Gastro-Highlights
Helicobacter, Ulkuskrankheit, Dyspepsie

10. Dezember 2022

Michael Gschwantler, Klinik Ottakring

- Helicobacter pylori
- Intestinale Metaplasie und Magenkarzinomrisiko
- Sicherheit von Protonenpumpenhemmern
- Therapie der Gastroparese
- Neue Therapiekonzepte bei Zöliakie

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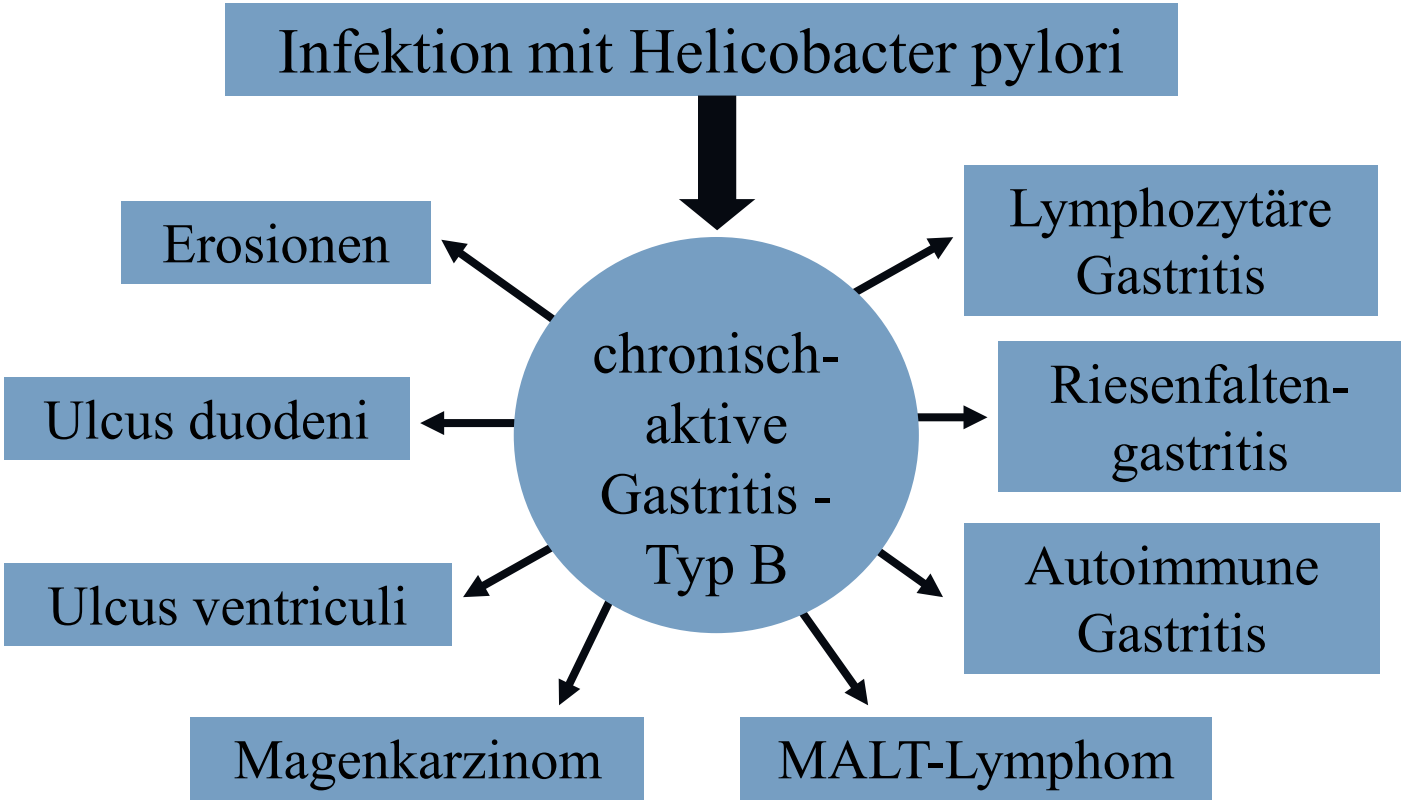
Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report

Peter Malfertheiner ,[1,2] Francis Megraud ,[3] Theodore Rokkas ,[4,5] Javier P Gisbert ,[6,7] Jyh-Ming Liou ,[8] Christian Schulz ,[1,9] Antonio Gasbarrini,[10] Richard H Hunt,[11,12] Marcis Leja ,[13,14] Colm O'Morain,[15] Massimo Rugge ,[16,17] Sebastian Suerbaum,[9,18] Herbert Tilg ,[19] Kentaro Sugano ,[20] Emad M El-Omar ,[21] On behalf of the European Helicobacter and Microbiota Study group

- „H.p. infection is formally recognised as an infectious disease, an entity that is now included in the International Classification of Diseases 11th Revision. This in principle leads to the recommendation that all infected patients should receive treatment.“

Malfertheiner P et al. Gut 2022; 71: 1724-1762

Mögliche Folgekrankheiten einer Helicobacter pylori induzierten chronischen Gastritis



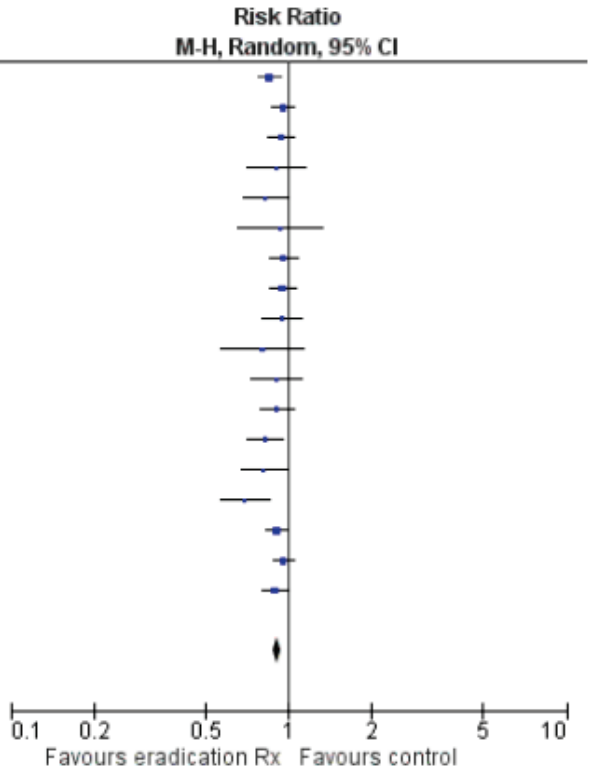
Efficacy of H.p.-eradication for functional dyspepsia – Metaanalysis of RCTs

- 29 RCTs with a total of 6.781 patients included
- **Effect on symptom cure:**

Study or Subgroup	H. pylori eradication Rx Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
McColl 1998	127	160	147	158	10.7%	0.85 [0.78, 0.93]	1998
Talley (ORCHID) 1999	115	135	127	143	10.4%	0.96 [0.88, 1.05]	1999
Talley (USA) 1999	128	170	134	167	6.9%	0.94 [0.84, 1.05]	1999
Miwa 2000	35	50	31	40	1.6%	0.90 [0.71, 1.16]	2000
Bruley des Varannes 2001	74	129	86	124	2.7%	0.83 [0.68, 1.00]	2001
Hsu 2001	34	81	36	80	0.8%	0.93 [0.66, 1.33]	2001
Alizadeh-Naeeni 2002	72	84	65	73	6.5%	0.96 [0.85, 1.08]	2002
Malfertheiner 2003	338	534	177	266	7.8%	0.95 [0.85, 1.06]	2003
Koelz 2003	67	89	73	92	3.8%	0.95 [0.81, 1.11]	2003
Veldhuyzen van Zanten 2003	31	75	42	82	0.8%	0.81 [0.57, 1.14]	2003
Ang 2006	49	71	45	59	2.2%	0.90 [0.73, 1.12]	2006
Mazzoleni 2006	39	46	42	45	4.4%	0.91 [0.79, 1.05]	2006
Shi 2006	65	88	77	86	4.5%	0.82 [0.71, 0.95]	2006
Gwee 2009	31	41	38	41	2.5%	0.82 [0.67, 0.99]	2009
Wu 2010	55	100	79	100	2.3%	0.70 [0.57, 0.85]	2010
Lan 2011	86	98	94	97	12.5%	0.91 [0.83, 0.98]	2011
Mazzoleni 2011	166	201	175	203	12.0%	0.96 [0.88, 1.04]	2011
Sodhi 2013	185	280	204	276	7.5%	0.89 [0.80, 1.00]	2013
Total (95% CI)		**2432**		**2132**	**100.0%**	**0.91 [0.88, 0.94]**	
Total events	1697		1672				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 18.21$, $df = 17$ ($P = 0.38$); $I^2 = 7\%$

Test for overall effect: $Z = 6.10$ ($P < 0.00001$)



NNT: 14

Ford AC et al. Gut 2022; 71: 1967-1975

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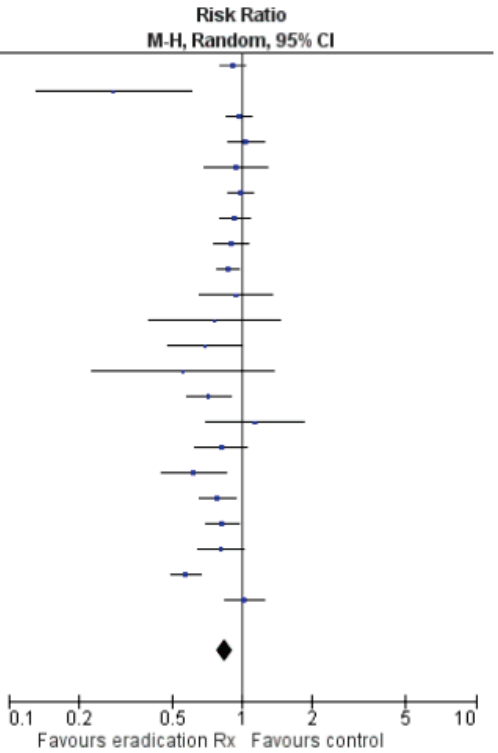
- 29 RCTs with a total of 6.781 patients included
- **Effect on symptom improvement:**

