



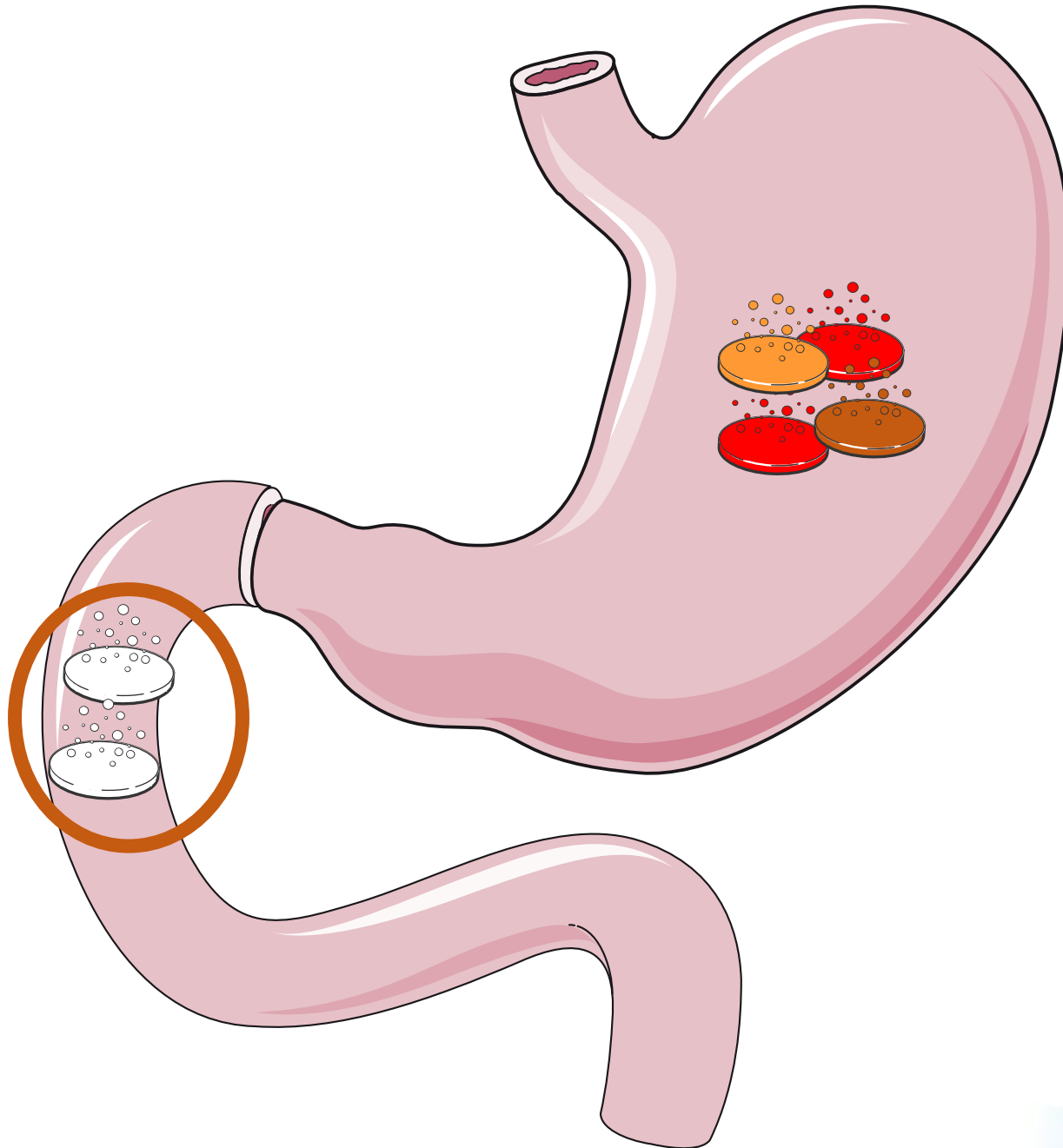
Papel de los IBPs De LI en la Enfermedad Acido Péptica

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Colombia

Profesor Titular de
Medicina
Universidad Nacional
de Colombia

Past president, Asociación
Colombiana de Endoscopia
Digestiva y Asociación
Colombiana de
Gastroenterología





Liberación Inmediata

“Enfermedad Ácido-péptica”

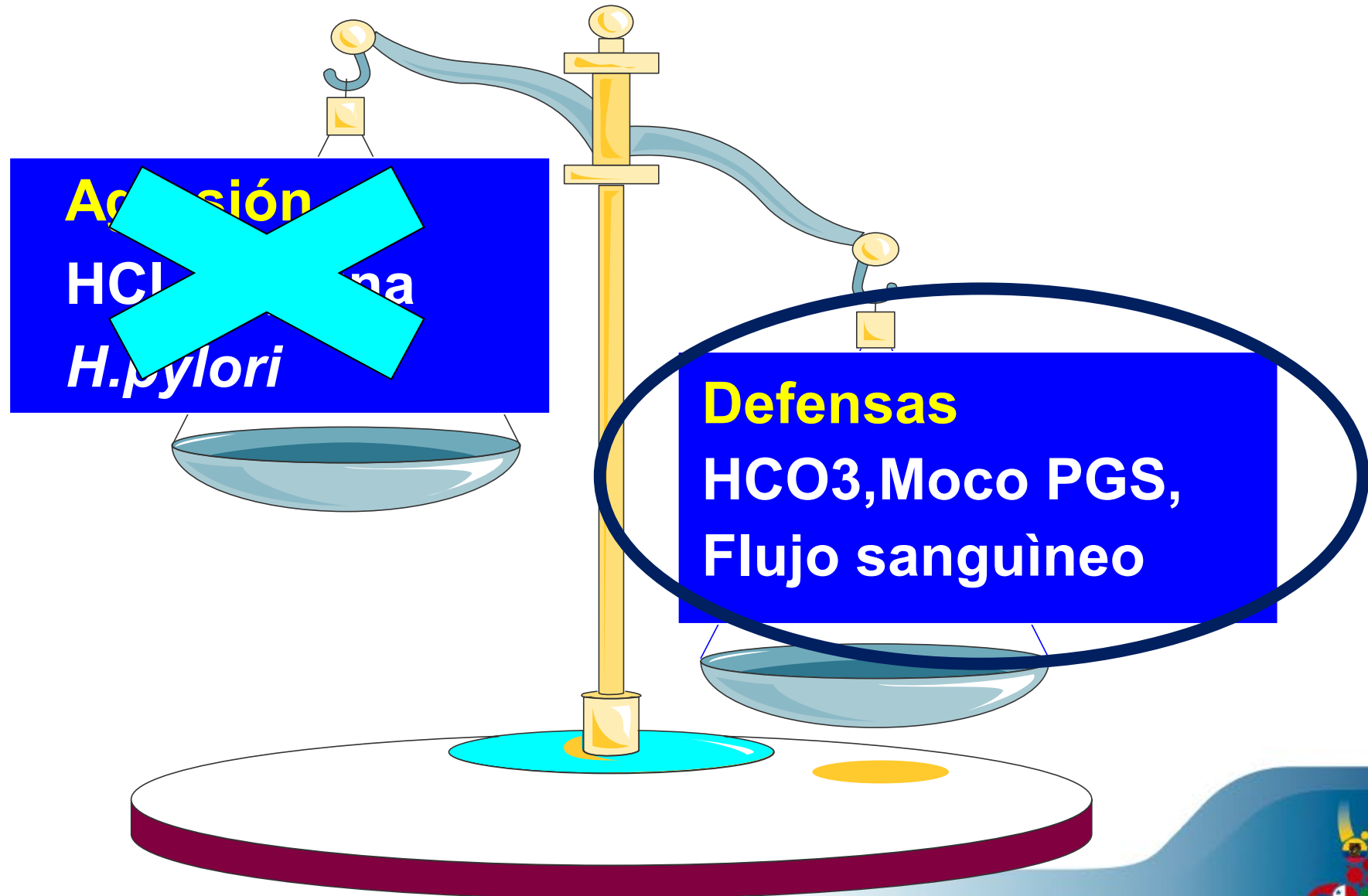


**No es un diagnóstico Específico,
Incluye Muchas enfermedades**



**Originadas por alteraciones
Del ácido y la pepsina**

Enfermedad “acido péptica”



~~Anticongulantes~~

~~Proton~~

~~Sucra~~

~~Prostaglandinas~~

~~Anticongulantes~~

Enfermedad
Acido péptica
HCl

~~Anti-irritina~~

Anti-H2
~~Proton~~
Famotidina
Roxatidina

N-Nitrosodimetil amina 400 veces
Carcinogenesis, 2016;37:625–634
FDA detuvo fabricación 2019

Detienen fabricación de Ranitidina por sustancia cancerígena

La FDA anunció que se han encontrado niveles bajos del químico cancerígeno NDMA



Oral intake of ranitidine increases urinary excretion of N-nitrosodimethylamine

Teng Zeng^{1,2,3} and William A. Mitch^{2,3,*}

Abstract

The H₂-receptor antagonist, ranitidine, is among the most widely used pharmaceuticals to treat gastroesophageal reflux disease and peptic ulcers. While previous studies have demonstrated that amines can form N-nitrosamines when exposed to nitrite at stomach-relevant pH, N-nitrosamine formation from ranitidine, an amine-based pharmaceutical, has not been demonstrated under these conditions. In this work, we confirmed the production of N-nitrosodimethylamine (NDMA), a potent carcinogen, by nitrosation of ranitidine under stomach-relevant pH conditions *in vitro*. We also evaluated the urinary NDMA excretion attributable to ingestion of clinically used ranitidine doses. Urine samples collected from five female and five male, healthy adult volunteers over 24-h periods before and after consumption of 150 mg ranitidine were analyzed for residual ranitidine, ranitidine metabolites, NDMA, total N-nitrosamines and dimethylamine. Following ranitidine intake, the urinary NDMA excreted over 24h increased 400-folds from 110 to 47 600 ng, while total N-nitrosamines increased 5-folds. NDMA excretion rates after ranitidine intake equaled or exceeded those observed previously in patients with schistosomiasis, a disease wherein N-nitrosamines are implicated as the etiological agents for bladder cancer. Due to metabolism within the body, urinary NDMA measurements represent a lower-bound estimate of systemic NDMA exposure. Our results suggest a need to evaluate the risks attributable to NDMA associated with chronic consumption of ranitidine, and to identify alternative treatments that minimize exposure to N-nitrosamines.

400 veces

Carcinogenesis, 2016;37:625–634

Exposure to Ranitidine and Risk of Bladder Cancer: A Nested Case-Control Study

Chris R. Cardwell, PhD¹, Ronald D. McDowell, PhD¹, Carmel M. Hughes, PhD², Blánaid Hicks, PhD¹ and Peter Murchie, MD, PhD³

Ranitidine and bladder cancer risk: A case-control study

Outcome

Bladder cancer cases ($n=3260$) and, population-based controls ($n=14037$) were identified from General Practice records.



Exposure

Ranitidine use was identified from prescription records.



Conclusion

Ranitidine was associated with a 22% increase in bladder cancer risk, after controlling for confounders. Future studies are required to replicate this finding.



➤ 3 años OR 1.43 (IC 95% 1.05–1.94).

Supresión àcido clorhidrico

IBP



Estàndar de oro

Mossner J, Dtsch Arztebl Int 2016;113:477-83

Targownik L, Am J Gastroenterol 2018;113:519-28

**Primeros cinco más vendidos
USA, 2009:7 billones
Mundo, 13 billones**

**Más prescrito en
Gastroenterología**

IBP

**“Medicamentos
Esenciales” OMS**

**Eficacia
Demostrada**

**Mossner J, Dtsch Arztebl Int 2016;113:477-83
Targownik L, Am J Gastroenterol 2018;113:519-28**

Indicaciones correctas de los IBPs



**Por períodos
Cortos <12 semanas**

Erradicación *H.pylori*
Úlceras pépticas
Úlcera péptica sangrante
Profilaxis úlceras estrés
Dispepsia funcional (“Gastritis”)
Esofagitis eosinofílica sin respuesta



**Por períodos
Indefinidos**

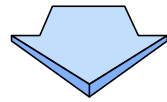
Esofagitis C y D
Esófago de Barrett
Úlcera péptica idiopática
Profilaxis AINES
Profilaxis antiplaquetarios
Esofagitis eosinofílica (+)
Fibrosis Pulmonar
Zollinger Ellison

Herszényi L, Dig Dis 2020;38:104-11

Targownik LE, Gastroenterology 2022;162:1334-42

63% Wang J, Hepatol Int. 2020; 14:385-98

IBP no indicados



Pancreatitis aguda o crónica
Cirrosis Descompensada
Hospitalizados en sala general
“Polimedicados”
Reflujo Faringo-laríngeo

Herszényi L, Dig Dis 2020;38:104-11

Targownik LE, Gastroenterology 2022;162:1334-42

Use of proton pump inhibitors to treat persistent throat symptoms: multicentre, double blind, randomised, placebo controlled trial

James O'Hara,^{1,2} Deborah D Stocken,³ Gillian C Watson,⁴ Tony Fouweather,⁵ Julian McGlashan,⁶ Kenneth MacKenzie,⁷ Paul Carding,⁸ Yakubu Karagama,⁹ Ruth Wood,⁴ Janet A Wilson¹⁰

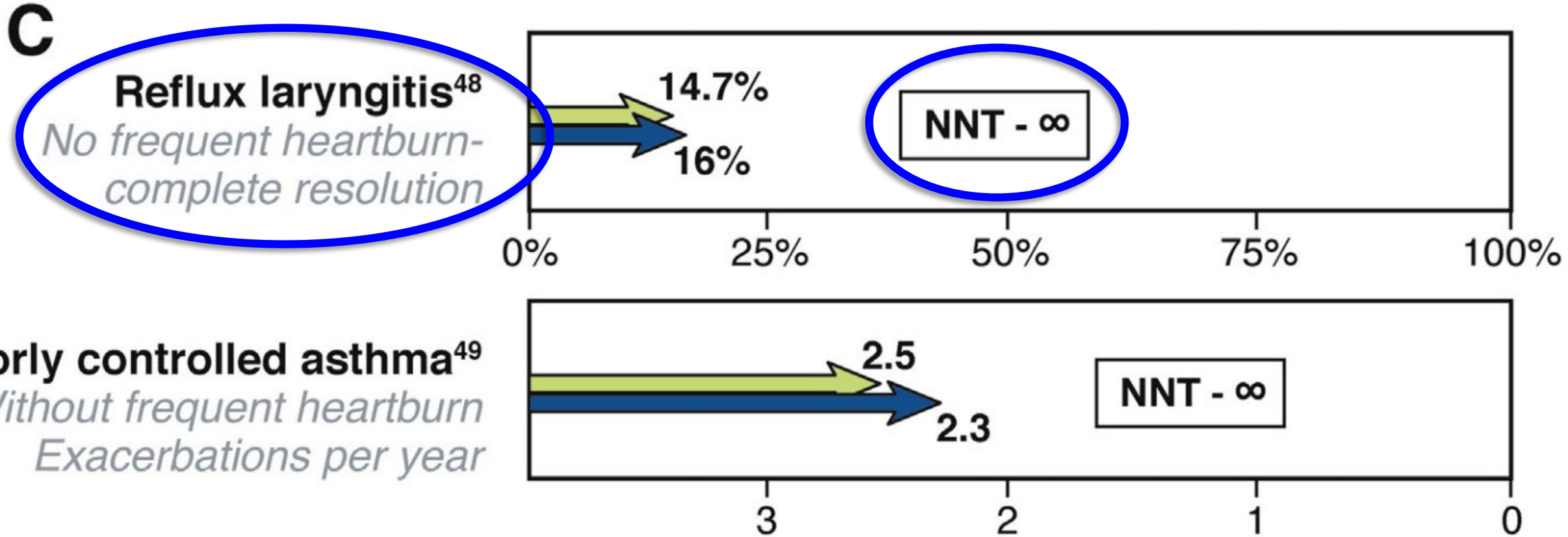
O'Hara J, BMJ 2021;372:4903.

Table 2 | Questionnaire outcome scores for compliant intention-to-treat group

| Questionnaires and intervention | No in group | Mean score at follow-up (95% CI) | | |
|---------------------------------|-------------|----------------------------------|---------------------|---------------------|
| | | Baseline | 16 weeks* | 12 months |
| RSI*: | | | | |
| Lansoprazole | 102 | 22.0 (20.4 to 23.6) | 17.4 (15.5 to 19.4) | 16.0 (13.6 to 18.4) |
| Placebo | 118 | 21.7 (20.5 to 23.0) | 15.6 (13.8 to 17.3) | 13.6 (11.7 to 15.5) |
| Differencet | | 0.3 (-1.7 to 2.3) | 1.8 (-0.8 to 4.4) | 2.4 (-0.6 to 5.4) |
| RSI-HB: | | | | |
| Lansoprazole | 102 | 20.3 (18.8 to 21.7) | 16.3 (14.5 to 18.1) | 14.7 (12.4 to 16.9) |
| Placebo | 118 | 19.8 (18.6 to 21.0) | 13.9 (12.2 to 15.5) | 11.9 (10.1 to 13.7) |
| Differencet | | 0.5 (-1.4 to 2.4) | 2.4 (-0.0 to 4.8) | 2.8 (0.5 to 5.1) |
| CReSS: | | | | |
| Lansoprazole | 102 | 50.3 (44.9 to 55.7) | 38.9 (33.4 to 44.3) | 36.6 (29.8 to 43.5) |
| Placebo | 118 | 51.1 (46.4 to 55.8) | 34.7 (29.6 to 39.9) | 31.8 (26.6 to 36.9) |
| Differencet | | -0.8 (-7.9 to 6.3) | 4.2 (-3.2 to 11.6) | 4.8 (-3.5 to 13.1) |
| LPR-HRQL: | | | | |
| Lansoprazole | 102 | 28.9 (24.5 to 33.3) | 20.5 (16.1 to 25.0) | 18.8 (13.7 to 23.8) |
| Placebo | 118 | 26.5 (22.5 to 30.5) | 17.1 (13.3 to 21.0) | 13.9 (10.0 to 17.8) |
| Differencet | | 2.4 (-3.5 to 8.3) | 3.4 (-2.4 to 9.2) | 4.9 (-1.3 to 11.1) |


O'Hara J, BMJ 2021;372:4903.

