Oral Presentations

WEDNESDAY, 6 JUNE 2012

Interstitial lung disease in rheumatic disease: an update

OP0001 DEVELOPING A DISEASE ACTIVITY AND THERAPEUTIC RESPONSE INDEX IN CONNECTIVE TISSUE DISEASE - INTERSTITIAL LUNG DISEASE (CTD-ILD): RESULTS FROM A DELPHI EXERCISE: CONSENSUS ON DOMAINS

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Background: Lack of reliable and valid measures of disease activity and clinical response in patients with CTD-ILD makes clinical trial design difficult. From a multi-tiered investigation to develop consensus on provisional criteria in both CTD-ILD and idiopathic pulmonary fibrosis (IPF), we report the results of expert voting from a 3-tiered Delphi exercise to identify domains "important" to measure in a one year randomized controlled trial (RCT) in IPF and CTD-ILD.
Methods: Using the international consensus organization, Outcome Measures in Rheumatology (OMERACT) methodology, 270 experts nominated 23 "domains" and 616 "instruments" that were assembled into an initial voting survey for a 3-tiered Delphi exercise with survey items anchored by degree of importance on a 9-point Likert scale with as a voting option. All stages of data collection used a custom-designed secure web-site that included related articles and opportunities for participants to upload commentary supporting or refuting importance of each item.
Tier 1 Analysis: A cut-off median <4 was applied to the results. Final review demanded 100% consensus agreement for dismissal of an item based on lack of: 1. Face validity, 2. Content validity (more suited to diagnostic, demographic, or inclusion criteria) and 3. Feasibility in a multicenter trial.
Tiers 2 and 3 Analysis: To protect against bias introduced by using an arbitrary cut-off, cluster analysis was implemented to identify patterns of consensus within the data.
Results: 90% of invited experts: 137 pulmonary, 102 rheumatology and 4 cardiology specialists from 32 countries/6 continents participated. 74% and 69% of participants considered ILD and rheumatologic lung disease respectively as their primary field of research or clinical interest. Recidivism after Tier 1 was <1% with each subsequent Tier. Five common domains were identified for CTD-ILD and IPF: DYSPNEA, HEALTH RELATED QUALITY OF LIFE, LUNG IMAGING, LUNG PHYSIOLOGY/FUNCTION and SURVIVAL.
Conclusions: Development of valid, discriminatory and feasible outcome measures to assess disease progression and therapeutic responses is essential for performing RCTs in CTD-ILD. This is the first comprehensive, multi-disciplinary, international effort to assess domains for study of ILD. Experts identified a core set of measures focused on radiographic, physiologic and patient-reported outcomes culled from a large number of candidate items. A research agenda focusing on candidate biomarkers and domains requiring instrument development has emerged. Broad participation from a multidisciplinary ILD research community reflects the high perceived need in this area.
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Long-term outcomes of modern treatment

OP0002 USE OF ANTI-TNF THERAPY IS ASSOCIATED WITH REDUCED CARDIOVASCULAR EVENT RISK IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is associated with increased risks for cardiovascular (CV) comorbidities because of an increased prevalence of traditional CV risk factors and the underlying chronic inflammatory process.
Objectives: To assess the effects of treatment with anti–tumor necrosis factor (anti-TNF) therapy, methotrexate (MTX), or other nonbiologic DMARDs on CV event risk in patients with RA.
Methods: Adult patients with $\geq$2 RA diagnoses (ICD-9 CM: 714.xx) and $\geq$1 filled prescription of anti-TNF therapy, MTX, or other nonbiologic DMARD were identified in the Thomson Reuters MarketScan® database (2003–2010). Patients were assessed from index fill date to first inpatient CV diagnosis of myocardial infarction (MI), stroke, unstable angina, or heart failure (HF) to the end of health plan enrollment or to 6 months after the discontinuation of their index drug, whichever came first. Cox proportional-hazards models assessed the effect of cumulative exposure to anti-TNF therapy, MTX, and other nonbiologic DMARDs on occurrence of CV events. We adjusted for baseline (ie, 1 year before index prescription) demographics; use of therapies for RA (eg, MTX, corticosteroid), CV-related medications, and smoking deterrents; comorbidities (eg, dyslipidemia, hypertension, diabetes); history of CV events; and medical resource use. Subgroup and sensitivity analyses also were conducted.
Results: The study identified 109,462 patients with 105,920 total patient-years (PYs) of follow-up, including 48,621 PYs of exposure to anti-TNF therapies (31,466 as monotherapy), 35,480 PYs of exposure to MTX (18,325 as monotherapy) and 52,994 PYs of exposure to other nonbiologic DMARDs (9,441 as monotherapy). A total of 1743 patients (1.6%) had a CV event after their index prescription. In the multivariate regression model, each additional 6 months of anti-TNF therapy significantly reduced the risk for any study CV event (hazard ratio [HR]=0.87, 95% confidence interval [CI]=0.80–0.96, *P*=.005) and for MI (HR=0.80, CI=0.67–0.95, *P*=.013), compared with patients without anti-TNF biologics, after adjusting for cumulative exposure to MTX or other nonbiologic DMARD. The effects of cumulative use of MTX and other nonbiologic DMARDs were not statistically significant. In the subgroup analyses, each additional 6 months of anti-TNF therapy use was significantly associated with a reduction in CV events in patients aged $\geq$50 years (HR=0.86, CI=0.77–0.96, *P*=.007) as well as in those without prior MTX use (HR=0.85, CI=0.73–0.98, *P*=.022). In the full sample, the multivariate regression model predicted that cumulative use of anti-TNF therapy for 1, 2, or 3 years would reduce CV event risks by 24%, 42%, and 56%, respectively, compared to not using anti-TNF therapies during those time periods, adjusting for background use of MTX or other nonbiologic DMARDs.
Conclusions: Use of anti-TNF therapies vs. non-use was associated with significantly lower risks for CV events (ie, inpatient diagnoses for MI, stroke, unstable angina, or HF) in patients with RA, older patients with RA, and patients without prior exposure to MTX, adjusting for use of MTX and other nonbiologic DMARDs.
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