Study or Subgroup	H. pylori eradication Rx Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Blum 1998	119	164	130	164	6.7%	0.92 [0.81, 1.03]	1998
Dhali 1999	6	32	20	30	1.0%	0.28 [0.13, 0.60]	1998
Talley (ORCHID) 1999	103	135	112	143	6.6%	0.97 [0.86, 1.11]	1999
Talley (USA) 1999	101	170	96	167	5.7%	1.03 [0.86, 1.24]	1999
Bruley des Varannes 2001	49	129	50	124	3.7%	0.94 [0.69, 1.28]	2001
Froehlich 2001	77	92	75	88	6.6%	0.98 [0.87, 1.11]	2001
Koskenpato 2001	61	77	63	74	6.2%	0.93 [0.80, 1.08]	2001
Alizadeh-Naeeni 2002	61	84	59	73	5.8%	0.90 [0.76, 1.07]	2002
Malfertheiner 2003	312	534	178	266	6.9%	0.87 [0.78, 0.98]	2002
Veldhuyzen van Zanten 2003	31	75	36	82	3.0%	0.94 [0.65, 1.35]	2003
Gisbert 2004	13	34	8	16	1.3%	0.76 [0.40, 1.46]	2004
Gonzalez Carro 2004	22	47	31	46	3.0%	0.69 [0.48, 1.00]	2004
Martinek 2005	5	20	9	20	0.7%	0.56 [0.23, 1.37]	2004
Ruiz Garcia 2005	46	79	64	79	5.0%	0.72 [0.58, 0.89]	2005
Ang 2006	26	71	19	59	2.1%	1.14 [0.70, 1.84]	2005
Mazzoleni 2006	30	46	36	45	4.4%	0.82 [0.63, 1.05]	2006
Shi 2006	33	88	52	86	3.5%	0.62 [0.45, 0.85]	2006
Lan 2011	62	98	78	97	5.7%	0.79 [0.66, 0.94]	2010
Mazzoleni 2011	107	201	131	203	5.9%	0.82 [0.70, 0.97]	2011
Xu 2013	105	262	66	134	4.8%	0.81 [0.65, 1.02]	2013
Liu 2014	100	200	174	200	6.2%	0.57 [0.50, 0.67]	2014
Yazdanbod 2015	99	186	90	173	5.4%	1.02 [0.84, 1.25]	2015
Total (95% CI)		**2824**		**2369**	**100.0%**	**0.84 [0.78, 0.91]**	
Total events	1568		1577				

Heterogeneity: Tau² = 0.02; Chi² = 67.54, df = 21 (P < 0.00001); I² = 69%

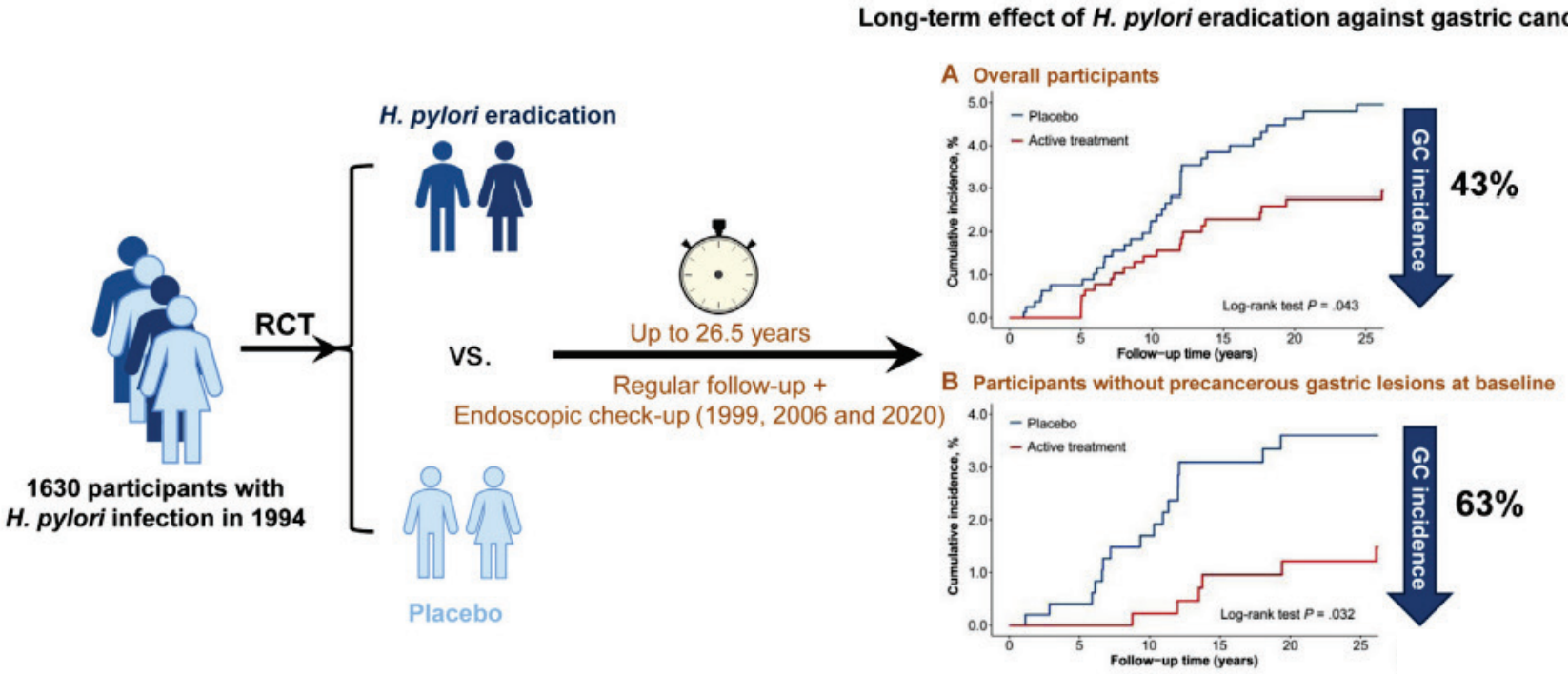
Test for overall effect: Z = 4.15 (P < 0.0001)



NNT: 9

Ford AC et al. Gut 2022; 71: 1967-1975

Effect of Helicobacter pylori eradication on gastric cancer prevention



Yan L et al. Gastroenterology 2022; 163: 154-162

Effect of Helicobacter pylori eradication on gastric cancer prevention

Trial group	Follow-up *H pylori* status[a]	No. of participants	Gastric cancers, n	Unadjusted		Adjusted[b]	
				HR (95% CI)	*P* value	HR (95% CI)	*P* value
Placebo	Positive	527	32	Reference	—	Reference	—
Placebo	Negative	47	0	—	—	—	—
H pylori eradication	Positive	133	4	0.40 (0.09–1.71)	.216	0.46 (0.11–1.94)	.289
H pylori eradication	Negative	625	16	0.45 (0.25–0.80)	.007	0.46 (0.26–0.83)	.009

[a]Participants received biannual ^{13}C urea breath test for *H pylori* status after *H pylori* or placebo treatment. The final *H pylori* status was determined by the result of ^{13}C urea breath test for *H pylori* status at 7.5 years of follow-up or last available *H pylori* status for subjects lost to follow-up or subjects with cancer until January 2002. Final *H pylori* status was available for 1332 participants (81.72%) and was modeled as time-dependent covariate.
[b]Adjustment for age, sex, daily smoking, green tea consumption, and baseline histopathology findings.

Yan L et al. Gastroenterology 2022; 163: 154-162

Effect of Helicobacter pylori eradication on gastric cancer prevention

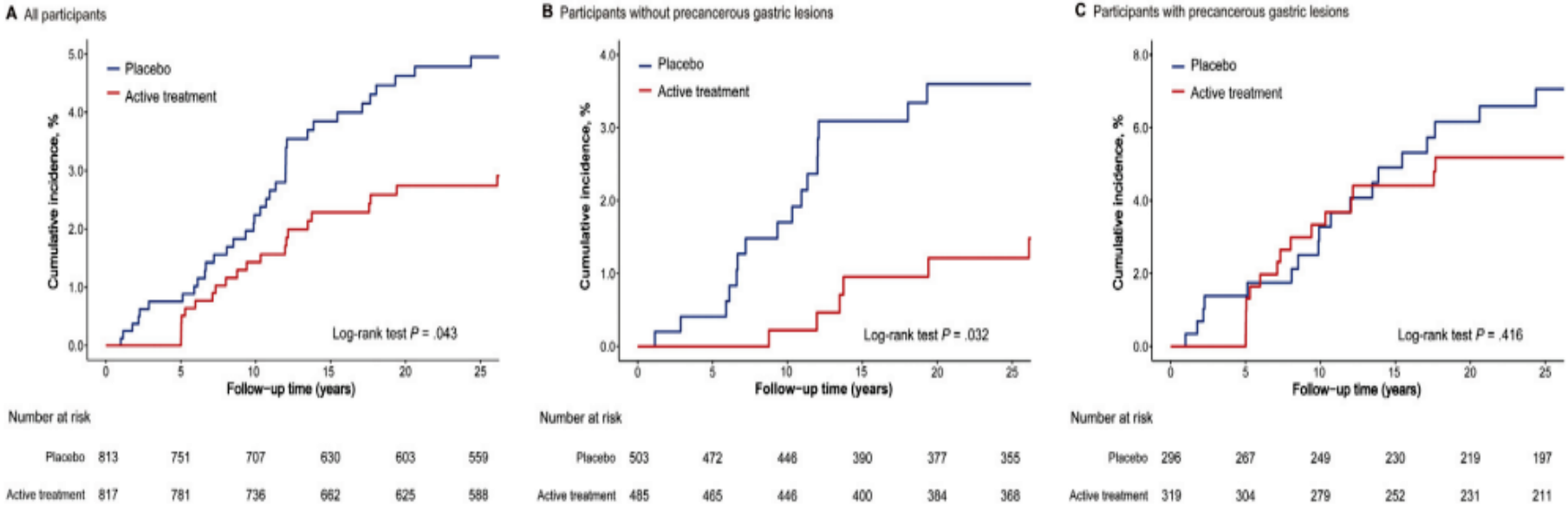


Figure 2. Nelson-Aalen cumulative incidence curves for gastric cancer by *H pylori* treatment arm. (*A*) For overall participants. (*B*) For participants without precancerous gastric lesions (normal mucosa or superficial gastritis) at baseline. (*C*) For participants with precancerous gastric lesions (chronic atrophic gastritis, intestinal metaplasia, and dysplasia) at baseline.