Síntomas extraesofágicos

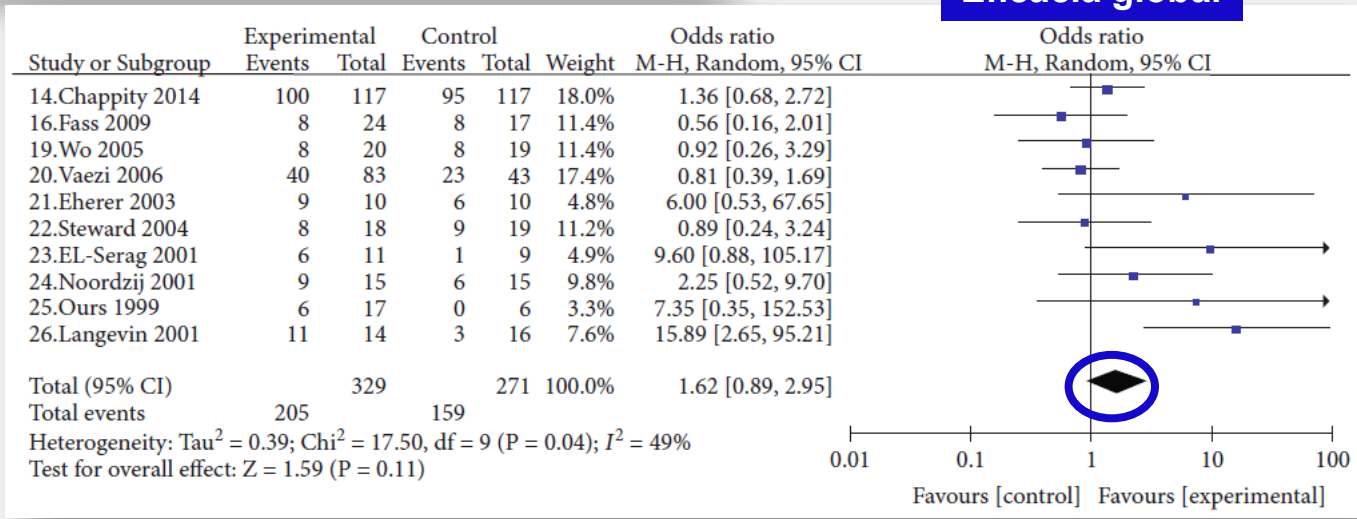


Katzka DA, Clin Gastroenterol Hepatol 2020;18:767-76

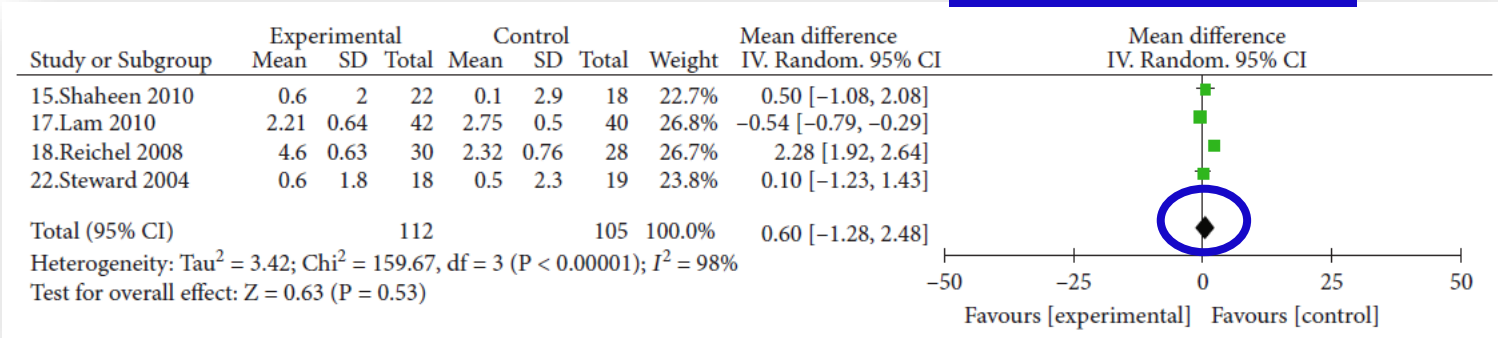
Meta-analysis of Proton Pump Inhibitors in the Treatment of Pharyngeal Reflux Disease

Xiulin Jin, Xufeng Zhou, Zongxian Fan, Yingchun Qin, and Junjie Zhan 

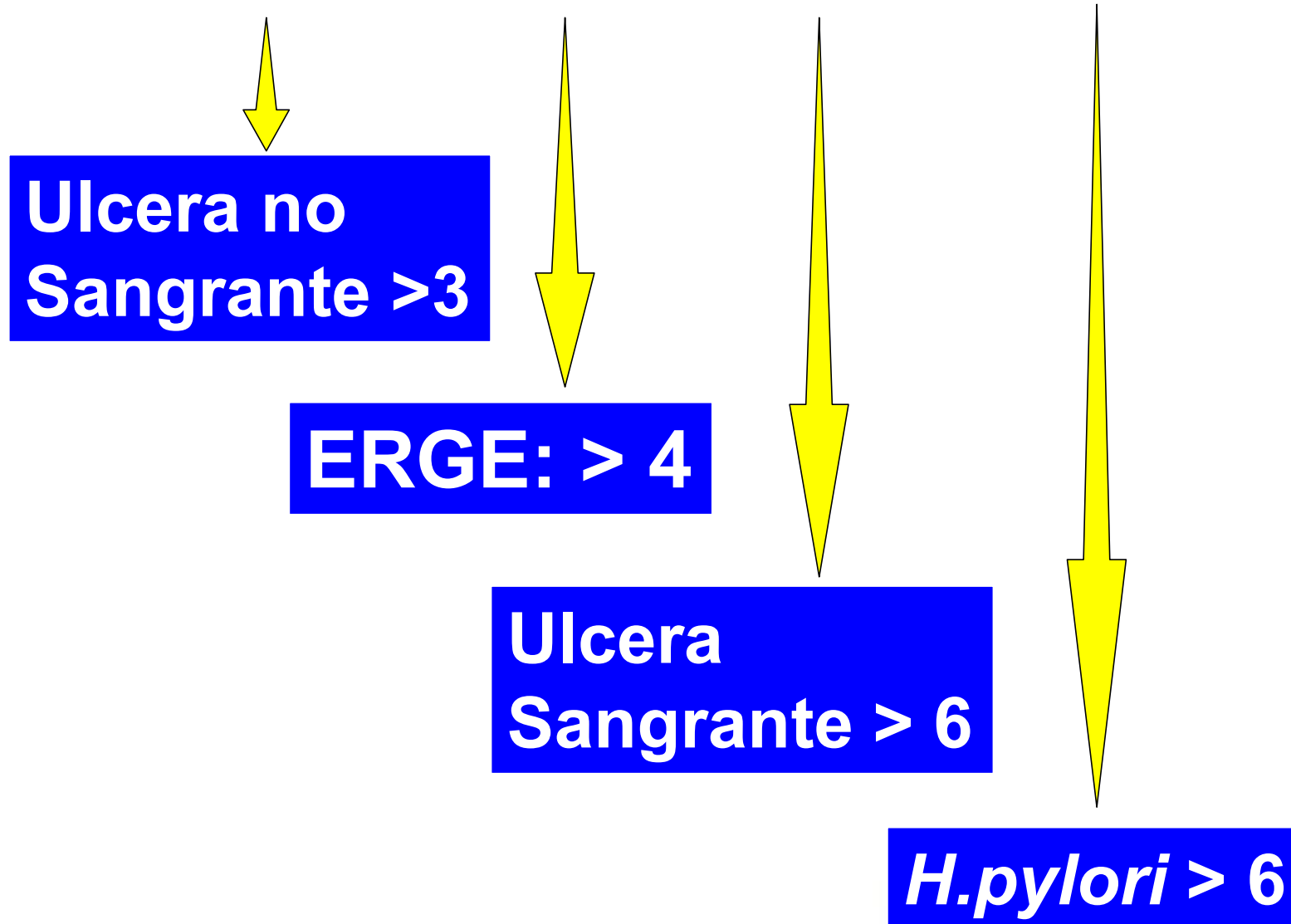
Eficacia global

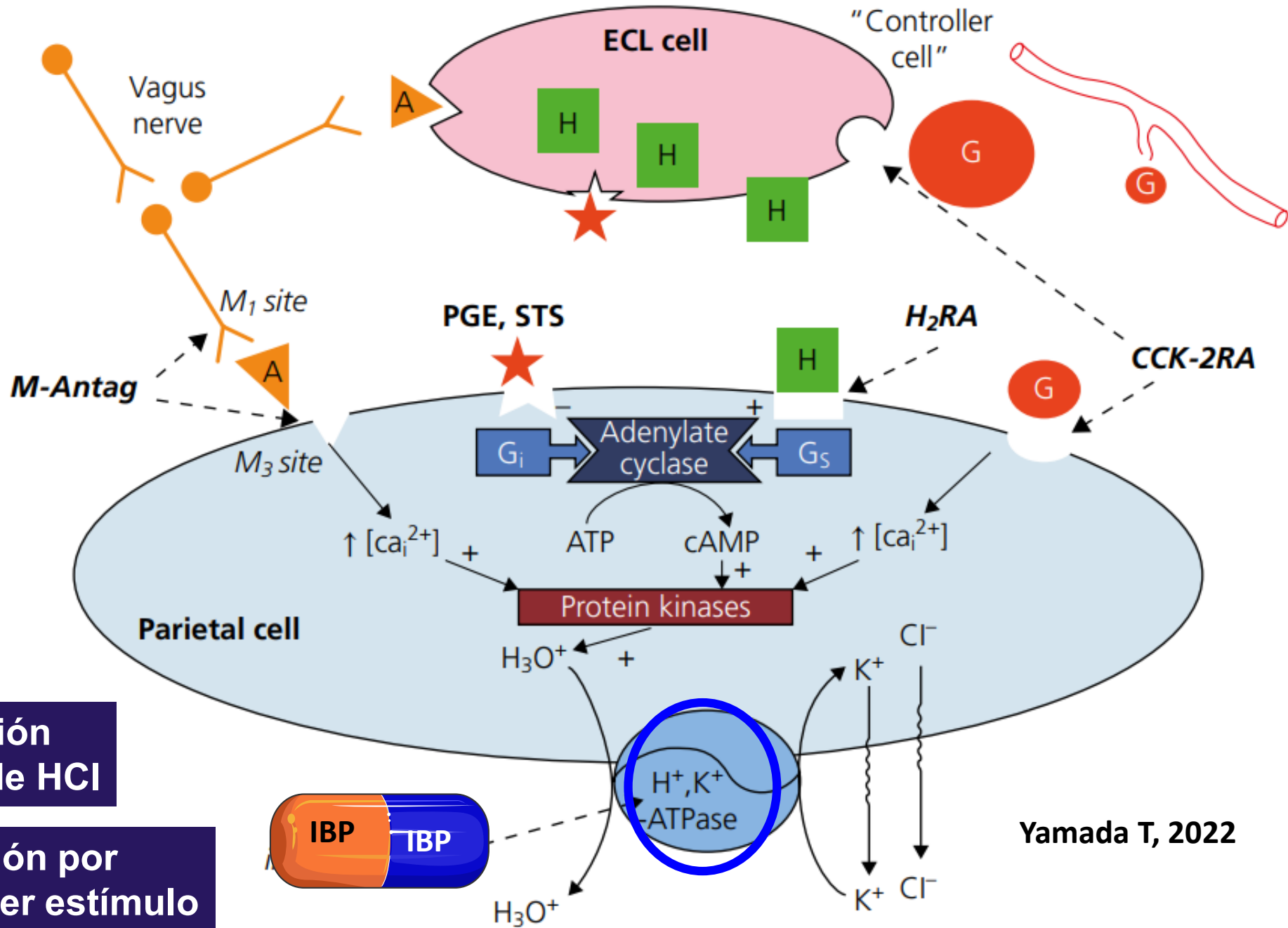


Puntaje sintomas



Para cada enfermedad un nivel de pH





Secreción Basal de HCl

Secreción por cualquier estímulo

Yamada T, 2022

IBP





Efectos sistémicos anti inflamatorios

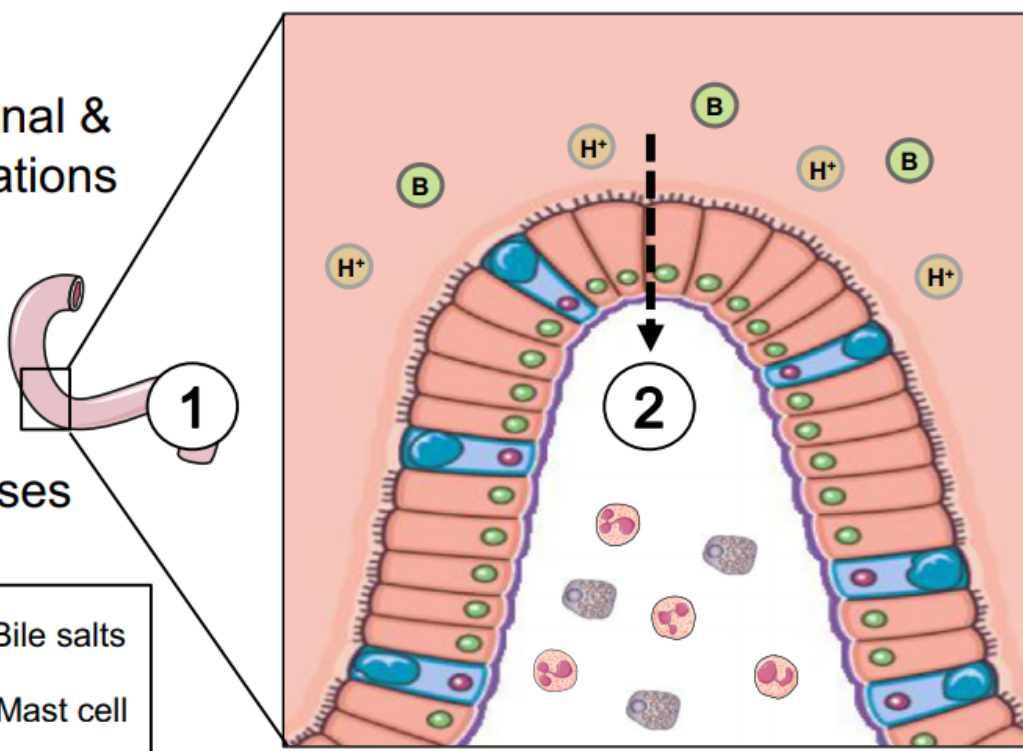
IBP y Dispepsia Funcional

Off-PPI:

duodenal luminal & mucosal alterations

systemic & stress responses

 Acid (pH)  Bile salts
 Eosinophil  Mast cell

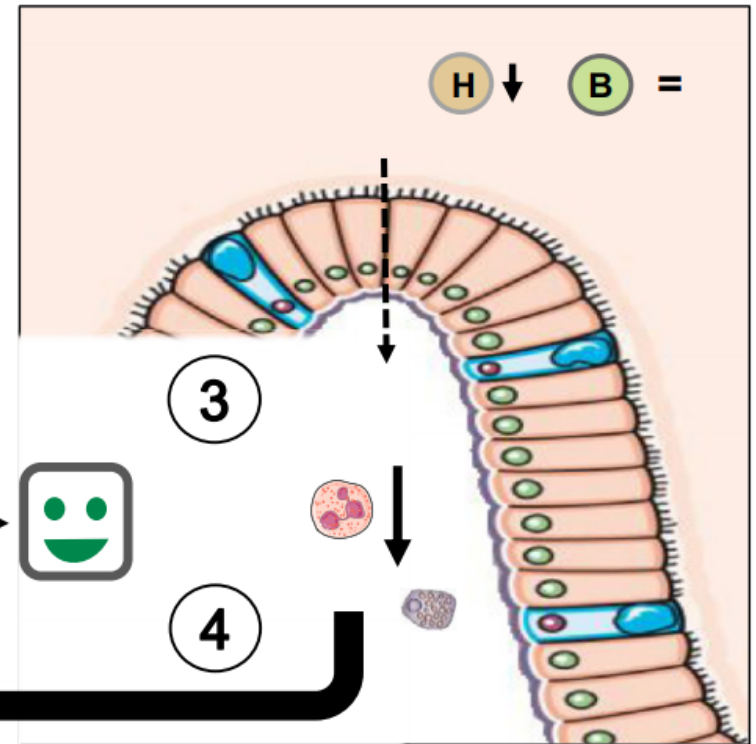


On-PPI:

↓ symptoms

= stress

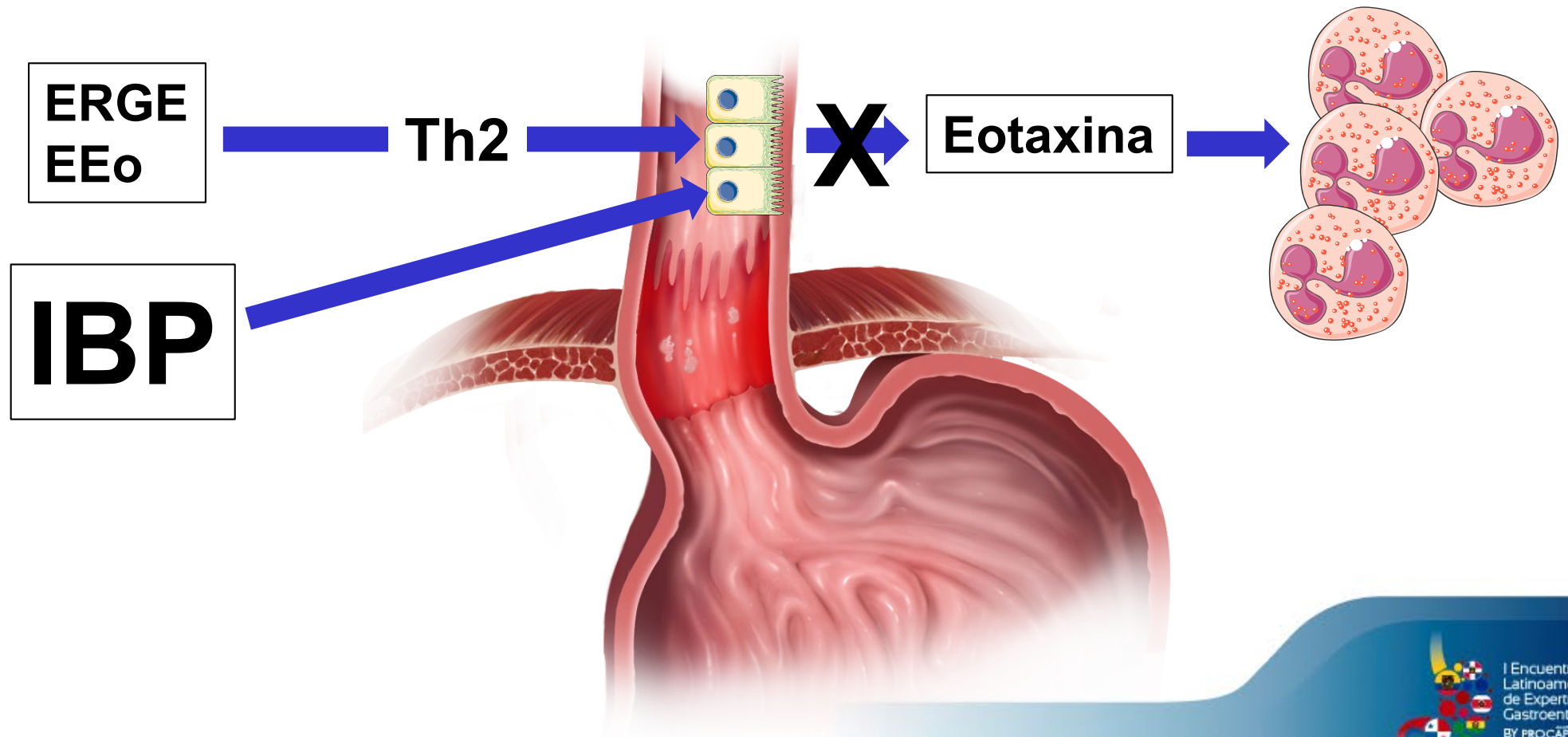
↓ cortisol



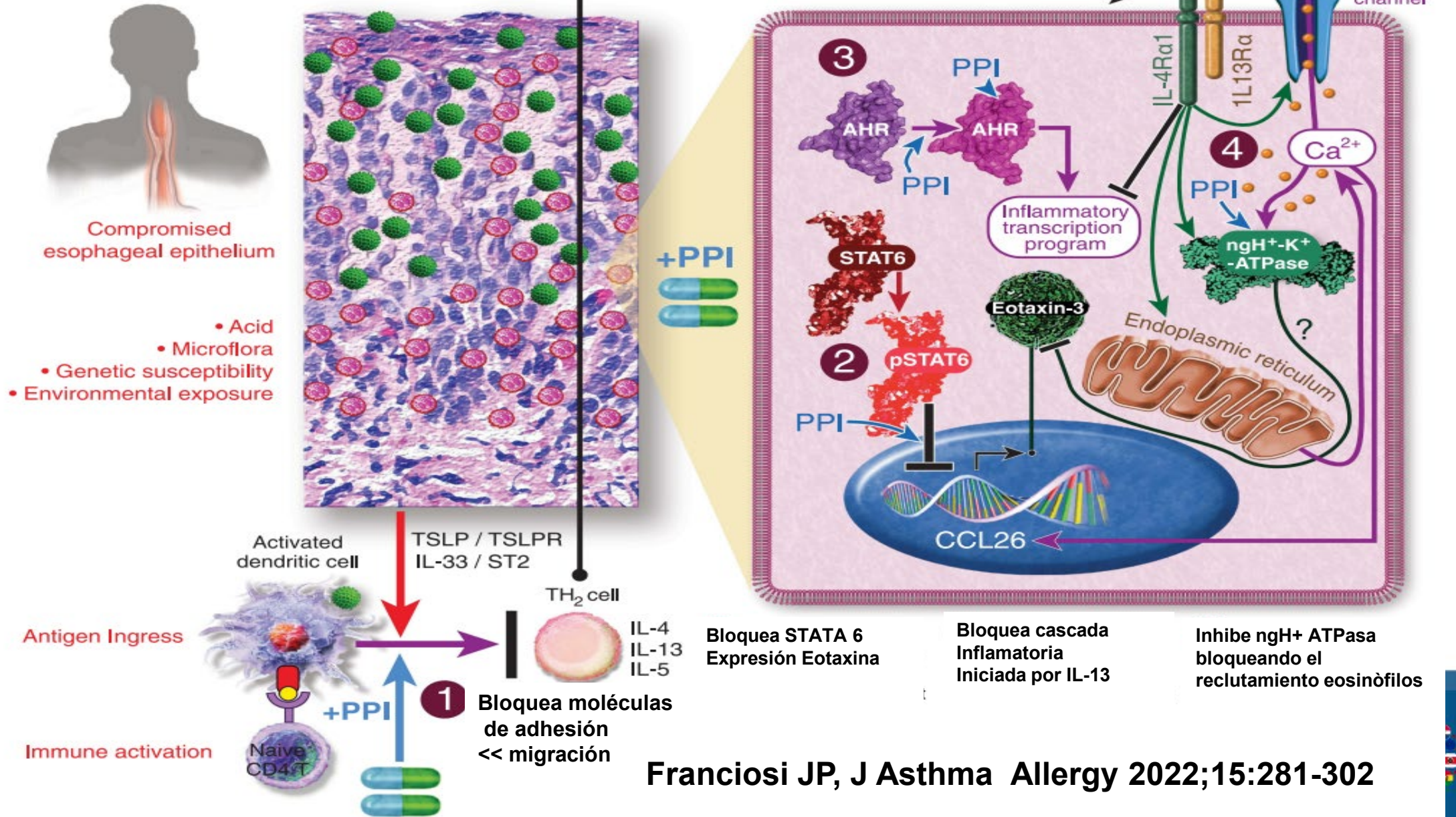
Wauters L, Gastroenterology 2021;160:1521-31

Omeprazole blocks eotaxin-3 expression by oesophageal squamous cells from patients with eosinophilic oesophagitis and GORD

Etaire Cheng,¹ Xi Zhang,² Xiaofang Huo,² Chunhua Yu,² Qiuyang Zhang,² David H Wang,² Stuart Jon Spechler,² Rhonda F Souza²



B Anti-Inflammatory Mechanisms



Franciosi JP, J Asthma Allergy 2022;15:281-302

Esofagitis eosinofílica

1990

2000

IBP Tratamiento EEO
Remisión síntomas 61%
Remisión Histología 51%

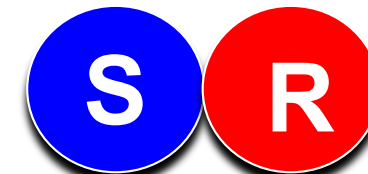
Reflujo con
Eosinofilia

Respuesta +
Eosinofilia
Esofàgica VS EEO

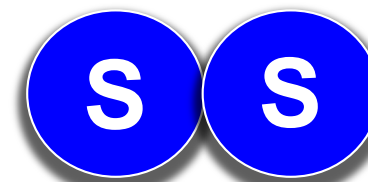
Franciosi JP, J Asthma Allergy 2022;15 281-302

Lucendo AJ, Clin Gastroenterol Hepatol 2016;14:13-22

Omeprazol 1988

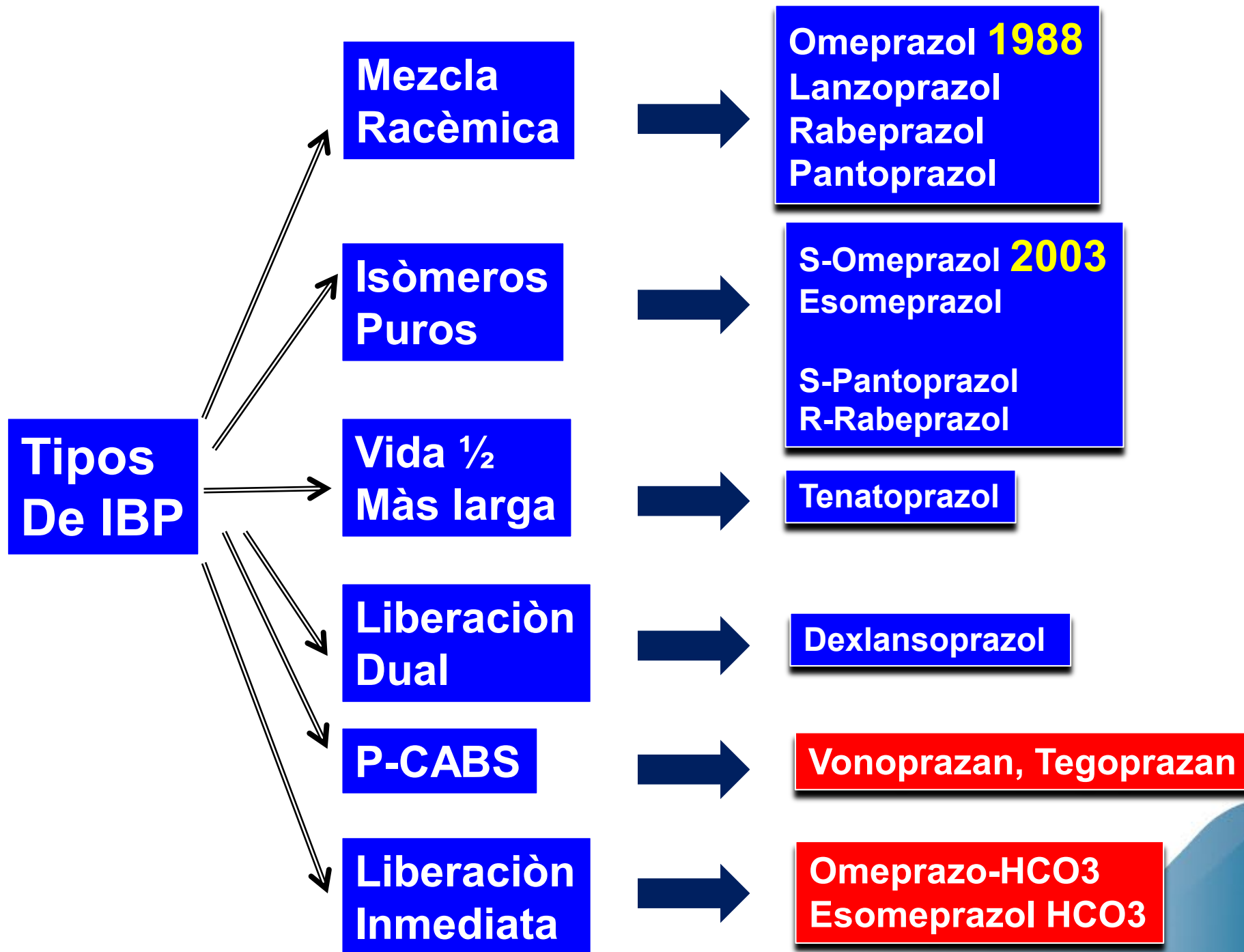


Esomeprazol 2003



**Isómero S
> Vida media**

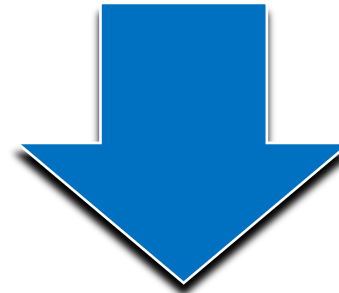
Scarpignato C, Curr Opin Pharmacol 2008;8:677-84



IBP No son iguales



Potencia




Farmacognètica

Potencia de los IBPs comparados con omeprazol

| Diferentes IBPs | Omeprazol mg |
|-------------------|------------------------|
| Rabeprazol 20 mg | 36 mg |
| Esomeprazol 20 mg | 32 mg <u>1.6 veces</u> |
| Omeprazol 20 mg | 20 mg |
| Lansoprazol 20 mg | 18 mg |
| Pantoprazol 20 mg | |

Más potente



Menos potente

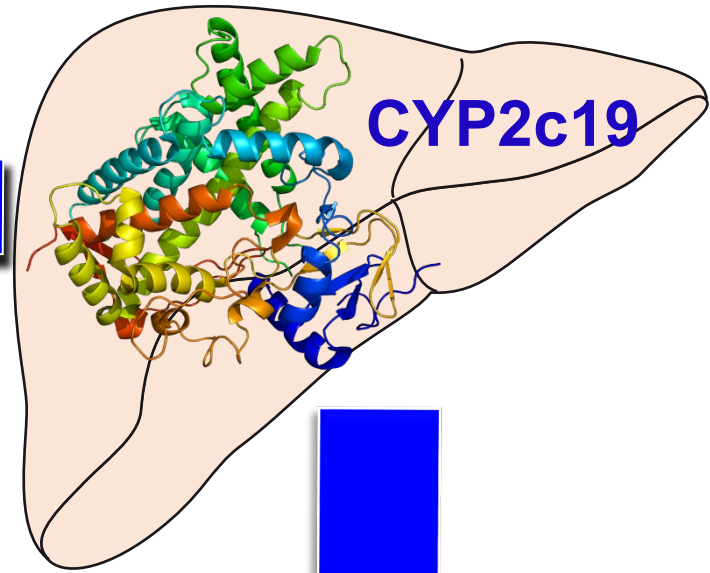
Graham DY, Clin Gastroenterol Hepatol. 2018;16:800-8

