7.4, p = 0.0065) among groups Vioxx, Cox2-Vioxx and Others in the adverse events rates of 5.84%, 5.00% and 3.83% respectively. Further Logistic regression analysis revealed that Vioxx and Cox2-Vioxx patients experienced higher events rate (group Vioxx vs. Others: OR = 1.218, 95%CI = 0.95–1.640; group Cox2-Vioxx vs. Others OR = 1.13, 95%CI = 0.834–1.532) with influencing factors adjusted, gender (male OR = 1.555, 95%CI = 1.190–2.031), age (OR = 1.080, 95%CI = 1.063–1.097) and comorbidities. CONCLUSIONS: The study demonstrated that Vioxx before withdrawn from market had highest heart attack/stroke events as compared to other Cox2 drugs or drug class. The other Cox2 drugs, Celebrex and Bextra, had higher adverse events than other painkiller classes such as NSAIDs. The follow up study with extended data is expected to confirm the finding.

**ARTHRITIS—Cost Studies**

**COST-EFFECTIVENESS ANALYSIS OF RITUXIMAB AS A NEW THERAPEUTIC OPTION FOR RHEUMATOID ARTHRITIS IN THE UK**

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OBJECTIVES: Rituximab (RTX; MabThera), a unique B-cell therapy, is a new option for rheumatoid arthritis (RA) patients who respond inadequately to anti-TNF therapies. This analysis evaluated the cost-effectiveness of introducing RTX from the perspective of the UK NHS. METHODS: The model simulated, over a patient’s expected lifetime, the real-life treatment sequence for 10,000 RA patients who respond inadequately to one anti-TNF therapy. Baseline characteristics were aligned with the REFLEX study. Clinical outcomes were based upon ACR response rates (adjusted for different study populations) and complemented with observational data. The model estimated the incremental cost per quality-adjusted life-year (QALY) of a typical treatment sequence containing RTX compared to the same treatment sequence without RTX. Average time-on-treatment for biological agents was up to 4.25 years. QALYs were mapped from a disease severity measure (HAQ score). Relevant costs (2004–5 Euros [€]) included those related to drug (including administration and monitoring) and indirect costs through reduced productivity. Costs and benefits were discounted at 3.5% per year. We assessed either adding RTX or using it instead of adalimumab. RESULTS: Annual average drug costs were €10,208 for RTX + MTX, €22,574 for adalimumab, €22,630 for etanercept, and €13,484 for infliximab. RTX as an additional treatment gave an additional 0.531 QALYs at an incremental total direct medical cost of €16,527 over the patient’s lifetime. With an incremental QALY of 0.665 this would result in an incremental direct medical cost of €24,844 per QALY. The corresponding ICERs were €25,985 and €17,058 per QALY gained. Using RTX as an alternative to adalimumab would produce a small incremental QALY gain, together with lifetime cost-savings of €23,143. CONCLUSIONS: In Germany, the incremental cost of adding RTX to options for RA-patients who respond inadequately to anti-TNF therapy is favourable using commonly accepted cost-effectiveness thresholds. As a replacement for a currently used drug in second-line biologic DMARD, RTX could lower average annual treatment costs.

