

I Linfomi dell'apparato gastroenterico La biologia dell'*Helicobacter Pylori*

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Urgenza
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Università degli Studi di Bologna

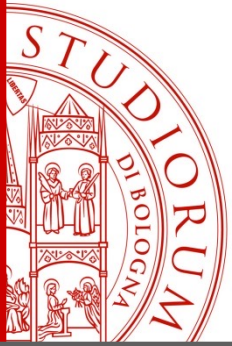
berardino.vaira@unibo.it

<http://www.unibo.it/docenti/berardino.vaira>

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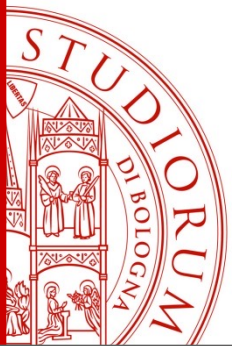
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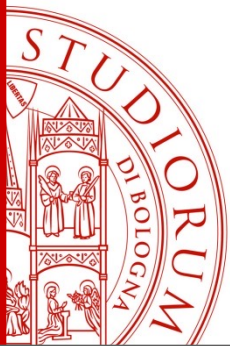


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Perché è importante l'Helicobacter?





Gastroenterology 2017;153:420–429

Global Prevalence of *Helicobacter pylori* Infection: Systematic Review and Meta-Analysis

James K. Y. Hooi,^{1,*} Wan Ying Lai,^{1,*} Wee Khoon Ng,^{1,2,*} Michael M. Y. Suen,^{1,*}
Fox E. Underwood,³ Divine Tanyingoh,³ Peter Malfertheiner,⁴ David Y. Graham,⁵
Vincent W. S. Wong,¹ Justin C. Y. Wu,¹ Francis K. L. Chan,¹ Joseph J. Y. Sung,¹
Gilaad G. Kaplan,^{3,§} and Siew C. Ng^{1,§}



4,4 MILIARDI DI PERSONE
NEL MONDO SONO
POSITIVE PER
L'INFEZIONE DA
HELICOBATER PYLORI!

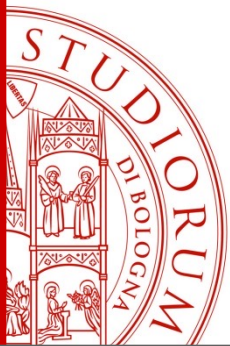
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IL PRESENTE MATERIALE È RISERVATO AL PERSONALE DELL'UNIVERSITÀ DI BOLOGNA E NON PUÒ ESSERE UTILIZZATO AI TERMINI DI LEGGE DA ALTRE PERSONE O PER FINI NON ISTITUZIONALI

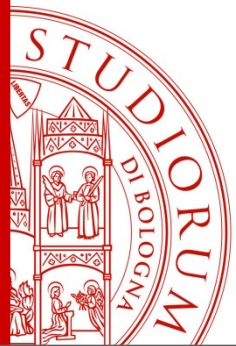


In Europa ci sono 743 milioni di abitanti
297.000 sono H pylori+



In Italia 24 milioni persone sono H pylori+





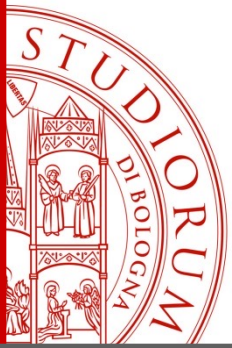
The cancer wars 3

Cancer survival: global surveillance will stimulate health policy and improve equity

Michel P Coleman

Lancet 2014; 383: 564-73





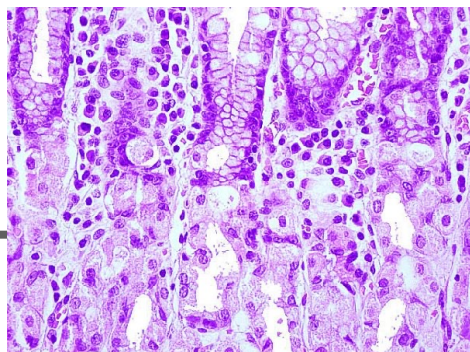
- 2010: about 8 million people died from cancer, 38% increase since 1990.
- by 2030 20 million people will be diagnosed with cancer every year with more than 13 million death.

Lancet 2014; 383: 564-73

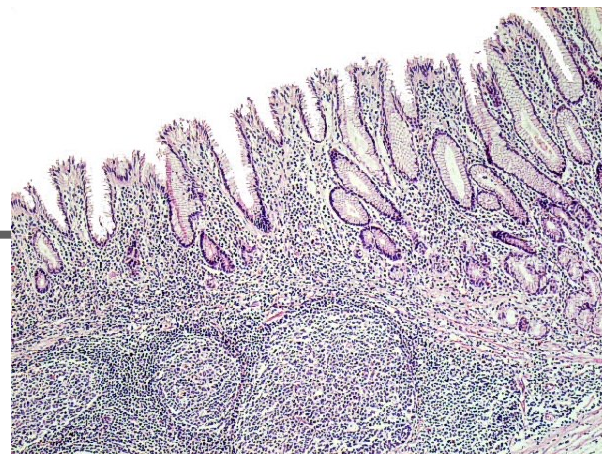




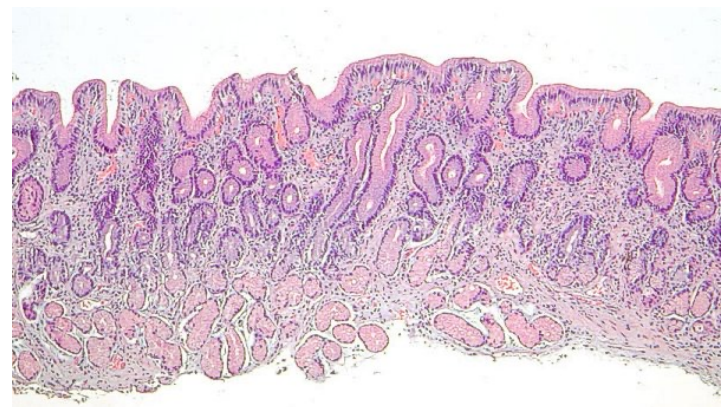
Active Inflammation



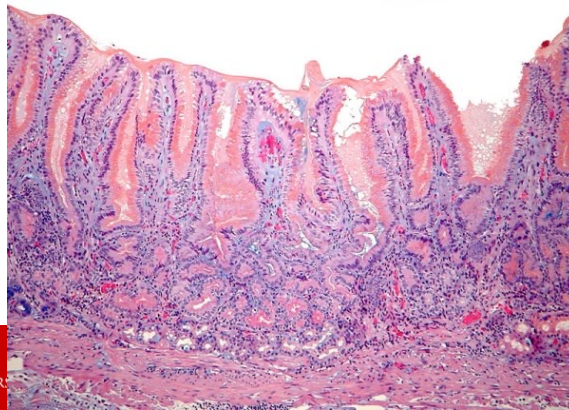
Chronic Gastritis



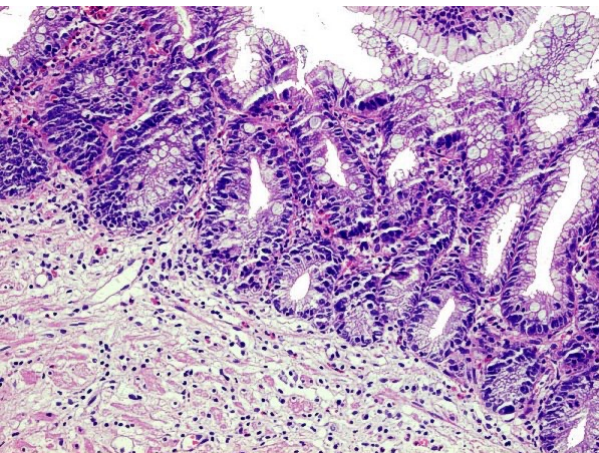
Atrophic Gastritis



Intestinal Metaplasia



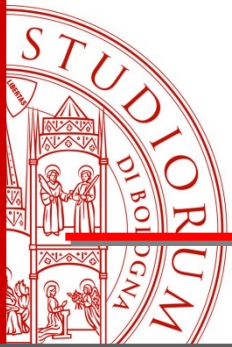
Dysplasia



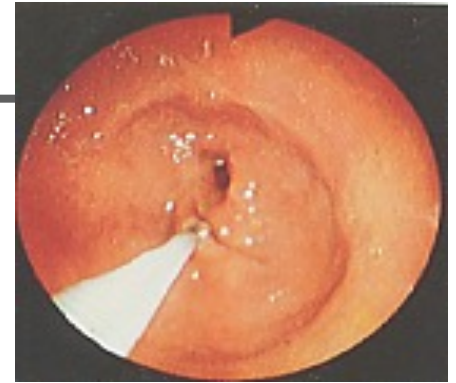
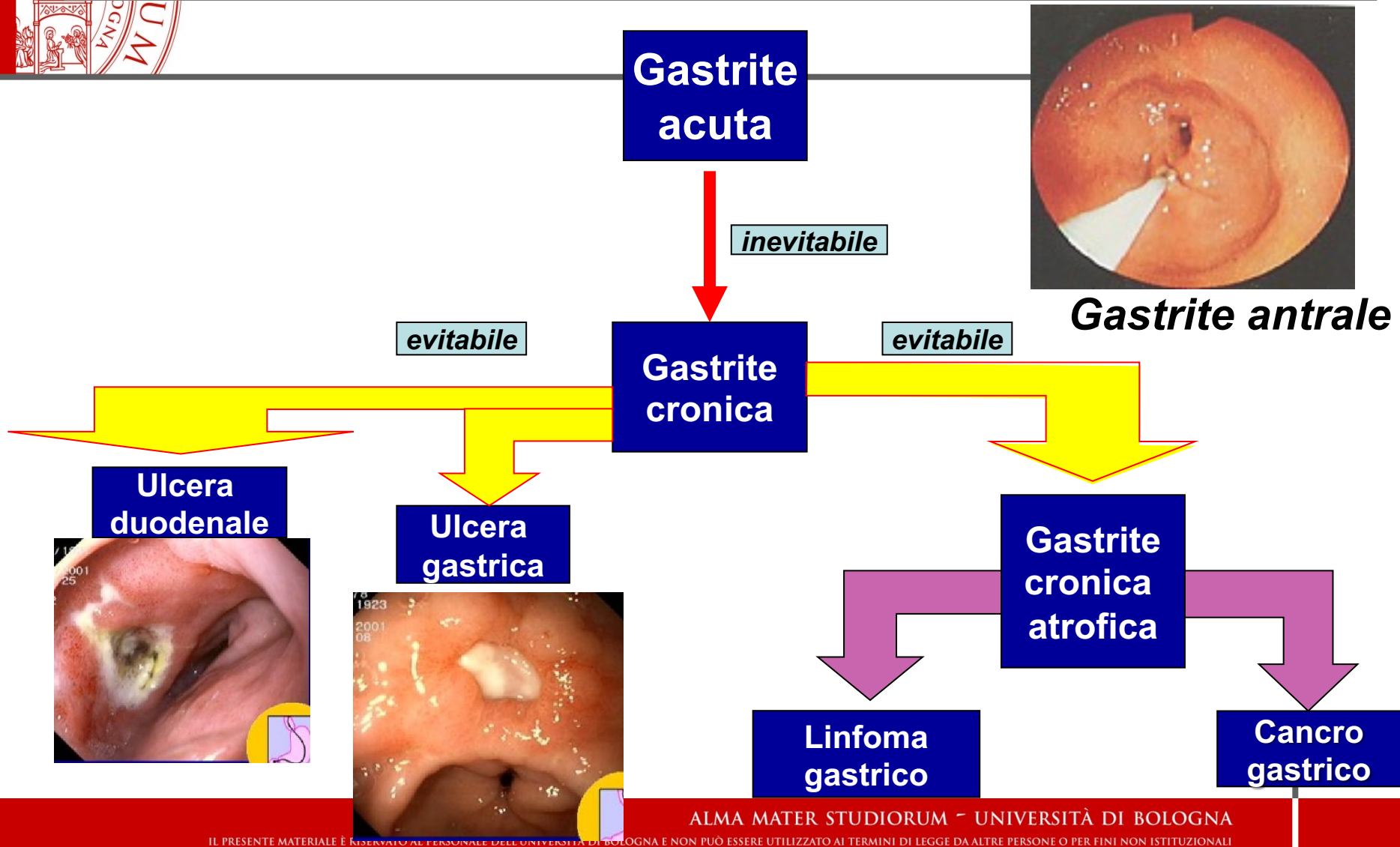
Dino Vaira

