GRAPPA Trainees Symposium 2012: A Report from the GRAPPA 2012 Annual Meeting

Neha Garg, Zahi Touma, and Christopher T. Ritchlin

ABSTRACT. The 2012 annual meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) in Stockholm, Sweden, began with a Trainees Symposium, which included 30 dermatology and rheumatology trainees currently involved with research in psoriasis or psoriatic arthritis. The 6 oral presentations and 24 posters presented at the meeting highlight the status of current basic and clinical research performed by members and trainees of GRAPPA. (J Rheumatol 2013;40:1413–8; doi:10.3899/jrheum.130452)

Key Indexing Terms:

GRAPPA	PSORIATIC ARTHRITIS	PSORIASIS
TRAINEE	RHEUMATOLOGIST	DERMATOLOGIST

The fifth Trainees Symposium was held at the 2012 annual meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) in Stockholm, Sweden. Since its inception in 2008, the symposium has become an integral part of GRAPPA meetings and serves as an open forum to encourage and develop potential future researchers[1,2,3]. Rheumatology or dermatology trainees, either GRAPPA members themselves or nominated by GRAPPA members, were invited to submit abstracts based on recent research in psoriasis or psoriatic arthritis (PsA). Each year, an increasing number of abstracts are submitted for consideration. The 2009 meeting attracted 19 fellows[1]; in 2010, 24 trainees presented[2]; and in 2011, 25 trainees presented[3]. At the 2012 meeting, a total of 30 trainees from over 10 countries in North America, South America, and Europe participated. Invited abstracts included those describing a primary research project or those presenting an evidence-based literature search with a proposal for a research project to follow. Trainees with the highest-scoring abstracts were invited to deliver an oral presentation (n = 6); the remaining trainees with satisfactory scores presented a poster (n = 24). The audience comprised 100 or more GRAPPA members who provided suggestions on improvement and further development of research plans. The session was chaired by Christopher Ritchlin (University of Rochester Medical Center, Rochester, NY, USA), who introduced the format of the symposium, and gave a brief summary of research advances to date by members of GRAPPA.

From the Division of Arthritis and Rheumatism, Oregon Health and Sciences University, Portland, Oregon, USA; University of Toronto, Psoriatic Arthritis Clinic, Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital, Toronto, Ontario, Canada; and Division of Allergy, Immunology, and Rheumatology, University of Rochester Medical Center, Rochester, New York, USA.

N. Garg, MD, Division of Arthritis and Rheumatism, Oregon Health and Sciences University; Z. Touma, MD, FACP, PhD, University of Toronto, Psoriatic Arthritis Clinic, Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital; C.T. Ritchlin, MD, MPH, Division of Allergy, Immunology, and Rheumatology, University of Rochester Medical Center.

Drs. Garg and Touma contributed equally to this report.

Address correspondence to Dr. C.T. Ritchlin, Allergy, Immunology, and Rheumatology Division, Center for Musculoskeletal Research, University of Rochester Medical Center, 601 Elmwood Avenue, Box 695, Rochester, NY 14642, USA. E-mail: christopher_ritchlin@urmc.rochester.edu

Oral Presentations

Wnt pathway inhibitors in patients with PsA and rheumatoid arthritis (RA) treated with anti-tumor necrosis factor-α (TNF-α) therapy (Agnes Szentpetery, Dublin, Ireland)

Dr. Szentpetery presented a study[4] comparing the effect of anti-tumor necrosis factor (anti-TNF) treatment on inhibitors of Wnt signalling; and analyzed the interplay of TNF-α, Dickkopf-1 (Dkk-1), sclerostin, and osteoprotegerin (OPG) in new bone formation. In 62 patients [35 rheumatoid arthritis (RA), 27 psoriatic arthritis (PsA)] with active disease recruited prior to starting anti-TNF therapy, serum levels of Dkk-1, sclerostin, OPG, and C-reactive protein (CRP) were measured by ELISA. No significant difference in Dkk-1 and sclerostin levels was observed between RA and PsA; however, a trend was noted for lower Dkk-1 levels in patients with PsA compared to those with RA after 12 months of anti-TNF therapy, a profile that may favor new bone formation in patients with PsA. High serum sclerostin levels were associated with low Dkk-1 levels after 12 months of therapy, suggesting that Dkk-1 but not sclerostin might be altered with anti-TNF therapy. Neither Dkk-1 nor sclerostin correlated with CRP at any timepoint, indicating that these Wnt inhibitors may not be linked to inflammation. OPG/Dkk-1 and OPG/sclerostin ratios reflecting remodeling balance were similar and did not change significantly in either RA or PsA. These findings raised further questions regarding the pathophysiology of bone formation in PsA and the mechanisms of action of anti-TNF therapy on new bone formation in PsA.

