

14 References

1. P&G MRD#US983190, data in Sponsor's file Yankelovich
2. Oliveria SM, Christos PJ, Talley NJ, Dannenberg AJ. Heartburn risk factors, knowledge, and prevention strategies: a population-based survey of individuals with heartburn. Arch Int Med 1999; 159:1592-1598.
3. P&G MRD#US972782, data in Sponsor's file
4. Nebel OT, Fornes MF, Castell DO. Symptomatic gastroesophageal reflux: incidence and precipitating factors. Dig Dis 1976; 21(11):953-956.
5. P&G MRD#US983190, data in Sponsor's file
6. ACNielsen/SmithKlineBeecham Survey. Profile of consumers in need: people with sour stomachs, by demographics. Prog Groc 1995; 74(9):98-99.
7. P&G MRD#US980801, data in Sponsor's file
8. P&G MRD#US991715, data in Sponsor's file
9. A Gallup Survey on Heartburn Across America, Gallup Organization, Inc., Princeton, NJ: 1988
10. Environmental Nutrition. Heartburn: why it occurs, and ways to gain relief. Environmental Nutrition 1988; (6):8.
11. Kurata JH, Nogawa AW, Chen YK, Parker CE. Dyspepsia in primary care: perceived causes, reasons for improvement, and satisfaction with care. J Fam Prac 1997; 44(3):281-288.
12. P&G MRD#US973358 Label Comprehension Study, data in Sponsor's file
13. P&G MRD#US960316, data in Sponsor's file
14. MRCA Survey 1994-1996, data in Sponsor's file
15. P&G MRD#US974088, data in Sponsor's file
16. P&G MRD#US996633, data in Sponsor's file
17. Gardner JD, Rodriguez-Stanley S, Robinson MG, et al. How do provocative meals cause heartburn? Integrated gastric acidity as the determinant of esophageal acid exposure. Gastroenterol 2000; 118:2605,A482.

18. Gardner JD, Rodriguez-Stanley S, Robinson MG, et al. Meal-induced heartburn: quantification of esophageal acid exposure and its relationship to gastric acidity. *Gastroenterol* 2000; 118:2606,A482.
19. Gardner JD, Rodriguez-Stanley S, Robinson MG, et al. Relationship between esophageal acid exposure and heartburn severity in meal-induced heartburn. *Gastroenterol* 2000; 118:2607,A482.
20. Lindberg P, Brandstrom A, Wallmark B, Mattsson H, Rikner L, Hoffmann K-J. Omeprazole: the first proton pump inhibitor. *Med Res Rev* 1990; 10: 1-54.
21. Andersson T. Pharmacokinetics, metabolism, and interactions of acid pump inhibitors; focus on omeprazole, lansoprazole, and pantoprazole. *Clin Pharmacokinet* 1996; 31:9-28.
22. Andersson T. Expert Report. Omeprazole; with special reference to drug interaction studies in combinations with metronidazole and clarithromycin, amoxicillin and metronidazole, or amoxicillin and clarithromycin. Clinical pharmacological documentation. May 1998.
23. Andersson T, Cederberg C, Edvardsson G, Heggelund A, Lundborg P. Effect of omeprazole treatment on diazepam plasma levels in slow vs. normal rapid metabolizers of omeprazole. *Clin Pharmacol Ther* 1990; 47:79-85.
24. Astra Hässle Clinical Study Report: Influence of cimetidine on the pharmacokinetics of omeprazole. (Study No. I-212) December 1982.
25. Andersson T, Bergstrand R, Cederberg C. Influence of acid secretory status on absorption of omeprazole from enteric coated granules. *Br J Clin Pharmacol* 1991; 31:275-8.
26. Andersson T, Andren K, Cederberg C, et al. Bioavailability of omeprazole as enteric-coated (EC) granules in conjunction with food on the first and seventh days of treatment. *Drug Invest* 1990; 2:184-188.
27. Lind T, Cederberg C, Ekenved G, et al. Effect of omeprazole - a gastric proton pump inhibitor - on pentagastrin-stimulated acid secretion in man. *Gut* 1983; 24:270-276.
28. Lind T, Cederberg C, Ekenved G, et al. Inhibition of basal and betazole- and sham-feeding-induced acid secretion by omeprazole in man. *Scand J Gastroenterol* 1986; 21:1004-1010.
29. Londong W, Londong V, Cederberg C, et al. Dose-response study of omeprazole on meal-stimulated gastric acid secretion and gastrin release. *Gastroenterol* 1983; 85:1373-1378.

30. Lind T, Cederberg C, Axelson M, et al. Long-term acid inhibitory effect of different daily doses of omeprazole 24 hours after dosing. *Scand J Gastroenterol* 1986; (Suppl 118):137-138.
31. Lind T, Cederberg C, Forsell H, et al. Relationship between reduction of gastric acid secretion and plasma gastrin concentration during omeprazole treatment. *Scand J Gastroenterol* 1988; 23:1259-1266.
32. Davis TC, Long SW, Jackson RH, et al. Rapid Estimate of Adult Literacy in Medicine: A Shortened Screening Instrument. *Clinical Research and Methods*. 1993 25,391-5.
33. Hartman K, Ciorciaro C, Kuhn M. Ulcer therapy agents: Adverse drug reaction profile of proton pump blockers compared to H₂-antagonists in the spontaneous reporting scheme. *Schweiz Med Wochenschr* 1996; 126(49):2114-2118.
34. Gustavson LE, Kaiser JF, Edmonds AL, Locke CS, DeBartolo ML, Schenck DW. Effect of omeprazole on concentrations of clarithromycin in plasma and gastric tissue at steady state. *Antimicrob Agents Chemother* 1995; 39(9):2078-2083.
35. Astra Hässle Clinical Study Report: An interaction between omeprazole, metronidazole and clarithromycin (SH-OMH-0014) 1997.
36. Astra Hässle Clinical Study Report: An interaction between omeprazole, amoxicillin and clarithromycin (SH-OMH-0016) 1997.
37. Andersson T. Pharmacokinetics of omeprazole in man with special reference to single and repeated administration, drug interactions, and polymorphic metabolism. Thesis: University of Göteborg (Sweden):41 pp, ISBN 91-628-0180-5, 2nd Edition; Vasastadens 1991.
38. Astra Hässle Clinical Study Report: Food interaction study on omeprazole. Comparison between a new multiple unit tablet with the commercially manufactured capsules. (Protocol No. SH-OME-0008) 1996.
39. Astra Hässle Clinical Study Report: Effect of omeprazole on diazepam plasma levels after I.V. diazepam. (Study No. I-285) April 1985.
40. Gugler R, Jensen JC. Omeprazole inhibits oxidative drug metabolism. Studies with diazepam and phenytoin *in vivo* and 7-ethoxycoumarin *in vitro*. *Gastroenterology* 1985; 89:1235-41.
41. Andersson T, Andren K, Cederberg C, Edvardsson G, Heggelund A, Lundborg P. Effect of omeprazole and cimetidine on plasma diazepam levels. *Eur J Clin Pharmacol* 1990; 39:51-4.
42. Astra Hässle Clinical Study Report: Effect of omeprazole and cimetidine on diazepam plasma levels after IV diazepam. (Report No. I-306) April 1987.