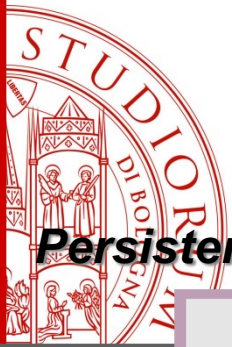


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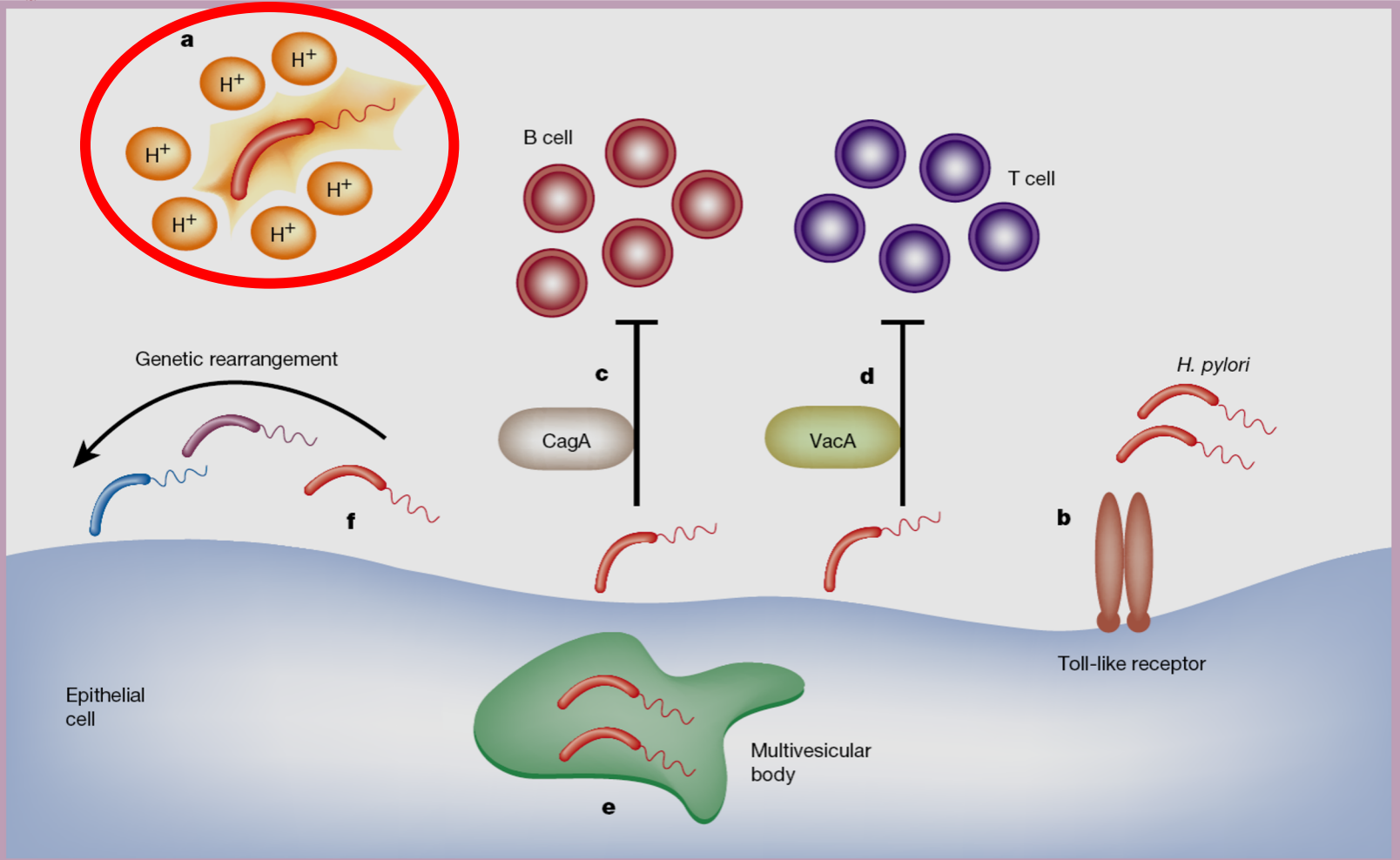
L'Hp può essere responsabile di patologie anche molto gravi





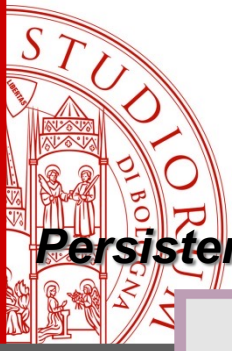
H pylori & Gastric Cancer

Persistent infection...



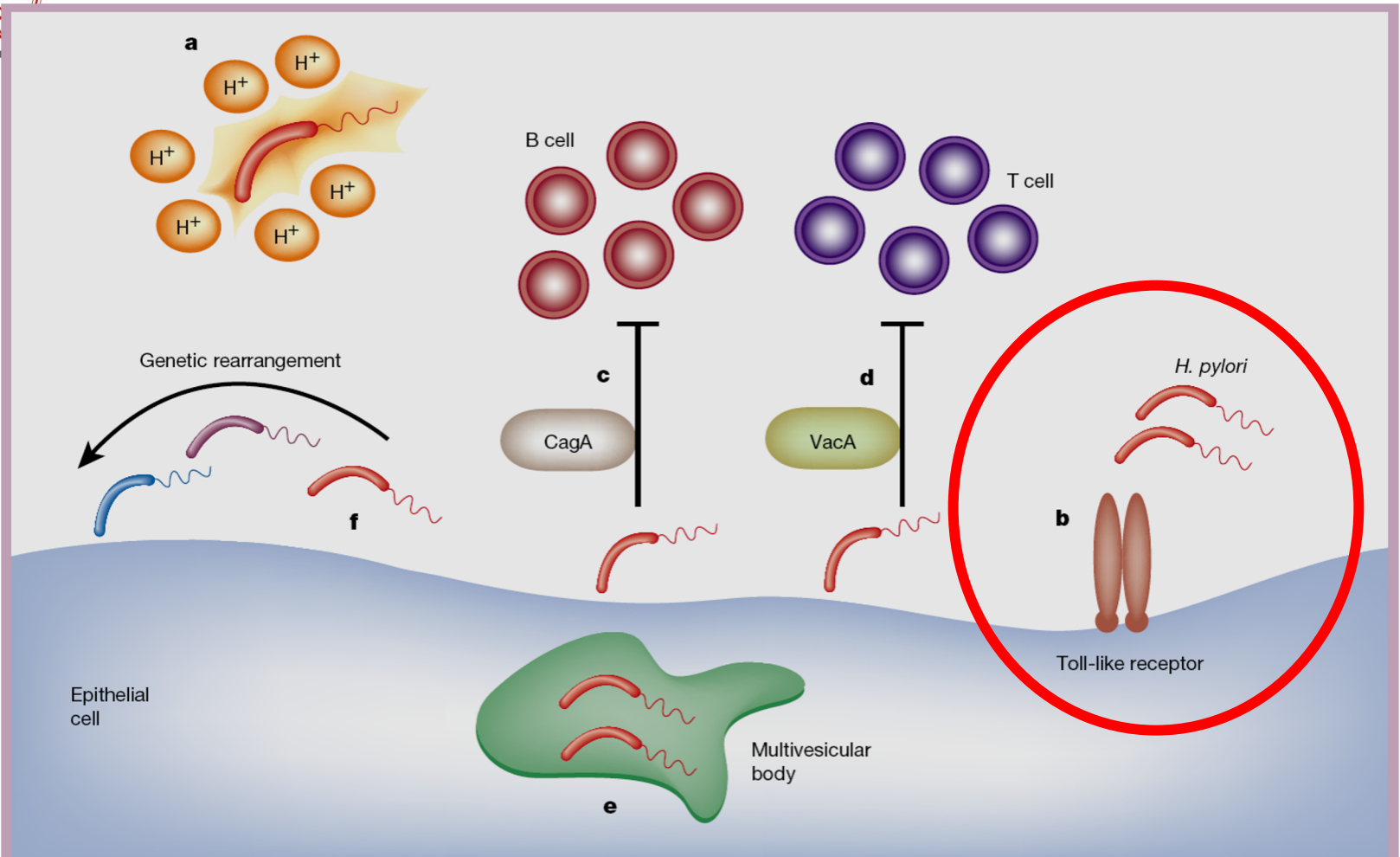
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Merrel DS et al. Nature 2004.



H. pylori & Gastric Cancer

Persistent infection...



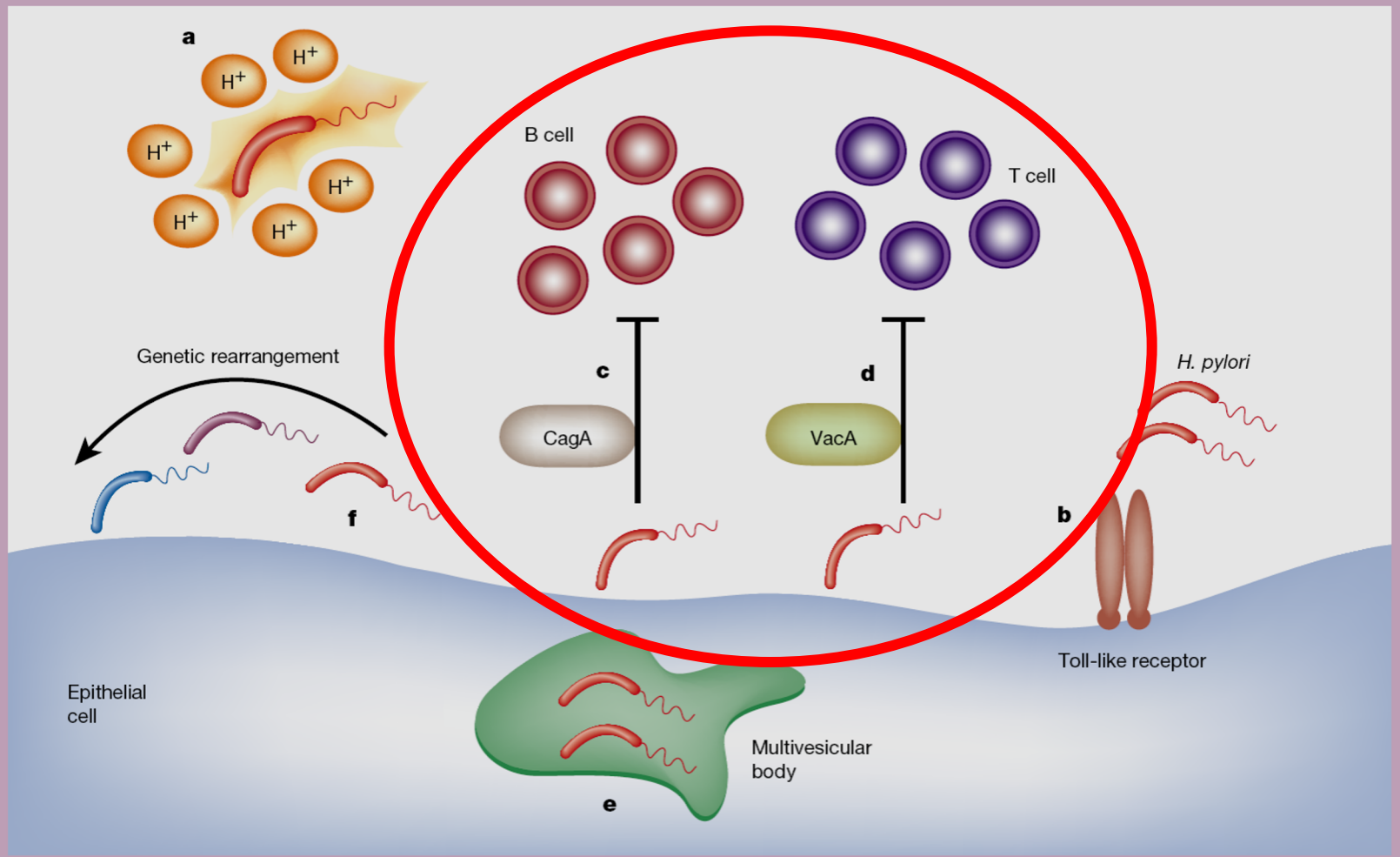
Dino Vaira

Merrel DS et al. Nature 2004.



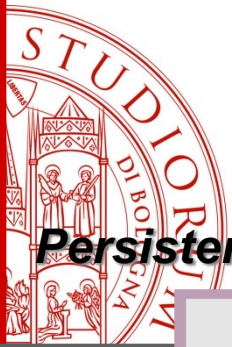
H pylori & Gastric Cancer

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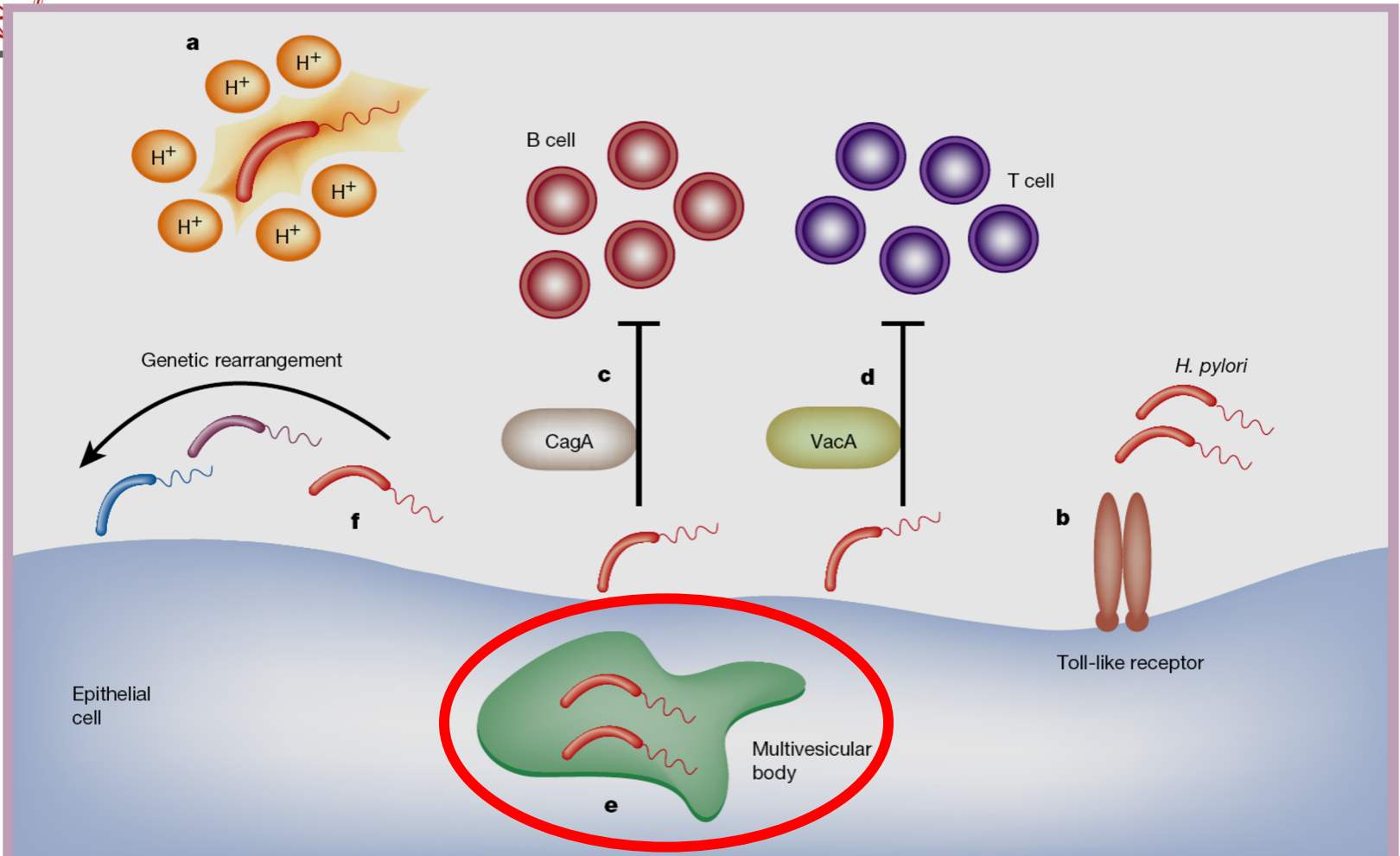
Dino Vaira

Merrel DS et al. Nature 2004.