Yan L et al. Gastroenterology 2022; 163: 154-162

Effect of Helicobacter pylori eradication on gastric cancer prevention

Causes of death	No. of deaths	Active, n (n = 817)	Placebo, n (n = 813)	Unadjusted		Adjusted[a]	
				HR (95% CI)	*P* value	HR (95% CI)	*P* value
All-cause deaths	253	127	126	0.98 (0.76–1.25)	.842	1.02 (0.80–1.30)	.885
Cause-specific deaths							
All cancer	116	58	58	0.97 (0.67–1.39)	.859	1.01 (0.70–1.46)	.958
Gastric cancer	32	14	18	0.75 (0.37–1.51)	.423	0.76 (0.38–1.53)	.443
Esophageal cancer	7	3	4	0.73 (0.16–3.28)	.685	0.76 (0.17–3.42)	.722
Liver cancer	26	15	11	1.32 (0.61–2.88)	.484	1.37 (0.63–3.00)	.429
Lung cancer	24	12	12	0.97 (0.44–2.15)	.935	1.06 (0.48–2.38)	.880
Other cancers	27	14	13	1.04 (0.49–2.21)	.919	1.06 (0.50–2.26)	.878
Cardiovascular diseases	51	25	26	0.93 (0.54–1.61)	.797	1.00 (0.58–1.74)	.998
Other	86	44	42	1.01 (0.66–1.55)	.949	1.05 (0.69–1.61)	.806

[a]Adjusted for age, sex, daily smoking, green tea consumption, and baseline histopathology findings.

Yan L et al. Gastroenterology 2022; 163: 154-162

Effect of Helicobacter pylori eradication on gastric cancer prevention - Should every H.p.-positive patient receive eradication therpy??

- Study was carried out in southern China – a region with a high incidence of gastric cancer
- Follow-up was 26.5 (!!) years
- Significant effect on gastric cancer incidence only in subgroup of patients without premalignant gastric lesions and in those without dyspepsia symptoms at baseline
- Despite of long follow-up there was no significant effect of eradication therapy on gastric cancer mortality
- → Indication for eradication therapy should consider patient age and other baseline characteristics

Yan L et al. Gastroenterology 2022; 163: 154-162

Maastricht VI/Florence consensus: treatment recommendations

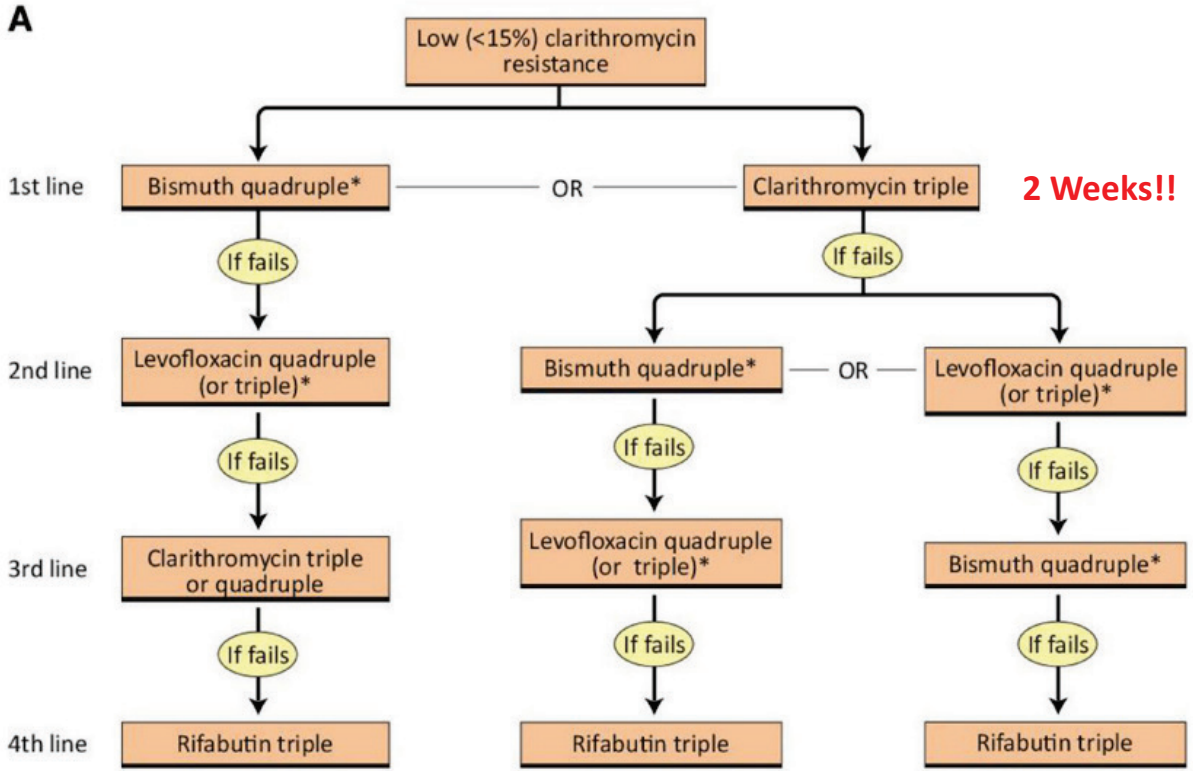


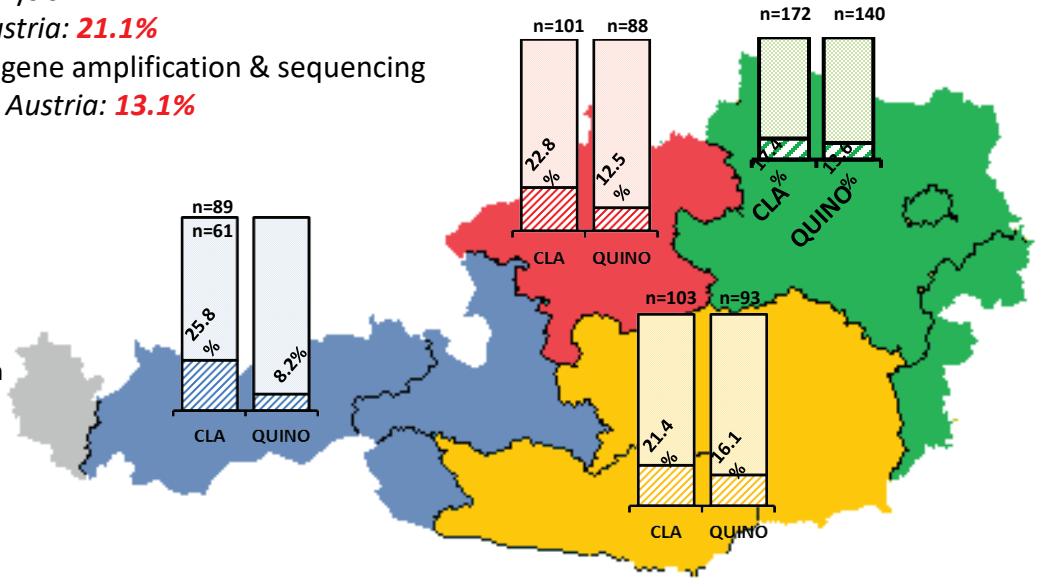
Figure 1 Algorithm for empirical *Helicobacter pylori* eradication if individual antibiotic susceptibility testing is not available. Bismuth quadruple: proton pump inhibitor (PPI), bismuth, tetracycline and metronidazole. Clarithromycin triple: PPI, clarithromycin and amoxicillin; only use if proven effective locally or if clarithromycin sensitivity is known. Non-bismuth quadruple (concomitant): PPI, clarithromycin, amoxicillin and metronidazole. Levofloxacin quadruple: PPI, levofloxacin, amoxicillin and bismuth. Levofloxacin triple: the same but without bismuth. In cases of high fluoroquinolone resistance (>15%), the combination of bismuth with other antibiotics, high-dose PPI-amoxicillin dual or rifabutin, may be an option. *High-dose PPI or P-CAB (vonoprazan where available) plus amoxicillin may be another option. P-CAB, potassium-competitive acid blocker; PPI, proton pump inhibitor.

Malfertheiner P et al. Gut 2022; 71: 1724-1762

Prospective, multi-center clinical trial on geographic antimicrobial resistance patterns of Helicobacter pylori

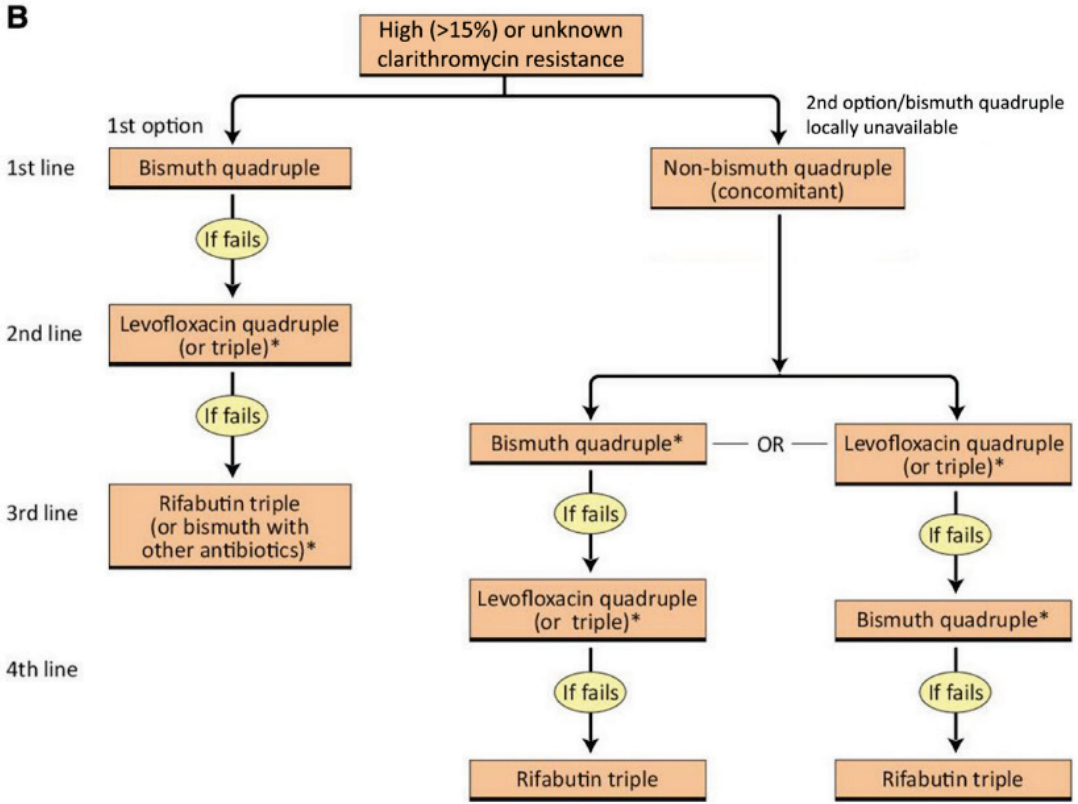
- 2000 patients included
  - Histopathological investigation: 515 HP+ (26%)
  - 23S rRNA *H. pylori*-specific realtime PCR: 466 HP+ (90% confirmation rate of histology results)
- Antimicrobial resistance testing
  - **Clarithromycin**: 23S rRNA gene amplification & melting point analysis
    Cla res. rate in Austria: ***21.1%***
  - **Quinolone**: *gyrA* gene amplification & sequencing
    Quino res. rate in Austria: ***13.1%***