43. Astra Hässle Clinical Study Report: Effect of omeprazole on diazepam plasma levels after IV diazepam in slow and in normal rapid metabolisers of omeprazole. (Study No. I-306,B) June 1988.
44. Astra Hässle Clinical Study Report: Effect of omeprazole on phenytoin plasma levels after I.V. phenytoin. (Study No. I-286) April 1985.
45. Prichard PJ, Walt RP, Kitchingman GK, Somerville KW, Langman MJS, et al. Oral phenytoin pharmacokinetics during omeprazole therapy. *Br J Clin Pharmacol* 1987; 24:543-5.
46. Astra Hässle Clinical Study Report: Effect of omeprazole on phenytoin plasma levels after oral phenytoin (Epanutin®). (Study No. I-289) December 1987.
47. Bachmann KA, Sullivan TJ, Jauregui L, Reese JH, Miller K, Levine L. Absence of an inhibitory effect of omeprazole and nizatidine on phenytoin disposition, a marker of CYP2C activity. *Br J Clin Pharmacol* 1993; 36:380-2.
48. Andersson T, Lagerstrom P-O, Unge P. A study of the interaction between omeprazole and phenytoin in epileptic patients. *Ther Drug Monit* 1990; 12:329-33.
49. Astra Hässle Clinical Study Report: A study of the interaction between omeprazole and phenytoin in epileptic patients. (Study No. I-362) March 1990.
50. Sutfin T, Balmer K, Böstrom H, Eriksson S, Höglund P, Paulsen O. Stereoselective interaction of omeprazole with warfarin in healthy men. *Ther Drug Monit* 1989; 11:176-84.
51. Astra Hässle Clinical Study Report: Effect of omeprazole treatment on warfarin pharmacokinetics in patients. (Report No. I-293) August 1987.
52. Unge P, Svedberg L-E, Nordgren A, Blom H, Andersson T, et al. A study of the interaction of omeprazole and warfarin in anticoagulated patients. *Br J Clin Pharmacol* 1992; 34:509-512.
53. Astra Hässle Clinical Study Report: A study of the interaction between omeprazole and warfarin in anticoagulant patients. (Study No. I-367) March 1992.
54. Chin TWF, Loeb M, Fong IW. Effects of an acidic beverage (Coca-Cola) on absorption of ketoconazole. *Antimicrob Agents Chemother* 1995; 39(8):1671-5.
55. Jaruratanasirikul S, Sriwiriyajan S. Effect of omeprazole on the pharmacokinetics of itraconazole. *Eur J Clin Pharmacol* 1998; 54(2):159-61.
56. Andersson T, Olsson R, Regarch C-G, et al. Pharmacokinetics of [¹⁴C]omeprazole in patients with liver cirrhosis. *Clin Pharmacokinet* 1993; 24:71-78.

57. Rinetti M, Regazzi MB, Villani P, et al. Pharmacokinetics of [¹⁴C] omeprazole in cirrhotic patients. *Arzneimittelforschung* 1991; 41:420-422.
58. Landahl D, Andersson T, Larsson M, et al. Pharmacokinetic study of omeprazole in elderly healthy volunteers. *Clin Pharmacokinet* 1992; 23:469-476.
59. Naesdal J, Andersson T, Bodemar G, et al. Pharmacokinetics of [¹⁴C] omeprazole in patients with impaired renal function. *Clin Pharmacol Ther* 1986; 40:344-351.
60. Astra Pharmaceuticals, L. P. Package Insert. Prilosec[®] (Omeprazole) Delayed-Release Capsules prescribing information. FDA approved labeling No. 9194131. December 1998;4.
61. Muller J, Kirchner T, Muller-Hermelink HK. Gastric endocrine cell hyperplasia and carcinoid tumors in atrophic gastritis type A. *Am J Surg Pathol* 1987; 11(12):909-17.
62. Capella C, Polak JM, Timson CM, Frigerio B, Solcia E. Gastric carcinoids of argyrophil ECL cells. *Ultrastruct Pathol* 1980; 1(3):411-418.
63. Borch K, Renvall H, Liedberg G. Gastric endocrine cell hyperplasia and carcinoid tumors in pernicious anemia. *Gastroenterology* 1985; 88(3):638-48.
64. Lehy T, Cadot G, Mignon M, Ruszniewski P, Bonfils S. Influence of multiple endocrine neoplasia type 1 on gastric endocrine cells in patients with the Zollinger-Ellison syndrome. *Gut* 1992; 33(9):1275-1279.
65. Cadot G, Laurent-Puig P, Thuille B, Lehy T, Mignon M, Olschwang S. Is the multiple endocrine neoplasia type 1 gene a suppressor for fundic argyrophil tumors in the Zollinger-Ellison syndrome? *Gastroenterology* 1993; 105(2):579-582.
66. Solcia E, Fiocca R, Villani L, Luinetti O, Capella C. Hyperplastic, dysplastic, and neoplastic enterochromaffin-like-cell proliferations of the gastric mucosa. Classification and histogenesis. *Am J Surg Pathol* 1995; 19(Suppl 1):S1-7.
67. Solcia E, Bordi C, Creutzfeldt W, Dayal Y, Dayan AD, Falkmer S, et al. Histopathological classification of nonantral gastric endocrine growths in man. *Digestion* 1988; 41(4):185-200.
68. Stolte M. Fundic gland polyps: a rare, innocuous, and reversible disturbance. *Gastroenterology* 1993; 105(5):1590-1591.
69. Cooper JE, Roberts-Thomson IC. Gastrointestinal: Fundic gland polyps. *J Gastroenterol Hepatol* 1999; 14(4):395.
70. Elster K. Histologic classification of gastric polyps. Grundmann E and Kirsten WH. Current topics in pathology. Vol. 63. Berlin: Springer-Verlag, 1976: 77-93.

