View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by Elsevier - Publisher Connector

integration of both quantity and quality of life into a single analysis to be used for treatment comparisons. **METHODS:** EORTC QLQ C-30, FACT-G&P were used to collect QoL data for 288 subjects with asymptomatic hormone refractory prostate cancer as part of a randomized, double-blind, placebo-controlled dose ranging study of atrasentan, a selective endothelin-A receptor antagonist. Both instruments were administered at baseline and then at every six weeks until disease progression. The missing QoL domain scores were imputed by last observation carried forward method. The QoL domain scores were converted to a unit scale, range 0–1, with a higher score indicating improved QoL. The conversion was implemented with a linear affine transformation of original score according to Ware et. al. Each subject's QADFS was computed as the sum of the product QoL weights and the duration for which the patient experienced that level of QoL. These QADFS times were then analyzed with Kaplan-Meier methodology. In order to analyze the effect of administrative censoring on the results an area under the curve analysis for each QoL domain was implemented with the assumption of equal length of follow-up (365 days). **RESULTS:** The mean QADFS were estimated and compared amongst the three treatment groups. These comparisons yielded results that were robust to the choice of QoL domains and the length of follow-up. CONCLUSIONS: Multidimensional QoL instruments may be used to provide a summary index for assessing the response of novel interventions for cancer patients. It accounts for patient's QoL for the duration of the trial unlike the traditional (e.g., ANOVA) methods of analyses.

GASTROINTESTINAL/URINARY/ RENAL DISORDERS

PGU1

IS HEALTH-RELATED QUALITY OF LIFE (HRQL) IMPROVED BY GASTRO-ESOPHAGEAL REFLUX DISEASE (GERD) DRUGS?

Chassany O, Duracinsky M, Bergmann JF
Therapeutic Research Unit, Hopital Lariboisiere, Paris, France

OBJECTIVE: Effective antisecretory drugs are available to treat GERD, and result in dramatic improvement of pyrosis over placebo. Assessing a similar improvement of HRQL would appear of value. **METHOD:** A critical appraisal of published controlled trials was performed using a checklist. **RESULTS:** Although trials comparing proton pump inhibitors (PPI) to placebo or to H2-blockers or cisapride showed a clinically significant difference in the rate of complete relief of pyrosis, none was able to show a clear and unbiased HRQL improvement. For each trial, several or all of the following issues that may help one to have confidence in study results are not presented or are missing: justification of the choice of questionnaires; hypotheses of changes in HRQL scores and power estimation (even if HRQL assessment is a secondary endpoint); justification of the use of several questionnaires (are they covering different concepts?); statistical analysis plan; description and imputation of missing data, and intent to treat analysis (e.g. 408 patients among 599 randomized in a trial are analyzed for HRQL with no explanation about missing data); adjustment for multiple statistical comparisons; presentation of all the scores. Generic questionnaires (Psychological General Well Being is the most frequently used) result most often in non significant differences or findings without clinical significance (effect size < 0.30). This raises the uncertainty of questionnaire responsiveness, knowing that pyrosis is largely improved and that the sample size of trials ranges from 300 to 800. Using the specific questionnaire, Gastrointestinal Symptom Rating Scale, leads to significant results, but it may be argued that this questionnaire is not simply a symptom scale, because only two items on the questionnaire concern bother about pyrosis and regurgitation. **CONCLUSION:** There is concern to conclude that despite a large improvement of pyrosis, especially with PPI, there is no definite demonstration that HRQL is improved in GERD.

PGU2

DEVELOPMENT AND PRELIMINARY PSYCHOMETRIC VALIDATION OF THE PATIENT ASSESSMENT OF UPPER GASTROINTESTINAL DISORDERS-SYMPTOM SEVERITY INDEX (PAGI-SYM) IN GI PATIENTS

Rentz A[1], Schmier A[1], de la Loge C[2], Dubois D[3], Jones R[4], Peeters K[3], Zodet M[1], Revicki D[1]
[1]Center for Health Outcomes Research, MEDTAP International, Bethesda, MD, USA; [2]MAPI Values, Lyon, France; [3]Health Economics, Johnson & Johnson, Beerse, Belgium; [4]Health Economics, Johnson & Johnson, Titusville, NJ, USA

OBJECTIVE: Patient-reported symptom severity measures are important for evaluating the effectiveness of treatments for gastrointestinal diseases because they are the only measures in clinical evaluation that directly reflect the patient experience. The objective of this study is to describe the development and initial testing of a new patient self-report instrument, the Patient Assessment of Upper GastroIntestinal Disorders-Symptom Severity Index (PAGI-SYM) in subjects with gastroesophageal reflux disease (GERD) or dyspepsia. **METHODS:** Instrument content was based on an extensive review of the published literature and interviews with patients and clinicians. A sample of 448 persons with GERD (249) or dyspepsia (199) were identified and recruited from a large population survey. Using telephone interviews, subjects completed the PAGI-SYM, the SF-36, and a measure of patient-rated change in GI-related symptoms, the Overall Treatment Effect Scale (OTE). Two-week reproducibility was evaluated in 68 subjects. **RESULTS:** The 37-item PAGI-SYM is comprised of 6 subscales: heartburn, reflux/regurgitation, nausea/vomiting, abdominal pain, bloating/early satiety, and other symptoms. Subscale internal consistency reliability was good (alpha = 0.74 to 0.92) with the exception of the two-item sub-

scale, other (alpha = 0.45); total score alpha levels were excellent (0.95). Item correlations by subscale were in the predicted direction; all were significant (r = 0.29 to 0.77; $P < .001$). Correlations between PAGI-SYM total and subscale scores and SF-36 PCS and MCS scores were in the predicted direction; all were significant (r = −0.28 to −0.64; $P < .0001$). CONCLUSIONS: Results suggest the PAGI-SYM is internally consistent with evidence of content and construct validity. Further research on the instrument's reproducibility, sensitivity to change and the definition of clinically-meaningful change in GERD and dyspepsia symptoms is needed before use in clinical studies.