Farmacogenética

Primera Generación

Omeprazol
Lansoprazol
Pantoprazol

Dependientes

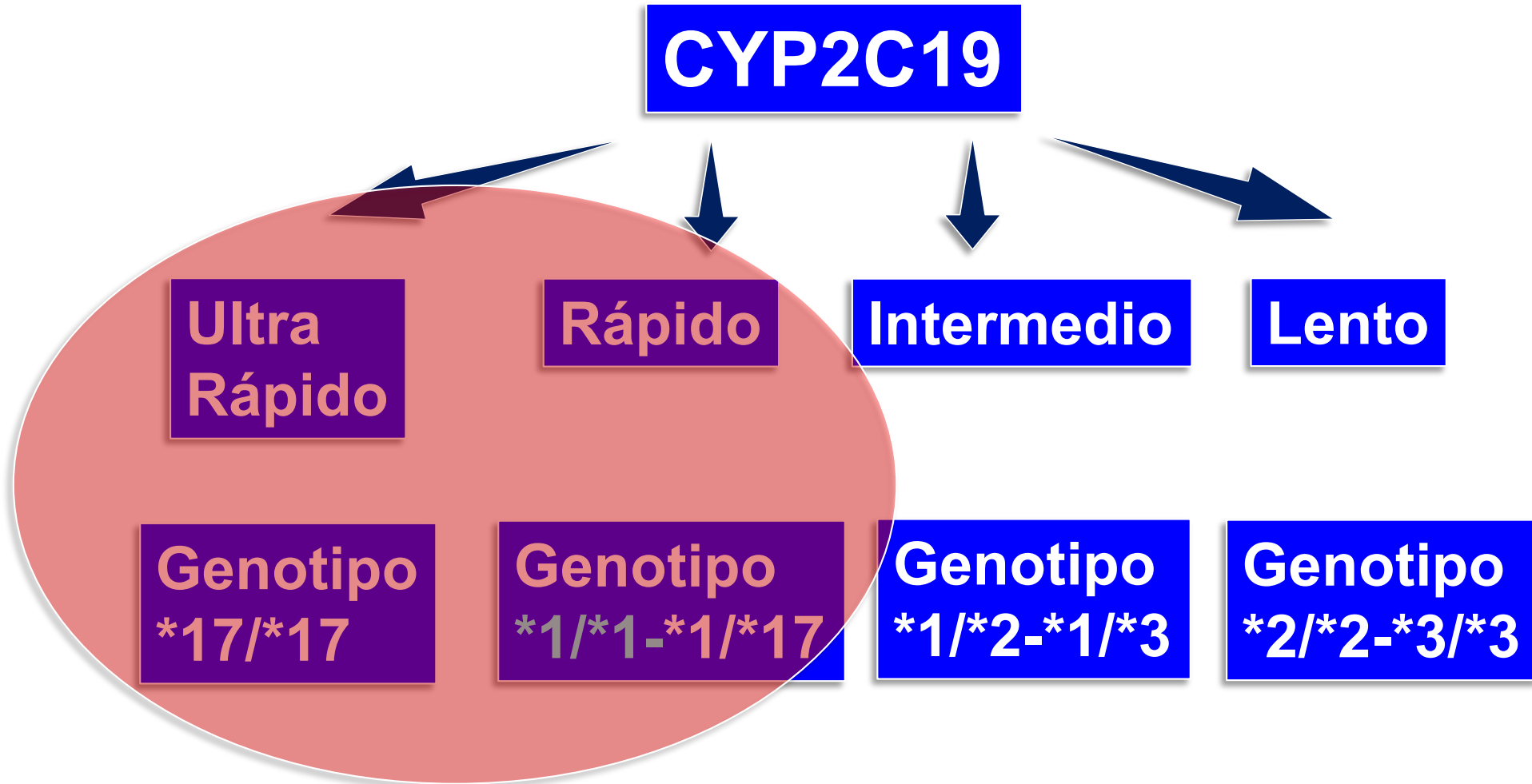


Menos dependientes

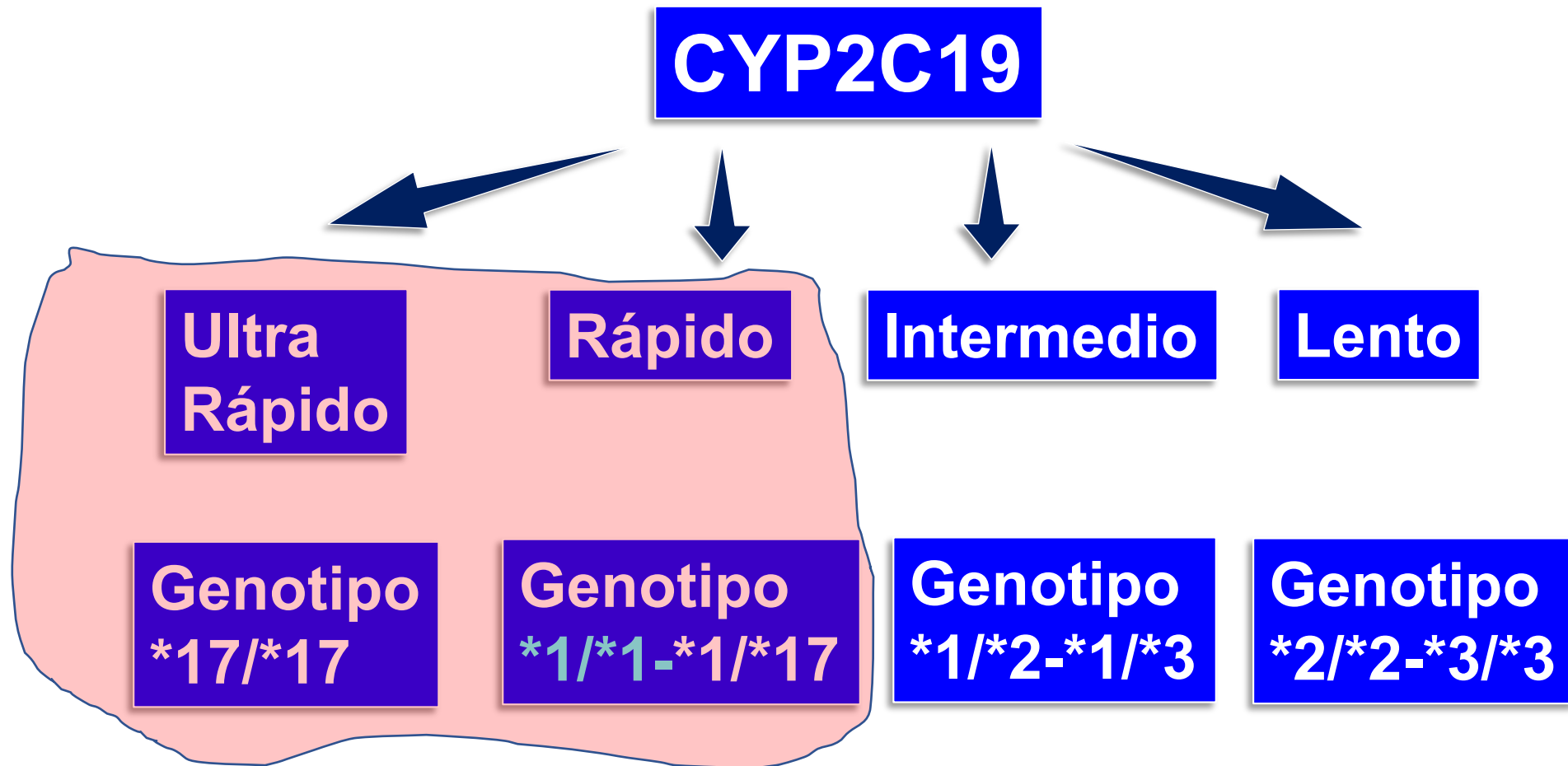
Segunda Generación

Esomeprazol
Rabeprazol

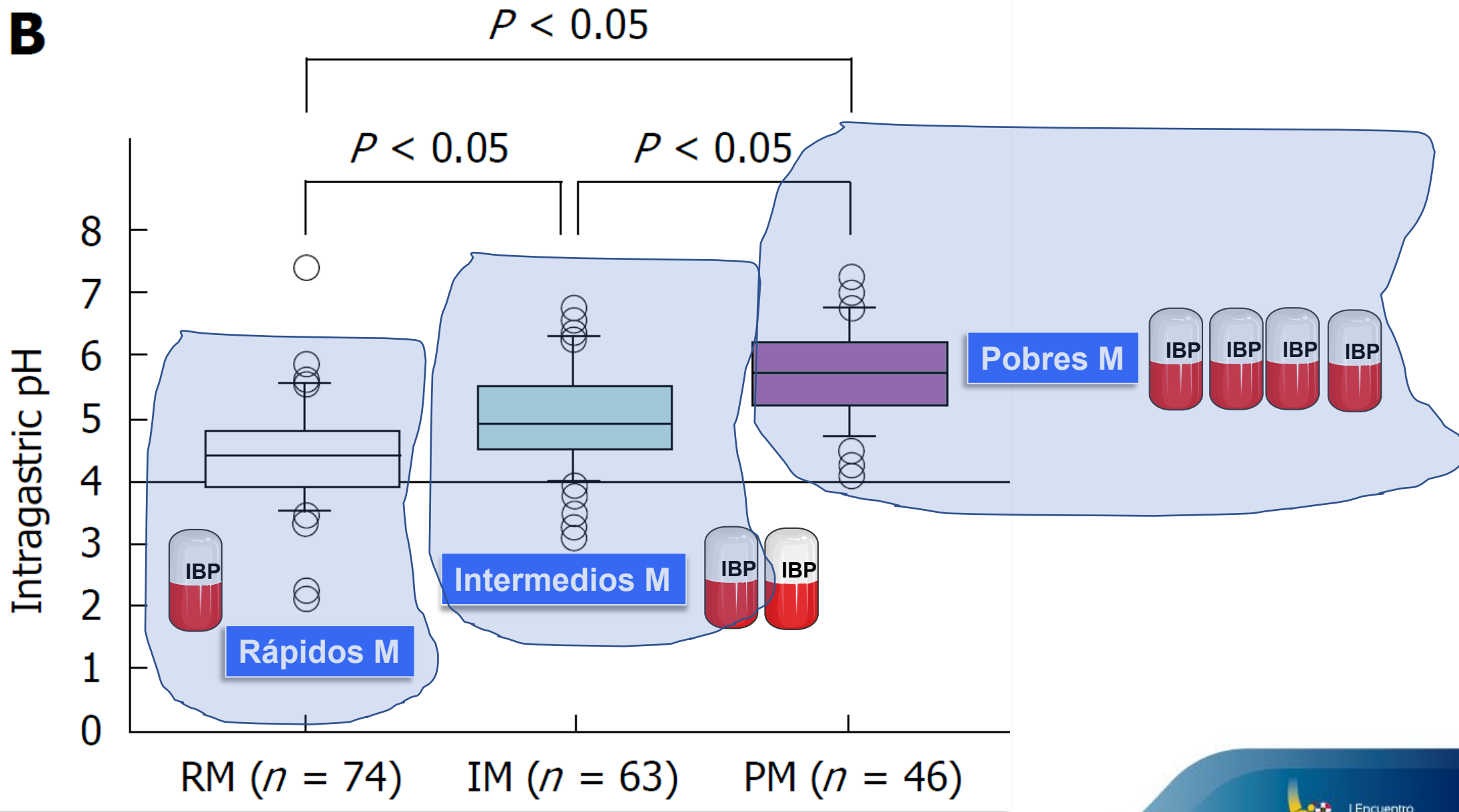
El Rouby N, Exp Opin Drug Metab Toxicol 2018;14:447-60
Hagymási K, Pharmacogenomics 2011;12:873-88



Arevalo A, Otero W, Trespalacios AA, et al. PLoS One 2021;16:e0245401



Arevalo A, Otero W, Trespacios AA, et al. PLoS One 2021;16:e0245401

B



Cyp2C19

**Rápido,
Ultrarrápido
80-84%**

***Esomeprazol* Rabeprazol
menos Influidos por el CYP
70% vs 90% OME**

Isaza C, BMC Clin Pharmacol. 2007;7:6.

Arévalo A, Tresplacios A, Otero W, Helicobacter 2019;24:e12574

Arevalo A, Otero W PLoS One. 2021;16:e0245401

Review article

A review of medical therapy for proton pump inhibitor nonresponsive gastroesophageal reflux disease

L. Hillman,¹ R. Yadlapati,² A. J. Thuluvath,³ M. A. Berendsen,⁴ J. E. Pandolfino²

SUMMARY. Up to 40% of patients report persistent gastroesophageal reflux disease (GERD) symptoms despite proton pump inhibitor (PPI) therapy. This review outlines the evidence for medical therapy for PPI nonresponsive GERD. A literature search for GERD therapies from 2005 to 2015 in PubMed, EMBASE, Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews identified 2928 unique citations. Of those, 40 unique articles specific to the impact of PPI metabolizer genotype on PPI response and the use adjunctive medical therapies were identified. Thirteen articles reported impacts on CYP genotypes on PPI metabolism demonstrating lower endoscopic healing rates in extensive metabolizers; however, outcomes across genotypes were more uniform with more CYP independent PPIs rabeprazole and esomeprazole. Twenty-seven publications on 11 adjunctive medications showed mixed results for adjunctive therapies including nocturnal histamine-2 receptor antagonists, promotility agents, transient lower esophageal sphincter relaxation inhibitors, and mucosal protective agents. Utilizing PPI metabolizer genotype or switching to a CYP2C19 independent PPI is a simple and conservative measure that may be useful in the setting of incomplete acid suppression. The use of adjunctive medications can be considered particularly when the physiologic mechanism for PPI nonresponse is suspected. Future studies using adjunctive medications with improved study design and patient enrollment are needed to better delineate medical management options before proceeding to antireflux interventions.

Esomeprazol/Rabeprazol

Erradicación de *H.pylori*

Host Genetic Determinants Associated With *Helicobacter pylori* Eradication Treatment Failure: A Systematic Review and Meta-analysis

Shailja C. Shah,^{1,2,3,4} Adam Tepler,⁵ Cecilia P. Chung,^{6,7} Giovanni Suarez,³ Richard M. Peek Jr,³ Adriana Hung,^{8,9} Christianne Roumie,^{8,10} and Neeraj Narula¹¹

57 estudios

Pacífico Asiático (Japón 24, Taiwan 6, Korea 5, Tailandia 1)

Europa (Alemania 3, Polonia 3, Italia 1)

Sur américa (Brazil 2)

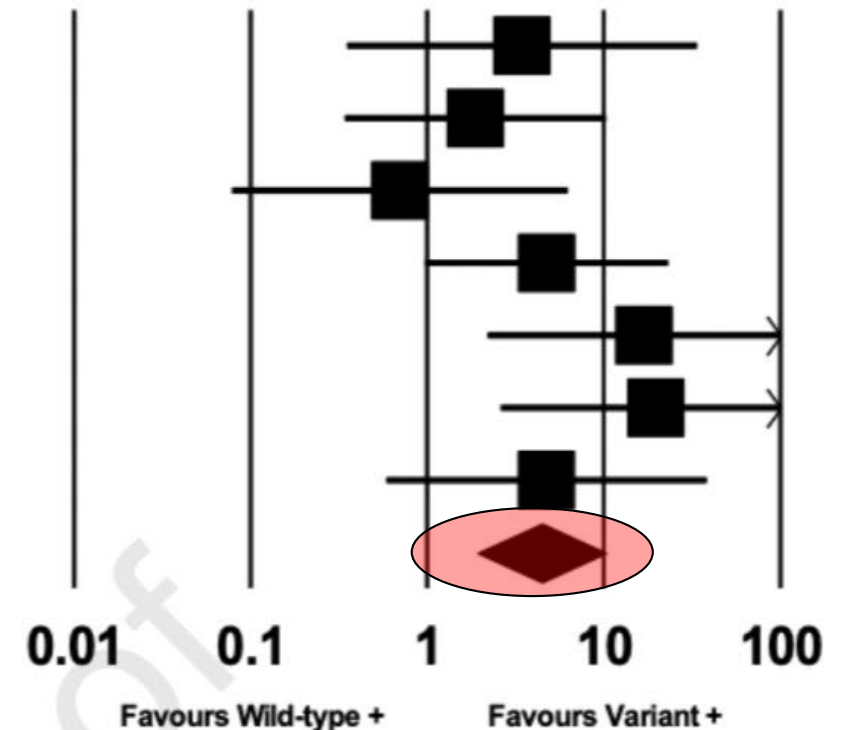
Gastroenterology 2021;161:1443–1459

H. pylori sensible a claritromicina o resistencia < 15% IBP Primera Generaciòn Lansoprazol, Omeprazol Pantoprazol Metabolizadores ràpidos

| Study name | Statistics for each study | | | | |
|----------------|---------------------------|-------------|-------------|---------|---------|
| | Odds ratio | Lower limit | Upper limit | Z-Value | p-Value |
| Isomoto, 2003 | 3.438 | 0.352 | 33.612 | 1.061 | 0.289 |
| Kawabata, 2004 | 1.875 | 0.342 | 10.269 | 0.725 | 0.469 |
| Miki, 2003 | 0.700 | 0.079 | 6.224 | -0.320 | 0.749 |
| Sheu, 2005 | 4.742 | 0.975 | 23.062 | 1.929 | 0.054 |
| Furuta, 2001 | 16.875 | 2.202 | 129.312 | 2.720 | 0.007 |
| Furuta, 2004 | 19.753 | 2.617 | 149.103 | 2.893 | 0.004 |
| Kang, 2008 | 4.738 | 0.589 | 38.140 | 1.462 | 0.144 |
| | 4.443 | 1.944 | 10.157 | 3.535 | 0.000 |

**Riesgo de
Falla terapèutica**

Odds ratio and 95% CI



Ràpids versus Pobres metabolizadors

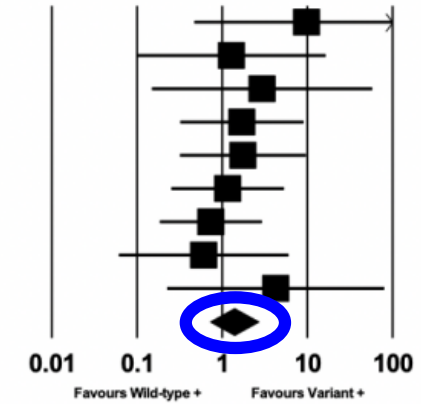
Esomeprazol
9 estudios

Rabeprazol
18 estudios

2B. Study name

| Study name | Statistics for each study | | | | |
|---------------|---------------------------|-------------|-------------|---------|---------|
| | Odds ratio | Lower limit | Upper limit | Z-Value | p-Value |
| Pan, 2010 | 9.783 | 0.473 | 202.374 | 1.475 | 0.140 |
| Pan*, 2010 | 1.286 | 0.101 | 16.340 | 0.194 | 0.846 |
| Miehlke, 2008 | 2.941 | 0.150 | 57.555 | 0.711 | 0.477 |
| Sheu, 2005 | 1.705 | 0.323 | 9.007 | 0.628 | 0.530 |
| Wu, 2011 | 1.750 | 0.321 | 9.554 | 0.646 | 0.518 |
| Song, 2016 | 1.159 | 0.253 | 5.304 | 0.191 | 0.849 |
| Okimoto, 2016 | 0.735 | 0.186 | 2.908 | -0.438 | 0.661 |
| Liou, 2011 | 0.606 | 0.061 | 5.985 | -0.429 | 0.668 |
| Kang, 2008 | 4.248 | 0.227 | 79.518 | 0.968 | 0.333 |
| | 1.387 | 0.723 | 2.662 | 0.984 | 0.325 |

Odds ratio and 95% CI



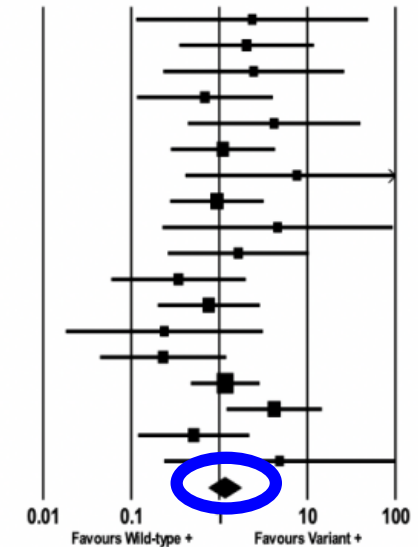
2C.