71. Watanabe H, Enjoji M, Yao T, Ohsato K. Gastric lesions in familial adenomatosis coli. *Hum Pathol* 1978; 9(3):269-283.
72. Iida M, Yao T, Watanabe H, Itoh H, Iwashita A. Fundic gland polyposis in patients without familial adenomatosis coli: its incidence and clinical features. *Gastroenterology* 1984; 86(6):1437-1442.
73. Sipponen P, Laxen F, Seppala K. Cystic 'hamartomatous' gastric polyps: a disorder of oxytic glands. *Histopathology* 1983; 7(5):729-737.
74. Lee RG, Burt RW. The histopathology of fundic gland polyps of the stomach. *Am J Clin Pathol* 1986; 86(4):498-503.
75. Kinoshita Y, Tojo M, Yano T, Kitajima N, Itoh T, Nishiyama K, et al. Incidence of fundic gland polyps in patients without familial adenomatous polyposis. *Gastrointest Endosc* 1993; 39(2):161-3.
76. Hizawa K, Iida M, Matsumoto T, Aoyagi K, Yao T, Fujishima M, et al. Natural history of fundic gland polyposis without familial adenomatosis coli: Follow-up observations in 31 patients. *Radiology* 1993; 189(2):429-432.
77. Odze RD, Marcial MA, Antonioli D. Gastric fundic gland polyps: A morphological study including mucin histochemistry, stereometry, and MIB-1 immunohistochemistry. *Hum Pathol* 1996; 27:896-903.
78. Graham JR. Gastric polyposis: onset during long-term therapy with omeprazole. *Med J Aust* 1992; 157:287-8.
79. Graham JR. Gastric polyposis: onset during long-term therapy with omeprazole. *Med J Aust* 1992; 157(4):646.
80. Graham JR. Omeprazole and gastric polyposis in humans [letter; comment]. *Gastroenterology* 1993; 104(5):1584.
81. Graham JR. Gastric acne: Omeprazole-induced fundic gland polyposis. *Med J Aust* 1998; 168(2):93.
82. Stolte M, Bethke B, Seifert E, Armbrecht U, Lutke A, Goldbrunner P, et al. Observation of gastric glandular cysts in the corpus mucosa of the stomach under omeprazole treatment. *Z Gastroenterol* 1995; 33(3):146-9.
83. Israel DM, Hassall E, Dimmick JE. Gastric polyps in children receiving omeprazole. *Gastroenterology* 1995; 108(4 Suppl):A121.
84. Hirt M, Lee SW, Weinstein WM. Fundic gland polyps: A comparison of the omeprazole-associated and the sporadic types. *Gastroenterology* 1996; 110(4 Suppl):A135.

85. Mogadam M, Houk RR. Long-term use of omeprazole is associated with development of benign epithelial gastric polyps. Am J Gastroenterol 1996; 91(9):1921.
86. El-Zimaity H, Jackson FW, Graham DY. Fundic gland polyps associated with omeprazole therapy in patients without *H. pylori* infection. Am J Gastroenterol 1996; 91(9):1911.
87. El-Zimaity HMT, Jackson FW, Graham DY. Fundic gland polyps appearing during omeprazole therapy for Barrett's with no *H. pylori* gastritis. Mod Pathol 1997; 10(1):54A.
88. El-Zimaity HMT, Jackson FW, Graham DY. Fundic gland polyps appearing during omeprazole therapy for Barrett's with no *H. pylori* gastritis. Lab Invest 1997; 76(1):54A.
89. El-Zimaity HMT, Jackson FW, Graham DY. Fundic gland polyps developing during omeprazole therapy. Am J Gastroenterol 1997; 92(10):1858-60.
90. Van Vlierberghe H, De Vos M, De Cock G, Cuvelier C, Elewaut A. Fundic gland polyps: Three other case reports suggesting a possible association with acid suppressing therapy. Acta Gastroenterol Belg 1997; 60(3):240-2.
91. Schenk BE, Kuiipers EJ, Klinkenberg-Knol EC, Eskes SA, Bloemena E, Meuwissen SGM. Gastric polyps during long-term omeprazole treatment for gastro-oesophageal reflux disease. Eur J Gastroenterol Hepatol 1997; 9(12):A2-3.
92. Dignan CR, Ladabaum U, Scheiman JM, Appelman HD, Greenson JK. Fundic gland polyps are associated with omeprazole use. Lab Invest 1998; 78(1):63A.
93. Dignan CR, Ladabaum U, Scheiman JM, Appelman HD, Greenson JK. Fundic gland polyps are associated with omeprazole use. Mod Pathol 1998; 11(1):63A.
94. Declerck P, Ferrara A, Galati F, Caruso S, Baldacci MP, Ambrosiani L. Do fundic gland polyps develop under long-term omeprazole therapy? Am J Gastroenterol 1998; 93(8):1393.
95. Naegels S, Urbain D. Omeprazole and fundic gland polyps. Am J Gastroenterol 1998; 93(5):855.
96. Jackson FW, Gordon SJ. Regression of fundic gland polyps after discontinuation of omeprazole. Am J Gastroenterol 1998; 93(9):1639.
97. Pashankar D, Israel DM. Endoscopic gastric changes in children on long-term omeprazole therapy. J Pediatr Gastroenterol Nutr 1998; 27(4):479.

