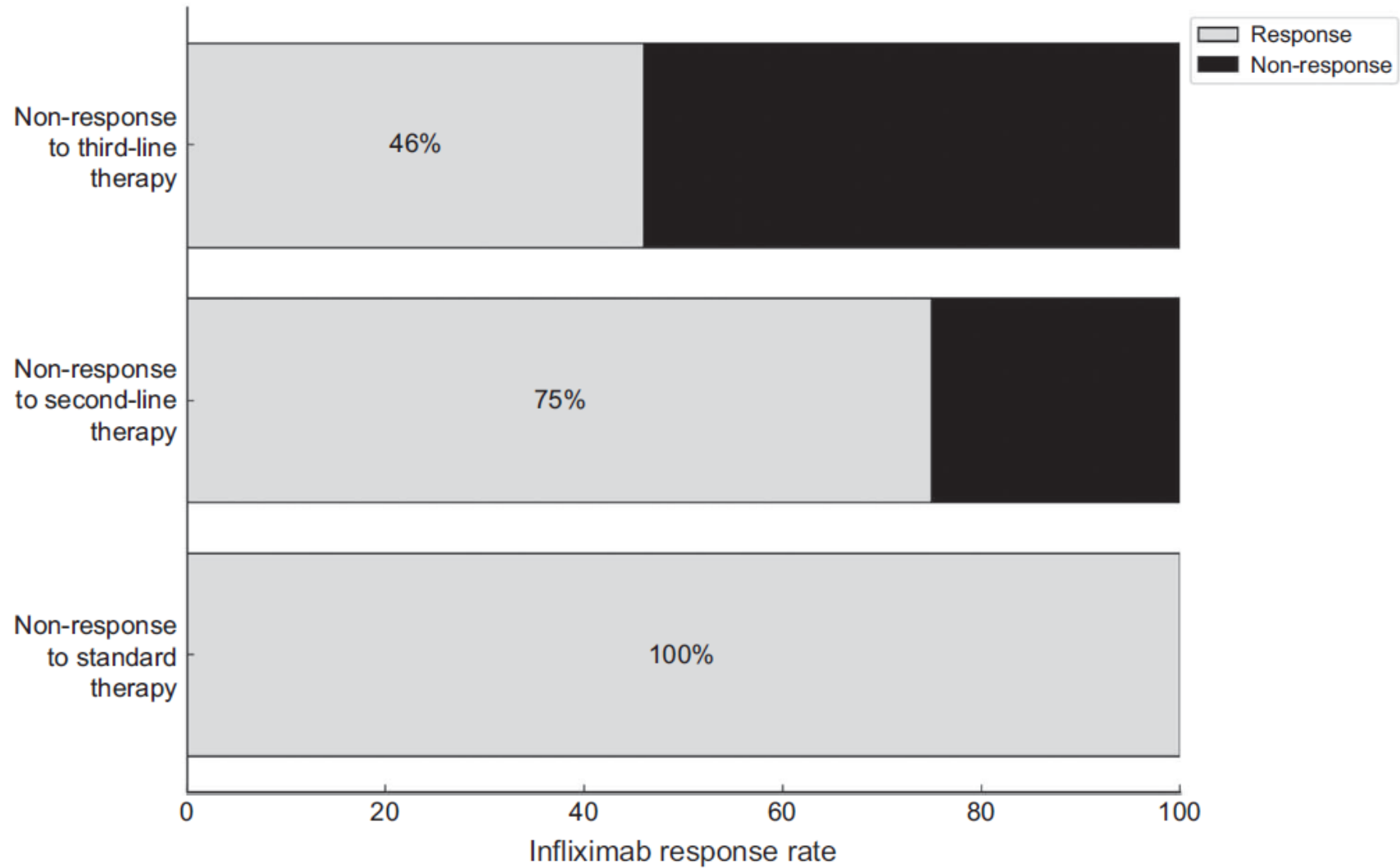
Infliximab bei refraktärer AIH

- Retrospective Cohort; N=11; single center -



Infliximab bei refraktärer AIH

- Retrospective Cohort; N=42; 21 centers in 12 countries -



Non-Response / Slow response

- **Question the diagnosis (e.g. Wilson? Toxic? Vascular? Infectious??)**
- **Prednisolone 100-250 mg/d i.v.**
- **Consider additional fast-acting immunosuppressives (tacrolimus, infliximab, cyclophosphamide....)**
- **If severe, prepare for emergency liver transplant after 7 days**
- **If mild-moderate, be patient, optimise standard therapy before progressing to 2nd and 3rd line drugs**

Autoimmunhepatitis – Überblick Therapie

- Therapie der Grunderkrankung -

- **Therapie-naiv** Steroide (0.5 – 1.0 mg/kg KG/d)
sequentiell Azathioprin 1.5–2.0 mg/kg KG/d (6-TGN)
oder MMF 1-2 g/d
- **Zweit-/Drittlinien-Therapie** MMF 1-2 g/d, Tacrolimus, CsA, mTOR Inhibitoren,
Biologica (Infliximab, Rituximab, Belimumab, etc.)
- **Fulminante AIH /
dekomponierte Zirrhose** Transplantation rechtzeitig (!) erwägen

Vielen Dank!



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