Endoplasmic reticulum aminopeptidase 1 (ERAP1) not associated with axial disease in PsA as it is in ankylosing spondylitis (Deepak Jadon, Bath, UK)

Dr. Jadon discussed the association between ankylosing spondylitis (AS)-associated genes *ERAP1* (rs30187), interleukin 23 receptor (*IL23R*; rs11209026, rs7530511), and *IL12B* (rs6887695) and specific psoriatic arthritis (PsA) subphenotypes, stratified by HLA-B27 and HLA-Cw*0602 status. In a prospective study of 262 PsA cases with comparison controls drawn from the Wellcome Trust Case Control Consortium[5], genotype data for HLA-Cw*0602 (rs10484554) and HLA-B27 (rs4349859) were obtained by imputation for PsA cases.

A statistically significant association was found between presence of homozygous allele for rs6887695 (*IL12B*) with presence of PsA (OR 1.7, 95% CI 1.32–2.18, $p < 0.001$). A trend was observed for the minor allele of rs11209026 (*IL23R*) to be less frequent in patients with erosive joint disease than those without erosions. HLA-Cw*0602 was more frequent in patients with type 1 psoriasis than in those with type 2 psoriasis.

Dr. Jadon noted that PsA cases carrying the minor allele of rs30187 (*ERAP1*) were equally likely to experience radiographic axial disease or sacroiliitis, even after stratifying by HLA-B27 or HLA-Cw*0602 status, suggesting that spinal involvement in psoriatic disease is not genetically identical to that in AS. This study was unique in exploring *ERAP1* polymorphisms in PsA and raises further questions in the genetic pathophysiology of axial disease in PsA and possibly suggesting an association with *IL12B*.

Simple questions in dermatology office may reasonably exclude but do not reliably identify PsA patients: Results from the Center of Excellence for Psoriasis And PsA (CEPPA) (Neha Garg, Portland, OR, USA)

Dr. Garg described the disease characteristics in a new psoriasis cohort in Oregon, where dermatologists determined early identification of patients for referral to rheumatology for evaluation of PsA using 4 questions: "Do you have a history of joint pain or swelling," "Do you have morning stiffness," "Do you have stiffness after prolonged resting," and "Do you have PsA?" Of those who answered no to all 4 questions, 95.8% did not have PsA. However, of those who answered yes, 27.0% still did not have PsA, emphasizing the need for detailed assessment by rheumatologists.

Of the 547 psoriasis patients, 29.5% had PsA. Most patients were diagnosed with PsA within ≤ 25 years of onset of psoriasis; family history of psoriasis appeared to predispose to an 8-year earlier onset. Patients with PsA were more likely to have nail changes (OR 13.7, 95% CI 6.5–29.1, $p < 0.01$), and also a significantly worse quality of life (QOL) based on Routine Assessment of Patient Index Data, 12-item Psoriasis Quality of Life Questionnaire, and Medical Outcomes Study 12-Item Short Form scores ($p < 0.01$). Percentage of body surface area (BSA) involvement did not correlate with presence of PsA.

The relatively high prevalence of PsA in this population compared to the general population (10%–30%) could be the result of referral bias or early identification by dermatologists with expertise in identification of PsA, which suggests that PsA may be routinely missed in other dermatology offices. Dr. Garg emphasized the good sensitivity of these 4 questions and proposed that, with further validation, they could be used to easily and quickly identify patients who would benefit from referral to a rheumatologist.

Clinical and demographic characteristics of erosion-free and erosion-present status in psoriatic arthritis in a prospective cohort study (Zahi Touma, Toronto, Canada)

Dr. Touma studied the predictors of erosion-free PsA in patients with ≥ 10-year period of followup in the Toronto PsA cohort. Among 290 patients, 12.4% were erosion-free patients (EFP) and 87.6% erosion-present patients (EPP). EFP were diagnosed with psoriasis at a younger age (22.5 ± 14.7 yrs) compared to EPP patients (27.6 ± 12.1 yrs; $p = 0.02$). No statistically significant differences were found in ethnicity, gender, age at diagnosis of PsA, or duration of psoriasis and PsA among EFP and EPP.