98. Choudhry U, Boyce HW Jr, Coppola D. Proton pump inhibitor-associated gastric polyps: A retrospective analysis of their frequency, and endoscopic, histologic, and ultrastructural characteristics. *Am J Clin Pathol* 1998; 110(5):615-21.
99. Collins S, Tydd T. Gastric polyps and long term omeprazole. *J Gastroenterol Hepatol* 1998; 13(Suppl 1):A149.
100. Toribara NW, Sleisenger MH. Screening for colorectal cancer. *N Engl J Med* 1995; 332(13):861-867.
101. Penman ID, McColl KEL. Gastrin and colorectal cancer: Where now? *Eur J Gastroenterol Hepatol* 1998; 10(4):285-8.
102. Baldwin GS, Shulkes A. Gastrin, gastrin receptors and colorectal carcinoma. *Gut* 1998; 42(4):581-4.
103. Joshi SN, Gardner JD. Gastrin and colon cancer: A unifying hypothesis. *Dig Dis* 1996; 14(6):334-44.
104. Begos DG, Modlin IM. Editorial: Gastrin and colon cancer. Clarifying the controversy. *J Clin Gastroenterol* 1994; 18(3):189-193.
105. Baldwin GS, Whitehead RH. Gut hormones, growth and malignancy. *Baillieres Clin Endocrinol Metab* 1994; 8(1):185-214.
106. Creutzfeldt W, Lamberts R. Is hypergastrinemia dangerous to man? *Scand J Gastroenterol* 1991; (Suppl 180):179-91.
107. Renga M, Brandi G, Paganelli GM, Calabrese C, Papa S, Tosti A, et al. Rectal cell proliferation and colon cancer risk in patients with hypergastrinaemia. *Gut* 1997; 41(3):330-2.
108. Orbuch M, Venzon DJ, Lubensky IA, Weber HC, Gibril F, Jensen RT. Prolonged hypergastrinemia does not increase the frequency of colonic neoplasia in patients with Zollinger-Ellison syndrome. *Dig Dis Sci* 1996; 41(3):604-13.
109. Wong K, Beardshall K, Waters CM, Calam J, Poston GJ. Postprandial hypergastrinaemia in patients with colorectal cancer. *Gut* 1991; 32(11):1352-4.
110. Finley GG, Koski RA, Melhem MF, Pipas JM, Meisler AI. Expression of the gastrin gene in the normal human colon and colorectal adenocarcinoma. *Cancer Res* 1993; 53(12):2919-26.
111. Seitz JF, Giovannini M, Gouvernet J, Gauthier AP. Elevated serum gastrin levels in patients with colorectal neoplasia. *J Clin Gastroenterol* 1991; 13(5):541-5.
112. Smith JP, Wood JG, Solomon TE. Elevated gastrin levels in patients with colon cancer or adenomatous polyps. *Dig Dis Sci* 1989; 34(2):171-4.

113. Kikendall JW, Glass AR, Sabin LH, Bowen PE. Serum gastrin is not higher in subjects with colonic neoplasia. Am J Gastroenterol 1992; 87(10):1394-7.
114. Yapp R, Modlin IM, Kumar RR, Binder HJ, Dubrow R. Gastrin and colorectal cancer. Evidence against an association. Dig Dis Sci 1992; 37(4):481-4.
115. Suzuki H, Matsumoto K, Terashima H. Serum levels of gastrin in patients with colorectal neoplasia. Dis Colon Rectum 1988; 31(9):716-717.
116. Penman ID, el-Omar E, Ardill JE, McGregor JR, Galloway DJ, O'Dwyer PJ, et al. Plasma gastrin concentrations are normal in patients with colorectal neoplasia and unaltered following tumor resection. Gastroenterology 1994; 106(5): 1263-70.
117. Vanderstraeten EF, De Vos MM, Versieck JM, Elewaut AP. Serum gastrin levels and colorectal neoplasia. Dis Colon Rectum 1995; 38(2):172-176.
118. Annibale B, Rindi G, D'Ambra G, Marignani M, Solcia E, Bordi C, et al. Antral gastrin cell hyperfunction and *Helicobacter pylori* infection. Aliment Pharmacol Ther 1996; 10(4):607-15.
119. Kuipers EJ, Pals G, Pena AS, van Uffelen CWJ, Kik A, Westerveld BD, et al. *Helicobacter pylori*, pepsinogens and gastrin: relationship with age and development of atrophic gastritis. Eur J Gastroenterol Hepatol 1996; 8(2):153-156.
120. Maconi G, Lazzaroni M, Sangaletti O, Bargiggia S, Vago L, Bianchi Porro G. Effect of *Helicobacter pylori* eradication on gastric histology, serum gastrin and pepsinogen I levels, and gastric emptying in patients with gastric ulcer. Am J Gastroenterol 1997; 92(10):1844-8.
121. Perez-Paramo M, Albilllos A, Calleja JL, Salas C, Del Carmen Marin M, Marcos ML, et al. Changes in gastrin and serum pepsinogens in monitoring of *Helicobacter pylori* response to therapy. Dig Dis Sci 1997; 42(8):1734-1740.
122. Gupta A, Rana SV, Goenka MK, Kukreja RS. Transcriptional expression of gastrin mRNA in *Helicobacter pylori* infected patients. Indian J Med Res 1997; 105:136-40.
123. Bretagne J-F, Heresbach D. *Helicobacter pylori*, achlorhydria and gastric atrophy: What sort of triangle? Gastroenterol Clin Biol 1997; 21(2):117-23.
124. Parente F, Imbesi V, Maconi G, Cucino C, Manzionna G, Vago L, et al. Effects of *Helicobacter pylori* eradication on gastric function indices in functional dyspepsia. Scand J Gastroenterol 1998; 33(5):461-7.
125. Gisbert JP, Boixeda D, Al-Mostafa A, Vila T, de Rafael L, Alvarez Baleriola I, et al. Basal and stimulated gastrin and pepsinogen levels after eradication of *Helicobacter pylori*: A 1-year follow-up study. Eur J Gastroenterol Hepatol 1999; 11(2):189-200.