- 2 biopsy samples from each patient (antrum & corpus)
  - HP infection in both sites of the stomach **94.5%**
  - HP infection only in antrum **2%**
  - HP infection only in corpus **3.5%**



Bilgilier C et al. Clin Microbiol Infect 2018; 24: 267-272

Maastricht VI/Florence consensus: treatment recommendations



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H.p.-Eradikation 2022 bei hoher Clarithromycinresistenz

Pylera® Kapseln

4 x 3 Kapseln täglich

(1 Kapsel = 140mg Bismuth subcitrat,

125mg Metronidazol,

125mg Tetracyclin)

plus

PPI 2 x 1

Therapiedauer: 10 Tage

Amoxicillin 2 x 1000 mg

plus

Clarithromycin 2 x 500 mg

plus

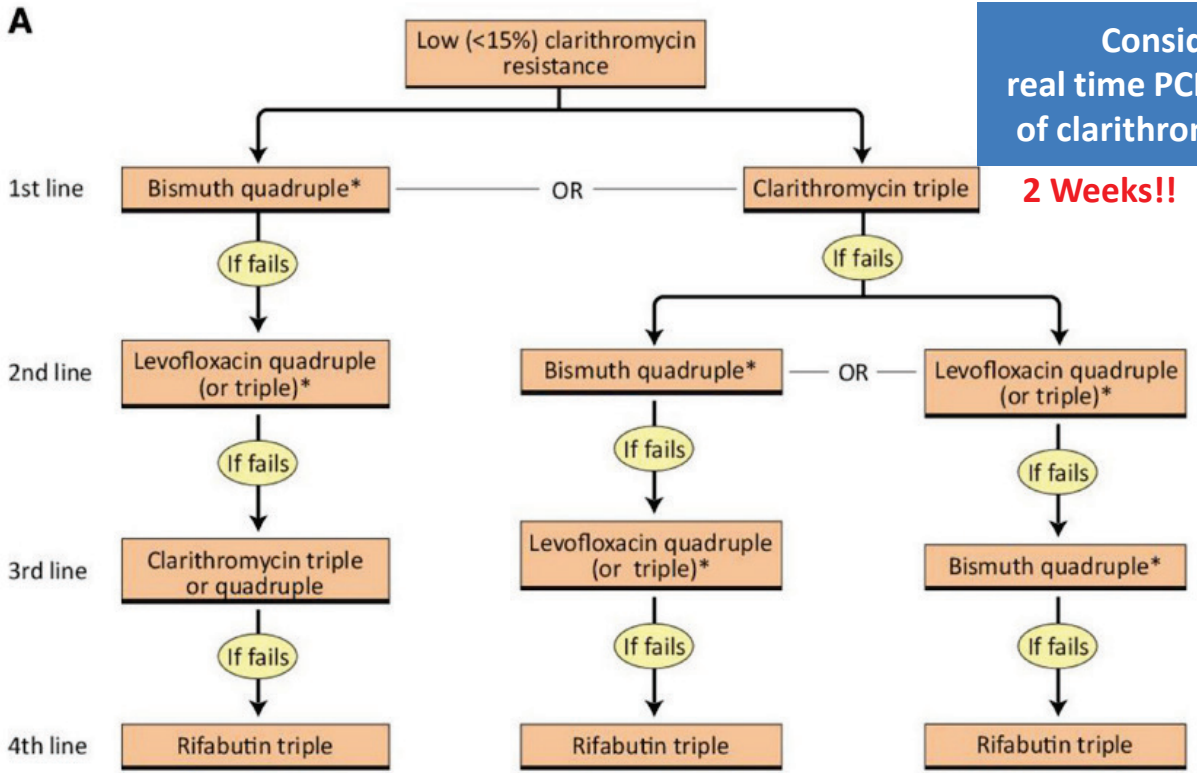
Metronidazol 2 x 500 mg

plus

PPI 2 x 1

Therapiedauer: 14 Tage

Maastricht VI/Florence consensus: treatment recommendations



Consider routine real time PCR for assessment of clarithromycin resistance

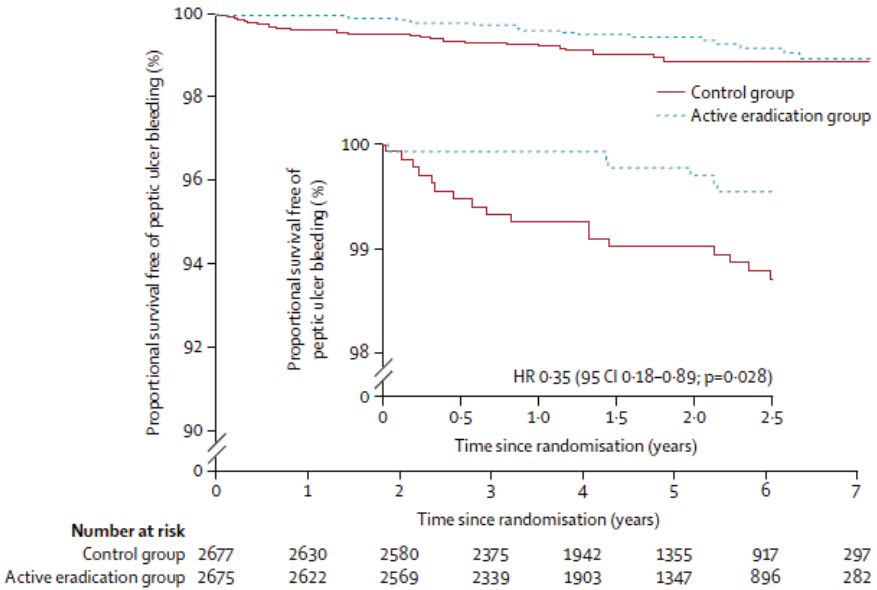
2 Weeks!!

Figure 1 Algorithm for empirical *Helicobacter pylori* eradication if individual antibiotic susceptibility testing is not available. Bismuth quadruple: proton pump inhibitor (PPI), bismuth, tetracycline and metronidazole. Clarithromycin triple: PPI, clarithromycin and amoxicillin; only use if proven effective locally or if clarithromycin sensitivity is known. Non-bismuth quadruple (concomitant): PPI, clarithromycin, amoxicillin and metronidazole. Levofloxacin quadruple: PPI, levofloxacin, amoxicillin and bismuth. Levofloxacin triple: the same but without bismuth. In cases of high fluoroquinolone resistance (>15%), the combination of bismuth with other antibiotics, high-dose PPI-amoxicillin dual or rifabutin, may be an option. *High-dose PPI or P-CAB (vonoprazan where available) plus amoxicillin may be another option. P-CAB, potassium-competitive acid blocker; PPI, proton pump inhibitor.

Malfertheiner P et al. Gut 2022; 71: 1724-1762

H.p.-eradication for primary prevention of peptic ulcer bleeding in older patients on low-dose aspirin

- **Design:** double-blind, randomised, placebo-controlled trial
- **Patients:** 5.352 patients, older than 60 years, with a prescription of low-dose aspirin, all H.p.-positive
- **Treatment:** H.p.-eradication (C+M+PPI for 7d) versus placebo
- **Results:**

