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USE OF TNF-INHIBITORS IN THE UNITED STATES: UTILIZATION PATTERNS AND DOSE-ESCALATION FROM A REPRESENTATIVE UNITED STATES RA POPULATION

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OBJECTIVES: TNF-inhibitors were the first biological therapies approved for RA treatment and five are approved by the US FDA: etanercept (ETN), adalimumab (ADA), infliximab (IFX), certolizumab pegol (CZP) and golimumab (GOL). The study objective was to understand "real-life" dosing patterns, including dose-escalation, which may impact costs/outcomes of TNF-inhibitor therapy. **METHODS:** We used a longitudinal claims database (i3 Pharma Informatics) to assess RA patients receiving ETN, ADA, or IFX. Due to product launch date, CZP and GOL were excluded. Patients having a TNF-inhibitor claim, RA diagnosis (ICD-9: 714.0), at least 6 months pre-biologic eligibility and 24-months enrollment post-claim from January 2007–March 2009 were included. Dose-escalation was defined as an increase in bi-weekly dosing from 40 to 80mg for ADA, an increase in weekly dosing from 25 to 50/100mg or 50 to 100mg for ETN, and the addition of 1 vial to the subsequent 8-weekly maintenance treatment dose, or a reduction in weeks between IFX treatments. **RESULTS:** A total of 59,928 patients filled a TNF-inhibitor prescription and 3448 were eligible for inclusion in this analysis. Dose-escalation rates were 13% for ADA, 3% for ETN, and 39% for IFX. Additionally, 6% of patients initiated on 25mg ETN experienced dose-escalation versus baseline. Switching to another biologic occurred in 14% (ETN), 16% (ADA) and 17% (IFX). **CONCLUSIONS:** These "real-life" data confirm dose-escalation occurs in clinical practice. Further analyses including all anti-TNF approvals should be performed to further elucidate the clinical and cost implications for physicians and payers. A limitation of this study is lack of standardized methodology for calculating anti-TNF doses from claims data. Previous studies report a range of dose-escalation rates for ETN (1-17%), ADA (0-12%), and IFX (30-53%). In this study, cut-points were based on current standards of care correlated with frequency distributions within a closed system, ensuring resulting dose-escalation rates are clinically representative.

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ESTIMATING THE ECONOMIC BENEFITS OF POSITIVE SHIFTS IN FIBROMYALGIA SEVERITY

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OBJECTIVES: Fibromyalgia (FM) is a chronic condition characterized by widespread pain and can impose substantial economic burden. This study estimates the annualized differences in healthcare costs associated with improvement in FM severity among pregabalin-treated patients. **METHODS:** Data from 3 similarly designed, 3-month placebo-controlled, clinical trials of pregabalin in FM patients were modeled. Extrapolation of efficacy results was based on a 1-year open-label study. Mean annual costs (direct and indirect) were assigned based on FM severity levels (mild: $10,219; moderate: $26,217; severe: $42,456) and were derived from the US Fibromyalgia Burden of Illness Study. FM severity levels were defined using established cutpoints on the Fibromyalgia Impact Questionnaire. Mean annualized costs at endpoint were estimated for all patients within each cohort and the mean differences in costs were compared between cohorts using a regression model. **RESULTS:** Relative to placebo, the proportion of mild subjects at endpoint was significantly higher with pregabalin 450mg and significantly lower for severe subjects. Mean total costs were lower with pregabalin (300mg, $25,721; 450mg, $24,103) than placebo ($26,162). Relative to placebo, the difference in mean annual costs was $2059 lower for pregabalin 450mg (P=0.003) and $441 lower for pregabalin 300mg (P=0.52). Mean direct costs were higher with pregabalin (300mg, $4,962; 450mg, $4820) than placebo ($4,364). Relative to placebo, the difference in mean annual direct costs was significantly higher for pregabalin 450mg by $456 (P<0.0001) and by $599 for pregabalin 300mg (P<0.0001). Mean indirect costs for pregabalin (300mg, $20,783; 450mg, $19,306) were lower than placebo ($21,735). Relative to placebo, the difference in mean annual direct costs for pregabalin 450mg was significantly lower by $2,429 (P<0.0001), and for pregabalin 300mg was lower by $951 (P=0.12). **CONCLUSIONS:** Improvements in FM severity are associated with overall reductions in costs that may offset the costs of treatment with pregabalin.

PMS56

HEALTH CARE UTILIZATION AND PATIENT FINANCIAL BURDEN ANALYSIS OF PRE- VERSUS POST-DIAGNOSIS OF FIBROMYALGIA SYNDROME (FMS)

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OBJECTIVES: While the etiology of fibromyalgia syndrome (FMS) is unknown, the incidence of FMS has been on the rise over the years. There is no known cure or universally accepted treatment for FMS and the treatment is typically aimed at symptom management. Although patients with FMS are known to have higher pharmacy-related costs compared to those without FMS due to high usage of pain-relieving medications, the true financial burden on newly diagnosed FMS patients remains unclear. The purpose of this study was to compare health care utilization and patient financial burden of FMS patients at pre- and post-diagnosis. **METHODS:** Nationwide commercial claims database which includes EPO, PPO, HMO and POS managed care systems was used to identify 194 patients who were newly diagnosed with FMS in year 2008 (identified by ICD-9-CM of 729.10). Patients with chronic comorbidities including other musculoskeletal diseases, cancer, HIV/AIDS, or asthma/COPD were excluded from the study. Health care utilization (defined by number of outpatient medical services) and patient financial burden (defined by out-of-pocket [OOP] costs including co-pay, deductible, and coinsurance) were assessed for two time intervals – six months prior to and after the diagnosis of FMS. **RESULTS:** Mean age of newly diagnosed FMS patients was 44 years (SD=14) and 143 of 194 patients were females. The majority of patients (74%) were enrolled in point of service managed care systems. FMS patients had higher health care utilization post-diagnosis when compared to pre-diagnosis but the results were not statistically significant (28 vs. 26, respectively; p=0.35). OOP costs remained relatively unchanged for the two time periods (p=0.59). **CONCLUSIONS:** Patients newly diagnosed with FMS use only slightly higher health care utilization upon diagnosis of FMS when compared with pre-diagnosis period while studies involving pharmacy utilization indicate significantly higher utilization.