H pylori & Gastric Cancer

Persistent infection...

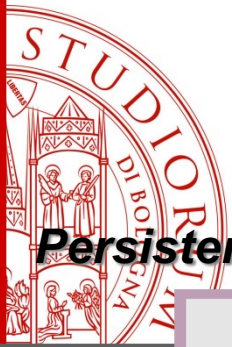


Dino Vaira

Merrel DS et al. Nature 2004.

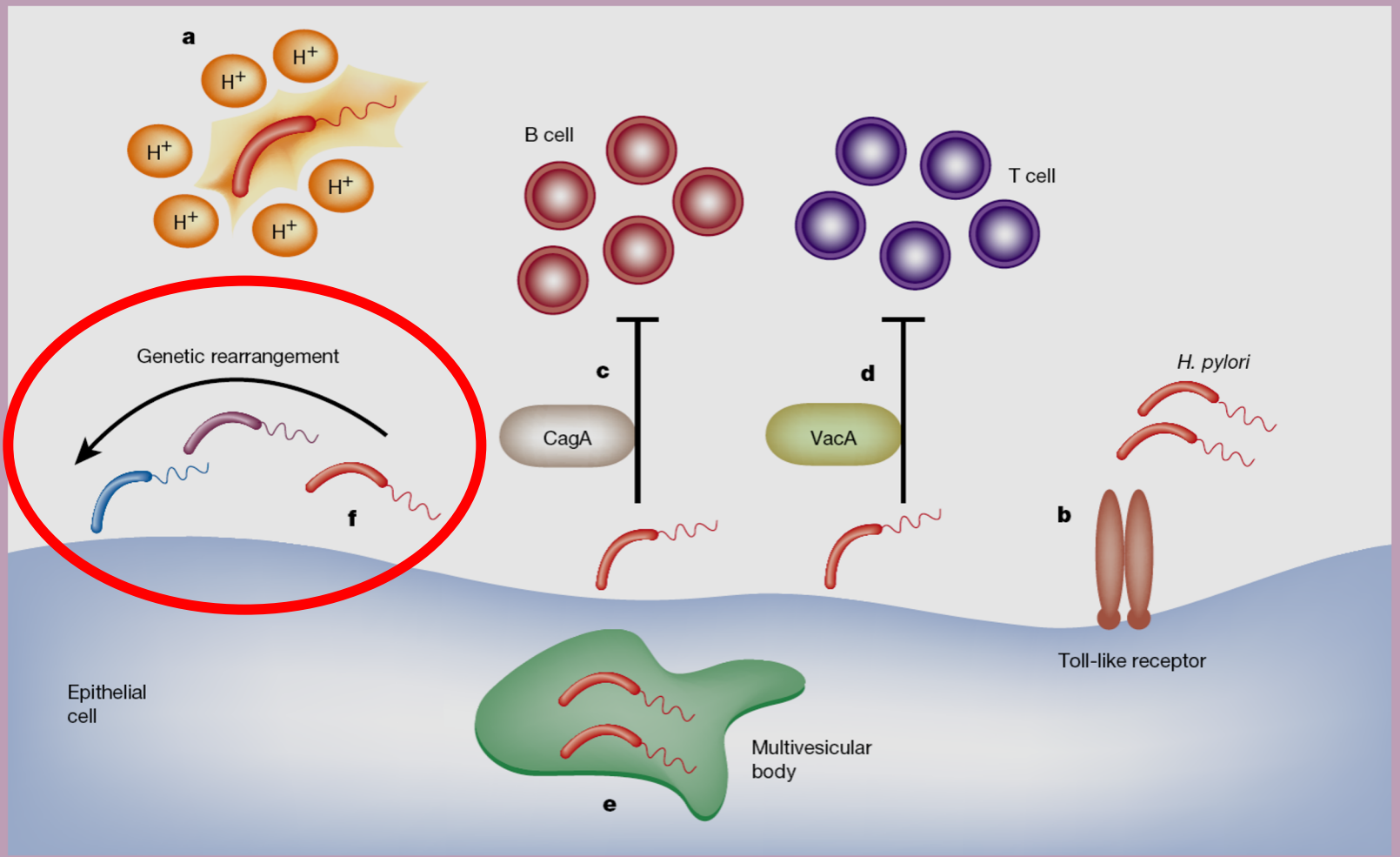
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H pylori & Gastric Cancer

Persistent infection...



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Merrel DS et al. Nature 2004.



Napoleone Bonaparte nacque nel 1769 e morì il 5 maggio 1821 dopo 6 anni di esilio

Fase 1-3: ottobre 1817-gennaio 1819
Dolore, nausea, mal di testa, alvo alterno, febbre, ittero, urine marsalate (post-mortem “sludge biliare”)

Fase 4: ottobre 1820-febbraio 1821
Sarcofobia, disfagia, calo ponderale, (“per me, ogni azione è come se affrontassi le prove di Ercole...”)

Fase 5: marzo -maggio 1821
Dolore, febbre, sudorazione (“era costretto a cambiare abito molte volte durante la notte”), ematemesi, melena

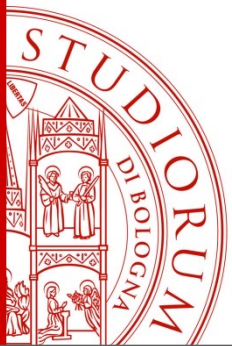
Egli ha avuto una infezione da *H pylori* con conseguente ulcera pre-pilorica ed evoluzione a cancro gastrico

Dino Vaira

Lugli A & Genta RM. Nat Cli Pract Gastr. Hepatol; gennaio 2007



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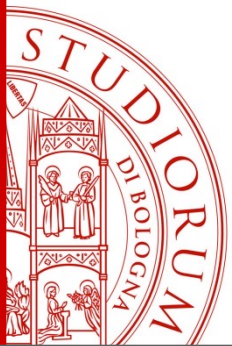


Infection = lymphoma???

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RUOLO DEL GASTROENTEROLOGO

1

Sintomi tipici



2

Quadri endoscopici patognomonic



3

Come fare correttamente le biopsie



4

Come trattare

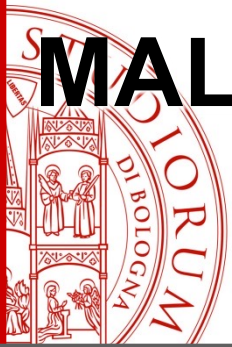


5

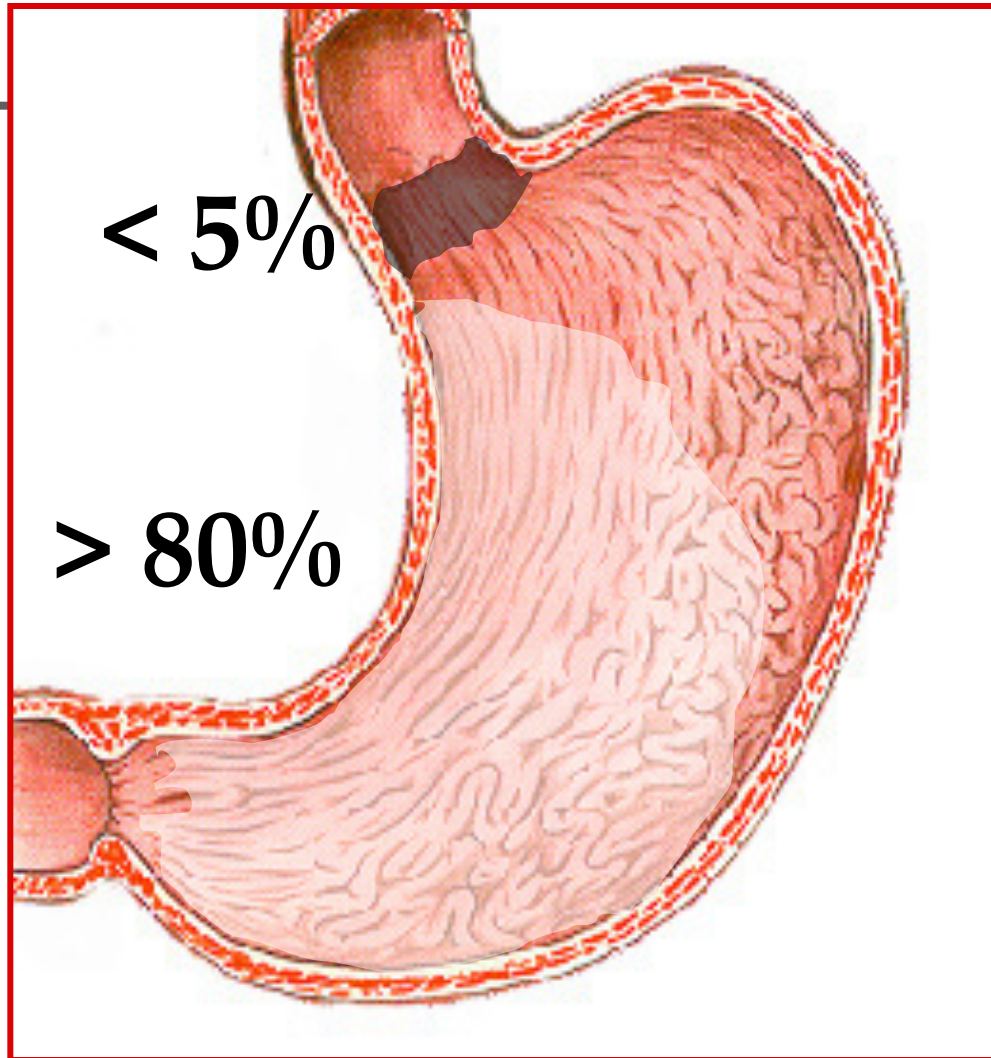
Come fare il follow-up



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MALToma sites



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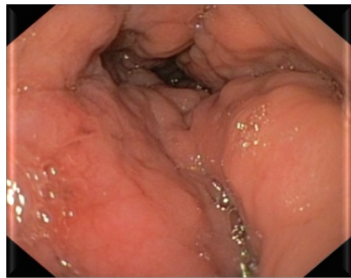
Effects of *Helicobacter pylori* Eradication on Early Stage Gastric Mucosa-Associated Lymphoid Tissue Lymphoma

ANGELO ZULLO,* CESARE HASSAN,* FRANCESCA CRISTOFARI,* ALESSANDRO ANDRIANI,‡
VINCENZO DE FRANCESCO,§ ENZO IERARDI,§ SILVERIO TOMAO,|| MANFRED STOLTE,¶ SERGIO MORINI,*
DINO VAIRA#

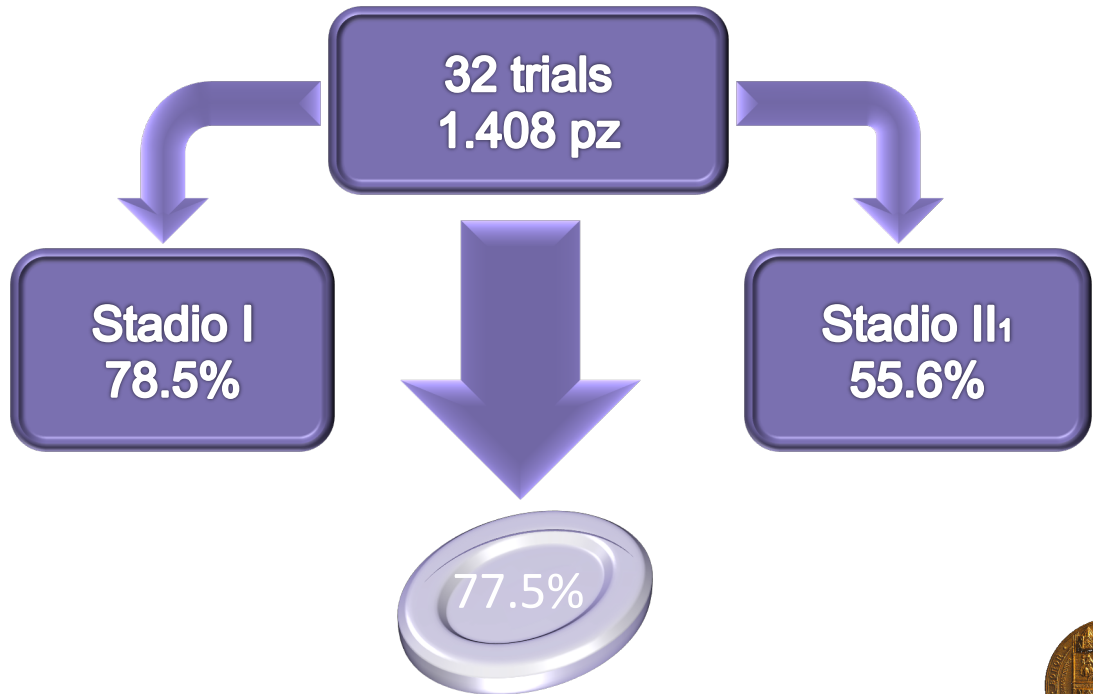
CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2010;8:105-110



Gastrite follicolare



Linfoma MALT



Effects of *Helicobacter pylori* Eradication on Early Stage Gastric Mucosa-Associated Lymphoid Tissue Lymphoma

ANGELO ZULLO,* CESARE HASSAN,* FRANCESCA CRISTOFARI,* ALESSANDRO ANDRIANI,[‡]
VINCENZO DE FRANCESCO,[§] ENZO IERARDI,[§] SILVERIO TOMAO,^{||} MANFRED STOLTE,[¶] SERGIO MORINI,* and
DINO VAIRA*

H. pylori eradication:

1,408/1,436
(98%)

Lymphoma remission:

1,091/1,408
(77.5%)
(95% CI: 75.3-79.7)

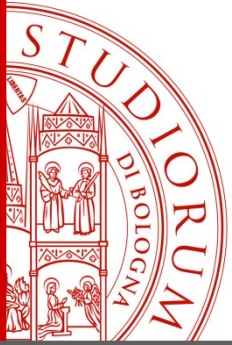
Stage II₁:

30/54
(55.6%)

Stage I:

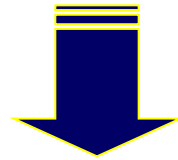
1061/1,354
(78.4%)

RESULTS 2



H. pylori eradication:

1,408/1,436
(98%)