Study name

Statistics for each study

| Study name | Statistics for each study | | | | |
|-----------------------------|---------------------------|-------------|-------------|---------|---------|
| | Odds ratio | Lower limit | Upper limit | Z-Value | p-Value |
| Isomoto*, 2003 - 7 days | 2.368 | 0.114 | 49.041 | 0.558 | 0.577 |
| Isomoto*, 2003 - 14 days | 2.045 | 0.354 | 11.820 | 0.800 | 0.424 |
| Yang, 2009 | 2.462 | 0.232 | 26.114 | 0.748 | 0.455 |
| Pan, 2010 | 0.688 | 0.117 | 4.056 | -0.414 | 0.679 |
| Inaba, 2002 | 4.200 | 0.442 | 39.943 | 1.249 | 0.212 |
| Miyoshi, 2001 | 1.100 | 0.283 | 4.282 | 0.137 | 0.891 |
| Lay, 2010 | 7.638 | 0.414 | 140.829 | 1.367 | 0.172 |
| Okimoto, 2016 | 0.942 | 0.278 | 3.189 | -0.096 | 0.924 |
| Lin, 2017 | 4.600 | 0.227 | 93.032 | 0.995 | 0.320 |
| Dojo, 2001 | 1.647 | 0.262 | 10.359 | 0.532 | 0.595 |
| Miki, 2003 | 0.345 | 0.060 | 1.993 | -1.190 | 0.234 |
| Lee, 2003 | 0.762 | 0.201 | 2.884 | -0.400 | 0.689 |
| Phiphatpatthamaamphan, 2016 | 0.238 | 0.018 | 3.121 | -1.093 | 0.274 |
| Kawabata, 2003 | 0.231 | 0.045 | 1.197 | -1.746 | 0.081 |
| Lee, 2010* | 1.169 | 0.478 | 2.862 | 0.343 | 0.732 |
| Kuwayama, 2007 | 4.211 | 1.216 | 14.585 | 2.268 | 0.023 |
| Hokari, 2001 | 0.513 | 0.120 | 2.190 | -0.902 | 0.367 |
| Jiang, 2005 | 4.846 | 0.237 | 98.960 | 1.025 | 0.305 |
| | 1.153 | 0.761 | 1.748 | 0.674 | 0.501 |

Odds ratio and 95% CI



Influence of *Cytochrome P450 2C19* Genotype on *Helicobacter pylori* Proton Pump Inhibitor-Amoxicillin-Clarithromycin Eradication Therapy: A Meta-Analysis

OPEN ACCESS

Edited by:

*Yuko Morino*¹, *Mitsushige Sugimoto*^{2*}, *Naoyoshi Nagata*², *Ryota Niikiura*², *Eri Iwata*²,
*Mariko Hamada*², *Yusuke Kawai*², *Tatsuhiko Fujimiya*³, *Hironori Takeuchi*⁴, *Sakae Unezaki*³
and *Takashi Kawai*²

25 ensayos clínicos controlados aleatorizados

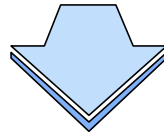
**24 ASIA, 1 Suramérica (Colombia), 5318 pacientes,
Tasa resistencia: Amoxi 8.9%, Cla 13%**

Morino Y, Front Pharmacol 2021;12:759240

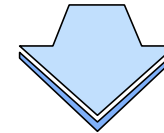
Influence of *Cytochrome P450 2C19* Genotype on *Helicobacter pylori* Proton Pump Inhibitor-Amoxicillin-Clarithromycin Eradication Therapy: A Meta-Analysis

Yuko Morino¹, Mitsushige Sugimoto^{2*}, Naoyoshi Nagata², Ryota Niikiura², Eri Iwata², Mariko Hamada², Yusuke Kawai², Tatsuhiro Fujimiya³, Hironori Takeuchi⁴, Sakae Unezaki³ and Takashi Kawai²

Extensos metabolizadores



**Lansoprazol y omeprazol
Menor tasa erradicación**



**Esomeprazol y rabeprazol
No son influidos**

CLINICAL PRACTICE UPDATE

AGA Clinical Practice Update on the Management of Refractory *Helicobacter pylori* Infection: Expert Review



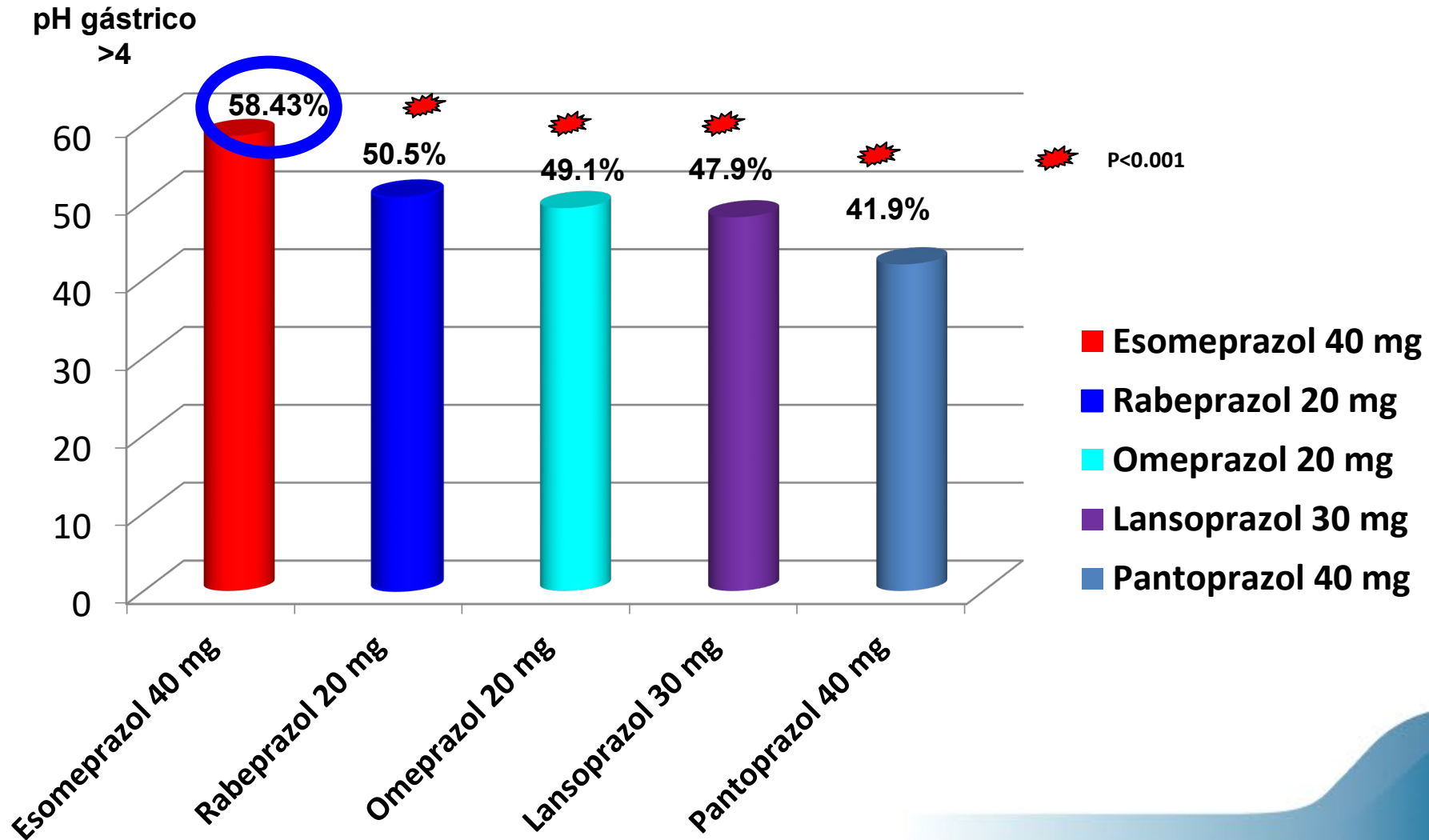
Shailja C. Shah,^{1,2,3} Prasad G. Iyer,⁴ and Steven F. Moss⁵

Best Practice Advice 7: Inadequate acid suppression is associated with *H pylori* eradication failure. The use of high-dose and more potent PPIs, PPIs not metabolized by *CYP2C19*, or potassium-competitive acid blockers, if available, should be considered in cases of refractory *H pylori* infection.

Opció n Rabeprazol, Esomeprazol, Vonoprazan, Tegoprazan o aumentar dosis de IBP 1era generaci3n

Gastric Acid Control With Esomeprazole, Lansoprazole, Omeprazole, Pantoprazole, and Rabeprazole: A Five-Way Crossover Study

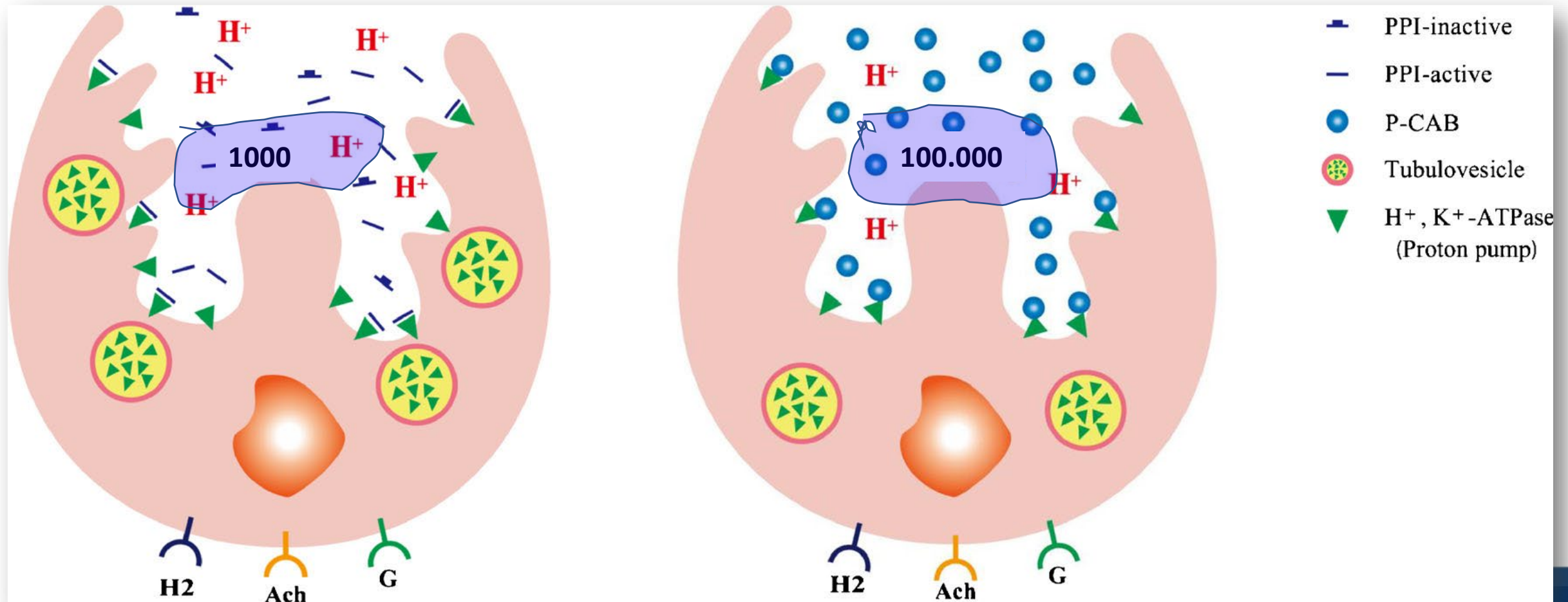
Philip Miner, Jr., M.D., Philip O. Katz, M.D., Yusong Chen, Ph.D., and Mark Sostek, M.D.



Am J Gastroenterol 2003;98:2616-20

Novedades para bloquear la secreción de HCl

IBP 3^a Generación competitivos de K: P-CABs



Shibli F, Curr Gastroenterol Rep 2020; 22:16

Hunt RH, Curr Opt Treat Gastroenterol 2018;16:57-90

**Vonoprazan
P-CABs**

**Superior a IBPs
Convencionales**

P-CABs

Vonoprazan

**Japón
Filipinas
Singapur
Tailandia
Malasia**

Tegoprazan

**Corea del
Sur**

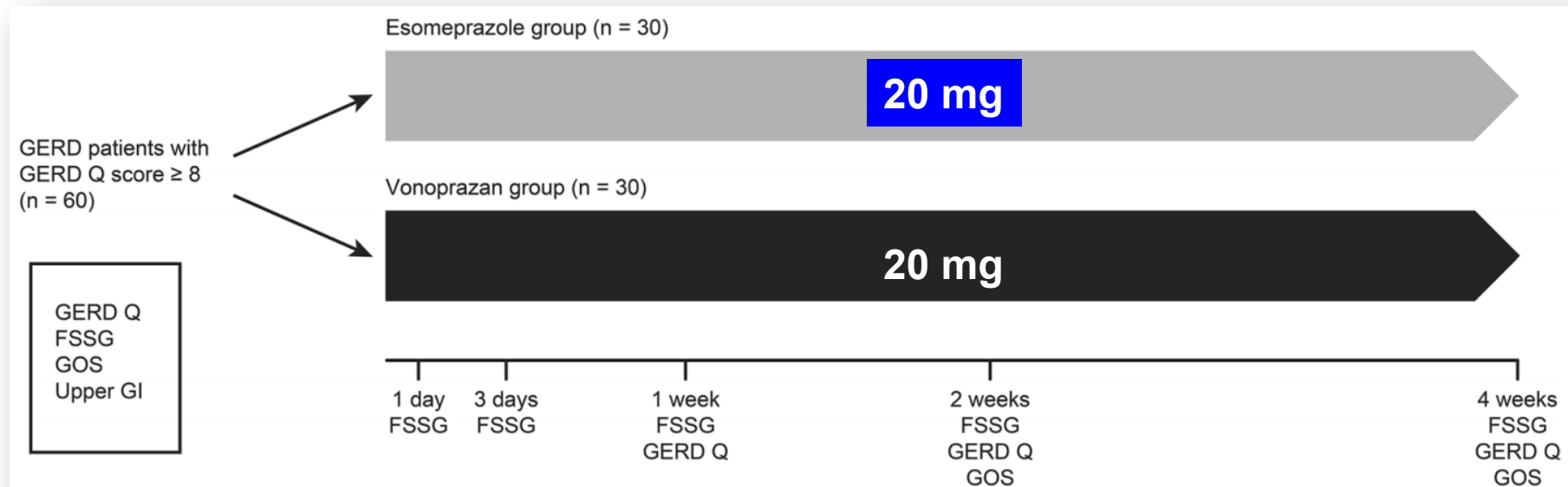
Oshima T, *J Neurogastroenterol Motil.* 2018;24:334–44.
Scarpignato C, *Aliment Pharmacol Ther.* 2019;50:960–62.