PGU3

DECISION ANALYSIS OF OMEPRAZOLE VERSUS LAPAROSCOPIC NISSEN FUNDOPLICATION FOR TREATING PATIENTS WITH SEVERE GASTROESOPHAGEAL REFLUX DISEASE

Cantrell CR[1], Wilde SW[2], Martin BC[1]
[1]University of Georgia College of Pharmacy, Athens, GA, USA; [2]Northeast Georgia Gastroenterology Associates, Athens, GA, USA

OBJECTIVE: To calculate the break-even point as the number of years after Laparoscopic Nissen fundoplication surgery where the surgery's costs are equivalent to the costs associated with omeprazole maintenance therapy for patients with severe gastroesophageal reflux disease (GERD). **METHODS:** A Markov decision analytic model was developed to estimate the direct medical costs of each alternative for treating patients with severe GERD. The payer perspective was utilized and a literature review was conducted to identify the direct costs associated with each approach. The probabilities used in the model were estimated from published clinical trials. The Markov model cycle was set equal to one year and the break-even point was identified as the year in which the expected values of the costs of each treatment were equal. Sensitivity analyses were performed. **RESULTS:** The break-even point of the two therapies is approximately 12 years. By subtracting 12 years from the average US life expectancy, the break-even age is 64 years in which the costs of surgical treatment for persons under the age of 64 is less than omeprazole for the remaining years of life. The results of the sensitivity analyses will be reported. **DISCUSSION:** This study provides evidence that Laparoscopic Nissen fundoplication becomes a cost saving approach relative to omeprazole therapy when omeprazole therapy is expected to last more than 12 years. This model assumes omeprazole therapy is taken continuously over a patient's lifetime to treat severe GERD and assumes that successful surgery does not require maintenance omeprazole and lasts a patient's lifetime. This procedure is a relatively new technique and there is no long-term data on the success rate. The standard prognosis of success for the surgery used by gastroenterologists has been 10 years. The surgical procedure may not be cost saving if the success rate declines after 10 years.

PGU4

UTILIZATION AND COSTS OF GASTROINTESTINAL DRUGS IN RELATION TO HELICOBACTER-PYLORI ERADICATION; PHARMACOECONOMIC ANALYSIS FOR THE NETHERLANDS

Postma MJ, van den Berg PB, Klok RM, Brouwers JRBJ, De Jong-van den Berg LTW
Groningen University Institute for Drug Exploration/Groningen Research Institute of Pharmacy (GUIDE/GRIP), Groningen, The Netherlands

OBJECTIVE: In the new Dutch General-Practitioner's guidelines, *Helicobacter pylori* (Hp) eradication is indicated for patients with peptic ulcer disease (ulcus duodeni and ulcus ventriculli). Pharmacotherapy for Hp-eradication comprises a combination of an antibiotic and a proton-pump inhibitor (PPI) or a bismuth preparation. Our objective is to estimate gastrointestinal drug utilization and related costs prior and post Hp-eradication. **METHODS:** For the analysis we used a regional pharmacists' database in the North of the Netherlands ("Interaction Database"; total population: 130,000; period covered: 1994–98). We selected all patients with two prescriptions on one day from the same doctor: one prescription for antibiotics and one for PPI. In total 1210 potential eradications were found. Over 95% of the patients received at least one of the following combinations: (i) PPI and amoxicillin; (ii) PPI, clarithromycin and metronidazole; (iii) PPI, clarithromycin and amoxicillin. **RESULTS:** Preliminary results indicate that in the four months prior to eradication, 30% of the patients were on ranitidine maintenance therapy and 25% used PPIs, but 45% used neither. Costs of PPIs amount to approximately €500 per patient in the year prior to eradication. Post-Hp-eradication results indicate that in the year after eradication, costs per patient for PPIs decrease to approximately €250. Updated results, comprising data for 1999 as well, will be presented at the conference. **CONCLUSIONS:** Preliminary results suggest that a significant share of Hp-eradications occur in patients not using PPIs or ranitidine. Furthermore, on the short-term, costs per patient per year for PPIs are reduced by 50% through Hp-eradication.

PGU5

THE BURDEN OF ILLNESS OF IRRITABLE BOWEL SYNDROME (IBS) USING THE ROME II CRITERIA

Badia X[1], Mearin F[2], Balboa A[3], Baró E[1], Caldwell E[4], Cucala M[4], Díaz-Rubio M[5], Fueyo A[6], Ponce J[7], Roset M[1], Talley NJ[8]
[1]Health Outcomes Research Europe, Barcelona, Spain; [2]Hospital Valle Hebron, Barcelona, Spain; [3]Hospital Comarcal de la Selva, Blanes, Spain; [4]Novartis Farmacéutica, Barcelona, Spain; [5]Hospital Clínico San Carlos, Madrid, Spain; [6]Glaxo Wellcome, Madrid, Spain; [7]Hospital de la Fe, Valencia, Spain; [8]University of Sydney, Sydney, Australia