**COST-EFFECTIVENESS OF RITUXIMAB AS A NEW TREATMENT MODALITY FOR RHEUMATOID ARTHRITIS IN GERMANY**

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OBJECTIVES: Rituximab (RTX; MabThera), a unique selective B-cell therapy, represents a new option for patients with rheumatoid arthritis (RA) who have responded inadequately to anti-TNF therapies. We analysed the cost-effectiveness of RTX from a German societal perspective. METHODS: We developed a model using published ACR response rates for RTX and current treatment choices (adjusted for study population differences), plus available observational data, German registry resource-utilisation data and baseline patient characteristics from the REFLEX study. We modelled real-life treatment for 10,000 RA patients who had responded inadequately to one anti-TNF therapy over the patient’s lifetime, assuming an average treatment duration for biological therapy (in combination with methotrexate) of up to 4.25 years. QALYs were mapped from a disease severity measure (HAQ score). Relevant costs (2004–5 Euros [€]) included those related to drug (including administration and monitoring) and indirect costs through reduced productivity. Costs and benefits were discounted at 3.5% per year. We assessed either adding RTX or using it instead of adalimumab. RESULTS: Annual average drug costs were €10,208 for RTX + MTX, €22,574 for adalimumab, €22,630 for etanercept, and €13,484 for infliximab. RTX as an additional treatment gave an additional 0.531 QALYs at an incremental total direct medical cost of €16,527 over the patient’s lifetime. With an incremental QALY of 0.665 this would result in an incremental direct medical cost of €24,844 per QALY. The corresponding ICERs were €25,985 and €17,058 per QALY gained. Using RTX as an alternative to adalimumab would produce a small incremental QALY gain, together with lifetime cost-savings of €23,143. CONCLUSIONS: In Germany, the incremental cost of adding RTX to options for RA-patients who respond inadequately to anti-TNF therapy is favourable using commonly accepted cost-effectiveness thresholds. As a replacement for a currently used drug in second-line biologic DMARD, RTX could lower average annual treatment costs.

**MODELING THE IMPACT OF PATIENT AND CLINICAL HETEROGENEITIES ON THE COST-EFFECTIVENESS OF SELECTIVE COX-2 INHIBITORS SUCH AS LUMIRACOXIB AND CONVENTIONAL NSAIDS IN PATIENTS WITH OSTEOARTHRITIS**

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OBJECTIVES: To explore influences of patient and clinical characteristics on the cost-effectiveness of selective COX-2 inhibitors and traditional NSAIDs in patients with osteoarthritis. METHODS: A published cost-effectiveness model (Arthritis Rheum 2003;49:283–92) was modified to incorporate important clinical characteristics that can influence the risk of gastrointestinal (GI) complications such as age, gender, history of GI bleed, and low-dose aspirin intake. The modified model used data from a large clinical trial (TARGET) to estimate base GI
event rates. Differences between NSAIDs were modeled from observed rates of GI events and adverse effects after adjusting for differences in population characteristics across three clinical trials (TARGET, CLASS and VIGOR). Other enhancements included modeling: 1) serious hepatic, renal, and skin adverse events (AEs); 2) proton pump inhibitor use after dyspepsia, while taking an NSAID; and 3) multiple occurrences of myocardial infarction (MI) (as opposed to one per patient). Health state utilities for AEs were assigned a value equal to that for the hospitalized surgical management of a complicated GI event. For MI, a 5% discount factor was used to reduce the patient’s utility score. Patients switching to acetaminophen because of an AE can experience reduced analgesic effect compared with NSAIDs; therefore utilities were discounted by 20%.

RESULTS: The modified model produced lower estimates of LYS and QALYs (approximately 0.05 and 0.08 less, respectively) compared with the original model which could be clinically meaningful in a 3-year model. Patient and clinical characteristics that defined low GI-risk subgroup versus high GI-risk group produced differences in LYS and QALYs of up to 1.40 and 0.7 QALY.

CONCLUSION: Effectiveness can vary considerably across patients with varying clinical characteristics. Therefore, the cost-effectiveness of treatment in any population should consider the heterogeneity of patients. This model provides flexible means to compare cost-effectiveness of treatment for patients with osteoarthritis.

MODELLING OF THE COST-EFFECTIVENESS OF RITUXIMAB FOR TREATMENT OF RHEUMATOID ARTHRITIS IN ITALY

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OBJECTIVES: Rituximab (RTX), a unique selective B-cell therapy, is a new option for rheumatoid arthritis (RA) patients who respond inadequately to anti-TNF therapies. This study reports a cost-effectiveness analysis modelling the introduction of RTX in Italy. METHODS: We used ACR response rates (adjusted for differences in study populations), plus observational data from EU registries and simulated real-life treatment for 10,000 RA patients who had responded inadequately to anti-TNF therapy, using baseline patient characteristics from the REFLEX study. We assumed an average treatment duration for biological therapy (in combination with methotrexate) of up to 4.25 years over the patient’s remaining lifetime. QALYs were mapped from a disease-severity measure (HAQ score) and based on registry data. Relevant costs included (2004–5 Euros [€]) drug costs (including administration and monitoring) and those related to reduced productivity (indirect costs). We assessed RTX as either a new treatment step or instead of adalimumab.