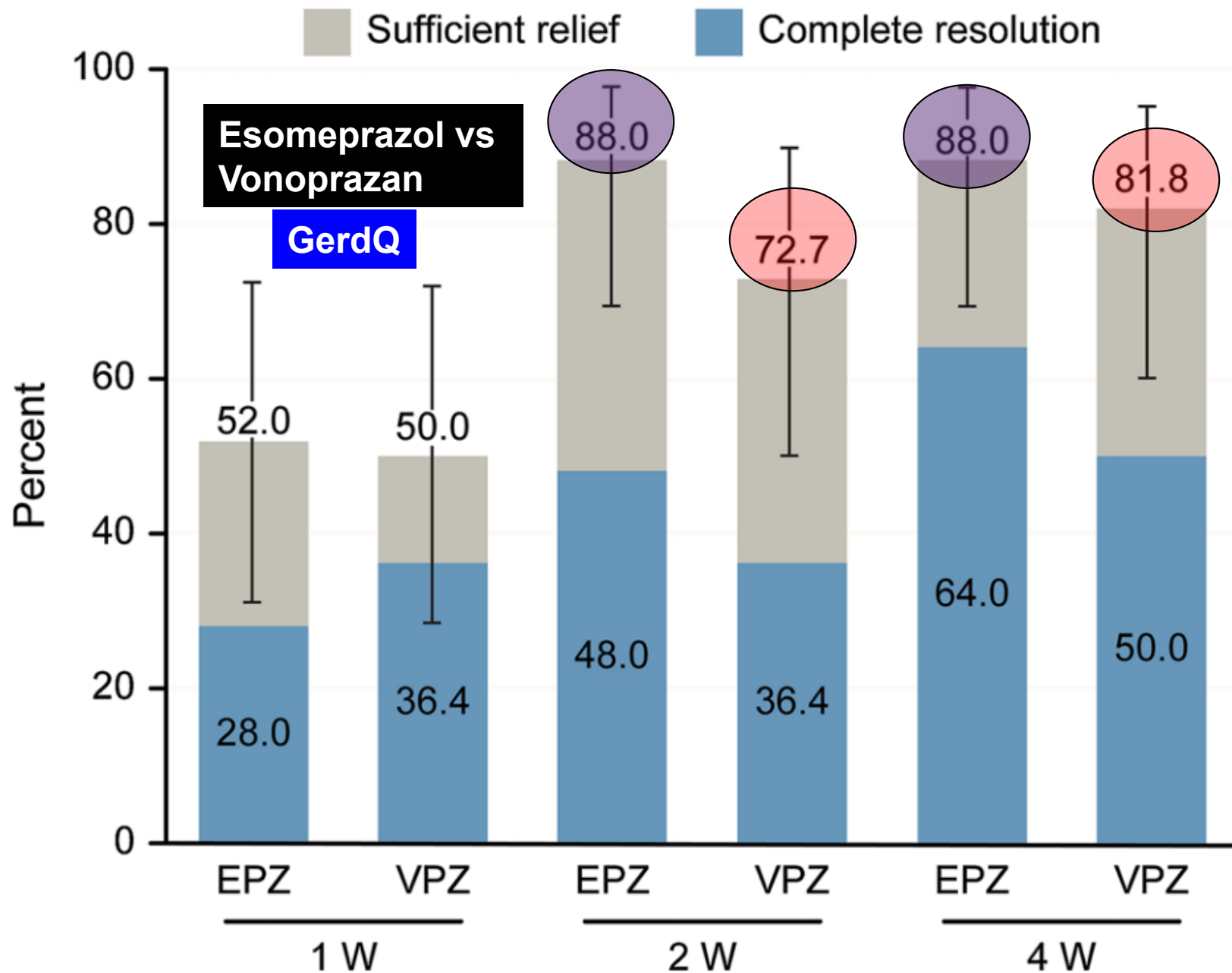
USA-Europa Ensayos 2021-22

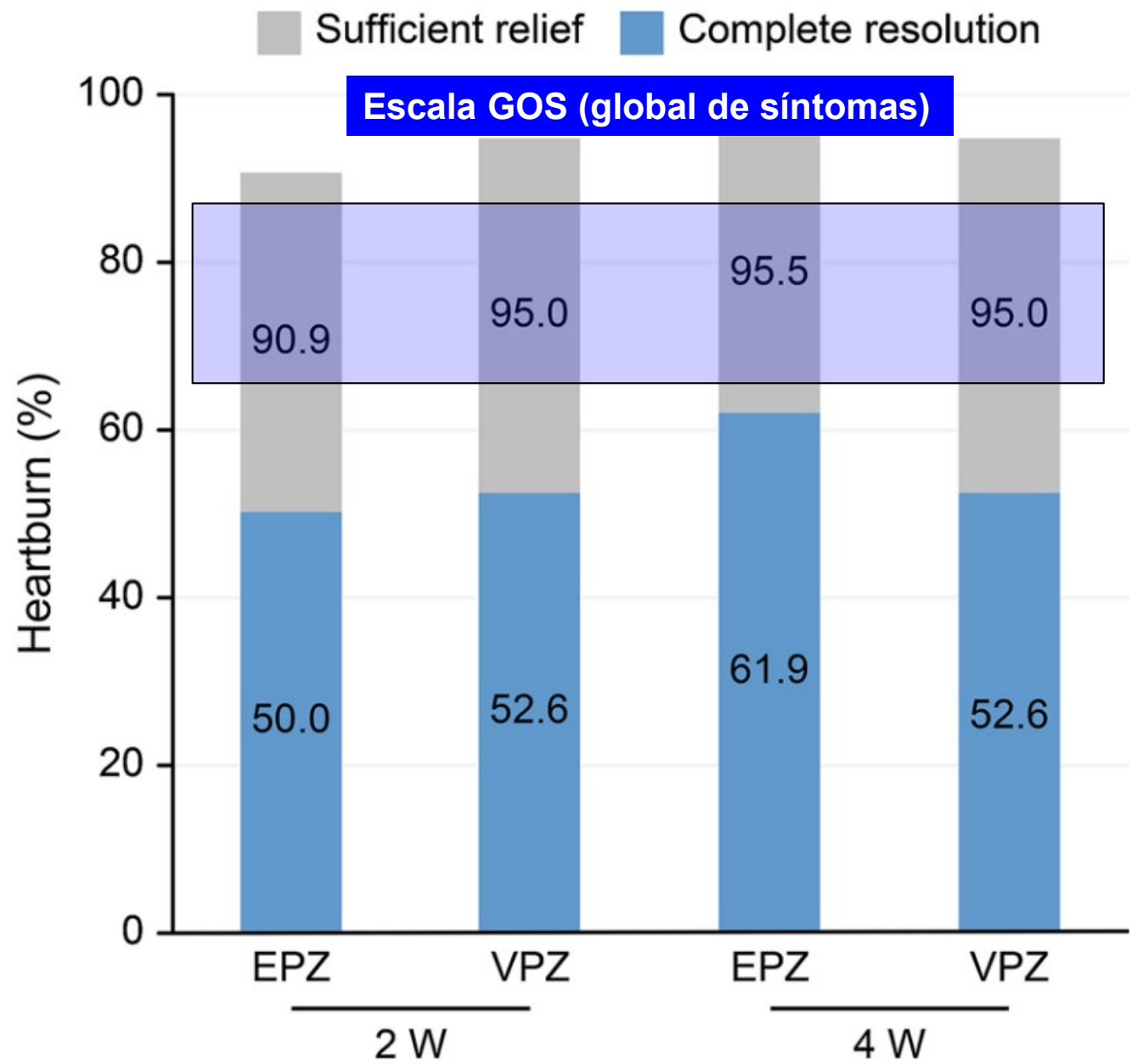
ORIGINAL ARTICLE

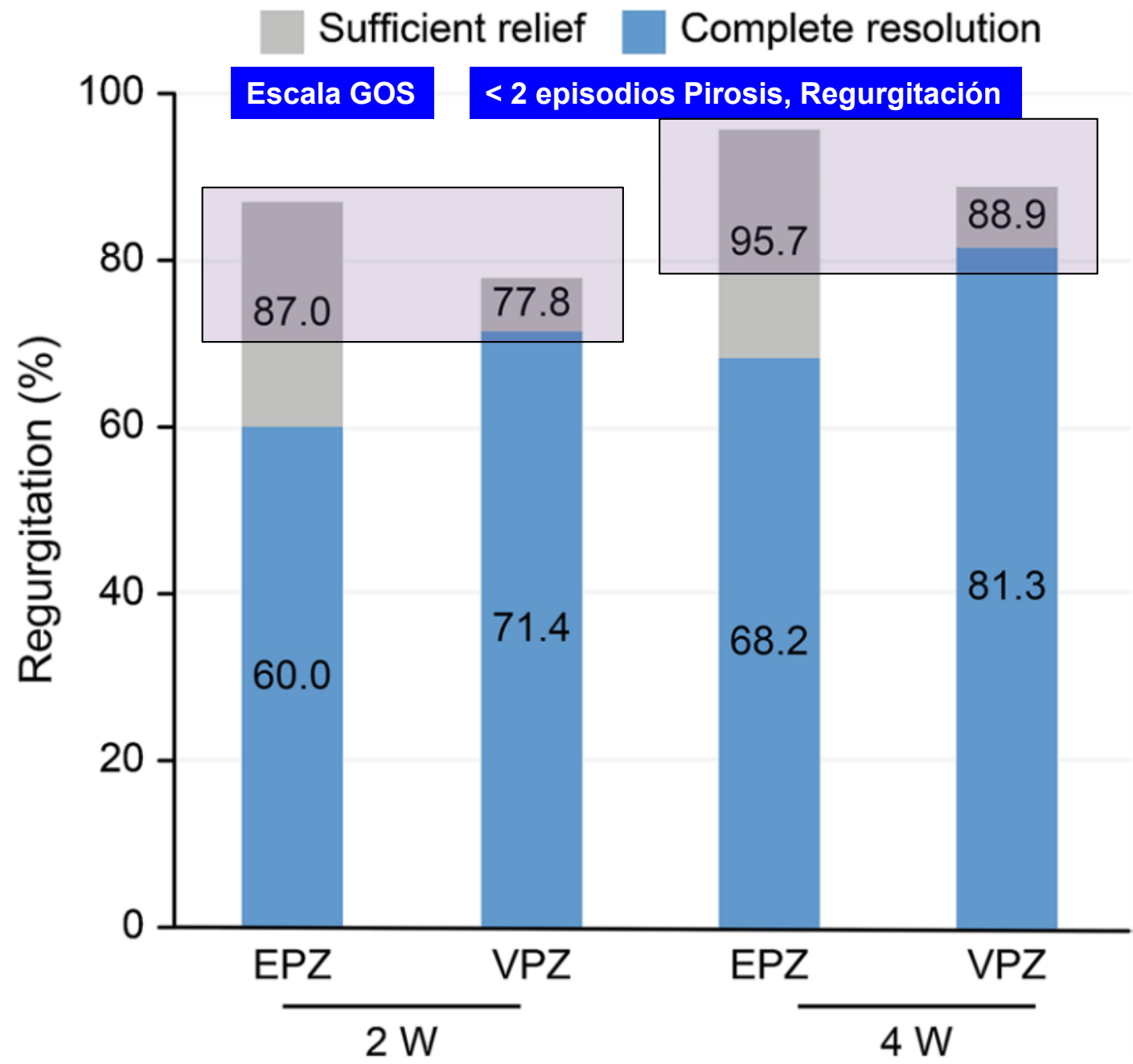
Short-Term Symptomatic Relief in Gastroesophageal Reflux Disease: A Comparative Study of Esomeprazole and Vonoprazan

Kouichi Sakurai¹ · Hiroko Suda¹ · Satomi Fujie¹ · Takayuki Takeichi¹ · Ayako Okuda¹ · Tetsuya Murao¹ · Kiwamu Hasuda¹ · Masahiro Hirano² · Kiyoharu Ito³ · Katsuie Tsuruta⁴ · Masahiro Hattori¹









ERGE Vonoprazan versus Esomeprazol

**Esomeprazol
Convencional**



Vonoprazan

**Esomeprazol
Liberación inmediata ?**

**IBP liberación
Inmediata
Varios países
Latinoamérica**



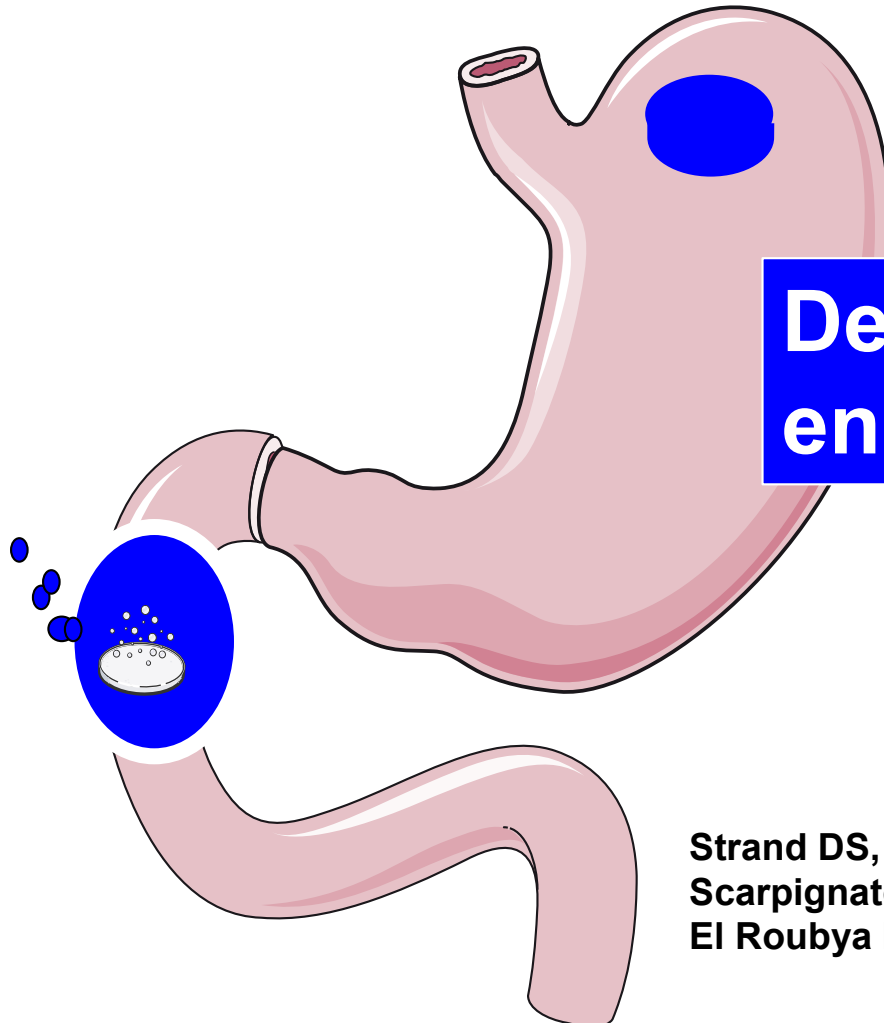
2022

IBP de liberación inmediata

**Hasta el momento los IBPs
Son de liberación retardada**

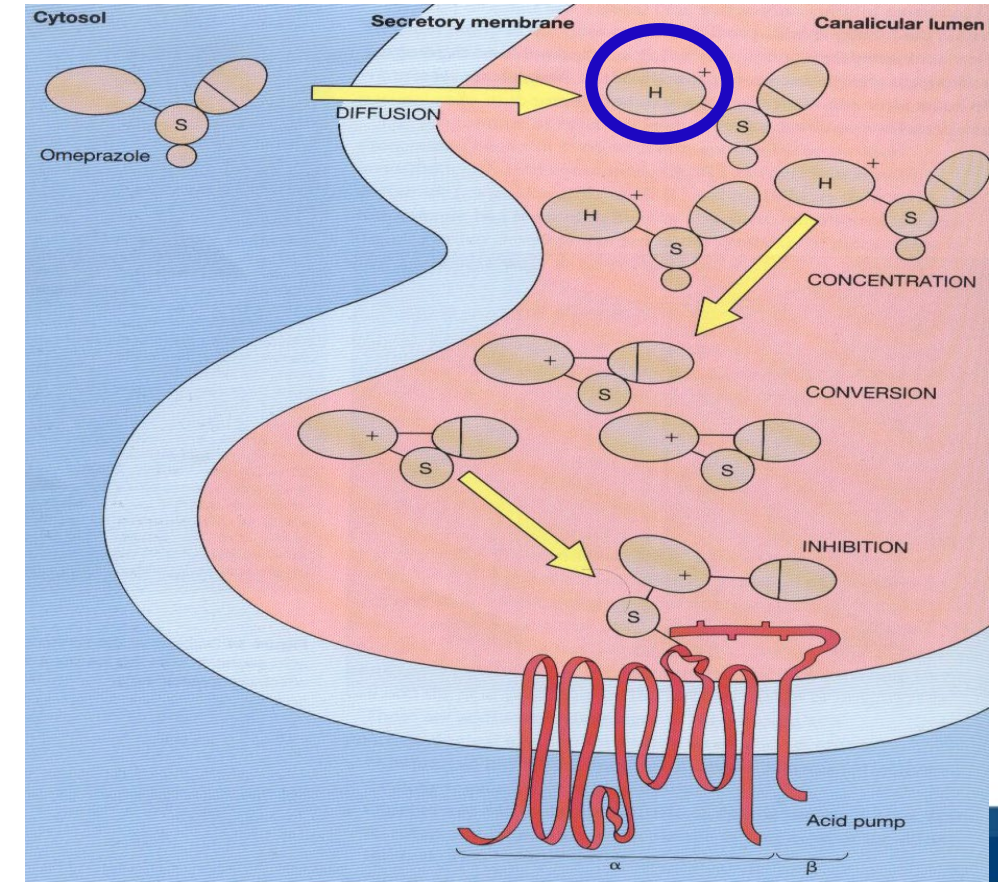
IBPs convencionales 1era y 2da Generación