Median

All but

3 pts: at 3

Table 2. Lymphoma Remission Rate After *H pylori* Eradication in Different Areas

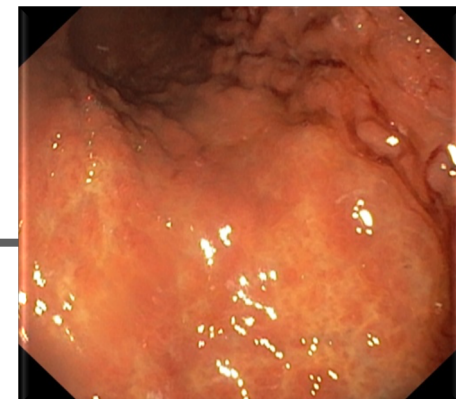
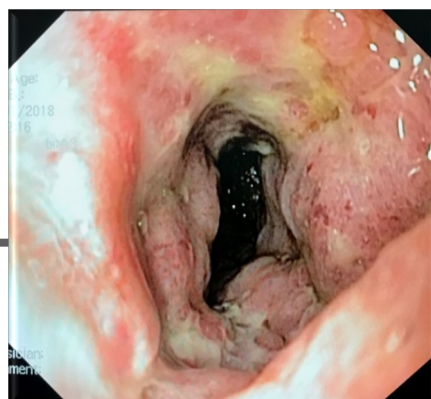
	Country		P value
	Asian, n (%)	Western, n (%)	
Stage I	401/478 (83.9)	660/876 (75.3)	.0005
Stage II ₁	22/25 (88.0)	8/29 (27.5)	.0001
Total	423/503 (84.1)	668/905 (73.8)	.0001

Stage II₁:

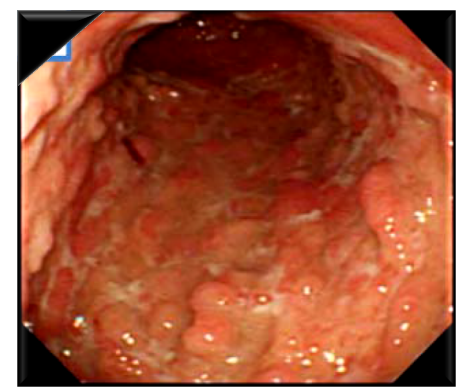
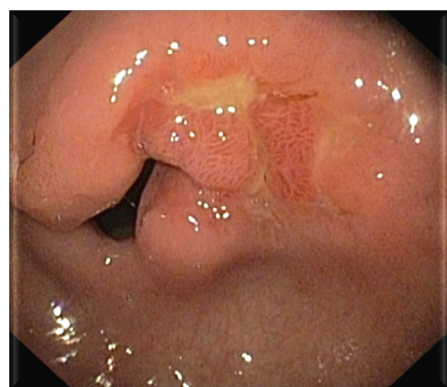
5.6%

3)

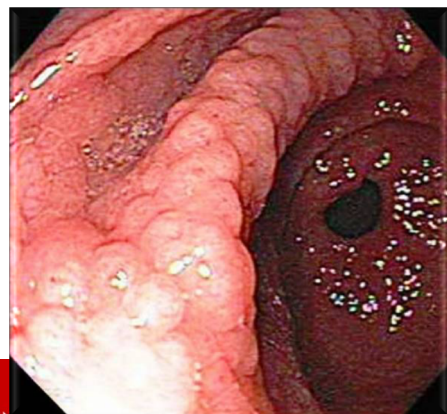
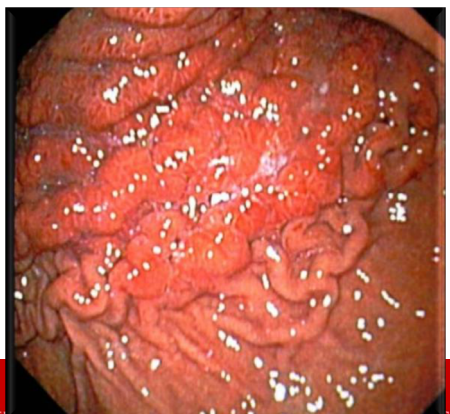
Esofitica (massa)



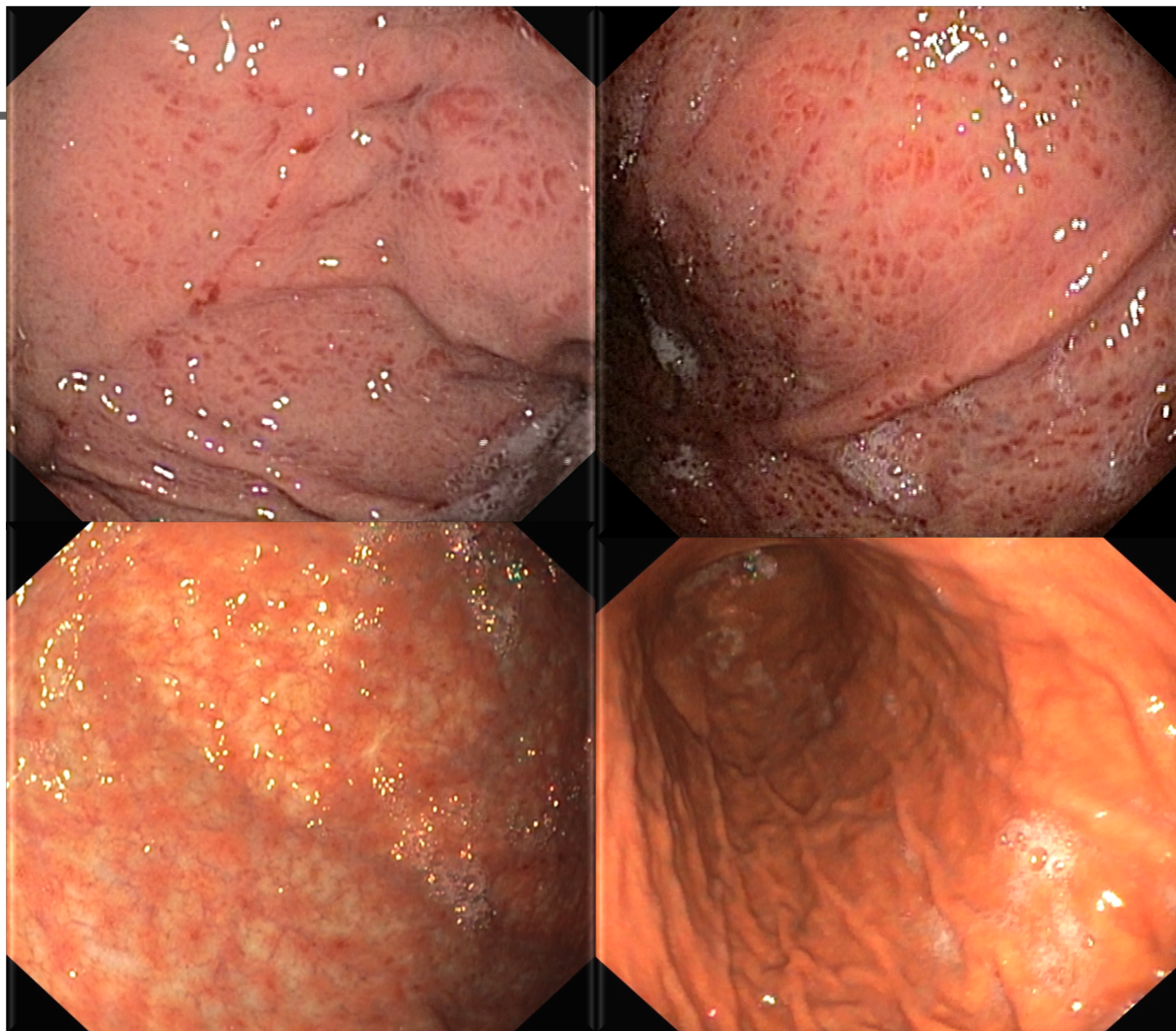
Ulcerativa (singola o multipla)



Ipertrofica (pliche giganti, nodularità)



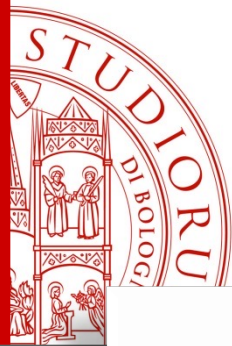
Mista



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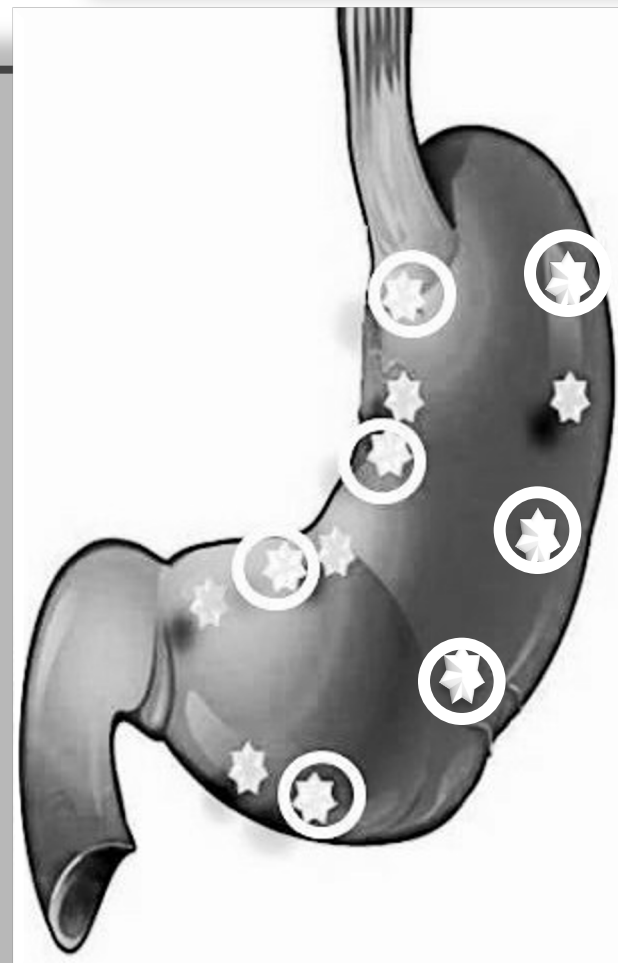
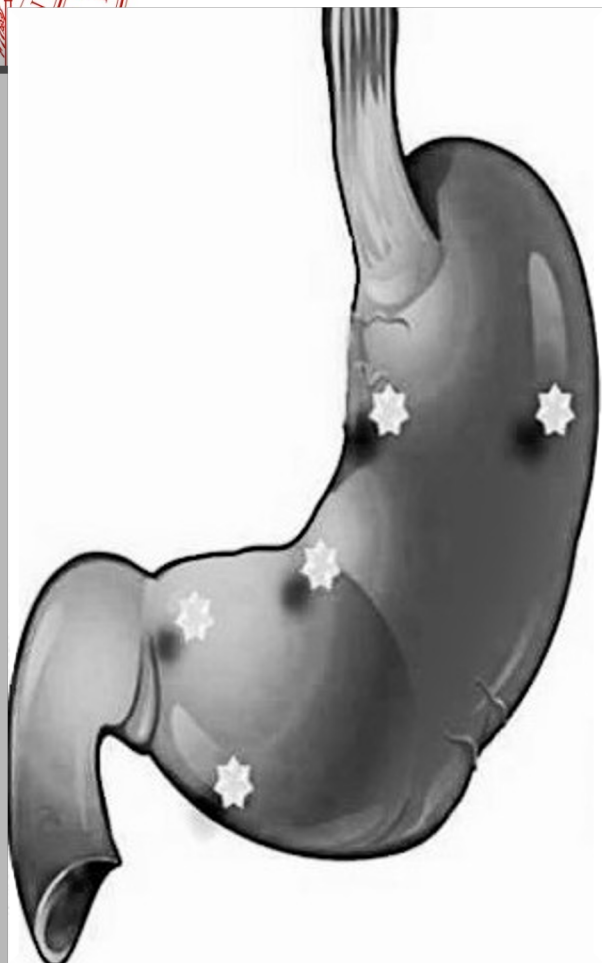
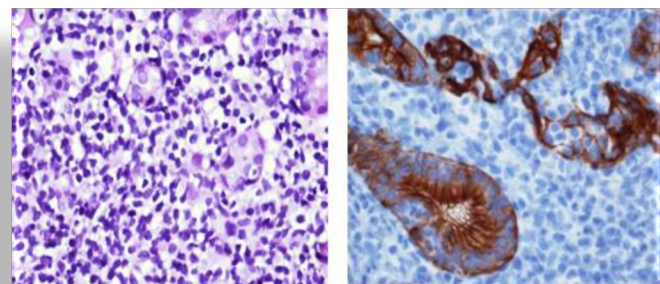