126. Thorburn CM, Friedman GD, Dickinson CJ, Vogelman JH, Orentreich N, Parsonnet J. Gastrin and colorectal cancer: A prospective study. *Gastroenterology* 1998; 115(2):275-280.
127. Elsborg L, Mosbech J. Pernicious anaemia as a risk factor in gastric cancer. *Acta Med Scand* 1979; 206(4):315-8.
128. Lieberman DA, Ippoliti AF, Weber LJ, Weinstein WM. Long-term omeprazole is not associated with an increased incidence of colon neoplasia. *Gastroenterology* 1996; 110(4):A176.
129. Robinson M, Earnest D, Rodriguez-Stanley S, et al. Heartburn requiring frequent antacid use may indicate significant illness. *Arch Intern Med* 1998; 158:2373-2376.
130. Talley NJ. Dyspepsia and heartburn: a clinical challenge. *Aliment Pharmacol Ther* 1997; 11(suppl 2):1-8.
131. Corder AP, Jones RH, Milward-Sadler GH, et al. Heartburn oesophagitis and Barrett's oesophagus in self-medicating patients in general practice. *BJCP* 1996; 50(5): 245-248.
132. Sampliner RE. Adenocarcinoma of the esophagus and gastric cardia: is there progress in the face of increasing cancer incidence? *Ann Intern Med* 1999; 130:67-69.
133. Cohen S, Parkman HP. Heartburn- a serious symptom. *N Engl J Med* 1999; 340:878-9. Letter.
134. Chow WH, Finkle WD, McLaughlin JK, Frankl H, Ziel HK, Fraumeni JF Jr. The relation of gastroesophageal reflux disease and its treatment to adenocarcinoma of the esophagus and gastric cardia. *JAMA* 1995; 274:474-477.
135. Lagergren J, Bergstrom R, Lindgren A, Nyren O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. *N Engl J Med* 1999; 340:825-831.
136. Spechler SJ. Epidemiology and natural history of gastro-esophageal disease. *Digestion* 1992; 51(suppl1):24-29.
137. Cameron AJ, Zinsmeister AR, Ballard DJ, Carney JA. Prevalence of columnar-lined (Barrett's) esophagus: comparison of population-based clinical and autopsy findings. *Gastroenterol* 1990; 99:918-922.
138. Cameron AJ, Lomboy CT, Barrett's esophagus: age, prevalence and extent of columnar epithelium. *Gastroenterology* 1992; 103:1241-1245.

139. Johnston MH, Hammond AS, Laskin W, Jones DM. The prevalence and clinical characteristics of short segments of specialized intestinal metaplasia in the distal esophagus on routine endoscopy. *Am J Gastroenterol* 1996; 91(8):1507-1511.
140. Eloubeidi MA, Provenzale D. Does this patient have Barrett's esophagus? The utility of predicting Barrett's esophagus at the index of endoscopy. *AM J Gastroenterol* 1999; 94(4):937-943.
141. Protocol SK&F 92334/B0025. An epidemiological study to establish the prevalence of endoscopically identified acid-peptic disorders in patients frequently taking antacids. *NDA* 20-238:158-166.
142. Burnham DB, Friedman CJ, Asbel-Sethi N. The prevalence of endoscopic lesions in the upper gastrointestinal (UGI) tract of frequent antacid users. *Gastroenterology* 1993; 104(suppl 4):A49.
143. Pappa KA, Giefer EE, Payne JE, et al. Endoscopic findings in a target population for over-the-counter treatment of heartburn. *Gastroenterology* 1996; 106,4(A):146.
144. DeVault KR, Castell DO. Guidelines for the diagnosis and treatment of gastroesophageal reflux disease. *Arch Inter Med* 1995;155:2165-73.
145. DeVault KR, Castell DO. Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. *Am J Gastroenterol* 1999; 94(6): 1434-1442.
146. Lind T, Cederberg C, Idstrom JP, Lonroth H, Olbe L, Lundell L. 24-Hour intragastric acidity and plasma gastrin during long-term treatment with omeprazole or ranitidine in patients with reflux esophagitis. *Scand J Gastroenterol* 1991; 26(6):620-626.
147. Gillen D, Wirz AA, Ardill JE, McColl KEL. Rebound hypersecretion after omeprazole and its relation to on-treatment acid suppression and Helicobacter pylori status. *Gastroenterology* 1999; 116(2):239-247.
148. Lamberts R, Creutzfeldt W, Struber HG, Brunner G, Solcia E. Long-term omeprazole therapy in peptic ulcer disease: Gastrin, endocrine cell growth, and gastritis. *Gastroenterology* 1993; 104(5):1356-1370.
149. Lind T, Cederberg C, Ekenved G, Haglund U, Olbe L. Effect of omeprazole - a gastric proton pump inhibitor - on pentagastrin stimulated acid secretion in man. *Gut* 1983; 24(4):270-276.
150. Sharma BK, Walt RP, Pounder RE, Gomes MD, Wood EC, Logan LH. Optimal dose of oral omeprazole for maximal 24 hour decrease of intragastric acidity. *Gut* 1984; 25(9):957-964.
151. Müller P, Seitz HK, Simon B, Dammann HG, Feurle G, et al. 28-day omeprazole treatment: Gastric acid secretion and basal hormone levels in man. *Z Gastroenterol* 1984; 22(5):236-240.