At baseline, 93% of EPP had active joints compared to 72% of EFP ($p < 0.0001$); EPP displayed a greater number of actively inflamed joints (10.1 ± 9.1) compared to EFP (4.8 ± 5.3; $p = 0.0007$); and 40.6% of EPP had damaged joints compared to 8.3% in EFP ($p = 0.0002$). EPP had a higher body mass index (BMI) compared to EFP ($p = 0.03$). More EPP were taking nonsteroidal antiinflammatory drugs ($p = 0.04$) and sulfasalazine ($p = 0.02$). EFP were all employed versus 69.8% of EPP ($p = 0.05$).

Of the 254 EPP, 60% already had erosions at first visit, and 40% had no erosions at first visit but developed them later; in this latter group, the mean time to development of erosion was 2.96 ± 5.23 years.

In multivariate analysis, actively inflamed joint count (OR = 1.09, $p = 0.02$) and damaged joint count (OR = 2.29, $p = 0.03$) were predictive of the development of erosions. A longer duration of psoriasis at baseline decreased the odds of developing erosions (OR = 0.95, $p = 0.01$). Dr. Touma concluded that among patients with PsA followed for ≥ 10 years, 12% never develop erosions in the peripheral joints. The presence of actively inflamed and damaged joints at baseline increases the odds of developing erosions. A longer duration of psoriasis at baseline has a protective effect on development of erosions.

Joint disease and obesity among pediatric psoriasis population in the United States: A population study using NAMCS and NHAMCS (Mary Ann N. Johnson, University of California, Davis, CA, USA)

Dr. Johnson examined whether children with psoriasis aged

2–18 years have increased joint diseases and symptoms compared to children without psoriasis, using data from outpatient visits to US physicians from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey. Between 2005 and 2009, 797 million outpatient visits occurred; 913,716 visits were children with psoriasis. Compared to children without psoriasis, the OR for the combined outcome of overweight stature and obesity in the pediatric psoriasis populations was 0.09 (95% CI 0.01–0.92). The exploratory analyses found that children with psoriasis appear to have statistically nonsignificant greater odds of joint diseases and symptoms and statistically significant decreased odds of obesity compared to children without psoriasis. Dr. Johnson emphasized that larger population studies are necessary to elucidate the relationships between joint diseases, obesity, and pediatric psoriasis.

Ultrasound for monitoring disease activity in early PsA: Comparison of clinical responders and non-responders (Axel Philipp Nigg, University of Munich, Munich, Germany)

Dr. Nigg conducted a prospective study to analyze the correlation between a semiquantitative ultrasound (US) score and clinical parameters during the course of early PsA. In each of 23 patients who completed a minimum of one followup visit, 56 joints were examined by greyscale US and power Doppler. Patients received standard of care treatment. European League Against Rheumatism (EULAR) response criteria and minimal disease activity, in addition to the Health Assessment Questionnaire (HAQ) and C-reactive protein (CRP), were defined for each followup period.

At baseline, US synovitis score showed a highly significant correlation with tender joint count 68 ($r = 0.57$), swollen joint count 66 ($r = 0.63$), physician global activity ($r = 0.54$), and Disease Activity Score (DAS) 28-CRP ($r = 0.42$). Longitudinal data showed a significant correlation between relative changes in US synovitis score and clinical parameters within one followup period. Dr. Nigg concluded that US findings correlate with parameters of clinical disease activity, and clinical responders showed a higher relative reduction of US synovitis.

Poster Presentations

Maria Laura Acosta Felquer (Buenos Aires, Argentina) described correlations of different remission criteria and activity indices in 55 patients with PsA using the Composite Psoriatic Disease Activity Index (CPDAI), Psoriatic Arthritis Screening and Evaluation, Disease Activity in Psoriatic Arthritis, MDA criteria in PsA, DAS28, Simplified Disease Activity Index (SDAI), Clinical DAI, and American College of Rheumatology/EULAR Boolean RA remission criteria. All indices showed good discriminative power for a change in treatment (area under the curve for all 0.8–0.9). DAS28 and minimal disease activity (MDA) seemed to be less stringent in PsA than the other indices. CPDAI showed the poorest correlation with all the other indices.