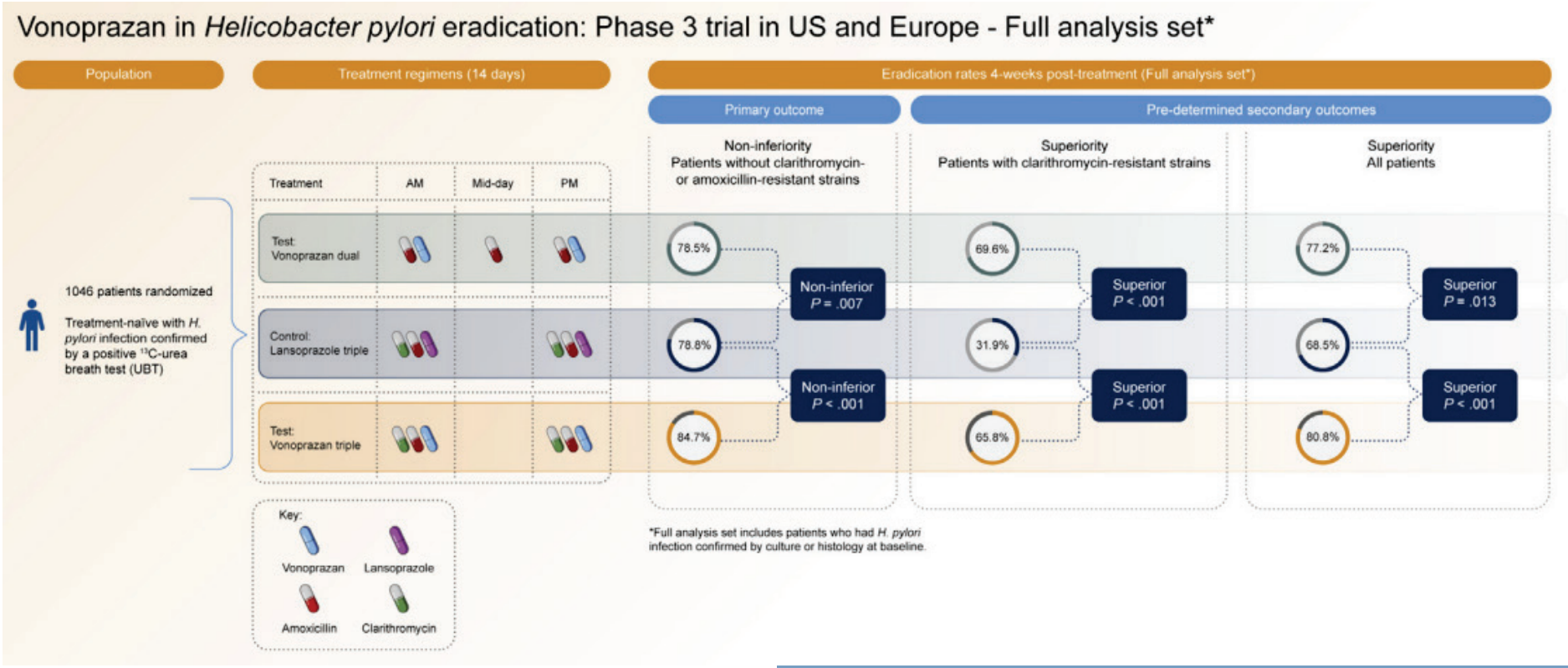


Hawkey C et al. Lancet 2022; 400: 1597-1606

Vonoprazan zur H.p.-Eradikation

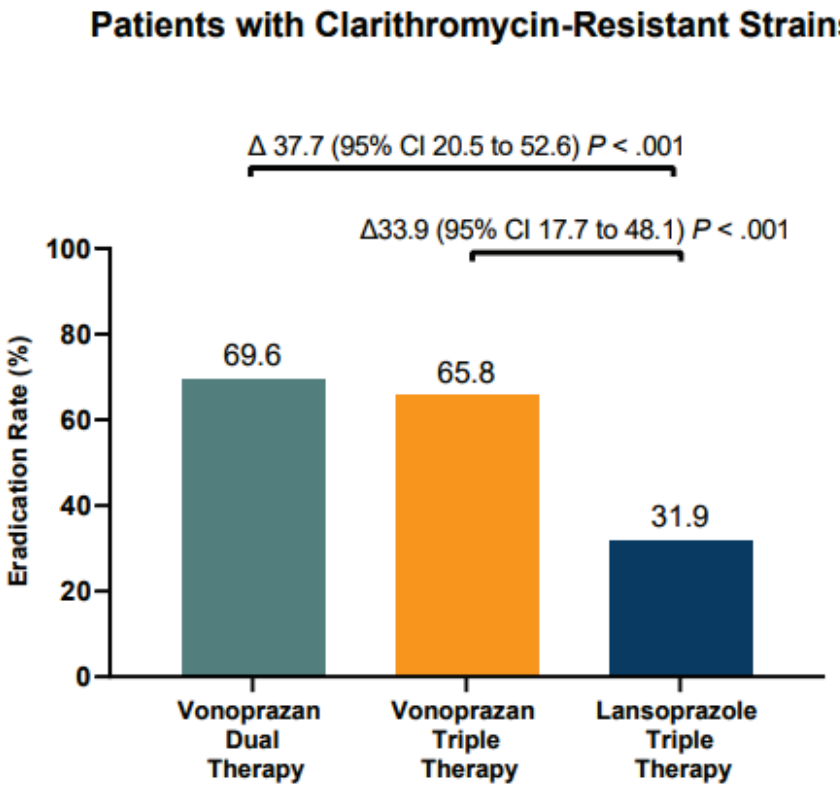
- Vonoprazan ist ein „first in class“ kalium-kompetitiver Protonenpumpenhemmer
- In Japan seit Februar 2015 zugelassen
- Vorteil: benötigt keine säureinduzierte Aktivierung; volle Säuresuppression bereits nach erster Dosis (PPI entfalten volle Wirkung erst nach 3-5 Tagen)
- Die Sensitivität von H.p. gegen Antibiotika hängt vom pH-Wert ab; daher könnte profunde Säuresuppression Eradikationsraten steigern – dies wäre insbesondere bei clarithromycin-resistenten Stämmen wichtig

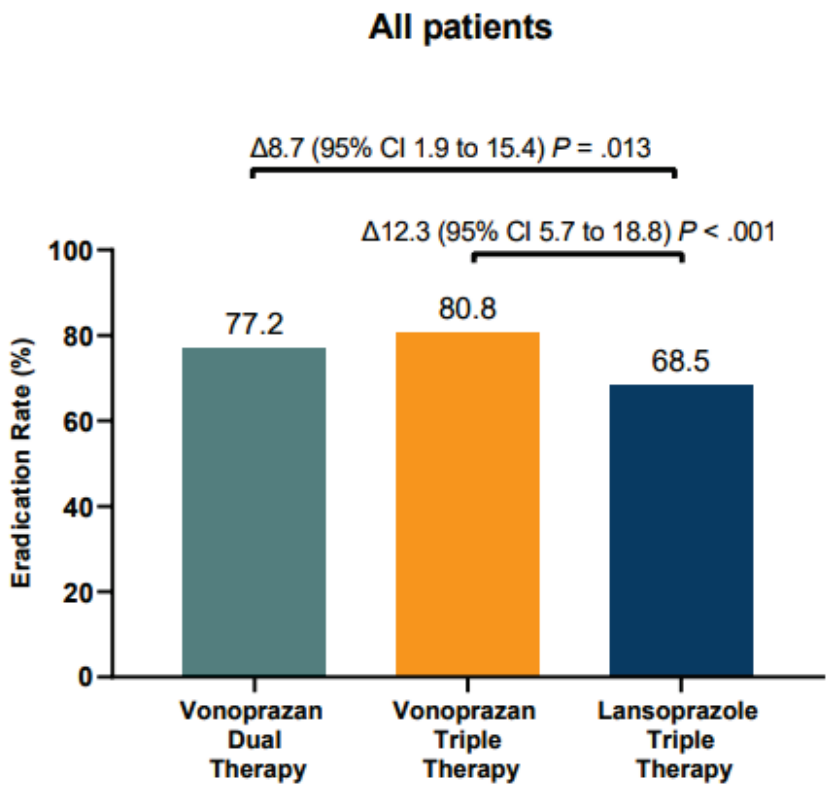
Vonoprazan triple and dual therapy for H.p.-eradication – a randomized clinical trial conducted in the United States and Europe



Chey WD et al. Gastroenterology 2022; 163: 608-619

Vonoprazan triple and dual therapy for H.p.-eradication – a randomized clinical trial conducted in the United States and Europe





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Grading of chronic gastritis according to OLGIM

(Operative Link on Gastric Intestinal Metaplasia Assessment)

		Corpus			
	IM score	**Not fat: no IM (score 0)**	**Mild IM (score 1)**	**Moderate IM (score 2)**	**Severe IM (score 3)**
Antrum (including incisura angularis)	No IM (score 0)	Stage 0	Stage I	Stage II	Stage II
	Mild IM (score 1)	Stage I	Stage I	Stage II	Stage III
	Moderate IM (score 2)	Stage II	Stage II	Stage III	Stage IV
	Severe IM (score 3)	Stage III	Stage III	Stage IV	Stage IV

IM, Intestinal metaplasia; *OLGIM*, operative link on gastric intestinal metaplasia assessment.

Capelle LG et al. Gastrointest Endosc 2010; 71: 1150-1158

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	Mild IM (score 1)	S		St	
	Moderate IM (score 2)	Stage II	Stage II	St	
	Severe IM (score 3)	Stage III	Stage III	Stage IV	

OLGIM I/II:
Low risk of gastric cancer

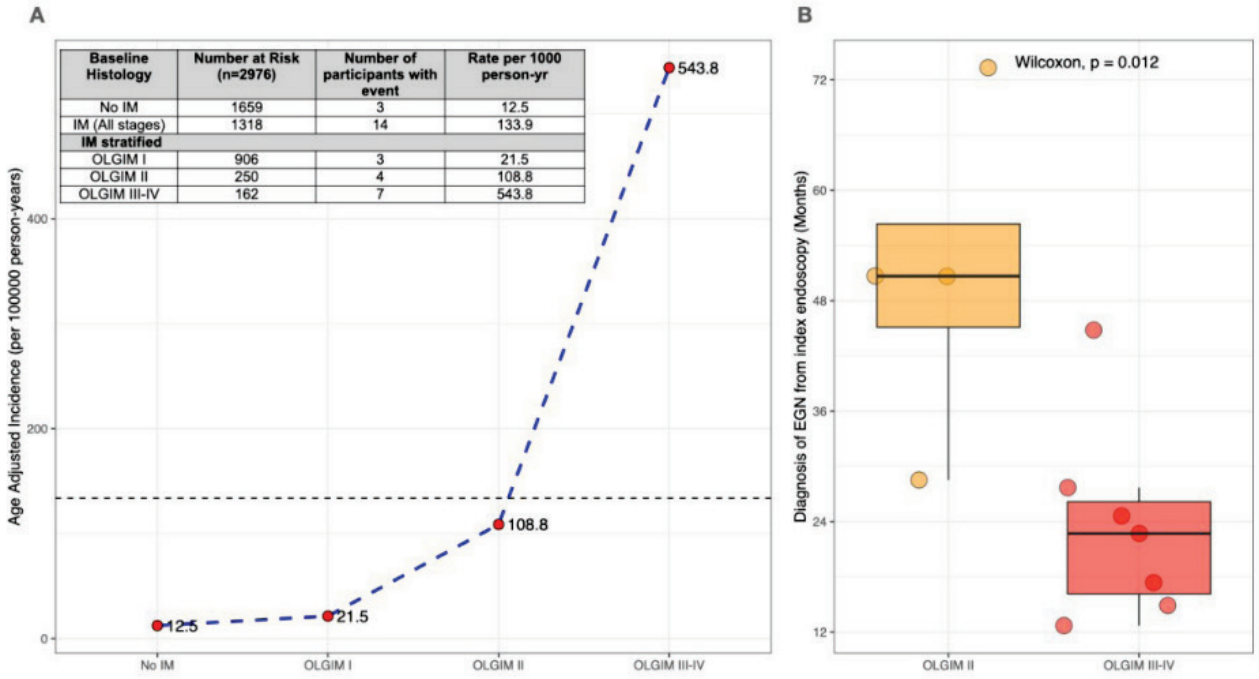
OLGIM III/IV:
High risk of gastric cancer

IM, Intestinal metaplasia; *OLGIM*, operative link on gastric intestinal metaplasia assessment.