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3

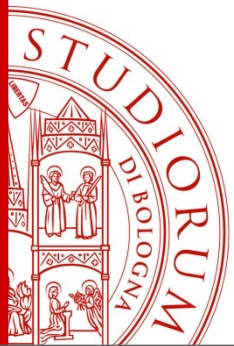
Prelievi bioptici



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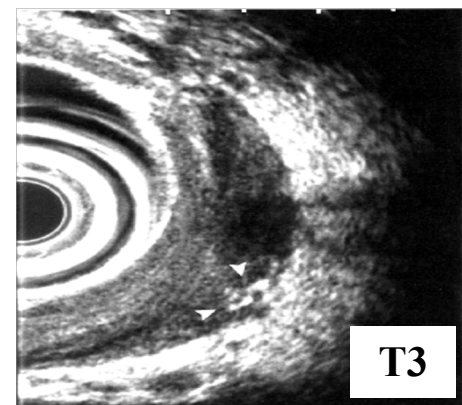
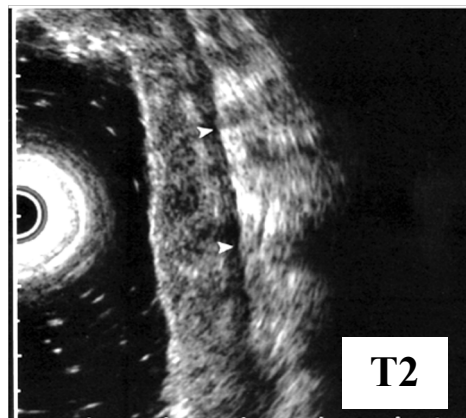
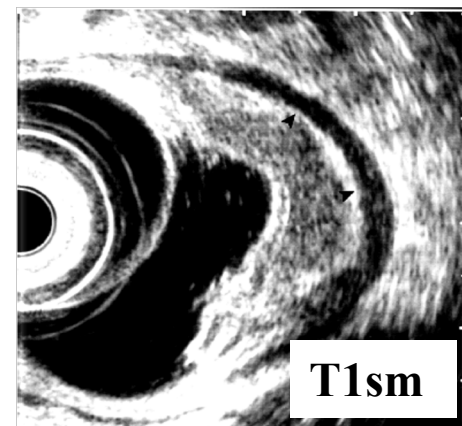
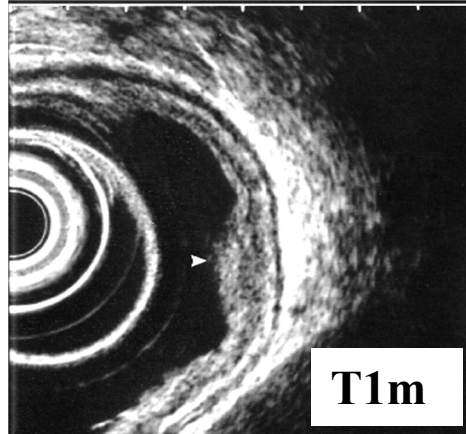
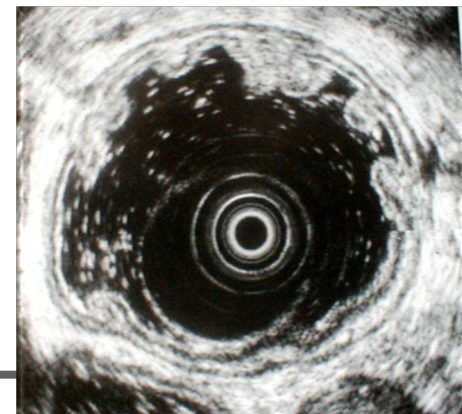
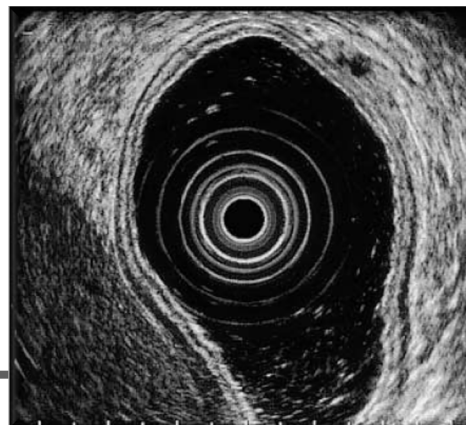


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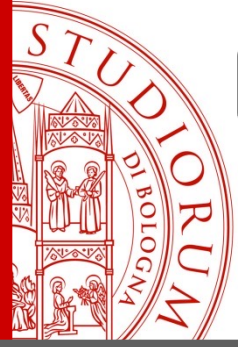


3

Eco-endoscopia

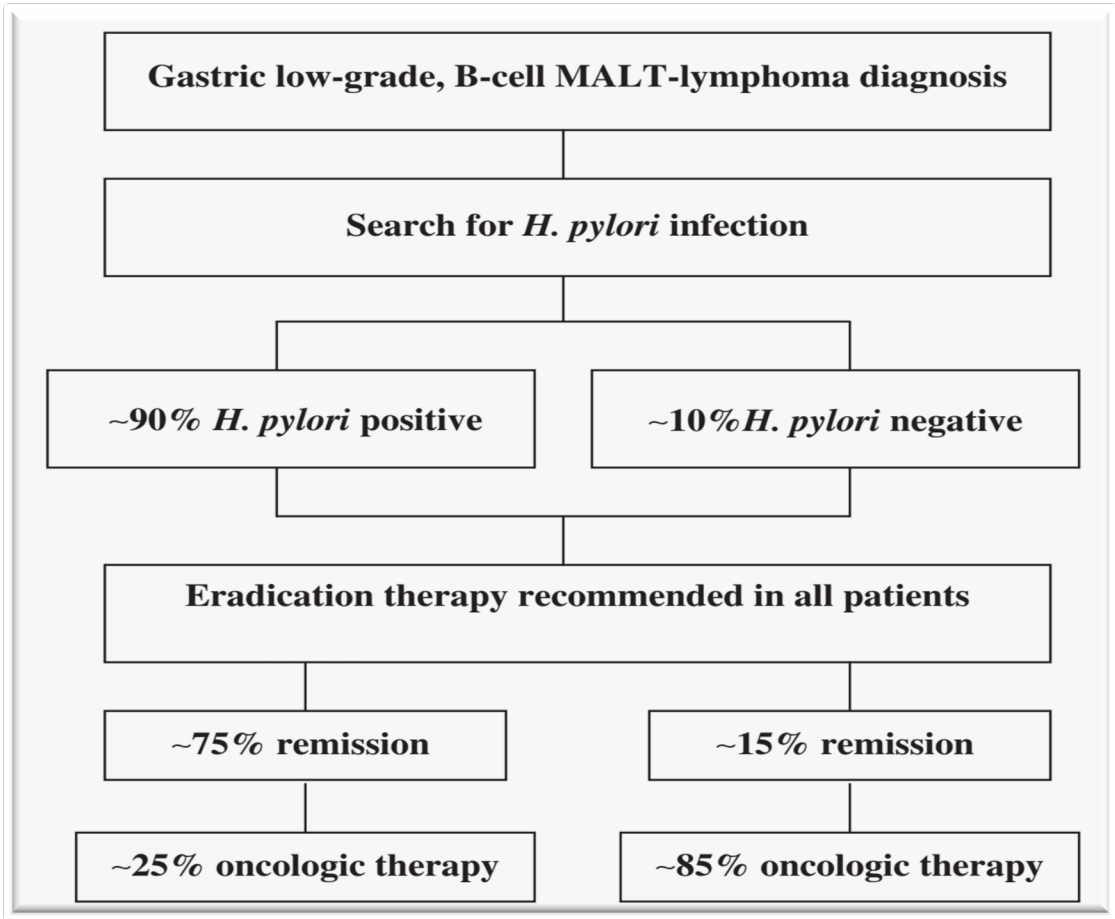


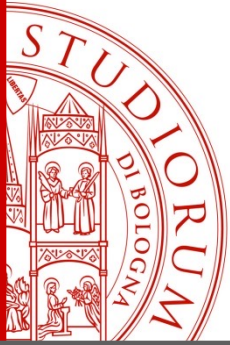
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4

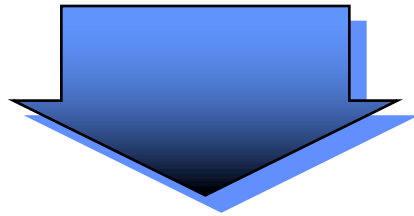
Come trattare





Terapia “5+5”

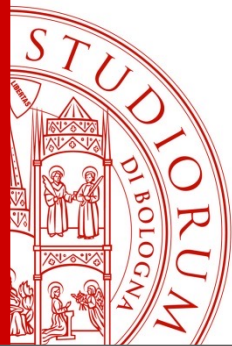
Esomeprazolo 40 mg bid
Amoxicilina 1 g bid 5 giorni



Seguito da

Esomeprazolo 40 mg bid
Clarithromicina 500 mg bid 5 giorni
Tinidazolo 500 mg bid





Sequential Therapy versus Standard Triple-Drug Therapy for *Helicobacter pylori* Eradication

A Randomized Trial

Dino Vaira, MD; Angelo Zullo, MD; Nimish Vakil, MD; Luigi Gatta, MD; Chiara Ricci, MD; Federico Perna, PhD; Cesare Hassan, MD; Veronica Bernabucci, MD; Andrea Tampieri, MD; and Sergio Morini, MD

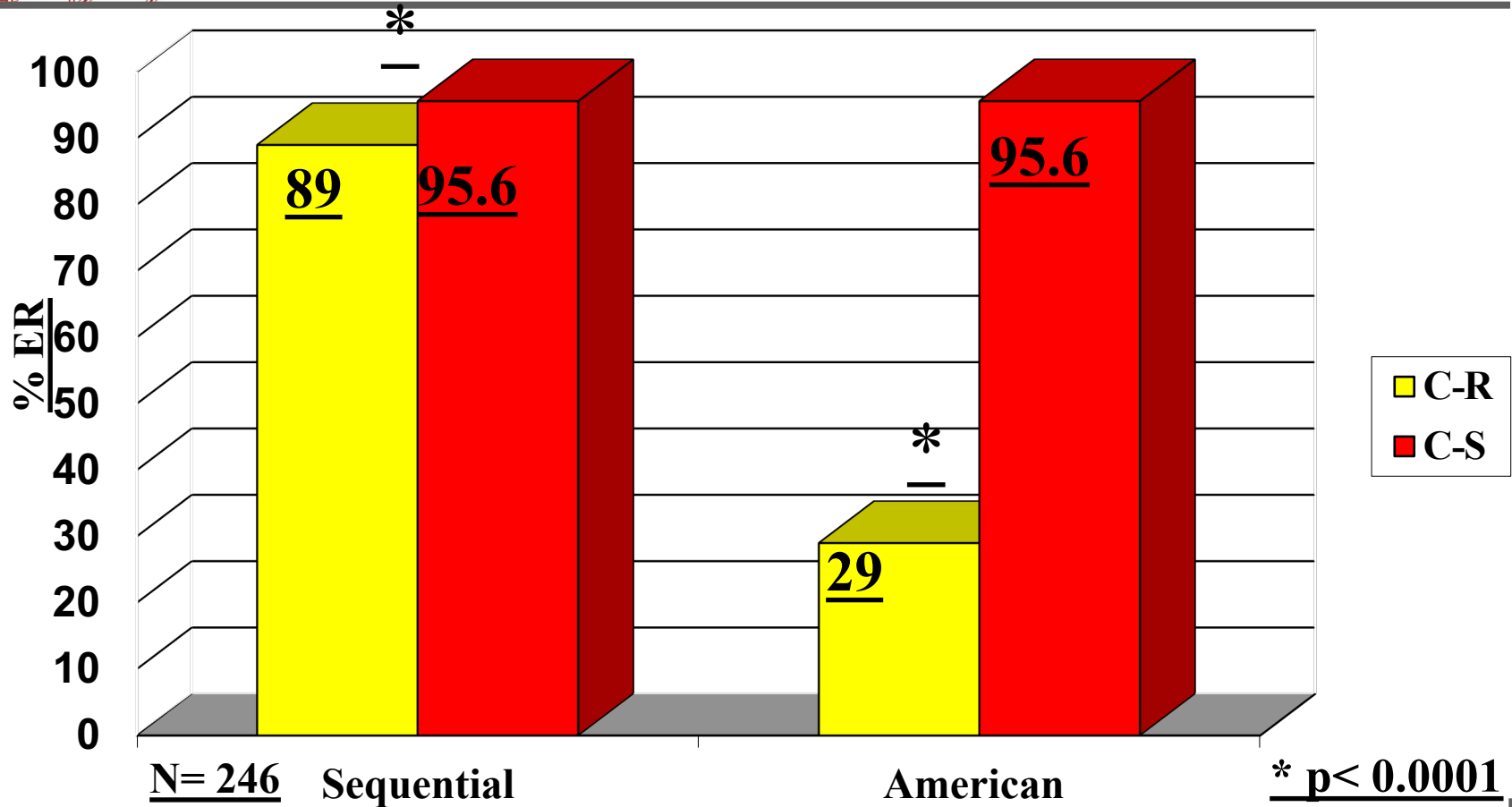
Table 2. *Helicobacter pylori* Eradication Rates with Sequential and Standard Therapy

Variable	Sequential Therapy		Standard Therapy		Difference (95% CI), %	P Value
	Patients, n	Eradication Rate, %	Patients, n	Eradication Rate, %		
Standard intention-to-treat analysis	150	89	150	77	12 (3–20)	0.0134
Modified intention-to-treat analysis*	146	91	149	78	13 (5–21)	0.0022
Per-protocol analysis	143	93	146	79	14 (6–21)	0.0010

* All patients who took at least 1 dose of medication are included.



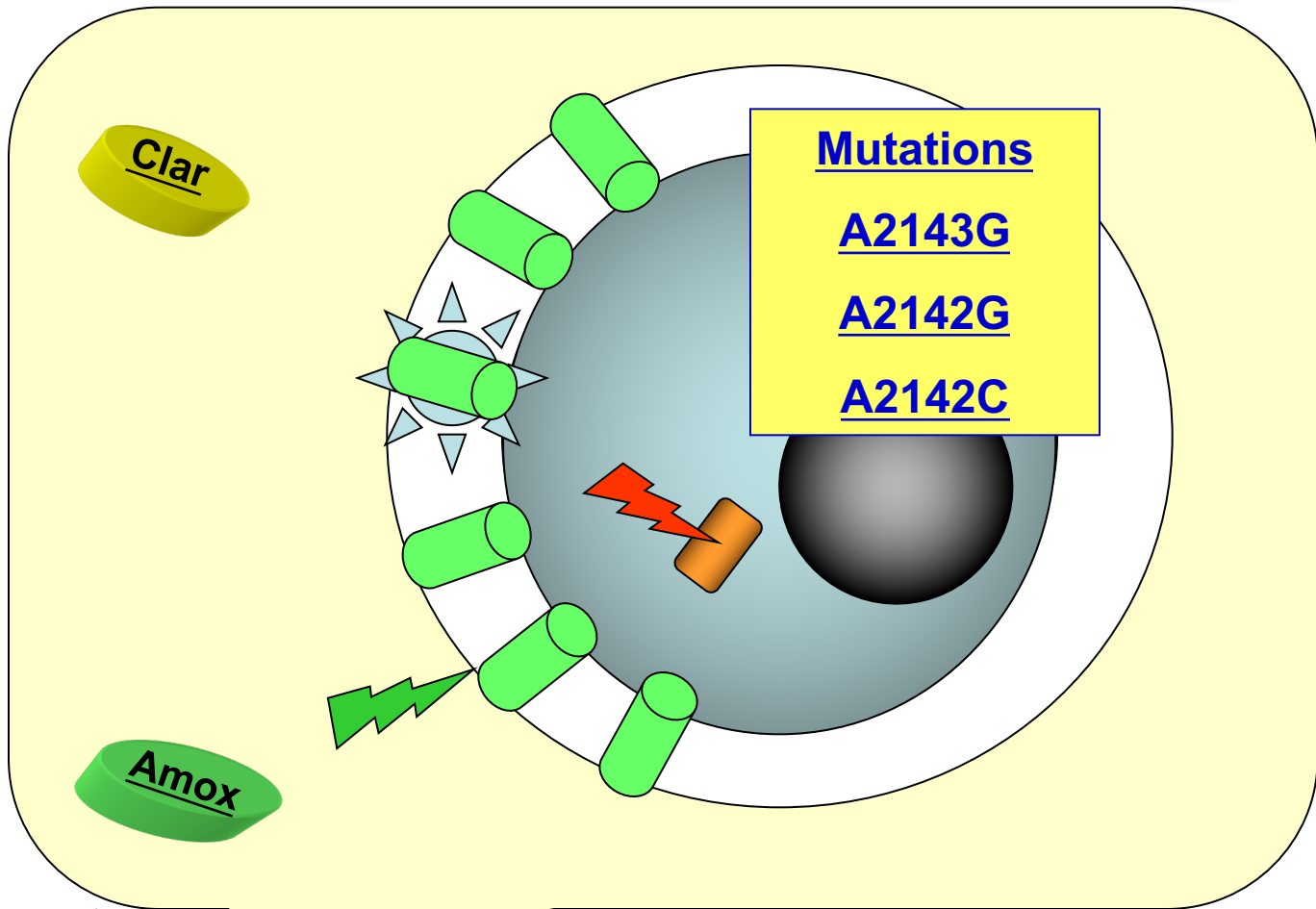
Double-blind placebo-controlled trial sequential vs American first-line treatment



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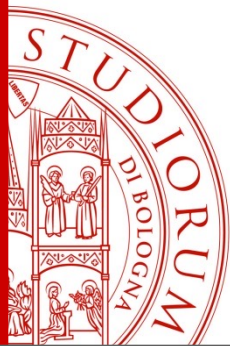


De Francesco V. *Ann Int Med* 2006;144;94-100.