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ASSOCIATION OF CLINICAL REMISSION AND NORMALIZED PATIENT REPORTED OUTCOMES: A VALIDATION OF TREAT-TO-TARGET FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS USING POOLED DATA FROM 3 PHASE III GOLIMUMAB CLINICAL TRIALS

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OBJECTIVES: Assess the impact of disease remission, a treatment target in the management of rheumatoid arthritis (RA) recommended by the International Task Force, on patient-reported outcomes (PROs). **METHODS:** Golimumab (GLM) efficacy and safety were assessed in methotrexate (MTX)-naïve RA patients (GO-BEFORE, N=637), RA patients with inadequate MTX response (GO-FORWARD, N=444) and anti-TNFa-experienced patients with baseline MTX use (GO-AFTER, N=305). Patients received placebo+MTX, or GLM (50 or 100mg)+MTX q4wks. Clinical remission was defined as a 28-joint Disease Activity Score (DAS28)<2.6. PRO assessments included Health Assessment Questionnaire (HAQ), 36-item short-form health survey (SF-36) physical/mental component summary (PCS/MCS) scores, Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Pain Severity Score of Brief Pain Inventory (BPI-Pain) and a visual analog scale of daily work productivity An ANOVA on van der Waerden normal scores or Chi-square test was performed for between-group comparisons. **RESULTS:** At wk24, greater proportions of GLM+MTX-treated patients achieved DAS28 remission versus PBO+MTX (GO-BEFORE: 22.3% vs. 11.3%, GO-FORWARD: 21.4% vs. 6.0%, GO-AFTER: 14.8% vs. 2.0%; all p<0.01). GLM+MTX-treated patients had greater PRO improvement versus PBO+MTX. From wk24-104, the overall SF-36 PCS score distribution shifted significantly towards the normal distribution. More patients in remission than not at wk24 achieved HAQ≤0.5 (72.2% vs. 24.3%), SF-36 PCS≥50 (general population median) (48.3% vs. 7.6%) and SF-36 MCS≥50 (66.3% vs. 40.3%), regained employability (39.6% vs. 24.1%) and significantly improved work productivity (80.1% vs. 25.6%) from baseline (all p<0.01). Greater median improvements in FACIT-Fatigue (wk24: 12.0 vs. 5.0) and BPI-Pain (wk14: 2.1 vs. 0.8) scores were observed among patients in, versus not in, remission. After achieving remission, MTX-naïve RA patients (GO-BEFORE) had greater improvements in PROs than MTX-inadequate responders (GO-FORWARD) or anti-TNF-experienced patients (GO-AFTER). **CONCLUSIONS:** Analysis results indicate controlling RA activity is crucial to regaining a normal life, and treating-to-target earlier (e.g., DAS28 remission) leads to better patient outcomes.

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BURDEN OF RHEUMATOID ARTHRITIS DISEASE FLARES

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OBJECTIVES: To assess the association of disease flares with clinical outcomes, health status, and work productivity loss among patients with RA. **METHODS:** Data were collected from individuals aged ≥18 and reporting an RA diagnosis through a cross-sectional, self-administered, Internet-based questionnaire. Frequency of disease flares were categorized as: no flares (reference group), <1 per month, 1 per month, 2-3 per month, 1 per week, 2-3 per week, 4-6 per week, and daily. Clinical outcomes included the Health Assessment Questionnaire (HAQ) and severity of morning stiffness, fatigue, and pain, measured as 1=none experienced to 10=severe. Health status was assessed using the SF-36, and work productivity loss (employed individuals only) and activity impairment were assessed using the Work Productivity and Activity Impairment questionnaire. Patient demographics and comorbidities were adjusted using linear regression and negative binomial regression as appropriate. **RESULTS:** Of 2,135 patients, 47.4% (n=1,011) experienced a disease flare in the past six months and 52.7% (n=1,124) experienced no flares. Greater frequency of flares was significantly associated with greater functional disability; greater severity of morning stiffness, fatigue, and pain; poorer physical and mental health status; greater lost work productivity and activity impairment. Specifically, daily flares were associated with greater functional disability (HAQ: regression coefficient b=0.56, p<0.001); greater severity of morning stiffness (b=2.27, p<0.001), fatigue (b=2.20, p<0.001), and pain (b=2.51, p<0.001); poorer health status (SF-36 physical component summary: b=-8.76, p<0.001 and mental component summary: b=-7.48, p=0.005); and greater work impairment (event ratio=2.20, p<0.001) and activity impairment (event ratio=1.68, p<0.001). **CONCLUSIONS:** RA disease flares are associated with worse clinical outcomes, poorer health status, and greater lost work productivity. However, due to the cross-sectional nature of the study, the direction of these associations cannot be determined. Treatments that minimize disease flares may provide additional benefit in clinical outcomes, health status, and work productivity.