THE FERRARA CONSENSUS REPORT THIRD ITALIAN GUIDELINES ON DIAGNOSIS AND TREATMENT OF HELICOBACTER PYLORI INFECTION

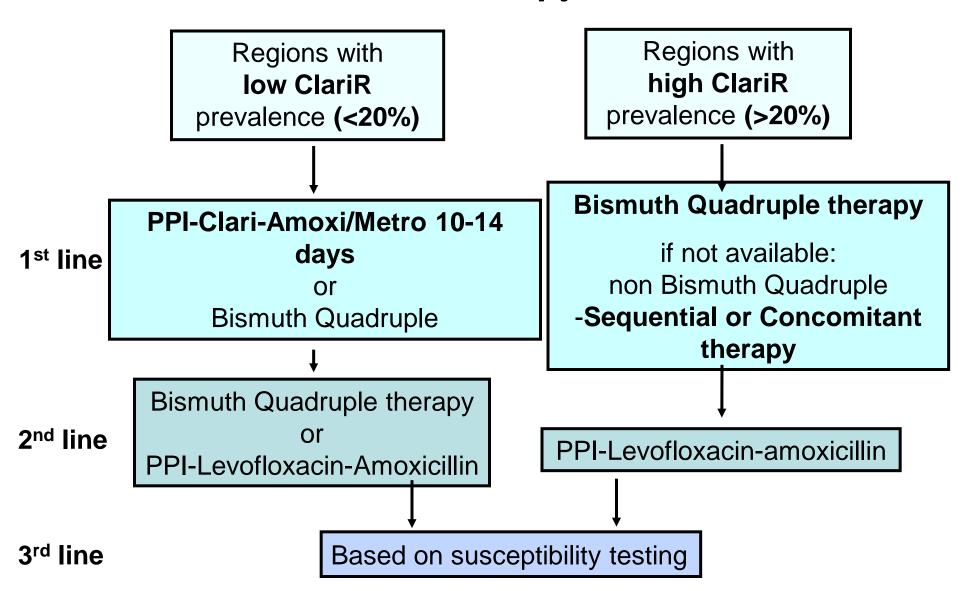
FERRARA 4-5 APRIL 2014

Diagnosi:

- · La coltura: come, quando e perchè.
- Quando è certa l'avvenuta eradicazione ? Dopo 1 mese, 6 mesi, 1 anno ?

Rocco Maurizio Zagari Università di Bologna

Maastricht/Florence IV: Treatment of *Helicobacter pylori* infection



Culture and antimicrobial susceptibility test

Guidelines



Management of *Helicobacter pylori* infection—the Maastricht IV/ Florence Consensus Report

Peter Malfertheiner, ¹ Francis Megraud, ² Colm A O'Morain, ³ John Atherton, ⁴ Anthony T R Axon, ⁵ Franco Bazzoli, ⁶ Gian Franco Gensini, ⁸ Javier P Gisbert, ⁹ David Y Graham, ¹⁰ Theodore Rokkas, ¹¹ Emad M El-Omar, ⁷ Ernst J Kuipers, ¹² The European Helicobacter Study Group (EHSG)

Statement 5: Culture and standard susceptibility testing should be considered in all regions before second line treatment if endoscopy is carried out for another reason and generally when a second-line treatment has failed.

Evidence level: 5 Grade of Recommendation: D

Statement 5: if standard susceptibility testing is not possible, molecular tests can be used to detect H. pylori and clarithromycin and/or fluoroquinolone resistance directly on gastric biopsies.

Evidence level: 1a

Grade of Recommendation: A

Susceptibility-based third-line

Pros and cons

- ✓ Tailored therapy
- ✓ Sensitivity: 73-90%
- ✓ High cost and not widely available
- Most community hospitals do not perform culture and susceptibility antimicrobial testing
- In vitro antibiotic susceptibility does not necessarily lead to eradication in vivo

Regimens available

Guidelines



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PPI-Clarithromycin triple therapies for 10-14 days

PPI-Clari-Amoxi or Metro (Tinidazole)

Sequential therapy for 10 days

All antibiotics : 5 day of PPI + Amoxi followed by 5 day of PPI + Claritro + Tinidazole

Concomitant therapy for 10 days

(non bismuth quadruple therapy)
All antibiotics togheter: PPI + amoxi+ Clari+ Metro (tinidazole)