Murakami K. *J Antimicrob Agents* 2002;19;67-70.




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RESEARCH

Global eradication rates for *Helicobacter pylori* infection: systematic review and meta-analysis of sequential therapy

 OPEN ACCESS

Luigi Gatta *physician and gastroenterologist*^{1,2}, Nimish Vakil *clinical professor of medicine*³, Dino Vaira *professor of internal medicine*⁴, Carmelo Scarpignato *professor of pharmacology and therapeutics; associate professor of gastroenterology*²

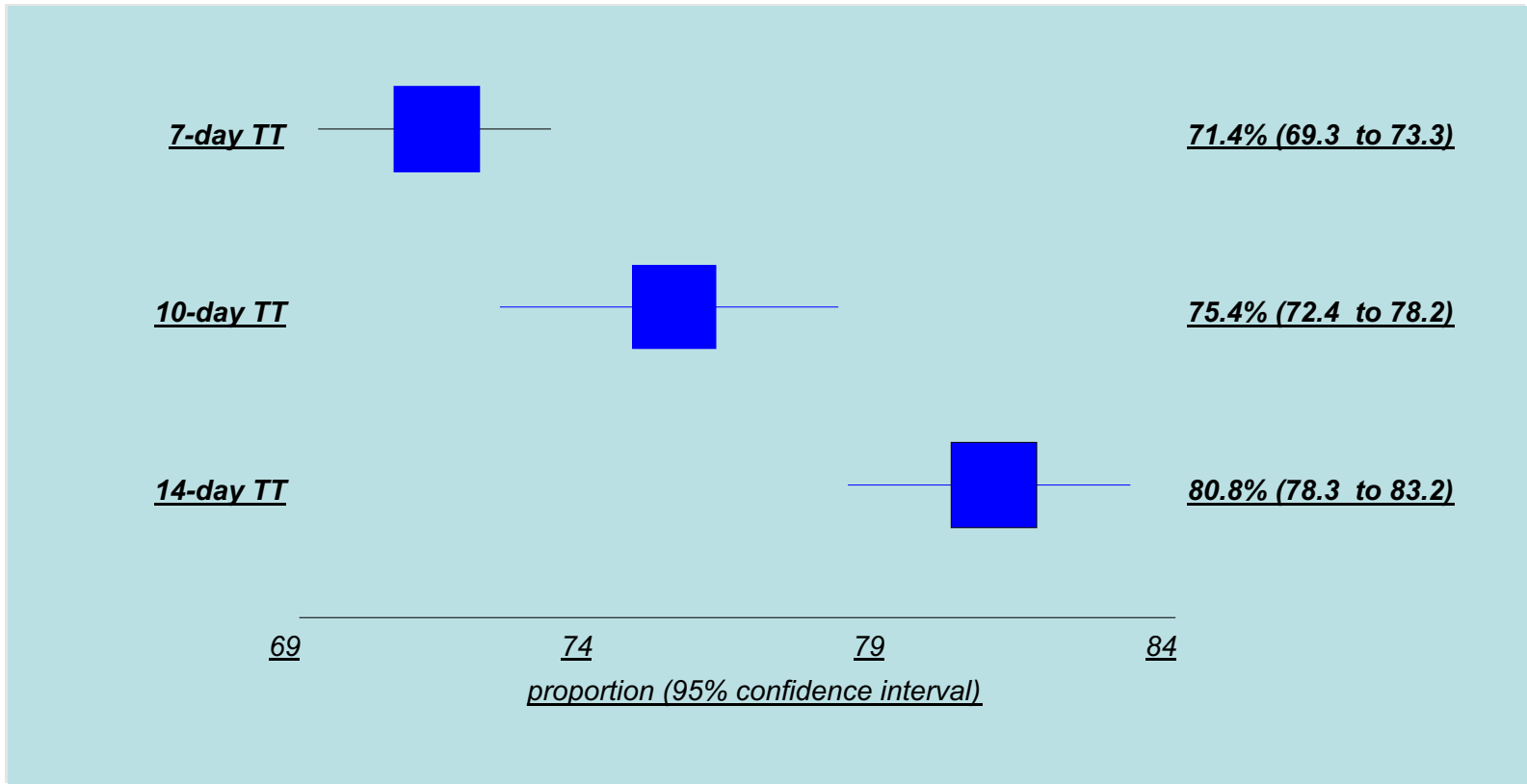
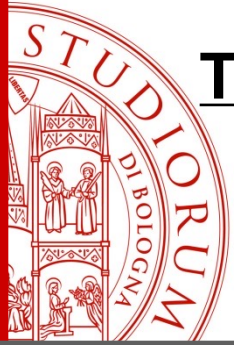
¹Gastroenterology and Endoscopy Unit, Versilia Hospital, Lido di Camaiore, Italy; ²Department of Clinical and Experimental Medicine, University of Parma, Parma, Italy; ³Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; ⁴Department of Medical and Surgical Sciences, University of Bologna, Italy

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Tasso di eradicazione totale della triplice terapia (meta-analisi)



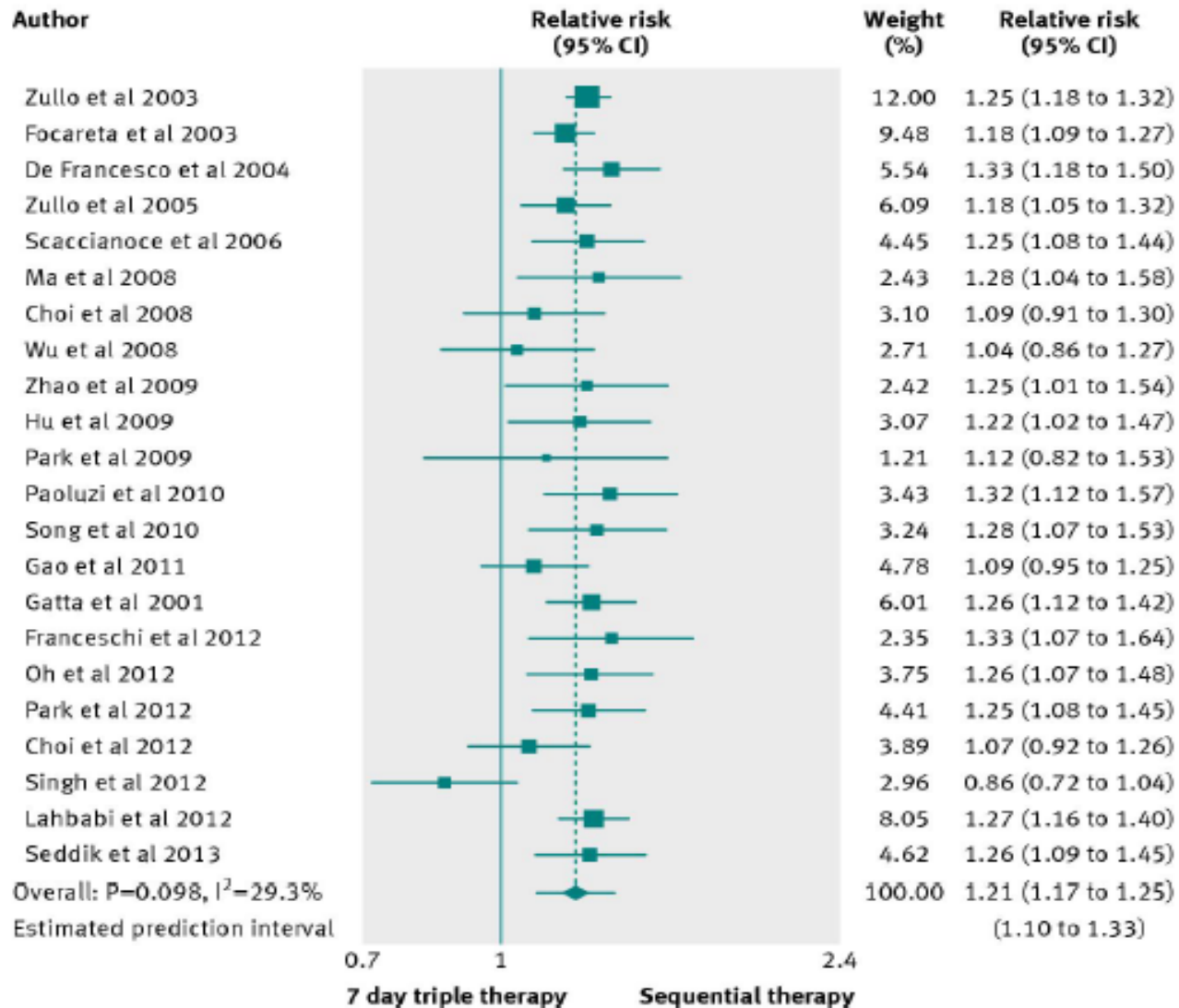
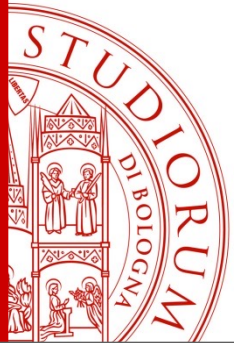


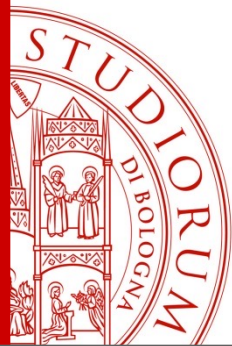
Fig 2 Forest plot of sequential therapy versus seven day triple therapy

Gatta, Vakil, Vaira & Scarpignato BMJ 2013

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Aliment Pharmacol Ther. 2018 May;47(9):1261-1269

WILEY AP&T Alimentary Pharmacology & Therapeutics

Impact of primary antibiotic resistance on the effectiveness of sequential therapy for *Helicobacter pylori* infection: lessons from a 5-year study on a large number of strains

L. Gatta^{1,2}  | C. Scarpignato²  | G. Fiorini³ | J. Belsey⁴ | I. M. Saracino³ |
C. Ricci⁵ | D. Vaira³

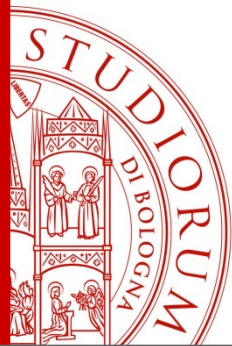
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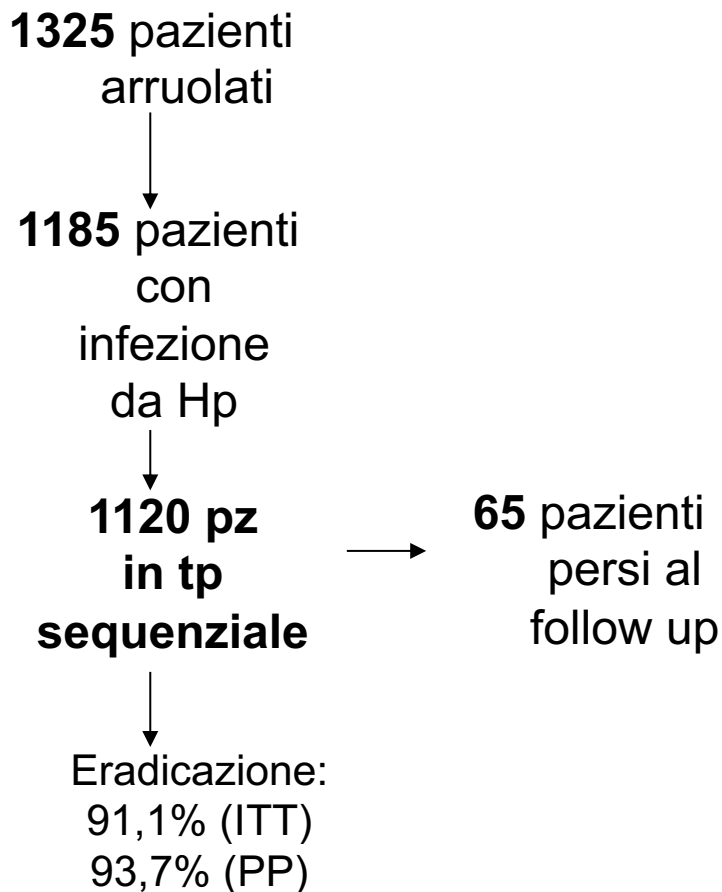
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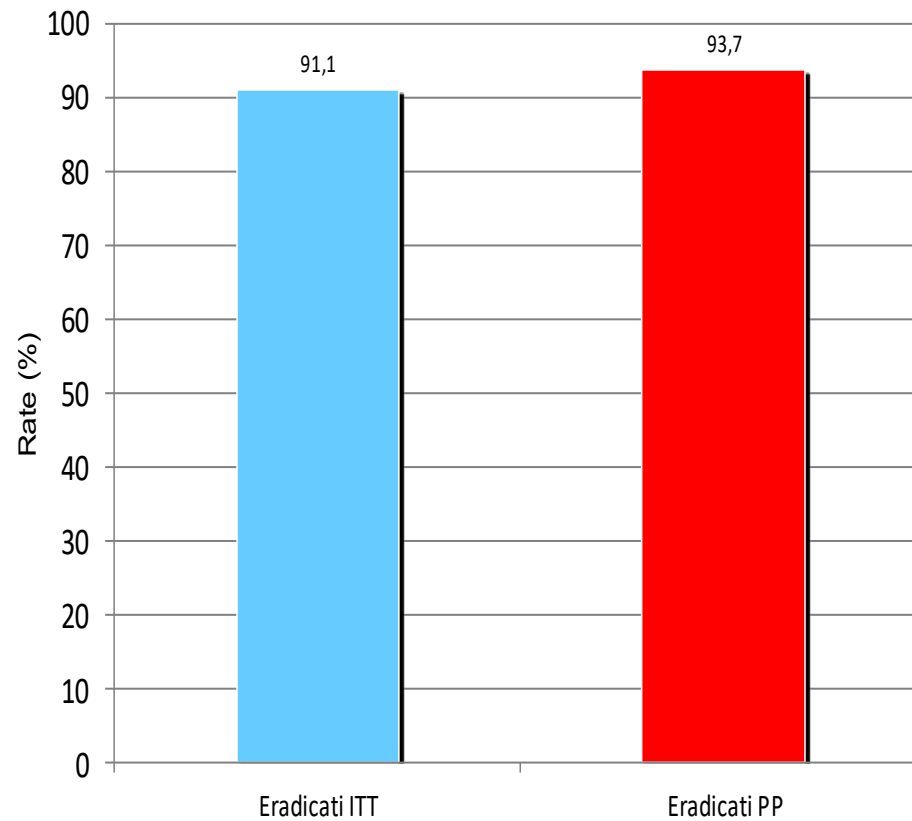
IL PRESENTE MATERIALE È RISERVATO AL PERSONALE DELL'UNIVERSITÀ DI BOLOGNA E NON PUÒ ESSERE UTILIZZATO AI TERMINI DI LEGGE DA ALTRE PERSONE O PER FINI NON ISTITUZIONALI