Capelle LG et al. Gastrointest Endosc 2010; 71: 1150-1158

Severity of gastric intestinal metaplasia predicts gastric cancer risk

- **Design:** prospective, longitudinal and multicentre study in Singapore
- **Patients:** 2.980 patients undergoing screening gastroscopy; follow-up gastroscopies after 3 and 5 years
- **Primary endpoint:** incidence of early gastric neoplasia



Lee JWJ et al. Gut 2022; 71: 854-863

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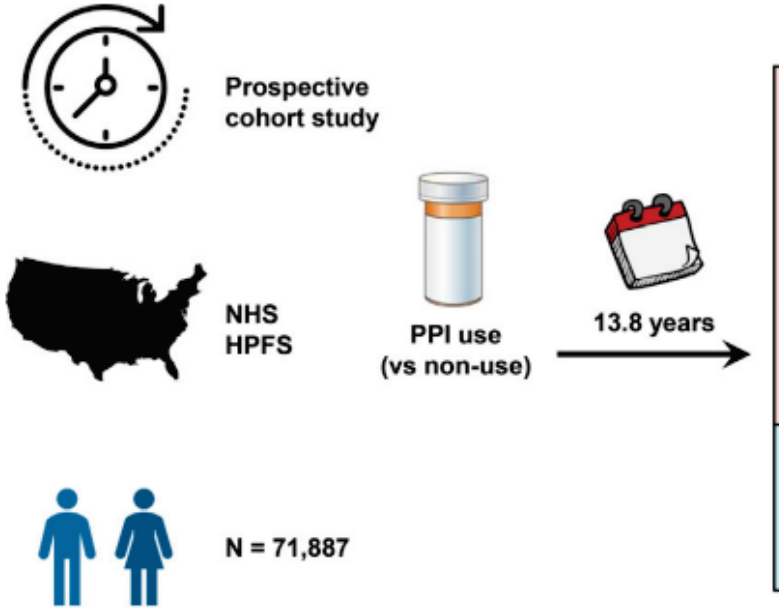
Einfluss von PPI auf Mortalität



	Without lag-time	With lag-time
Mortality risk	• All causes • Cancer • Cardiovascular diseases • Respiratory diseases • Digestive disease	• All causes • Cancer • Cardiovascular diseases • Respiratory diseases • Digestive diseases • Neurological diseases • Infectious diseases
No increase in mortality risk	• Neurological diseases • Infectious diseases	

NHS: Nurses´Health Study (2004-2018)
HPFS: Health Professionals Follow-up Study (2004-2018)

Problem bei Mortalität „without lag-time“: **protopathic bias**

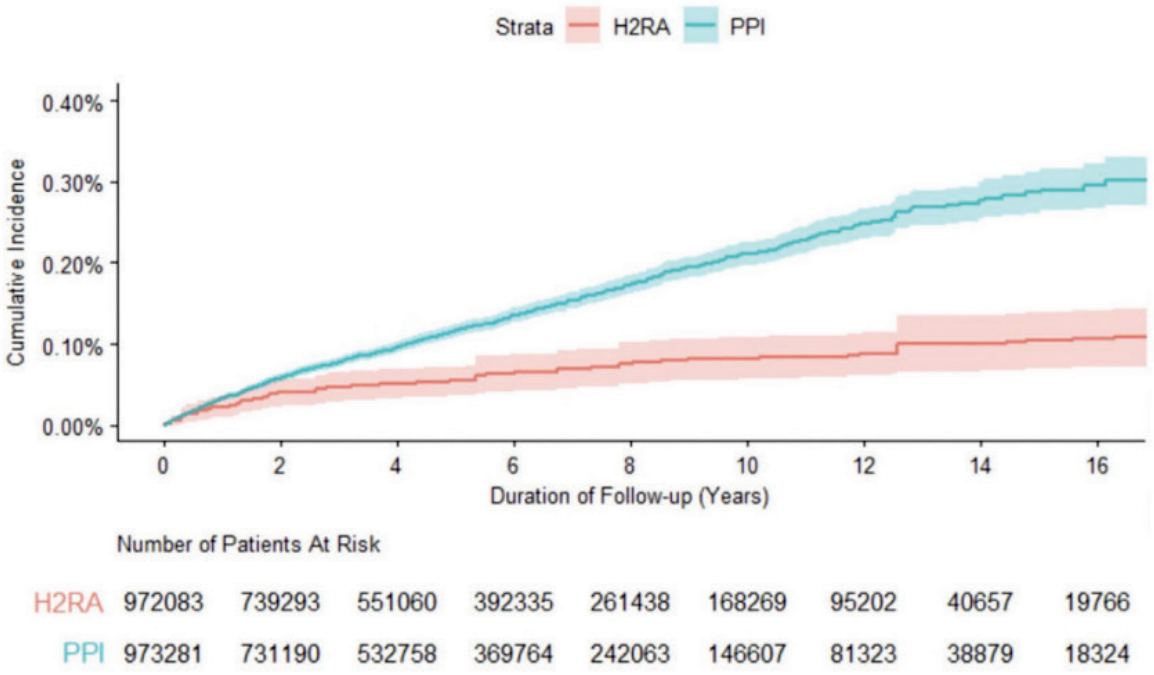
Lo CH et al. Gastroenterology 2022; 163: 852-861

PPI versus H_2-RA and the risk of gastric cancer

- **Design:** population-based cohort study using the UK Clinical Practice Research Datalink
- **Patients:** 973.281 new users of PPI versus 193.306 new users of H_2-RA (identified between 1 January 1990 and 30 April 2018)
- **Follow-up:** median follow-up of 5.0 years
- **Primary endpoint:** risk of gastric cancer
- **Results:**
- After 5 years the use of PPI was associated with a 45% increased risk of gastric cancer compared with the use of H_2-RA (HR 1.45; 95% CI 1.06 to 1.98)
- The number needed to harm was 2.121 after 5 years and 1.191 after 10 years

Abrahami D et al. Gut 2022; 71: 16-24

PPI versus H_2-RA and the risk of gastric cancer



Possible mechanisms:

- PPI cause hypergastrinaemia (gastrin is considered a potent growth factor)
- Long-term PPI use may lead to changes in the gut microbiom and thus contribute to an increased risk of gastric cancer
- Long-term acid suppression may be associated with atrophic gastritis

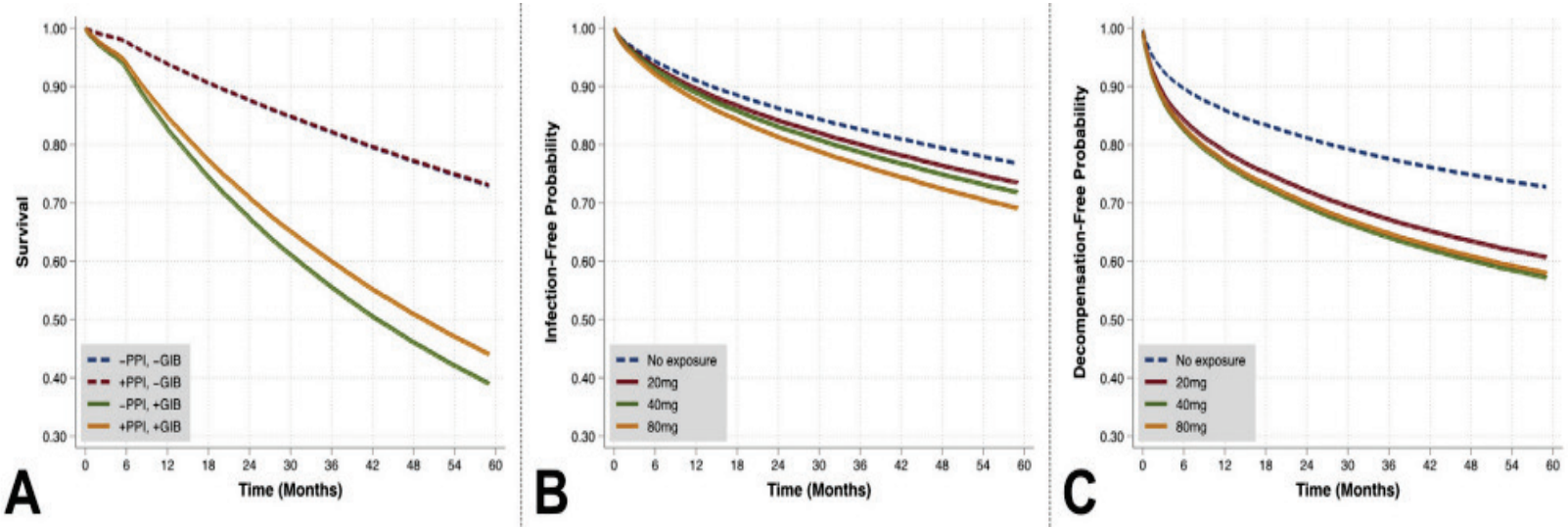
Abrahami D et al. Gut 2022; 71: 16-24

Einfluss von PPI auf „Liver-related outcomes“ bei Leberzirrhose

- **Design:** retrospektive Studie von Patienten mit Leberzirrhose in der „Veterans Health Administration“
- **Patienten:** n = 76.251; davon 23.628 mit PPI
- **Primärer Endpunkt:** Einfluss der PPI auf „Liver-related outcomes“ (nach Korrektur auf klinisch relevante andere Einflussfaktoren)
- **Ergebnisse:**
- PPI erhöht leberbezogene Mortalität (HR 1,23; 95% CI: 1,19-1,28)
- PPI senkt nicht-leberbezogene Mortalität (HR 0,88; 95% CI: 0,85-0,91)
- PPI reduziert Mortalität in der Untergruppe von Patienten, die wegen GI-Blutung aufgenommen wurden
- PPI signifikant assoziiert mit schweren Infektionen und Dekompensation

Mahmud N et al. Gastroenterology 2022; 163: 257-269

Einfluss von PPI auf „Liver-related outcomes“ bei Leberzirrhose



Mahmud N et al. Gastroenterology 2022; 163: 257-269

- Helicobacter pylori
- Intestinale Metaplasie und Magenkarzinomrisiko
- Sicherheit von Protonenpumpenhemmern
- Therapie der Gastroparese
- Neue Therapiekonzepte bei Zöliakie