Zoe Ash (Leeds, UK) explored the effects of anti-TNF therapy on improvements in psoriasis-related nail disease, specifically distal interphalangeal joint enthesitis, osteitis, and synovitis using high resolution magnetic resonance imaging (MRI) in 9 patients in a blinded fashion. Over 6-month followup, MRI scans surprisingly showed persistent subclinical inflammation (osteitis, synovitis, and enthesopathy) despite improvements seen in clinical and ultrasound parameters, possibly relating to either a time lag in imaging improvement or the sensitivity of the imaging techniques used.

Shiu-Chung Au (Boston, MA, USA) retrospectively compared the efficacy of biologic treatment for psoriasis to conventional systemic therapies and phototherapy using a Simple-Measure for Assessing Psoriasis Activity (S-MAPA, calculated by BSA multiplied by Physician's Global Assessment) and showed that biologics showed superior results to conventional systemic therapies (70% vs 40%; $p < 0.05$) for the treatment of patients with moderate to severe psoriasis at Week 24, despite the fact that patients taking biologics had greater baseline severity and had a greater number of previous treatments.

Andreea N. Boca (Cluj-Napoca, Romania) compared the expression of the immunomodulatory surface molecules CD25+, FoxP3, and GITR on CD4+ and CD8+ T lymphocytes isolated from peripheral blood mononuclear cells of 10 patients with severe psoriasis to those of 5 clinically healthy volunteers, and found increased frequency of Tregs, CD4+CD25+ and CD4+FoxP3+, CD8+CD25+ and CD8+GITR+ cells in the psoriasis group and CD8+FoxP3+ in the control group. With these encouraging results, the authors proposed a larger study to elaborate on the possible role of Treg cells in the pathogenesis of inflammation in psoriasis.

Elizabeth A. Brezinski (Davis, CA, USA) assessed awareness to screen psoriasis patients for cardiovascular (CV) risk factors using surveys among primary care physicians (PCP) and cardiologists randomly selected through professional society registries[6]. Approximately 43% of US physicians reported screening patients with psoriasis for hypertension, 11% for coronary artery disease, and 30% for obesity. Compared to PCP, cardiologists were 2.5 times more likely to be aware of an increased risk of CV events among patients with psoriasis and 3.5 times more likely to screen for dyslipidemia. No significant differences were observed in screening practices for hypertension, obesity, and diabetes between US PCP and cardiologists. More awareness of increased CV comorbidities was associated with rheumatoid arthritis and systemic lupus erythematosus than for psoriasis.

Lindsay Burns (Vancouver, BC, Canada) described a

cohort study to identify risk of pulmonary embolism (PE) and deep vein thrombosis (DVT) using incidence rate ratios (IRR) and hazard ratios (HR) in non-hospitalized psoriatic patients compared with a 1:8 matched non-psoriasis/PsA comparison cohort. They found IRR for PE and DVT of 0.90 and 2.0 per 1000 person-years with fully adjusted HR of 1.39 (1.00–1.92) for PE and 2.02 (1.61–2.54) for DVT. Highest risk was observed within a year following psoriasis/PsA diagnosis, supporting increased monitoring of venous thromboembolism in patients with psoriasis or PsA.

Solange Carrasco (São Paulo, Brazil) compared Toll-like receptor 2 (TLR2) expression of peripheral blood monocytes and neutrophils from 45 patients with PsA and healthy controls. Membrane-bound TLR2 expression was analyzed by flow cytometry by measuring geometric mean intensity of fluorescence. Increased expression of TLR2 was observed on monocytes from patients with PsA with both active and inactive disease compared to controls, whereas expression of TLR2 on neutrophils isolated from both patients and controls was similar. These data support a role for innate immune responses in the pathogenesis of the disease.

Rosemary deShazo (Salt Lake City, UT, USA) described the use and further validation of Treatment Satisfaction Questionnaire for Medications version II (TSQMII) in 404 patients with moderate to severe psoriasis. They found clinically significant correlation for each TSQMII subscale, with the exception of side effects (effectiveness $r = –0.25$, convenience $r = –0.24$, and global satisfaction $r = –0.29$; $p < 0.001$ for all 3). For every 10-unit increase in the TSQMII global satisfaction score, there was 26% less chance of treatment change. Treatment satisfaction is important in clinical decision-making, compliance, and overall success. This study validates the TSQMII and broadens its use in patients with moderate to severe psoriasis.