152. Prewett EJ, Hudson M, Nwokolo CU, Sawyerr AM, Pounder RE. Nocturnal intragastric acidity during and after a period of dosing with either ranitidine or omeprazole. *Gastroenterology* 1991; 100:873-877.
153. Bell NJ, Rohss K, Cederberg C, Hunt RH. Does tachyphylaxis and/or rebound acid secretion occur during/after treatment with omeprazole or ranitidine? *Gastroenterology* 1993; 104:A41.
154. Orr WC, Mellow MH. Omeprazole vs ranitidine: Comparisons of daytime and nocturnal reflux suppression. *Am J Gastroenterol* 1992; 87:1254.
155. Waldum HL, Arnestad JS, Brenna E, Eide I, Syversen U, Sandvik AK. Marked increase in gastric acid secretory capacity after omeprazole treatment. *Gut* 1996; 39(5):649-653.
156. Gillen D, Wirz AA, Ardill JES, McColl KEL. Rebound acid hypersecretion post-omeprazole correlates with on-treatment intragastric pH and on-treatment plasma gastrin. *Gastroenterology* 1998; 114(4 Suppl Pt 2):A133.
157. Fisher RS, Kushner M, Bonapace E, Knight LC, Parkman HP. Rebound acid hypersecretion after gastric acid suppressant therapy: A short-lived (<1-week) phenomenon. *Gastroenterology* 1998; 114(4 Suppl Pt 2):A13.
158. Weinstein WM, Ippoliti AF, Lee SW, Weber LJ, Leiberman DA. Acid hypersecretion, parietal cell hyperplasia, and endoscopic changes after withdrawal of long term high dose omeprazole therapy: a prospective study. *Gastroenterology* 1996; 110(4 Suppl):A294.
159. Gillen D, El-Omar EM, Wirz AA, Ardill JES, McColl KEL. The acid response to gastrin distinguishes duodenal ulcer patients from Helicobacter pylori - Infected healthy subjects. *Gastroenterology* 1998; 114(1):50-57.
160. Harris AW, Gummett PA, Phull PS, Jacyna MR, Misiewicz JJ, Baron JH. Recurrence of duodenal ulcer after Helicobacter pylori eradication is related to high acid output. *Aliment Pharmacol Ther* 1997; 11(2):331-334.
161. Bercik P, Verdu EF, Armstrong D, Cederberg C, Idstrom JP, et al. Apparent increase in acid output during omeprazole (OME) after cure of H. pylori infection (HPI). *Gastroenterology* 1997; 112(4 Suppl):A70.
162. Gibbons AH, Legon S, Walker MM, Ghatei M, Calam J. The effect of gastrin-releasing peptide on gastrin and somatostatin messenger RNAs in humans infected with Helicobacter pylori. *Gastroenterology* 1997; 112(6):1940-1947.
163. El-Omar E, Banerjee S, Wirz A, Penman I, Ardill JES, McColl KEL. Marked rebound acid hypersecretion after treatment with ranitidine. *Am J Gastroenterol* 1996; 91(2):355-359.

164. Klinkenberg-Knol EC. Eleven years' experience of continuous maintenance treatment with omeprazole in GERD-patients. *Gastroenterology* 1998; 114(4 Suppl Pt 2):A180.
165. Brown P, Ceravolo C, Zambelli A. Rebound rise in gastric acid secretion: study of cimetidine vs. trithiozine: a preliminary report. *Curr Ther Res* 1978; 23(6):706-708.
166. Nwokolo CU, Smith JTL, Pounder RE. Rebound intragastric hyperacidity after acute withdrawl of cimetidine, famotidine, or nizatidine is not mediated by persisting hypergastrinaemia. *Gut* 1989; 30:A725-A726.
167. Fullarton GM, McLauchlan G, Macdonald A, Crean GP, McColl KEL. Rebound nocturnal hypersecretion after four weeks treatment with an H₂ receptor antagonist. *Gut* 1989; 30(4):449-454.
168. Savarino V, Mela GS, Zentilin P, Sumberaz A, Bonifacino G, Celle G. Lack of gastric acid rebound after stopping a successful short-term course of nizatidine in duodenal ulcer patients. *Am J Gastroenterol* 1991; 86(3):281-284.
169. Atkinson TP, Kaliner MA. Anaphylaxis. *Med Clin N Amer* 1992;76:841-855.
170. Huitema ADR, Soesan M, Meenhorst PL, Koks CHW, Beijnon JH. A dose-dependent delayed hypersensitivity reaction to acetaminophen after repeated acetaminophen intoxications. *Hum Exp Tox* 1998;17:406-408.
171. Van Diem L, Grilliat JP. Anaphylactic shock induced by paracetamol. *Eur J Clin Pharmacol* 1990;38:389-390.
172. Ibanez MD et al. Delayed hypersensitivity reaction to paracetamol (acetaminophen). *Allergy* 1996;51:121-123.
173. Kounis NG. A review: Drug-induced bronchospasm. *Ann Allergy* 1976;37:285-291.
174. Brunner G, Thiesemann C, Ratz H. High plasma concentrations of proton pump inhibitors cause peripheral oedema in female patients. *Gastroenterology* 1993;104:A48.
175. Van der Klauw MM, Wilson JHP, Stricker BHCh. Drug-associated anaphylaxis: 20 years of reporting in the Netherlands (1974-1994) and review of the literature. *Clin Exp All* 1996;26:1355-1363.
176. D'Arcy PF. Drug reactions and interactions. *Int Pharm J* 1991;5:246-248.
177. Freemantle SN, Pearce GL, Wilton LV, et al. The incidence of the most commonly reported events with 40 newly marketed drugs – a study by Prescription-Event Monitoring. *Pharmacoepidemiology and Drug Safety* 1997;6(suppl 1):1-62.
178. Coulter D. Top ten adverse reactions to omeprazole in the IMMP. *Prescriber Update* 1997;14:28-31.