Endoscopic pyloromyotomy for severe and refractory gastroparesis

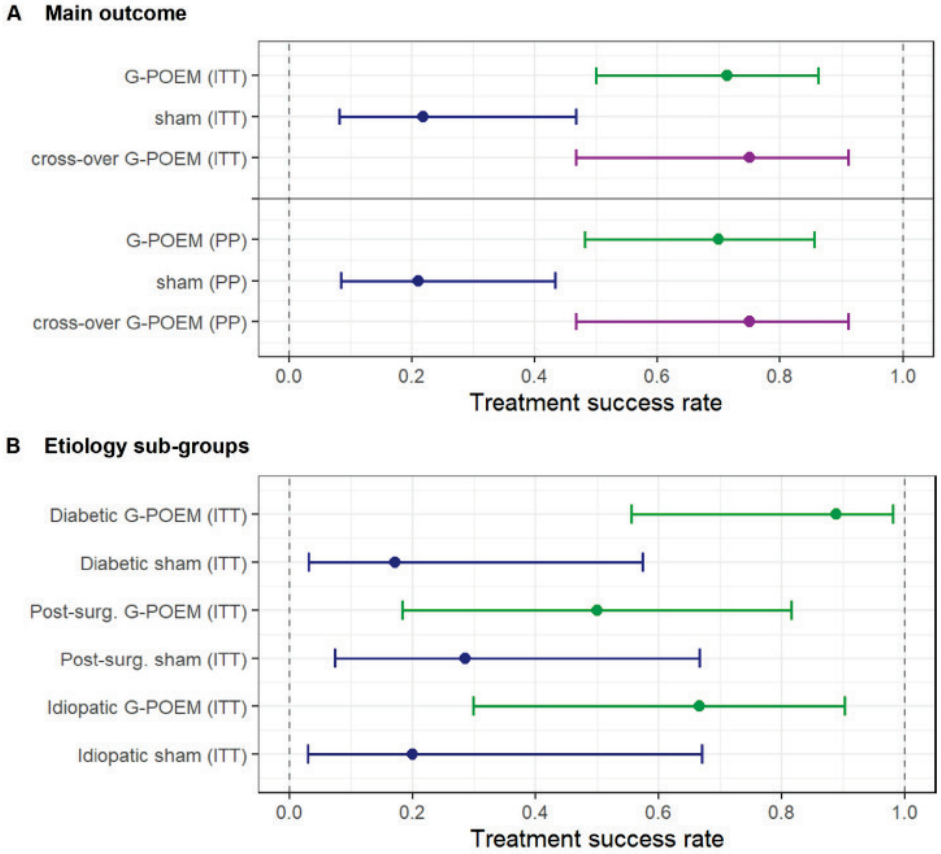
- **Design:** prospective randomised sham-controlled trial
- **Patients:** n = 41; G-POEM (n = 21) versus sham procedure (n = 20)
- **Primary endpoint:** proportion of patients with treatment success (defined as a decrease in the Gastroparesis Cardinal Symptom Index (GCSI) by at least 50%) at 6 months; patients randomised to the sham group with persistent symptoms were offered cross-over G-POEM
- Enrolment was stopped early after interim analysis of the first 41 patients, due to statistically significant results

Table 1 Demographic and clinical characteristics of the patients at baseline

Characteristic	G-POEM arm	Control (sham) arm
Number of patients	21	20
Sex—number (%)		
Female	11 (52.4)	11 (55.0)
Male	10 (47.6)	9 (45.0)
Age—median (Q1–Q3) (years)	43 (30 – 51)	51 (45 – 56)
BMI – median (Q1–Q3)(kg/m^2)	22 (19 – 28)	26 (21 – 28)
Aetiology—number (%)		
Diabetic; (diabetes type I/diabetes type II, number)	9 (42.9); (8/1)	8 (40.0); (6/2)
Post-surgical	6 (28.6)	7 (35.0)
Idiopathic	6 (28.6)	5 (25.0)
Previous therapy—number (%)		
Metoclopramide	12 (57.1)	10 (50.0)
Itopride	11 (52.4)	10 (50.0)
Domperidone	9 (42.9)	7 (35.0)
Other prokinetics	3 (14.3)	2 (10.0)
Enteral feeding via nasojejunal/nasogastric tube	3 (14.3)	1 (5.0)
Recurrent hospitalisation for gastroparesis-related symptom	8 (38.1)	7 (35.0)
Baseline GCSI score—median (Q1–Q3)*	3.5 (3.2–3.7)	3.2 (2.6–3.4)
Baseline PAGI-QOL score—median (Q1–Q3)†	2.1 (1.7–2.7)	2.5 (1.4–2.8)
Baseline 4 hours GES retention—median (Q1–Q3)(%)‡	22 (17–32)	26 (16–42)
Pre-procedure DI 40 mL—median (Q1–Q3)(mm^2/mm Hg)§	5.8 (4.8–9.8)	5.6 (3.5–6.2)

Martinek J et al. Gut 2022; 71: 2170-2178

Endoscopic pyloromyotomy for severe and refractory gastroparesis



- Clinical success was defined as reduction of the total Gastroparesis Cardinal Symptom Index (GCSI) by at least 50% from the baseline
- For the cross-over endoscopic pyloromyotomy (G-POEM), GCSI at 6 months after the sham procedure was considered as baseline
- The trial was not sufficiently powered to assess the effectiveness of G-POEM in the aetiology subgroups

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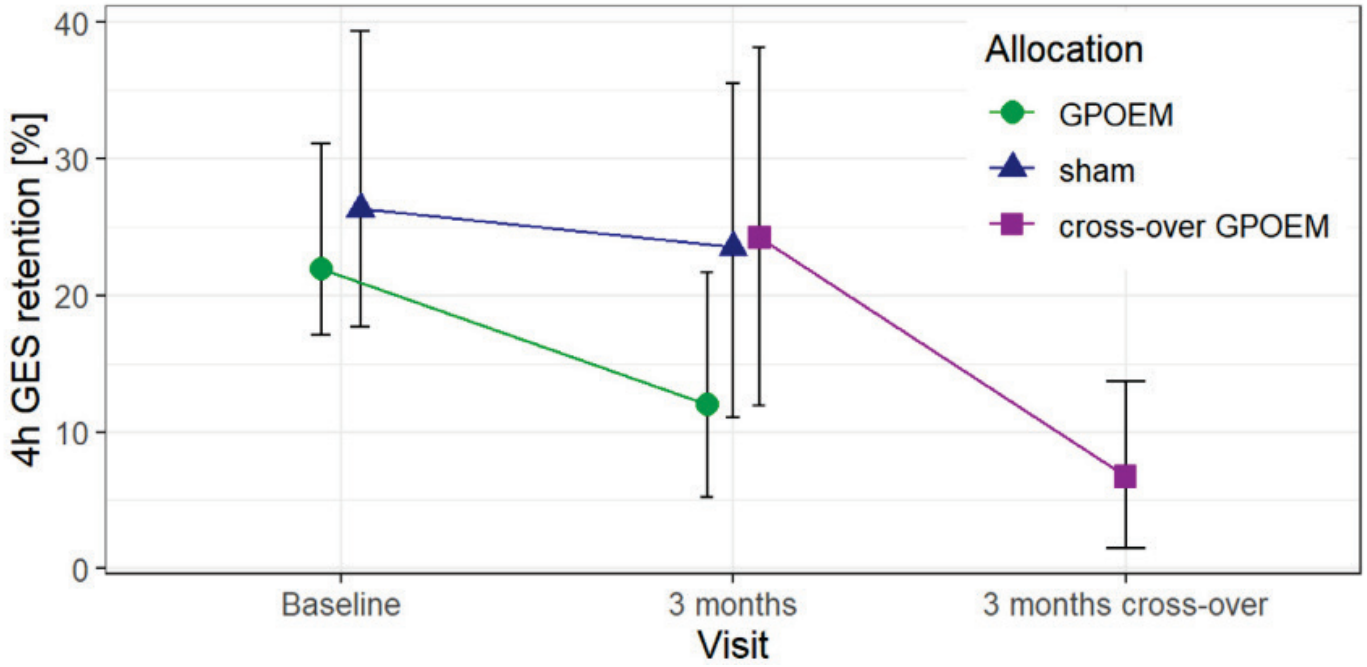
Endoscopic pyloromyotomy for severe and refractory gastroparesis



- Gastric retention at 4 hours significantly decreased after G-POEM and after the cross-over procedure but did not change after the sham procedure
- There was no correlation between GCSI and gastric retention at 3 months

GES: gastric emptying study; G-POEM: endoscopic pyloromyotomy

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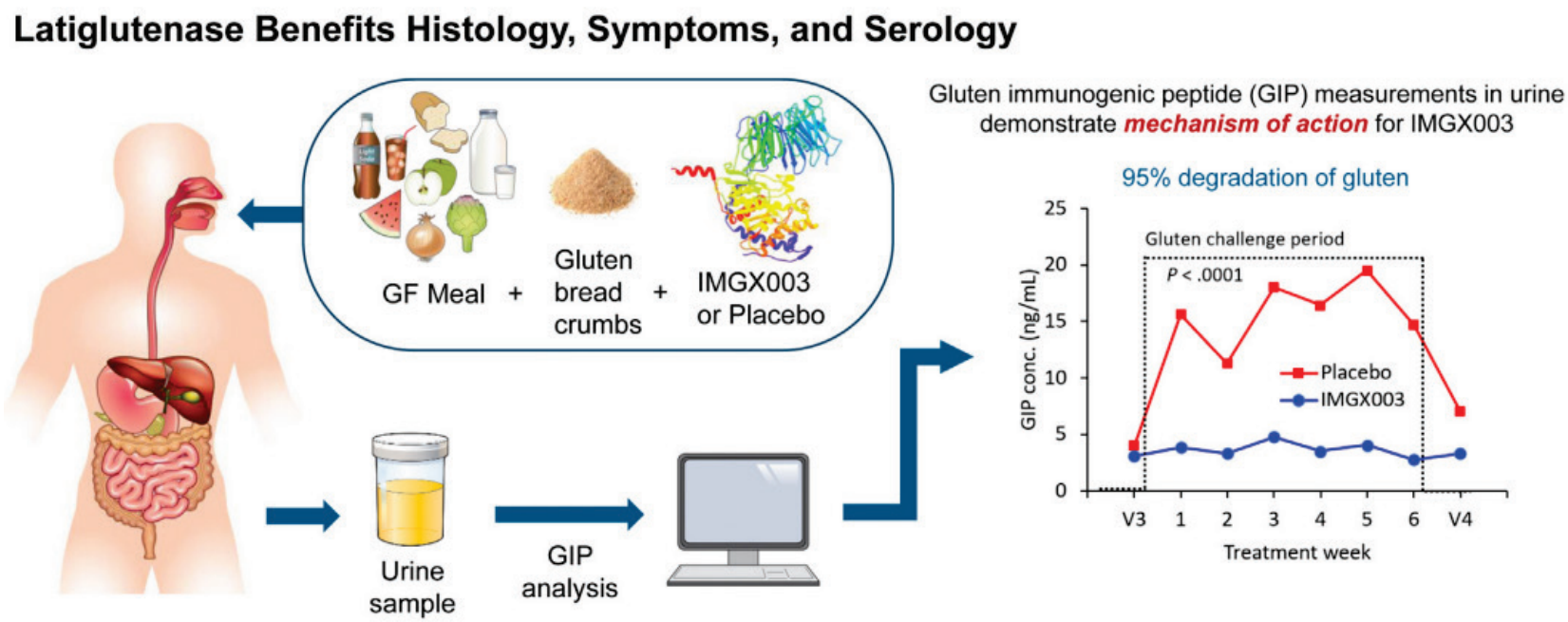
Neue Therapieoptionen bei Zöliakie - Hintergrund