Liberación Retardada



Debe darse en ayunas

Activación



Strand DS, Gut Liver 2017;11:27-37

Scarpignato C, Curr Opin Pharmacol 2008;;8:677-84

El Roubya N, Exp Opin Drug Met Toxicol 2018;14:447-60

Eficacia de los IBPs



**IBP con el desayuno
pH >4, 17.2%**

**IBP antes del desayuno
pH >4, 42%****

****p<0.01**

**Bombas activas
Pos comidas 70%
En ayunas 10%**



**Savarino V, Pharmacol Rev 2009;59:135-53
Shin JM, Curr Gastroenterol Rep 2008;10:528-34.**

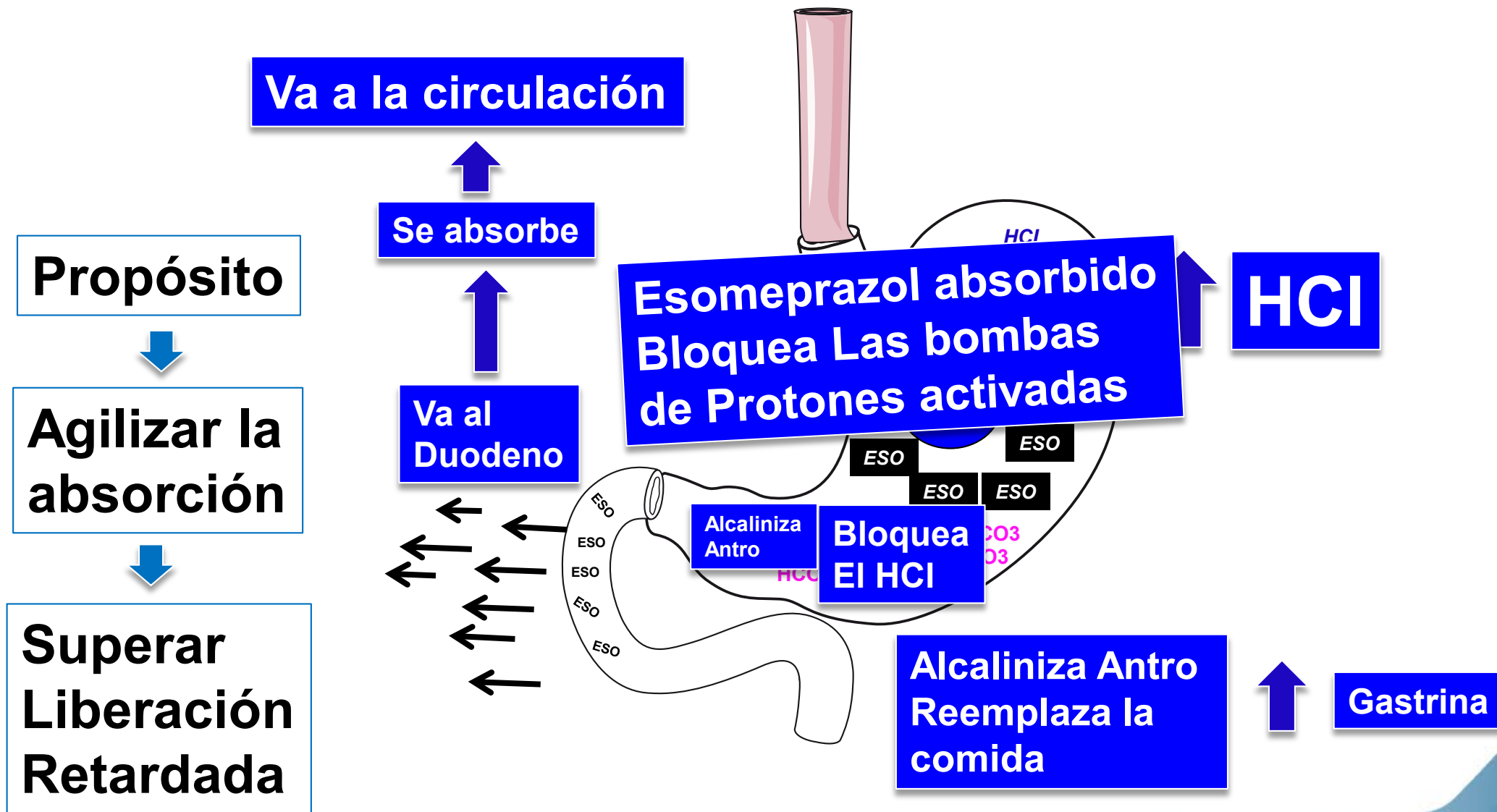
IBP de liberación Inmediata

**Qué
Es ?**



**Tiene
Ventajas ?**

IBP Liberación Inmediata: envoltura ácido-sensible



Adv Ther (2021) 38:1660–1676

<https://doi.org/10.1007/s12325-021-01644-7>

ORIGINAL RESEARCH

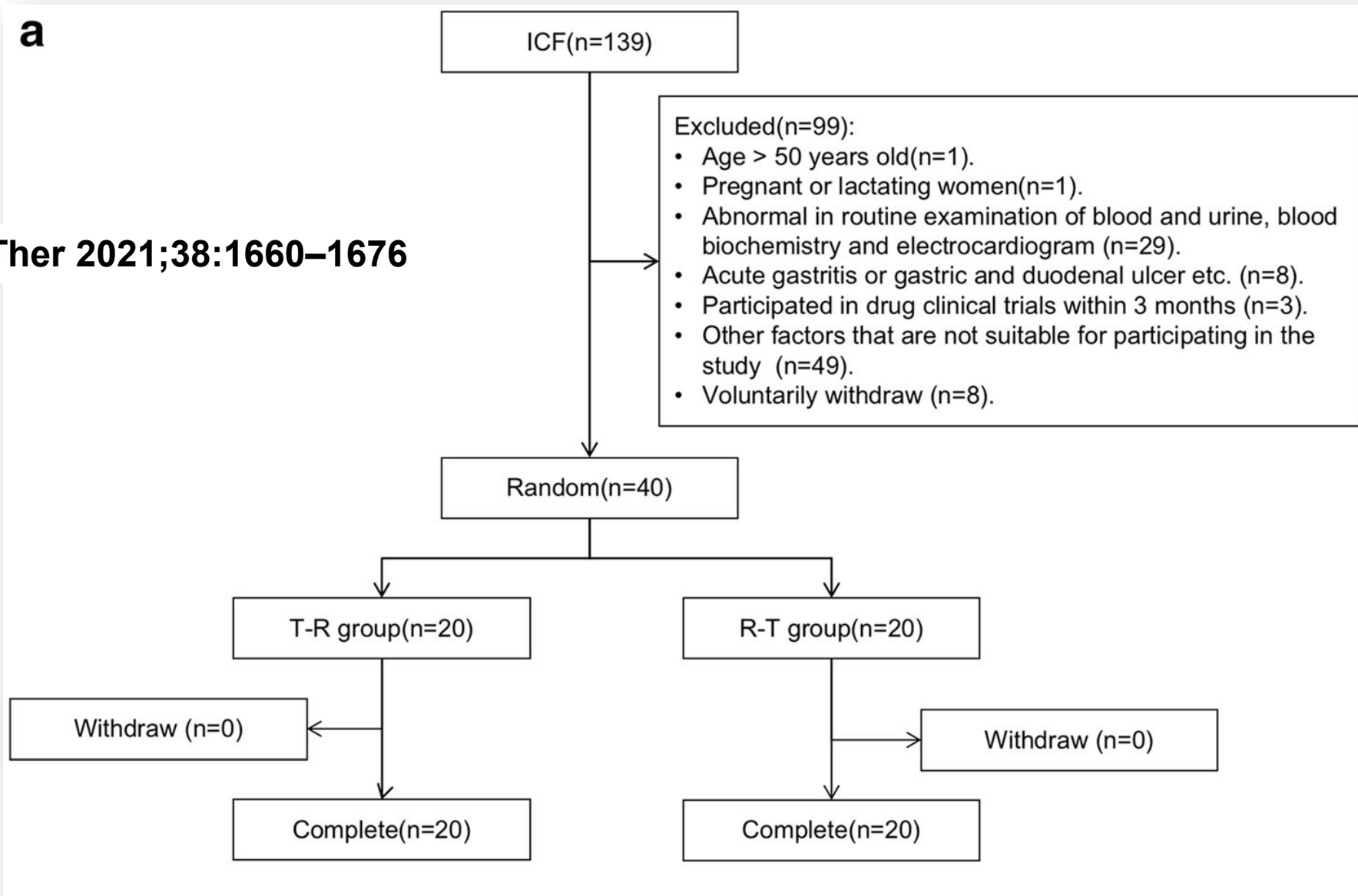
Changchun Haiyue Pharmaceutical have developed IR-ESO

Pharmacokinetics and Pharmacodynamics of **Esomeprazole/Sodium Bicarbonate Immediate-Release Capsules** in Healthy Chinese Volunteers: A Cross-Over, Randomized Controlled Trial

Shan Jing · Yue Zhu · Wenfang Liu · Kexu Yang · Lili Hu ·

Dan Deng · Chunyan Lu · Yang Lin

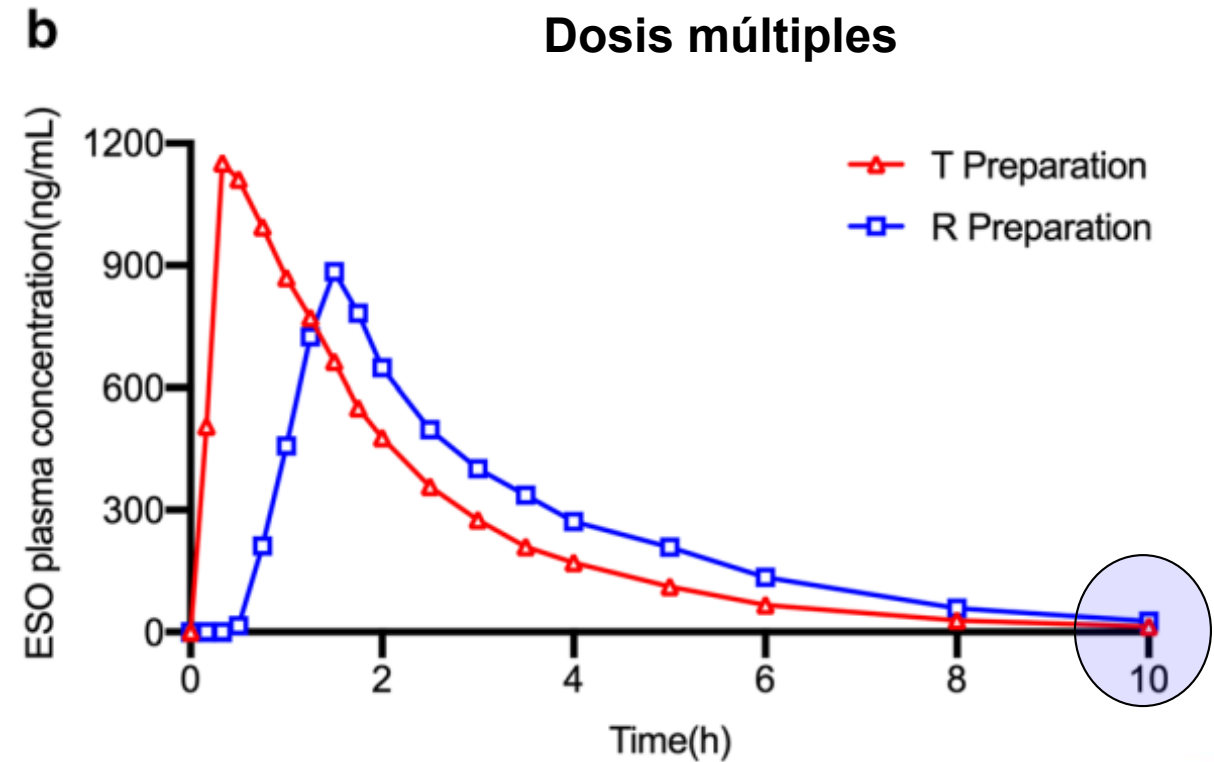
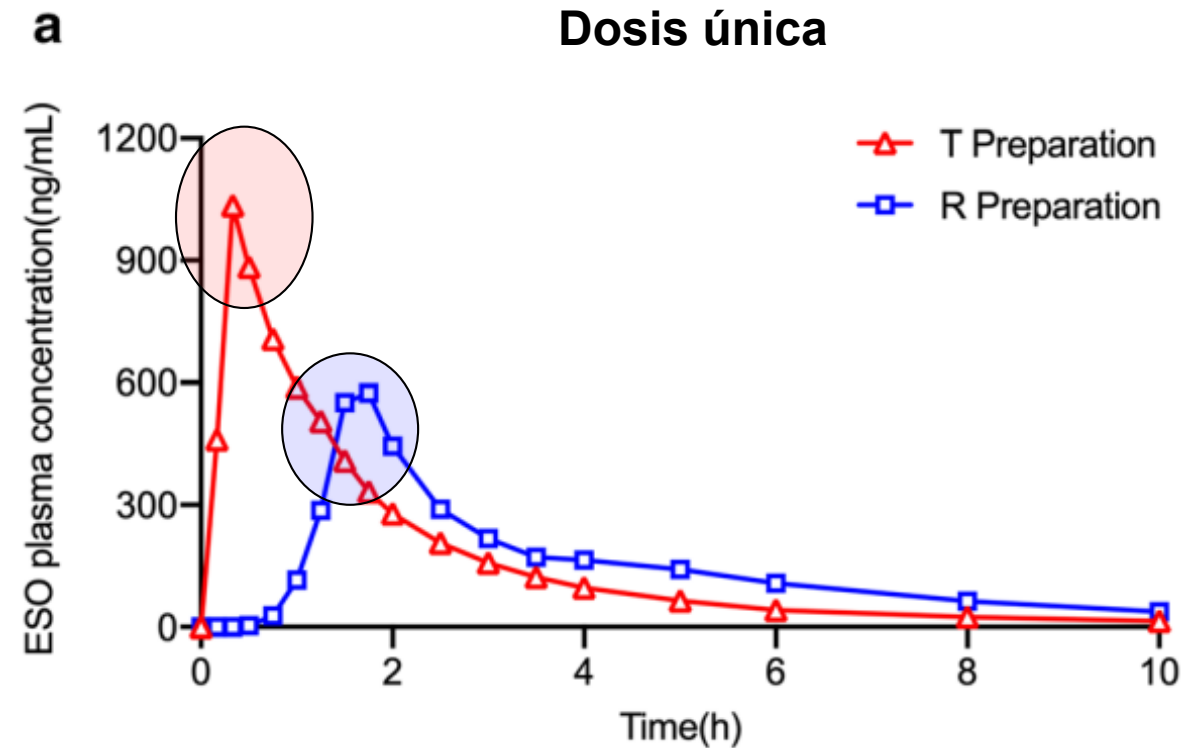
Jing S, Adv Ther 2021;38:1660–1676



ESO 20 mg + Sodium bicarbonate 1100 mg Changchun Haiyue Pharmaceutical

ESO 1 tableta 20 mg Astrazeneca (Nexium)

Esomeprazol liberación inmediata vs Liberación retardada



The safety, pharmacodynamics, and pharmacokinetics of immediate-release formulation containing esomeprazole 20 mg/sodium bicarbonate 800 mg in healthy adult male

40 voluntarios sanos

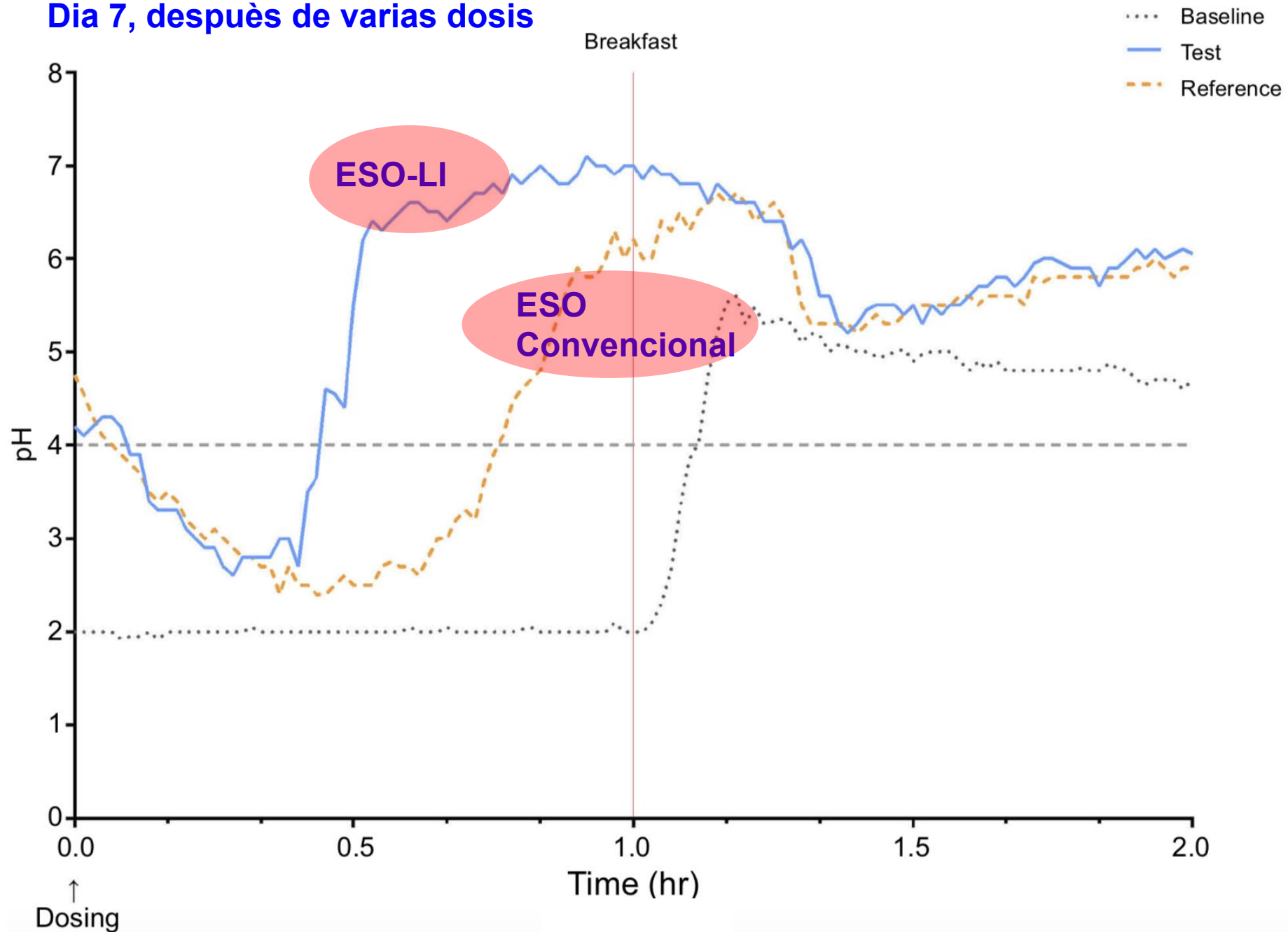
Dasohm Kim^{1,2}
Min Soo Park^{1,2}
Byung Won Yoo²
Taegon Hong²
Shin Jung Park³
Choon Ok Kim²

This article was published in the following Dove Press journal:
Drug Design, Development and Therapy

Background: Esomeprazole is the most effective treatment for acid-related disorders and is widely used with enteric coating due to rapid degradation in the acidic environment. However, the enteric-coated formulation delays absorption and onset of action. To overcome this limitation, an immediate-release formulation containing esomeprazole 20 mg and sodium bicarbonate 800 mg (IR-ESO) was developed.