Maureen Dubreuil (Philadelphia, PA, USA) evaluated the risk of incident diabetes in PsA and RA in a retrospective cohort study of a UK general population. They found increased risk of diabetes, with HR of 1.33 (1.09–1.61) in PsA, 1.21 (1.15–1.27) in psoriasis, and 0.94 (0.84–1.06) in RA after adjustment for age, sex, BMI, smoking, alcohol, glucocorticoid use, and comorbidity index, suggesting that, unlike RA, the risk of diabetes is increased in PsA regardless of other factors.

Ari Goldminz (Boston, MA, USA) assessed the prevalence of metabolic syndrome (MetS) in children with psoriasis or PsA in an ongoing cross-sectional study[7], comparing 20 children with psoriasis or PsA with over 1500 controls gathered from the National Health and Nutrition Examination Survey database. They found significantly high prevalence of MetS in psoriasis children compared to controls (30% vs 7.4%; $p = 0.45$) despite the lack of a significant difference in their BMI, suggesting a possible direct association of psoriasis and metabolic syndrome.

Rachel Grynszpan (Rio de Janeiro, Brazil) evaluated the role of anti-apoptotic proteins Bcl-2 and Bcl-X in 20 patients with active plaque psoriasis and found a statistically significant increase in epidermal expression of Bcl-2 ($p = 0.022$) and Bcl-X ($p = 0.036$) proteins after treatment with cyclosporine. Clinical improvement was evidenced by a reduction in Psoriasis Area and Severity Index (PASI) scores after 8 weeks of cyclosporin A 3 mg/kg/day. The results of this study suggested that suppressed apoptosis in psoriasis by inflammatory activity can be reversed and modified by cyclosporin A.

Amir Haddad (Toronto, ON, Canada) investigated the rate, type, characteristics, and predictors of infection in about 700 patients with PsA and 500 patients with psoriasis who were/were not taking biologic therapies. They found similar incidence rates of infection among patients with PsA (0.33/patient-year; 0.44 in those taking biologics) and among those with psoriasis alone (0.29/patient-year; 0.66 in those taking biologics). The most common infections were lung, sinus, skin, and genitourinary.

Muhammad Haroon (Dublin, Ireland) determined the prevalence of PsA among 200 psoriasis patients attending dermatology and rheumatology clinics and studied the clinical predictors of the development of PsA. Of psoriasis patients attending dermatology clinics, 29% had undiagnosed PsA. In multivariate analysis, only PASI scores were significantly associated with the diagnosis of PsA. Dr. Haroon also compared the performance of 3 PsA screening questionnaires (PsA Screening Evaluation, Psoriasis Epidemiological Screening Trial, Toronto PsA Screen) and found poor sensitivities (27%–41%) but high specificities (90%–98%) for all questionnaires when used in dermatology clinics.

Julie Jefferson (Portland, OR, USA) studied the characteristics of psoriatic patients with nail involvement among 30 patients with psoriasis including nail psoriasis seen at Oregon Dermatology and Research Center in Portland. Dr. Jefferson plans to evaluate if psoriatic nail disease is an indicator of comorbidities other than psoriasis and PsA.

Noori Kim (Boston, MA, USA) evaluated the efficacy of ustekinumab for the treatment of palmoplantar psoriasis in an open-label study[8]. Twenty subjects with moderate to severe psoriasis of the palms and soles were treated with ustekinumab at Weeks 0, 4, and 16. The primary endpoint was the percentage of subjects achieving clinical clearance (Palm-Sole Physician's Global Assessment ≤ 1) at Week 16. Results showed 35% of subjects achieved clinical clearance; of these, 67% of patients receiving 90 mg ustekinumab achieved clinical clearance compared to 9% receiving 45 mg ($p = 0.02$).

Stephanie Liu (Boston, MA, USA) described the development of a new scoring system for the assessment of inverse psoriasis, the Brigham Inverse Psoriasis Severity Index (BIPSI). The total BIPSI score is an estimation of the

overall severity of inverse disease ranging from 0–10, judged as very severe (9–10), severe (7–8), moderate (5–6), mild (3–4), and minimal (0–2). Additional studies are needed to assess the reliability and validity of the BIPSI.