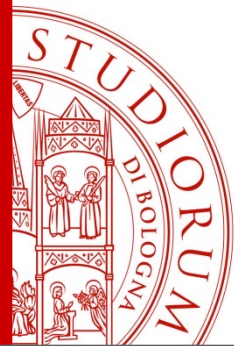


Risultati:



Eradicazione con terapia sequenziale





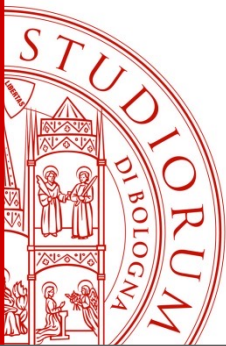
Pattern of strains	Numbers	%	Cum%	Eradication rate (%)
Cla-S Metro-S Levo-S	395	43,11	43,11	97,72
Cla-R Metro-R LevoR	99	10,81	53,93	90,91
Cla-R Metro-S Levo-S	88	9,61	63,54	94,32
Cla-R Metro-R Levo-S	79	8,62	72,16	84,81
Cla-S Metro-R Levo-S	78	8,52	80,68	97,44
Cla-S Metro-S Levo-R	55	6,00	86,68	94,55
Cla-S Metro-R Levo-R	45	4,91	91,59	100
Cla-R Metro-S Levo-R	30	3,28	94,87	93,33
Cla-I Metro-S Levo-S	28	3,06	97,93	96,43
Cla-I Metro-R Levo-S	13	1,42	99,35	100
Cla-I Metro-S Levo-R	3	0,33	99,68	100
Cla-I Metro-R Levo-R	3	0,33	100	100

Gatta et al. Aliment Pharmacol Ther. 2018 May;47(9):1261-1269

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antibiotics



Article

Trends in Primary Antibiotic Resistance in *H. pylori* Strains Isolated in Italy between 2009 and 2019

Ilaria Maria Saracino ¹, Giulia Fiorini ¹, Angelo Zullo ², Matteo Pavoni ¹, Laura Saccomanno ¹ and Dino Vaira ^{1,*}

¹ Department of Surgical and Medical Sciences, University of Bologna, 40126 Bologna, Italy; saracinoilariamaria@gmail.com (I.M.S.); giulia.fiorini@fastwebnet.it (G.F.); matteo.pavoni@studio.unibo.it (M.P.); laura.saccomanno@studio.unibo.it (L.S.)

² Gastroenterology Unit, Nuovo Regina Margherita Hospital, 00153 Rome, Italy; zullo66@gmail.com

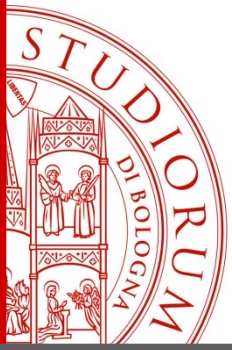
* Correspondence: berardino.vaira@unibo.it

Received: 18 December 2019; Accepted: 9 January 2020; Published: 13 January 2020

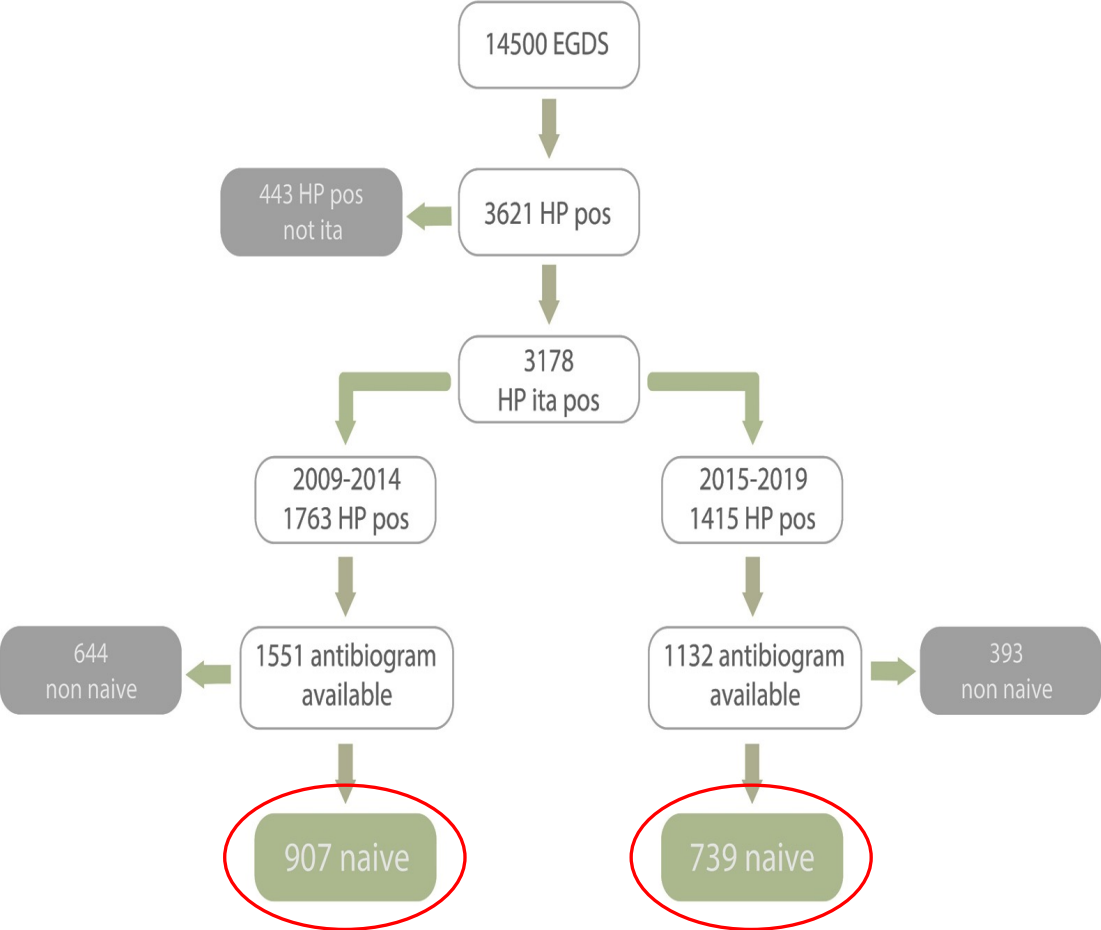
Dino Vaira

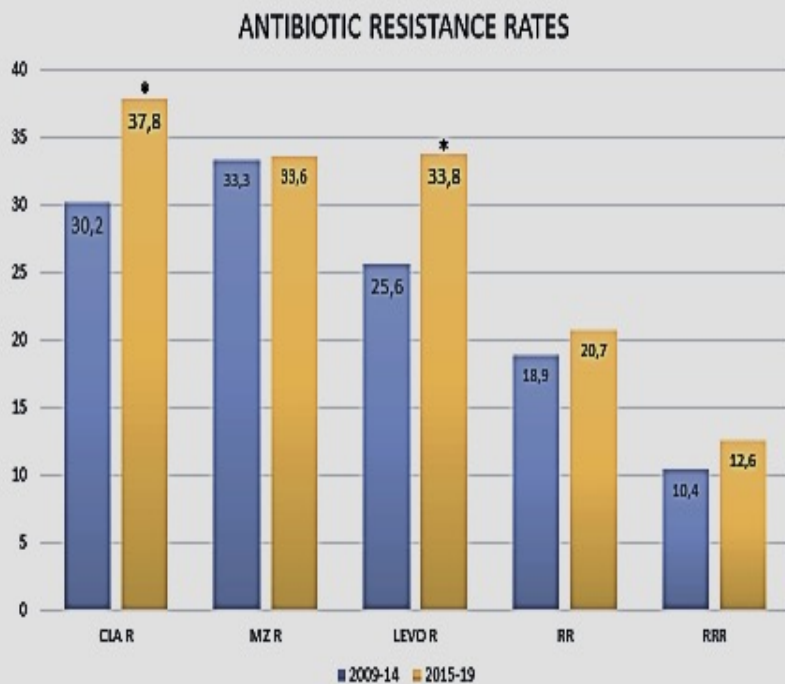


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Aim: evaluate, in Italian naïve patients, *H. pylori* antibiotic resistance trends and first line therapies eradication rates





H. pylori antibiotic resistance rates increase between 2009–2014 and 2015–2019. (* $p < 0,05$).

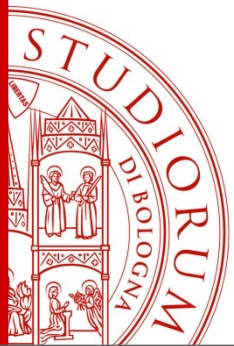
CLA: clarithromycin.

Mz: metronidazole.

Levo: levofloxacin.

R: resistant. RR: resistant to clarithromycin and metronidazole. RRR: resistant to clarithromycin, metronidazole and levofloxacin.

Conclusions: this data highlights an increase in primary *H. pylori* antibiotic resistance and strongly suggests the importance of drug susceptibility testing also in naïve patients.





antibiotics



Article

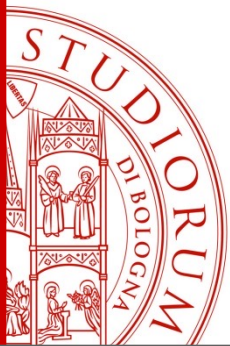
Antibiotic Resistance and Therapy Outcome in *H. pylori* Eradication Failure Patients

Saracino I.M. ^{1,†}, Pavoni M. ^{1,2,†}, Zullo A. ³, Fiorini G. ¹, Saccomanno L. ¹, Lazzarotto T. ⁴, Cavallo R. ⁵, Antonelli G. ² and Vaira D. ^{1,*}

Dino Vaira

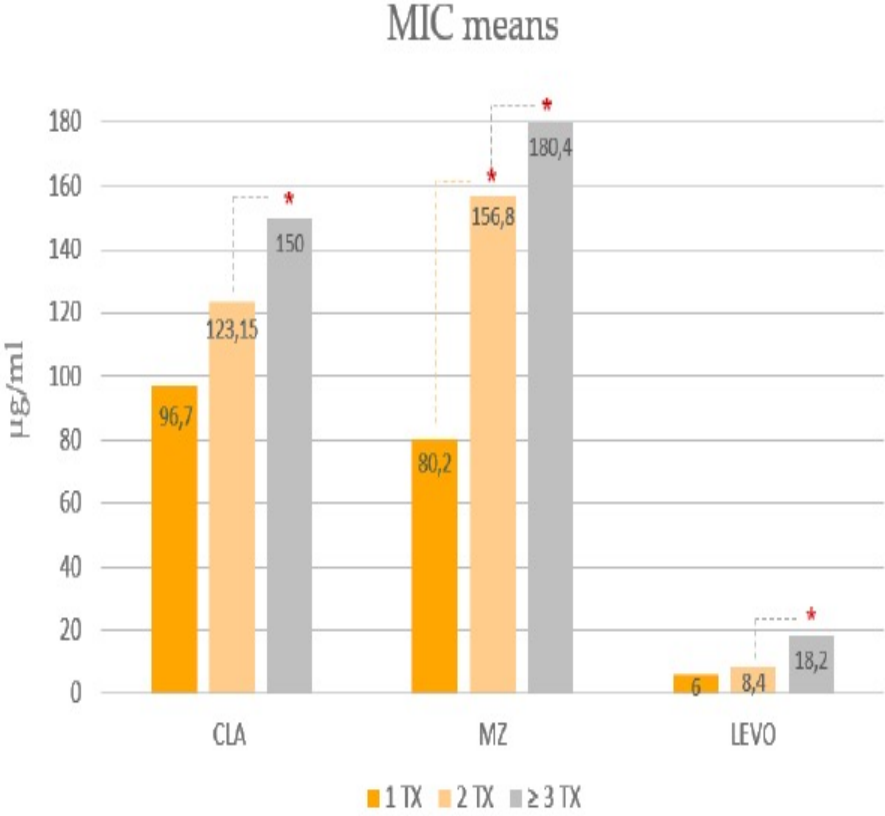


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Aim: to evaluate the development of antibiotic resistance, MIC values trends and therapeutic outcomes in patients who failed at least one *H. pylori* eradication therapy.