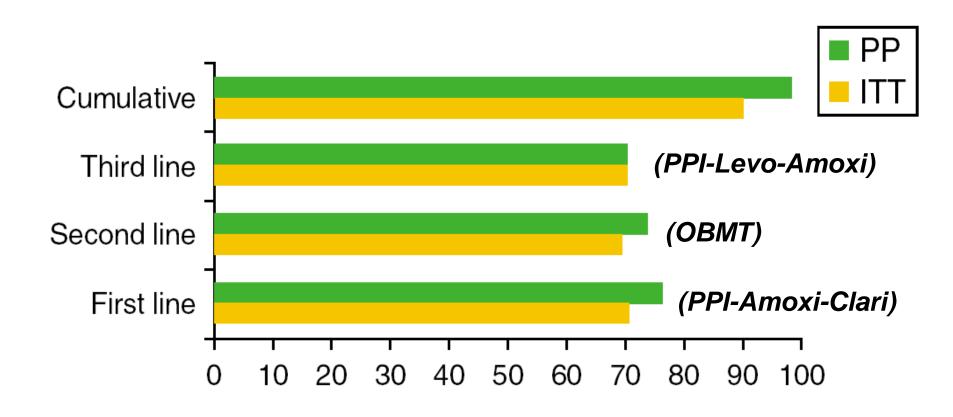
PPI-Levofloxacin triple therapy for 10 days

PPI Bismuth-based quadruple therapy for 10-14 days or -Rifabutin triple therapy for 10 days

H. Pylori resistance to antibiotics in Europe

Period	1998	2008-2009
Subjects	n. 1274	n. 1893
Antibiotic	% resistant	% resistant
Clarithromycin	9.9	17.5
Metronidazole	33.1	34.9
Levofloxacin	ND	14.1
Amoxicillin	0.8	0.7
Tetracycline	ND	0.9
Rifabutin	ND	1.1

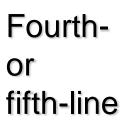
Cumulative *H.pylori* Eradication Rates in Clinical Practice by Adopting an <u>Empirical</u> Third-Line Regimen



Rifabutin in the treatment of refractory H.pylori infection

Third-line

Study or subgroup	Eradication rate	SE	Weight (%)	IV, Random, 95% CI	IV, Rando	m, 95% CI
Beales 2001 2tx	0.6 0.15	491933	6.3	0.60 [0.30, 0.90]		
Bock 2000 2tx	0.8 0.17	388544	5.5	0.80 [0.45, 1.15]		
Gisbert 2003 2tx	0.79 0.10	385771	8.1	0.79 [0.58, 1.00]		
Gisbert 2006 2tx	0.45 0.11	124298	8.0	0.45 [0.23, 0.67]		
Gisbert 2008 2tx	0.55 0.06	966305	9.8	0.55 [0.41, 0.69]		
Gonzalez-Carro 2007 2tx	0.61 0.05	085145	10.5	0.61 [0.51, 0.71]		
Miehlke 2008 2tx	0.9 0.04	160251	10.8	0.90 [0.82, 0.98]		-0-
Perri 2000 2tx	0.8	0.08	9.4	0.80 [0.64, 0.96]		
Qasim 2005 2tx	0.38 0.08	324309	9.2	0.38 [0.22, 0.54]		-
Van der Poorten 2007 2tx	0.64	0.12	7.7	0.64 [0.40, 0.88]		
Van Zanten 2010 2tx	0.5 0.15	311388	6.2	0.50 [0.19, 0.81]		-
Zullo 2010 2tx	0.85 0.09	903379	8.6	0.85 [0.66, 1.04]		
Total (95% CI)			100.0	0.66 [0.55, 0.77]		•
Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 57$. Test for overall effect: $Z = 11.42$		0001);	^{/2} = 81%	_	-1 -0.5	0.5 1



Study or subgroup	Eradication rate	e SE	Weight (%) IV, Fixed, 95% CI	IV, Fixed	l, 95% CI
Bock 2000 3tx	1	0		Not estimable		
Canducci 2001 ≥3tx	0.7	0.14491377	10.2	0.70 [0.42, 0.98]		
Gisbert 2008 3tx	0.71	0.17150593	7.3	0.71 [0.37, 1.05]		
Miehlke 2008 3tx	0.69	0.11217109	17.0	0.69 [0.47, 0.91]		
Miehlke 2008 ≥4tx	0.89	0.09894443	21.8	0.89 [0.70, 1.08]		
Perri 2000 ≥3tx	0.56	0.12409674	13.9	0.56 [0.32, 0.80]		
Van der Poorten 2007 ≥3tx	0.62	0.08717798	28.1	0.62 [0.45, 0.79]		
Van Zanten 2010 3tx	0.5	0.35355339	1.7	0.50 [-0.19, 1.19]	_	-
Total (95% CI)			100.0	0.70 [0.60, 0.79]		•
Heterogeneity: $\chi^2 = 6.12$, df = 6 ($P = 0.41$); $I^2 = 2\%$ Test for overall effect: $Z = 15.03$ ($P < 0.00001$)						0.5 1

Gisbert and Calvet, APT 2012

My point of view...

- ✓ Colture and standard susceptibility testing may be generally avoided in clinical practice.
- ✓ By adopting first-, second- and third line empirical regimens a high cumulative *H.pylori* eradication rate can be achieved.

- ✓ Colture and standard susceptibility testing are essential for local national resistance survey with appropriate sample sizes that are representative of the general population.
- ✓ Clinicians should take an antibiotic history before prescribing clarithromycin, metronidazole or levofloxacin for H. pylori.