Hernan Maldonado-Ficco (Buenos Aires, Argentina) evaluated the gender differences in a cohort of 2044 patients with spondylitis associated with psoriasis, inflammatory bowel disease, and primary AS followed in the multiethnic cohort of Ibero-American patients with spondyloarthritis. In this cohort, male patients were significantly younger, had longer diagnostic delay, worse total Bath AS Radiology Index scores, higher Bath AS Metrology Index scores, strikingly lower disease activity (Bath AS Disease Activity Index), and better QOL. In both primary AS and spondylitis associated with psoriasis, women had better spinal mobility and less radiographic damage.

Alexis Ogdie (Philadelphia, PA, USA) compared the mortality rates in patients with PsA, psoriasis, RA, and matched controls and the effects of disease-modifying antirheumatic drug (DMARD) prescriptions in 289 patients from The Health Improvement Network (THIN), a primary care medical record database in the United Kingdom[9]. This study demonstrated elevated mortality among patients with RA (HR 1.73 and 1.41, with and without DMARD, respectively) and psoriasis (1.41 and 1.08, with and without DMARD, respectively), but not in PsA (HR 0.98), with no effect of DMARD use.

Seema Qaiyumi (Washington, DC, USA) described the clinical characteristics of a diverse ethnic cohort of patients with psoriasis and PsA in an urban outpatient setting. Of 160 psoriasis patients, 93 (58%) were white and 67 (42%) were non-white (62 African American, 5 other). PsA occurred less frequently in African Americans, despite worse skin disease, than in whites, and African Americans received fewer DMARD and biologic therapies. While African Americans appeared to experience fewer psychological effects from their disease, their psoriasis-related QOL was reduced compared to whites.

Marcela Rodríguez (Bogotá, Colombia) evaluated the level of agreement between Colombian rheumatologists and dermatologists in the clinical assessment of psoriasis and PsA and whether a training session improved this agreement. Some agreement on assessments of the PASI and nail involvement was found between dermatologists and rheumatologists, and agreement improved after a short training program.

Junko Takeshita (Philadelphia, PA, USA) studied the potential link of microparticles between psoriasis and CV disease. Forty-seven psoriasis patients were compared to 41 healthy controls. Compared to healthy controls, higher absolute microparticle levels and concentration in psoriasis was identified in patients with psoriasis, with a predominance of endothelial-, platelet-, and, to a lesser extent, T lymphocyte-derived microparticles. The authors concluded that increased endothelial cell and platelet activation with turnover may contribute to heightened atherogenesis observed in psoriasis.

William Tillett (Bath, UK) investigated the impact of delay to diagnosis on physical function (using HAQ) in established PsA. Among 609 patients from the Bath longitudinal cohort, 267 patients with disease duration > 10 years were identified. This study showed that a delay in diagnosis of PsA, younger age at diagnosis, female sex, and smoking are associated with worse physical function in established PsA.

Jonathan Wollman (Tel Aviv, Israel) evaluated the effect of the extent of skin and joint involvement on the diagnosis of latent tuberculosis (TB) and compared the tuberculin skin test (TST) and QuantiFeron-TB Gold (QTF-G) in patients with psoriasis and PsA to patients with RA. Results showed that the extent of psoriasis severity does not affect the results of TST and QTF-G in patients with psoriasis. The level of agreement between TST and QTF-G was similar in RA and psoriasis.

Howa Yeung (Philadelphia, PA, USA) examined the prevalence of major systemic comorbidities (measured by Charlson Comorbidity Index) in patients with psoriasis compared to controls in over 9000 surveys utilizing THIN, an electronic medical records database of UK patients. The analysis showed a significantly higher comorbidity index in patients with mild (0.375 vs 0.347), moderate (0.398 vs 0.342), and severe psoriasis (0.450 vs 0.348) compared to respective matched controls ($p < 0.05$). Psoriasis overall was associated with higher odds of chronic pulmonary disease, diabetes, mild liver disease, myocardial infarction, peptic ulcer disease, peripheral vascular disease, renal disease, and rheumatologic disease but not with cancer or cerebrovascular disease.

Conclusion

Following the oral presentations, Dr. Ritchlin facilitated a discussion with all GRAPPA faculty. A ceremony was held during the gala dinner when prizes were awarded by Drs. Philip Mease and Philip Helliwell to the presenters of the oral presentations and posters. The next GRAPPA trainees symposium will be held in July 2013 in Toronto, Canada.

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