- Etwa 50% aller Patienten mit Zöliakie zeigen trotz Diät weiterhin pathologische Veränderungen in Histologie mit dem Risiko von Langzeitkomplikationen wie Lymphom oder Osteoporose.
- Die Einhaltung einer strikten glutenfreien Diät ist oft schwierig.
- Präparate, die bewirken, dass Diätfehler weder klinische Symptome noch pathologische Veränderungen induzieren, wären ein großer Fortschritt.
- Gluten-Peptide sind sehr resistent gegen den Abbau durch Proteasen im Dünndarm.
- Latiglutenase ist ein Präparat, das zwei Enzyme enthält, die nach oraler Zufuhr die Immunogenität von Gluten mitigieren.

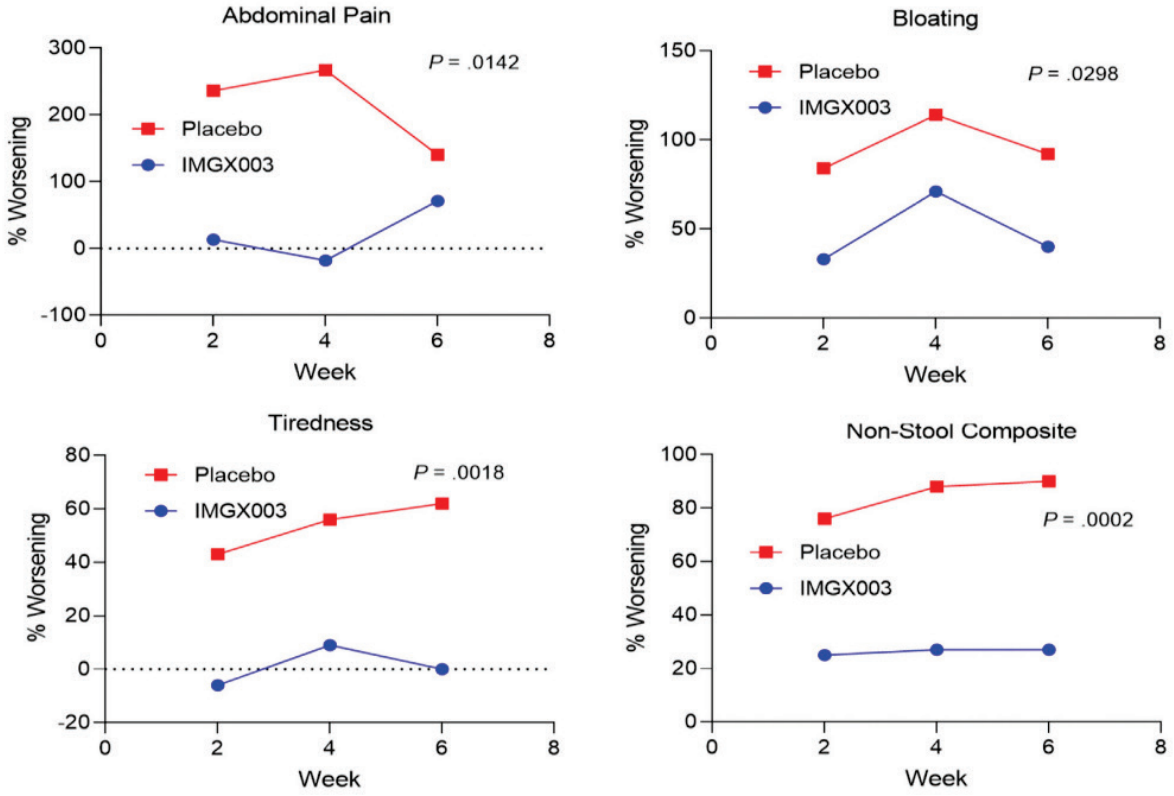
Latiglutenase zur Therapie der Zöliakie



n = 50 patients

Murray JA et al. Gastroenterology 2022; 163: 1510-1521

Latiglutenase zur Therapie der Zöliakie



Histologische Veränderungen (intraepitheliale Lymphozyten und Zottenatrophie) unter Latiglutenase deutlich geringer als unter Placebo

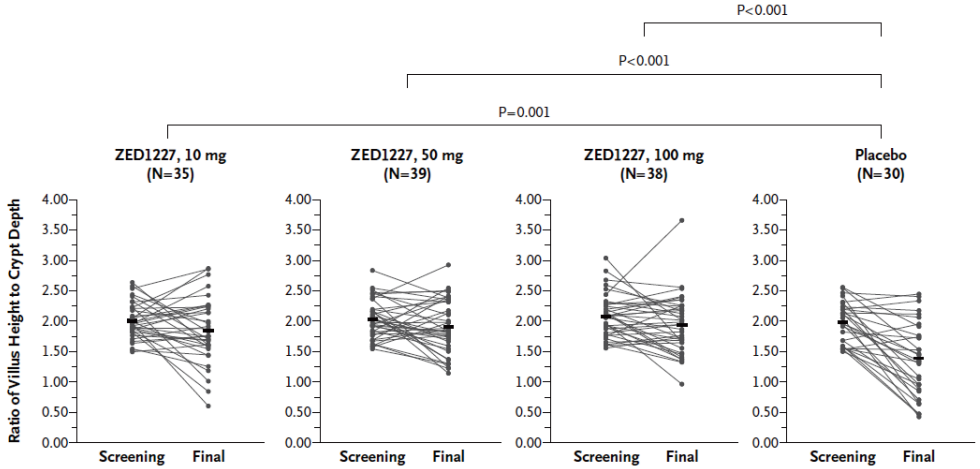
Murray JA et al. Gastroenterology 2022; 163: 1510-1521

Inhibition of transglutaminase 2 in celiac disease

- **Background:** In celiac disease (CD), small intestinal transglutaminase 2 causes deamidation of glutamin residues in gluten peptides, which enhances stimulation of T cells and leads to mucosal injury. Inhibition of transglutaminase 2 is a potent treatment for CD
- **Design:** double-blind, placebo-controlled, dose-ranging trial; patients were randomly assigned, in a 1:1:1:1 ratio, to one of four parallel groups to receive 10mg, 50mg, 100mg of ZED1227, or placebo, concurrent with the gluten challenge during six weeks
- **Primary endpoint:** attenuation of gluten-induced mucosal damage, as measured by the ratio of villous height to crypt depth.

Schuppan D et al. N Engl J Med 2021; 385: 35-45

Inhibition of transglutaminase 2 in celiac disease



Variable	ZED1227, 10 mg (N=35)	ZED1227, 50 mg (N=39)	ZED1227, 100 mg (N=38)	Placebo (N=30)
Ratio of villus height to crypt depth				
At baseline	2.01±0.30	2.04±0.32	2.09±0.35	1.98±0.33
After gluten challenge at wk 6	1.85±0.53	1.91±0.44	1.94±0.48	1.39±0.61
Change in ratio from baseline (95% CI)†	−0.17 (−0.33 to −0.01)	−0.12 (−0.27 to 0.03)	−0.13 (−0.28 to 0.03)	−0.61 (−0.78 to −0.44)
Estimated difference in ratio vs. placebo (95% CI)‡	0.44 (0.15 to 0.73)	0.49 (0.20 to 0.77)	0.48 (0.20 to 0.77)	—
P value	0.001	<0.001	<0.001	—

Schuppan D et al. N Engl J Med 2021; 385: 35-45

Take Home Messages I

- Durch H.p.-Eradikation kann auch in der Allgemeinbevölkerung das Magenkarzinomrisiko gesenkt werden, allerdings wird dieser Effekt erst nach sehr langem follow-up bemerkbar – die Indikation aus dieser Indikation sollte daher kritisch gestellt werden
- Bei H.p.-positiver funktioneller Dyspepsie ist die H.p.-Eradikation die Therapie der Wahl – die NNT ist allerdings 14
- Bei fehlender Resistenztestung ist in Österreich die first-line Therapie zur H.p.-Eradikation weiterhin Bismuth-Quadrupel oder A+C+M+PPI über 2 Wochen; routinemäßige Clarithromycinresistenztestung mittels Real time PCR sollte erwogen werden
- Bei Clarithromycin-sensiblen Stämmen sollte Tripeltherapie über 2 Wochen durchgeführt werden
- Vor low-dose Aspirin Testung auf H.p. und bei positivem Ergebnis Eradikationstherapie erwägen

Take Home Messages II

- Je ausgedehnter die intestinale Metaplasie desto höher das Magenkarzinomrisiko
- PPI sind sehr sichere Medikamente; durch eine Langzeittherapie wird jedoch wahrscheinlich das Magenkarzinomrisiko geringgradig erhöht
- Bei Leberzirrhose Indikation zur PPI-Therapie kritisch hinterfragen
- G-POEM ist eine vielversprechende Therapie bei Gastroparese
- Für Zöliakie sind vielversprechende neue Therapiekonzepte in Entwicklung