179. Coulter D. The New Zealand intensive medicines monitoring programme. *Pharmacoepidemiology and Drug Safety* 1998;7:79-90.
180. Hartmann K, Ciorciaro C, Kuhn M. Ulcer therapy agents: Adverse drug reaction profile of proton pump blockers compared with H₂-antagonists in the spontaneous reporting scheme. *Schweiz Med Wochenschr* 1996;126(49):2114-2118.
181. Arnold R. Safety of proton pump inhibitors - an overview. *Aliment Pharmacol Ther* 1994; 8(Suppl 1):65-70.
182. Massoomi F, Savage J, Destache CJ. Omeprazole: A comprehensive review. *Pharmacotherapy* 1993; 13:46-59.
183. Joelson S, Joelson IB, Lundborg P, Walan A, Wallander MA. Safety experience from long-term treatment with omeprazole. *Digestion* 1992; 51 (Suppl 1):93-101.
184. Klinkenberg-Knol EC, Festen HPM, Jansen JBMJ, Lamers CBHW, Nelis F, et al. Long-term treatment with omeprazole for refractory reflux esophagitis: efficacy and safety. *Ann Intern Med* 1994; 121:161-7.
185. Masubuchi N, Hakusui H, Okazaki O. Effects of pantoprazole on xenobiotic metabolizing enzymes in rat liver microsomes: A comparison with other proton pump inhibitors. *Drug Metab Dispos* 1997; 25(5):584-9.
186. McClain RM. Phenobarbital mouse liver tumors: implications of hepatic tumor promotion for cancer risk assessment. *Prog Clin Biol Res* 1995; 391:325-36.
187. Whysner J, Ross PM, Williams GM. Phenobarbital mechanistic data and risk assessment: enzyme induction, enhanced cell proliferation, and tumor promotion. *Pharmacol Ther* 1996; 71(1/2):153-191.
188. Rizzo N, Padoin C, Palombo S, Scherrman J-M, Girre C. Omeprazole and lansoprazole are not inducers of cytochrome P4501A2 under conventional therapeutic conditions. *Eur J Clin Pharmacol* 1996; 49(6):491-5.
189. Skare JA, Murphy VA, Bookstaff RC, Thompson GA, Heise MA, et al. Safety assessment of OTC drugs: doxylamine succinate. *Arch Toxicol Suppl* 1995; 17:326-40.
190. Olsen JH, Schulgen G, Boice JD, Whysner J, Travis LB, Williams GM, Johnson FB, McGee JO. Antiepileptic treatment and risk for hepatobiliary cancer and malignant lymphoma. *Cancer Res* 1995, 55: 294-7.
191. Gustavsson S, Adami H-O, Loof L, Nyberg A, Nyren O. Rapid healing of duodenal ulcers with omeprazole: double-blind dose-comparative trial. *Lancet* 1983; 2:124-5.
192. Loof L, Adami H-O, Gustavsson S, Nyberg A, Nyren O, Lundborg P. Omperazole: no evidence for frequent hepatic reactions. *Lancet* 1984; 1 135:1347-8.

193. McArthur KE, Collen MJ, Maton PN, Cherner JA, Howard JM, et al. Omeprazole: Effective, convenient therapy for Zollinger-Ellison syndrome. *Gastroenterology* 1985; 88:939-44.
194. Garcia Rodriguez LA, Wallander M-A, Stricker BHC. The risk of acute liver injury associated with cimetidine and other acid-suppressing anti-ulcer drugs. *Br J Clin Pharmacol* 1997; 43: 183-8.
195. Bashir RM, Lewis JH. Hepatotoxicity of drugs used in the treatment of gastrointestinal disorders. *Gastroenterol Clin North Am* 1995; 24(4):937-67.
196. Lewis JH. Hepatic effects of drugs used in the treatment of peptic ulcer disease. *Am J Gastroenterol* 1987; 82:987-1003.
197. Smallwood RA, Berlin RG, Castagnoli N, Festen HPM, Hawkey CJ, et al. Safety of acid-suppressing drugs. *Dig Dis Sci* 1995; 40(2 Suppl):63S-80S.
198. Anonymous. Notes on omeprazole. *Hepato-Gastroenterology*. 1994; 41: 596.
199. Schonhofer P. Intravenous omeprazole and blindness. *Lancet*. 1994; 343: 665.
200. Colin-Jones D. Safety of omeprazole and lansoprazole. *Lancet*. 1994; 343: 1369.
201. Schonhofer P. Safety of omeprazole and lansoprazole. *Lancet*. 1994; 343: 1369-1370.
202. Schonhofer P. Omeprazole and ocular damage: Author's reply. *BMJ*. 1998; 316: 68.
203. Kao LY, Huang L, Chen TT. Anterior ischemic optic neuropathy-recurrent attacks in one eye in a bilateral case. *Ann Ophthalmol*. 1989; 21: 71-74.
204. Kay MC. Ischemic optic neuropathy. *Neurologic Clinics*. 1991; 9: 115-129.
205. Burde RM, Optic disk risk factors for nonarteritic anterior ischemic optic neuropathy. *Am J Ophthalmol*. 1993; 116: 759-764.
206. Sadun AA. The efficacy of optic nerve sheath decompression for anterior ischemic optic neuropathy and other optic neuropathies. *Am J Ophthalmol*. 1993; 115: 384-389.
207. Katz DM, Trobe JD, Cornblath WT, Kline LB. Ischemic optic neuropathy after lumbar spine surgery. *Arch Ophthalmol*. 1994; 112: 925-931.
208. Arnold AC. Anterior ischemic optic neuropathy. *Seminars in Ophthalmology*. 1995; 10: 221-233.
209. Williams EL, Hart WM, Tempelhoff R. Postoperative ischemic optic neuropathy. *Anesth Analg*. 1995; 80: 1018-1029.