✓ A total of 1223 patients were *H. pylori* positive, and antibiotic susceptibility was available for 1037.



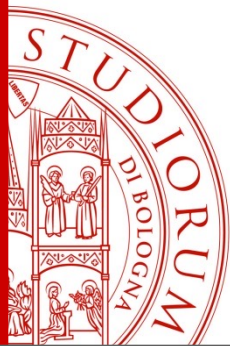
MIC values increase following one or more therapy failures.

TX = therapy. Cla: clarithromycin. Mz: metronidazole. Levo: levofloxacin. * p < 0.05.



Saracino et al Antibiotics 2020 Mar 13;9(3):121

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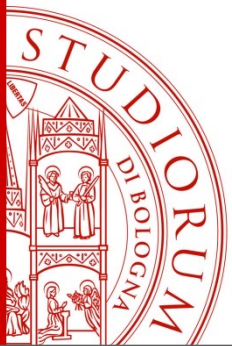
EFFECTIVENESS OF EMPIRICAL FIRST-LINE *H. PYLORI* ERADICATION THERAPY IN ITALY: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

Luigi Gatta ¹ Giulia Fiorini ², Ilaria Maria Saracino ², Matteo Pavoni ², Marco Romano ³, Antonietta Gravina ³, Rinaldo Pellicano ⁴, Antonio Gasbarrini ⁵, Alfredo Di Leo ⁶, Giuseppe Losurdo ⁶, Francesco Franceschi ⁷, Gerardo Nardone ⁸, Alba Rocco ⁸, Maria Pina Dore ⁹, Fabio Farinati ¹⁰, Matteo Ghisa ¹⁰, Ignasi Puig ¹¹, Olga P. Nyssen ¹², Francis Mégraud ¹³, Colm O'Morain ¹⁴, Dino Vaira ², and Javier P. Gisbert ¹², on behalf of the Hp-EuReg investigators

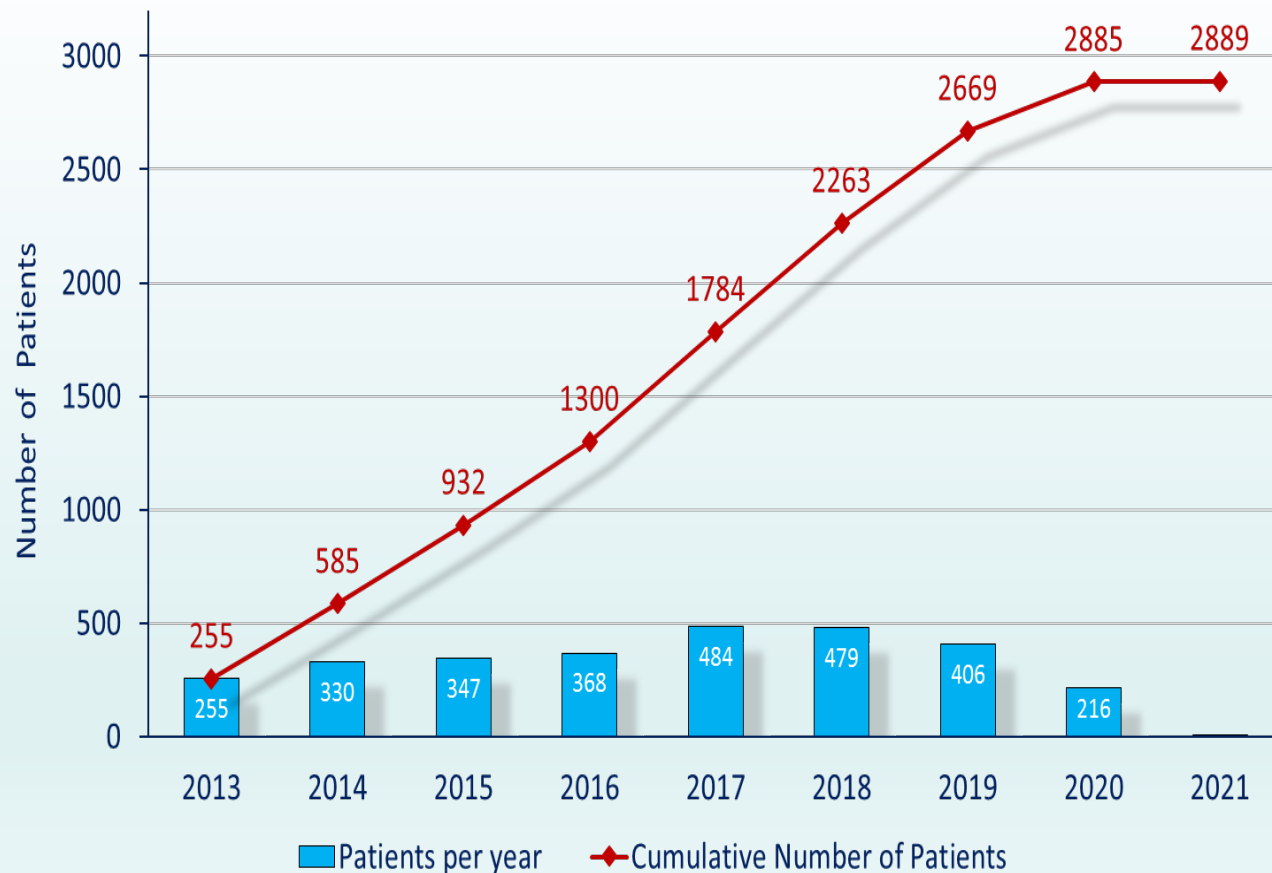
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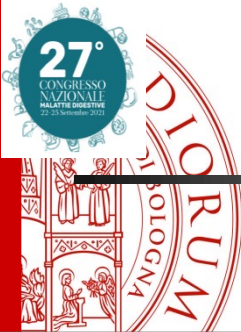


Aim: To assess the effectiveness of empirical first-line treatment evaluating the Italian data of the European Registry on the management of H. pylori (Hp-EuReg).



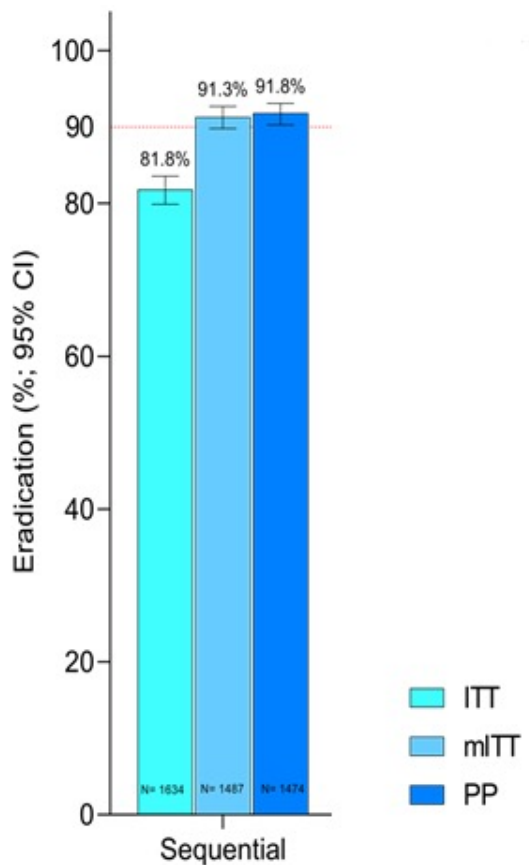
Dino Vaira

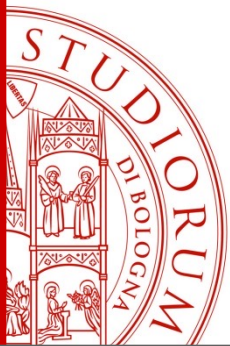
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Results

Eradication Rates for 10-day Regimens





120 Capsules in 10 blister cards
Each card contains 4 blisters.
Each blister contains 3 capsules.

NDC 58914-601-20

PYLERA[®]
CAPSULES

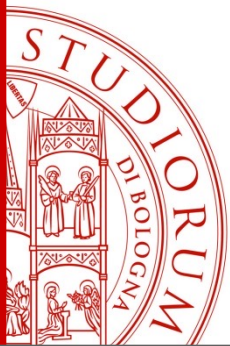
(bismuth subcitrate potassium 140 mg,
metronidazole 125 mg, tetracycline HCl 125 mg)

10 Day Therapy PAK

Rx only
Combination therapy indicated for the eradication of *Helicobacter pylori*
One blister card = 1 day of therapy

APTALISTM





Original article

Pylera and sequential therapy for first-line *Helicobacter pylori* eradication: a culture-based study in real clinical practice

Giulia Fiorini^a, Angelo Zullo^b, Ilaria M. Saracino^a, Luigi Gatta^c, Matteo Pavoni^a and Dino Vaira^a

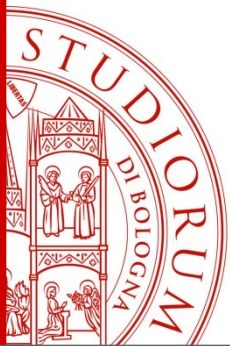
European Journal of Gastroenterology & Hepatology: June 2018 - Volume 30 - Issue 6 - p 621-625

doi: 10.1097/MEG.0000000000001102

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Schema Pylera per 10 giorni



Dopo colazione:

- Peptazol cpr 40 mg  1 cpr
- Pylera cpr  3 cpr

Dopo pranzo:

- Pylera cpr  3 cpr

Dopo cena:

- Peptazol cpr 40 mg  1 cpr
- Pylera cpr  3 cpr

Prima di coricarsi:

- Pylera cpr  3 cpr

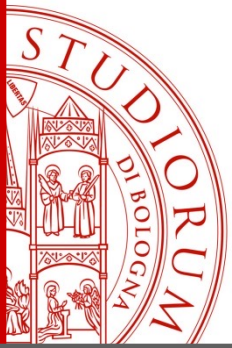
Dall'inizio della terapia e per **60 giorni**:

Controllo post terapia in data.....alle ore.....

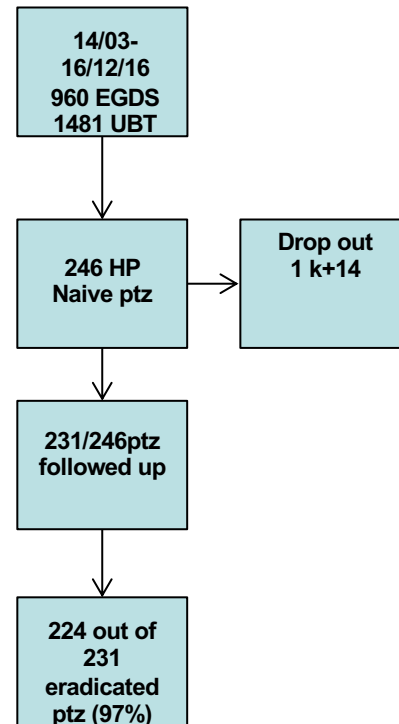
Con impegnativa per "Ricerca HP".

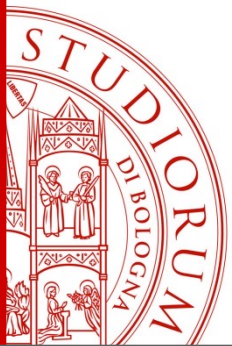
PRESENTARSI A DIGIUNO





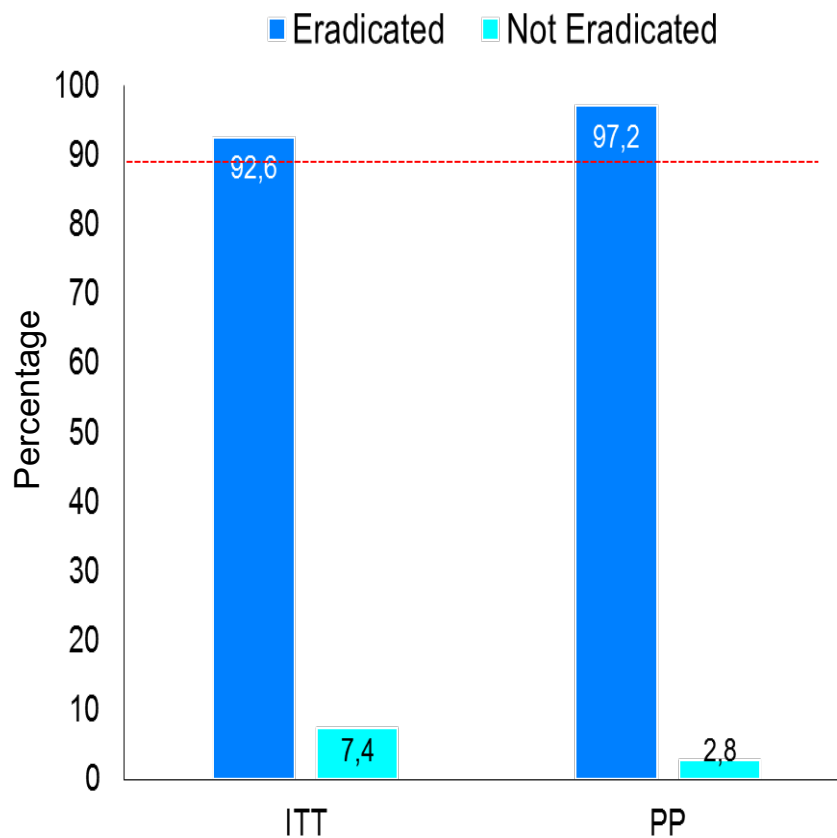
PYLERA Naïve





Overall Eradication Rate

PYLERA Naïve



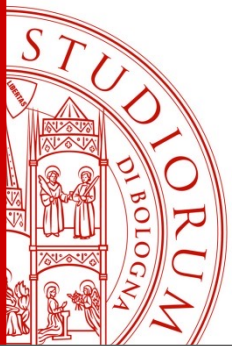
Dino Vaira

Fiorini et al Eur J Gastroenterol hepatol 2018 jun;30(6):621-25



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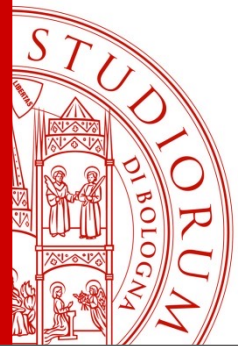
Therapies: duration, tablets

Therapy regimen	Duration (days)	Number of tablets
Sequential	10	50
Concomitant	14	112
Pylera	10	140

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Dio creò il medico...

ed il diavolo,

invidioso,

creò il collega...

Dino Vaira



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