Purpose: To evaluate the safety, pharmacokinetics (PK), and pharmacodynamics of IR-ESO compared to those of esomeprazole 20 mg (ESO).

Día 7, después de varias dosis



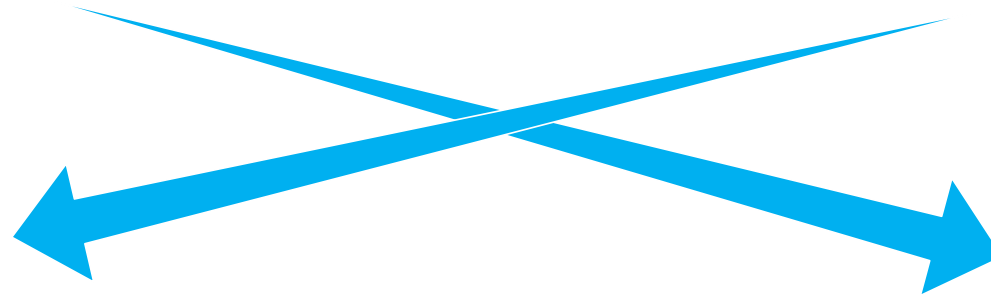
Oral buffered esomeprazole is superior to i.v. pantoprazole for rapid rise of intragastric pH: A wireless pH metry analysis

Rupa Banerjee,* D Nageshwar Reddy,* Nalini M Guda,[†] Rakesh Kalpala,* Swapna Mahurkar,* Santosh Darisetty* and G Venkat Rao*

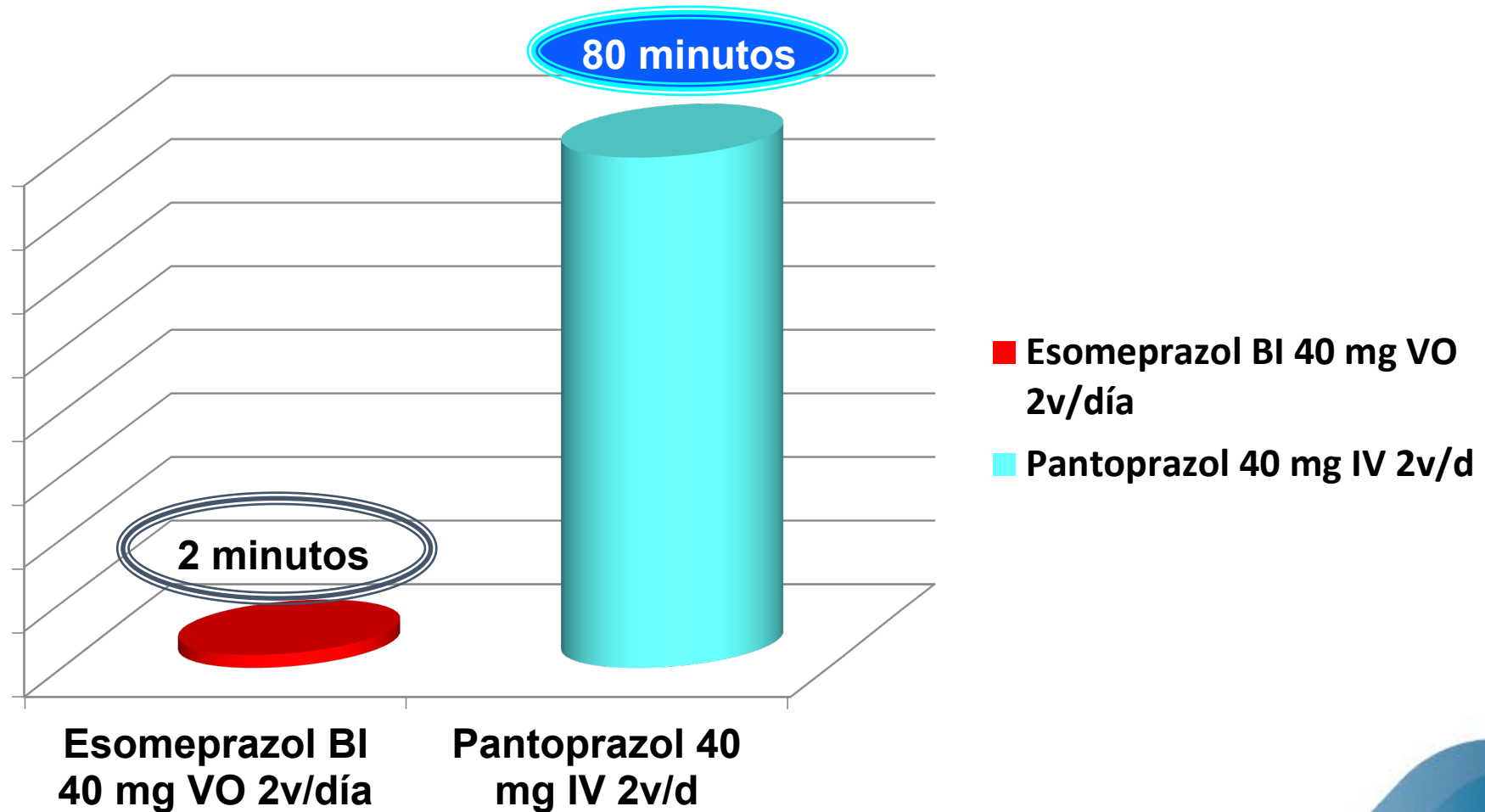
10 Voluntarios sanos (8H, 2M), 31 años, IMC 21kg/m², No anemia, *H.pylori* (-), perfil hepático normal. Dos dosis en 24 h
“washout” 2 semanas Crossover

**Esomeprazol BI
2v/día**

**Pantoprazol 40 mg IV
2v/día**



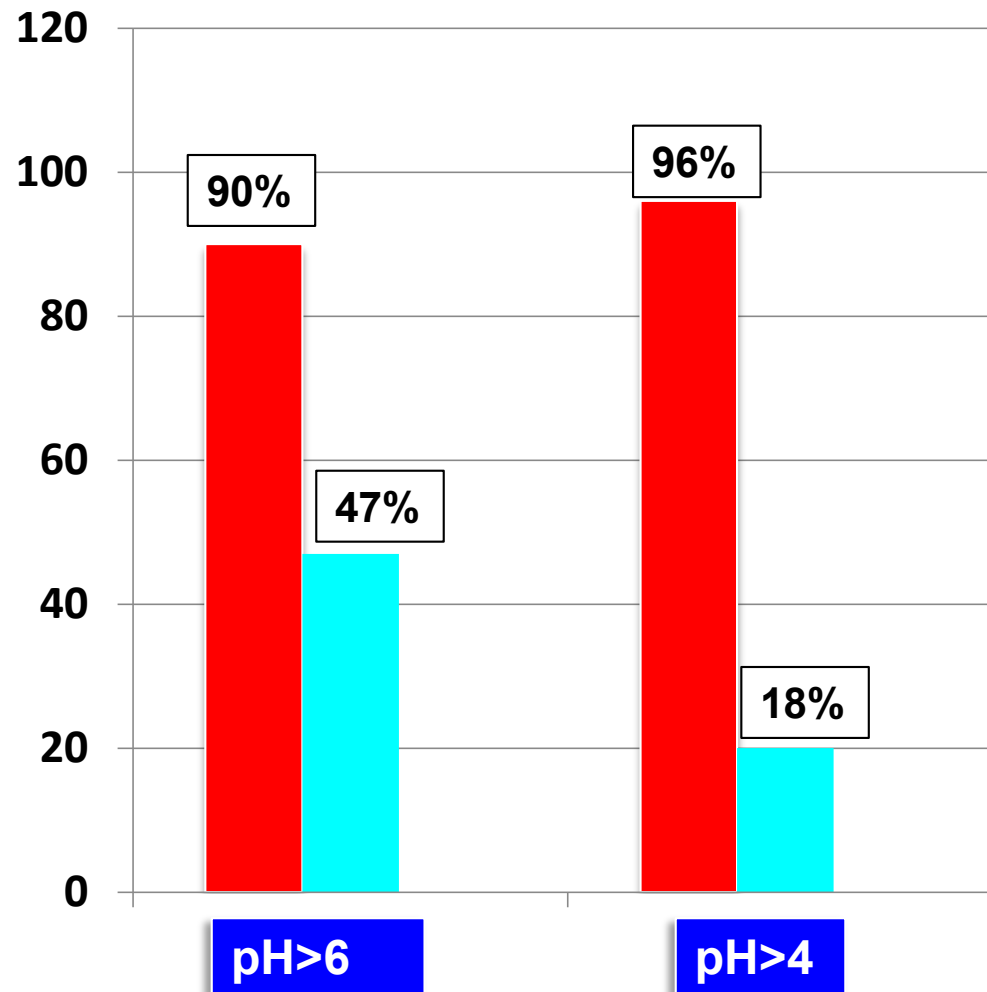
Tiempo para lograr pH > 6: Esomeprazol BI vs Pantoprazol IV/ 2v/día



Banerjee R, J Gastroenterol Hepatol 2010; 25: 43–47

% de 24 Horas con pH > 4 y >6
ESO BI 40 mg VO 2v/d VS Pantoprazol 40 mg IV/ 2v/día

pH
24 horas



La elevación del pH
Persistió después de 6h
de la 1era dosis: No es
por efecto local del HCO₃!

■ Esomeprazol BI
■ Pantoprazol

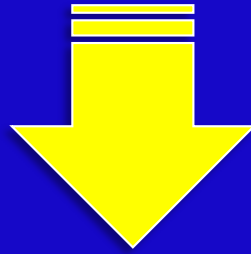
Abstract

Background and Aims: A pH of more than 6 is required for clot stability and hemostasis. Intravenous proton pump inhibitors have a rapid onset of action compared to oral and have been preferred for management of non-variceal bleeding. Intravenous pantoprazole has

**Por su rapidez de acción y
Elevación de pH >6,
Sería una excelente opción
En en hemorragia por
ulceras pépticas**

tration. It was significantly superior to i.v. pantoprazole in equivalent dosing. This finding could have implications in the management of non-variceal bleed where a rapid and sustained pH of more than 6 is desirable.

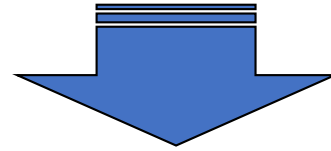
Úlceras pépticas Sangrantes



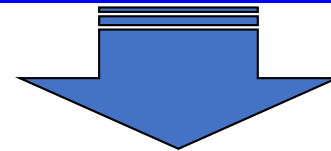
Objetivo
 $\text{pH} > 6$



Esomeprazol liberación inmediata



Actúa más rápido que Esomeprazol original liberación retardada



**Disolución en estómago
Acelera su absorción**

Esomeprazol LI- Resuelve desventajas IBPs 1ª Generación

**Esomeprazol
Independiente Cyp2C19
Más potente > inhibición HCl**

Bicarbonato

**Acción
Inmediata**

**No necesita darse
Antes de comida**

**Supera actividad
Esomeprazol original**



ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease

Philip O. Katz, MD, MACG¹, Kerry B. Dunbar, MD, PhD^{2,3}, Felice H. Schnoll-Sussman, MD, FACG¹, Katarina B. Greer, MD, MS, FACG⁴, Rena Yadlapati, MD, MSHS⁵ and Stuart Jon Spechler, MD, FACG^{6,7}

An omeprazole-sodium bicarbonate combination that is not enteric-coated provides good control of intragastric pH in the first 4 hours of sleep when dosed at bedtime (57).

Review article: rethinking the “ladder” approach to reflux-like symptom management in the era of PPI “resistance” a multidisciplinary perspective

Hungin APS Aliment Pharmacol Ther 2022;55;1492

A. Pali S. Hungin¹  | Carmelo Scarpignato² | Laurie Keefer³ | Maura Corsetti^{4,5}  | Foteini Anastasiou⁶ | Jean W. M. Muris⁷ | Juan M. Mendive⁸ | Peter J. Kahrilas⁹

There is little rationale for switching (almost all PPIs are similarly effective at equiactive antisecretory doses) unless the switch is toward a more effective antisecretory compound (e.g. esomeprazole,^{15,16} rabeprazole^{17,18}) or immediate release-omeprazole¹⁹).

Optimizaciòn IBP en ERGE

IBP 1v/D
Medidas
Generales

IBP en ayunas
IBP 2v/D?

Otro IBP
Esomeprazol
Rabeprazol
Vonopran

IBP
Liberaciòn
Inmediata

Hungin APS Aliment Pharmacol Ther 2022;55;1492
Katz PO, Am J Gastroenterol. 2022;117:27-56

Colombia, Serie de casos

68 pacientes síntomas nocturnos, ERGE 2-5 años, 28-60 años, 35 mujeres, Esofagitis B y C, IBP 2v/día

No mejoría, pirosis 3-4 v/semana

**Esomeprazol-Bicarbonato 40 mg (Ezolium ®)
Por la mañana o al acostarse 8 semanas**

**Persistencia
Síntomas 8%**

**Mejoría
Síntomas 10%**

**No síntomas
80%**

En las Mañanas

En la Mañana

Con el estómago vacío

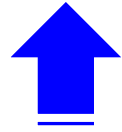
En la Noche

En la Tarde

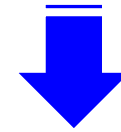
A demanda



**Superior a IBP
1era Generación**



Esomeprazol



**Similar a
Vonoprazan**

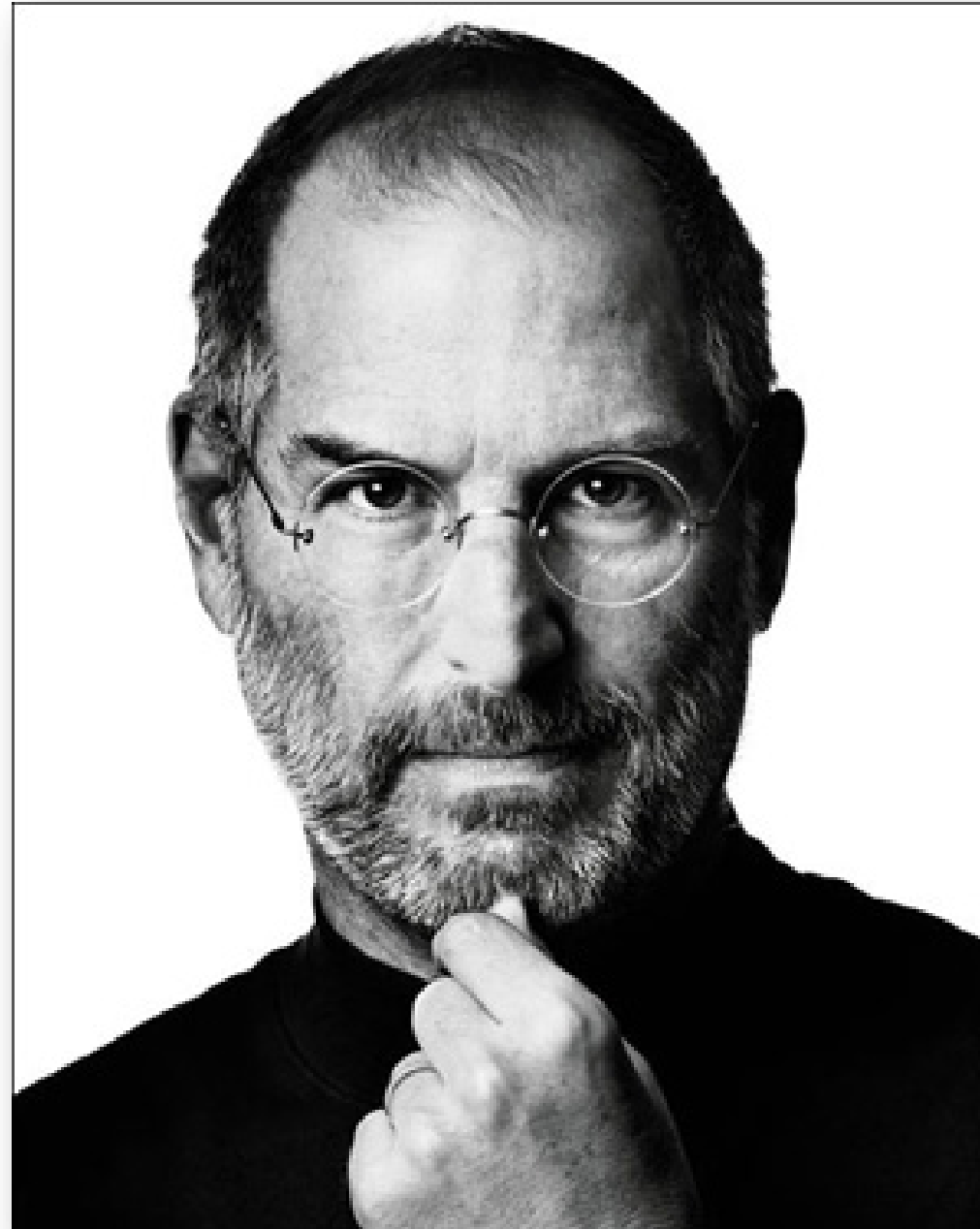
Mensajes para la casa

Esomeprazol superior a IBP 1ra generación
Similar a Vonoprazan 3ra generación
Con NaHCO₃ actúa inmediatamente 2 minutos
pH >4 más tiempo, noche
Evita horario rígido, cualquier hora
Es independiente del CYP2C19
Supera limitaciones tradicionales de “los IBP”

Esomeprazol + HCO₃, el Messi de los IBPs



La sencillez es la maxima expresiòn de la sofisticaciòn



**Lo difícil es
Hacerlo fácil**

Muchas gracias !