210. Schobel GA, Schmidbauer M, Millesi W, Undt G. Posterior ischemic optic neuropathy following bilateral radical neck dissection. *Int J Oral Maxillofacial Surgery*. 1995; 24: 283-287.
211. Lee AG, Brazis PW, Miller NR. Posterior ischemic optic neuropathy associated with migraine. *Headache*. 1996; 36: 506-509.
212. Altschuler E. Gastric helicobacter pylori infection as a cause of idiopathic Parkinson disease and non-arteritic anterior optic ischemic neuropathy. *Medical Hypotheses*. 1996; 47: 413-414.
213. Troger U, Meyer FP, Schonhofer PS, Werner B, Wille H. Visual impairment due to omeprazole, possible pathogenetic mechanisms and evaluation of case reports. *Eur J Clin Pharmacol*. 1995; 49. Abstract 165.
214. Schonhofer, P. Ocular damage associated with proton pump inhibitors. *BMJ*. 1997; 314: 1805.
215. Jensen K. Visual disturbance during treatment with omeprazole. *Ugeskr. Laeger* 1996; 158: 4790.
216. Kanamaru M, Nakashima M, Kajiho T, Matsuda Y, Oka T. Inhibition of gastric secretion by omeprazole, a proton pump inhibitor: Effect on basal and tetragastrin-stimulated gastric secretions in healthy volunteers. *J Clin Ther Med*. 1989; 5: 13-28.
217. Ferner RE, Allison TR. Omeprazole overdose. *Hum Exp Tox*. 1993; 12: 541-542.
218. Fireman Z, Kopelman Y, Sternberg A. Central nervous system side effects after proton pump inhibitor treatment. *J Clin Gastroenterol*. 1997; 25: 718.
219. Joseph J, Louis S. Transient ictal cortical blindness during middle age: A case report and review of the literature. *J Neuro-ophthalmol*. 1995; 15: 39-42.
220. Madan B, Schey SA. Reversible cortical blindness and convulsions with cyclosporin A toxicity in a patient undergoing allogeneic peripheral stem cell transplantation *Bone Marrow Transplant*. 1997; 20: 793-795.
221. Creutzfeldt WC, Blum AL. Safety of omeprazole. *Lancet*. 1994; 343: 1098.
222. Lundborg P, Walan A. Vision and hearing disorders under omeprazole therapy: Astra sees no causative correlation. *Deutsche Apotheker Zeitung*. 1994; 134: 980-981.
223. Labenz J, Stolte M. Vision and hearing disorders under omeprazole: the facts. *Leber Magen Darm*. 1995; 25: 6-8,11.
224. Riordan-Eva P, Sanders MD. Omeprazole and ocular damage: Facts of cases are unclear. *BMJ*. 1998; 316: 67.

225. Lessell S. Omeprazole and ocular damage: Concerns on safety of drugs are unwarranted. *BMJ*. 1998; 316: 67.
226. Sachs G. Omeprazole and ocular damage: Lack of causality holds true. *BMJ*. 1998; 316: 68.
227. Coca-Prados M, Fernandez-Cabezudo MJ, Sanchez-Torres J, Crabb JW, Ghosh S. Cell-specific expression of the human Na^+,K^+ -ATPase $\beta 2$ subunit isoform in the nonpigmented ciliary epithelium. *Invest Ophthalmol Vis Sci* 1995; 36: 2717-2728.
228. Fain GL, Smolka A, Cilluffo MC, Fain MJ, Lee DA, et al. Monoclonal antibodies to the $\text{H}^+ - \text{K}^+$ ATPase of gastric mucosa selectively stain the non-pigmented cells of the rabbit ciliary body epithelium. *Invest Ophthalmol Vis Sci* 1988; 29: 785-794.
229. Goves J, Oldring JK, Kerr D, Dallaras RG, Roffe EJ, Powell JA, et al. First line treatment with omeprazole provides an effective and superior alternative strategy in the management of dyspepsia compared to antacid/alginate liquid: A multicentre study in general practice. *Aliment Pharmacol Ther*. 1998; 12: 147-157.
230. Wilton L, Inman W, Kubota K, Pearce G, Skipp M. PEM report number 9: omeprazole. *Pharmacoepidemiol Drug Saf*. 1993; 2: 473-498.
231. The ADR Signals Analysis Project (ASAP) Team (Lindquist M, Pettersson M, Edwards IR, Sanderson J, Taylor N, Fletcher P, Schou J) and Fraunfelder FT. Omeprazole and visual disorders: Seeing alternatives. *Pharmacoepidemiol Drug Saf*. 1996; 5: 27-32.
232. Rodriguez LAG, Mannino S, Wallander MA. Ocular safety of antiulcer drugs. *Lancet*. 1995; 345: 1059-1060.
233. Rodriguez LAG, Mannino S, Wallander MA, Lindblom B. A cohort study of the ocular safety of anti-ulcer drugs. *Br J Clin Pharmacol*. 1996; 42: 213-216.
234. Mannino S, Troncon MG, Wallander MA, Cattaruzzi C, Romano F, Agostinis L, Marighi PE, et al. Ocular disorders in users of H_2 -antagonists and of omeprazole. *Pharmacoepidemiol Drug Saf*. 1998; 7(4):233-241.
235. American Society for Gastrointestinal Endoscopy. Guidelines for clinical application: the role of endoscopy in the management of GERD. ASGE publication no. 1006; 1998 December.
236. Blustein PK, Beck PL, Meddings JB, et al. The utility of endoscopy in the management of patients with gastroesophageal reflux symptoms. *Am J Gastroenterol* 1998; 93(12):2508-2512.
237. Bennett BM. On comparisons of sensitivity, specifically, and predictive value of a number of diagnostic procedures. *Biometrics* 1972.