RESULTS: Average annual treatment costs were €87,976 for RTX + MTX, €14,133 for adalimumab, €14,406 for etanercept, and €9,950 for infliximab. Compared with the current treatment sequence, RTX + MTX as a new treatment step produced a gain of 0.677 QALYs at an incremental total medical cost of €12,355 over the lifetime of each patient—an incremental cost-effectiveness ratio (ICER) of €18,259 per QALY gained. The incremental cost per QALY for drug therapy or total (direct + indirect) cost was €19,241 and €13,621. RTX used instead of adalimumab produced a similar QALY gain, but resulted in a total direct medical-cost saving of €11,389 over the patient’s lifetime.

CONCLUSIONS: RTX offers a highly acceptable incremental cost per QALY gained for Italian patients with RA who respond inadequately to anti-TNF therapy and the possibility of either treating more patients within an existing budget or reducing the overall treatment cost for RA patients.

USING MABTHERA IN PATIENTS WITH RHEUMATIC ARTHRITIS IN SPAIN: RESULTS OF COST-EFFECTIVENESS DATA BASED ON MICRO-SIMULATION

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Rituximab (RTX), is a new and unique selective B-cell therapy for rheumatoid arthritis (RA) patients who respond inadequately to anti-TNF therapies. OBJECTIVES: We determined the cost-effectiveness of introducing RTX in Spain. METHODS: Our cost-effectiveness model simulates a real-life Spanish treatment sequence for 10,000 RA patients who had responded inadequately to one anti-TNF therapy. We used ACR response rates for RTX and current treatment options, available epidemiological data from observational studies and baseline characteristics from the REFLEX study. The model estimated the incremental cost per QALY gained, with RTX as either a new or alternative treatment over each patient’s remaining lifetime, assuming time-on-treatment for biological agents (in combination with methotrexate) of up to 4.25 years. QALYs came from a disease severity measure (HAQ score). Costs included (2004–5 EURO) drug costs (including administration and monitoring) and costs related to disease progression, palliative care, and reduced productivity (indirect costs). Costs and benefits were discounted at 3.5% per annum. RESULTS: Annual average treatment costs were €7431 for RTX + MTX, €14,072 for adalimumab, €13,067 for etanercept, and €9823 for infliximab. Added to existing therapies, RTX would lead to a gain of 0.632 QALYs at an additional total direct medical cost of €11,350 over each patient’s lifetime. The corresponding incremental cost-effectiveness ratio (ICER) of RTX was €18,261 per QALY gained. Corresponding ICERs for drug therapy and total costs were €19,597 and €15,546 per QALY gained, respectively. Used in place of etanercept as second-line biologic DMARD, RTX + MTX were associated with lifetime drug cost-savings of over €17,000.

CONCLUSIONS: Adding RTX to the pool of available treatment options for Spanish patients with RA who respond inadequately to anti-TNF therapy results in a favourable incremental cost per QALY gained. When RTX is replacing another biologic DMARD, the average annual drug therapy costs can be lowered.

A PHARMACOECONOMIC EVALUATION FOR THE TREATMENT OF ARTICULAR PAIN IN PATIENTS WITH OSTEARTHRITIS IN MEXICO

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OBJECTIVES: Nonsteroidal antiinflammatory drugs (NSAIDs) are in widespread use for rheumatic diseases in Mexico, but can cause peptic ulcers and gastrointestinal bleeding and perforation. The purpose of this study was to evaluate cost—effectiveness ratios of celecoxib compared with NSAIDs and acetylsalicylic acid in adult patients with osteoarthritis in four hospitals in the Social Security Mexican Institute. METHODS: A decision tree model was developed using a Bayesian approach. The model simulated treatment of a hypothetical cohort of 1000 patients diagnosed with osteoarthritis during a time horizon of 6 months. Patients could initiate treatment with celecoxib, NSAIDs (diclofenac, naproxen) and acetaminophen. Conditional probabilities of the