Boletín del
Colegio Mexicano de Reumatología
Órgano Informativo y de Vinculación del Colegio Mexicano de Reumatología

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DIRECTORIO

CONTENIDO

Boletín Mexicano de Reumatología

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Colegio Mexicano de Reumatología
Paseo del Río No. 157, Colonia Barrio Oxtopulco Universidad, Delegación Coyoacán
C.P. 04318, México, D.F. Tels.: (55) 5662-4965, 5662-5014, 5662-5983

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Acta de la Sesión Mensual Ordinaria correspondiente a octubre de 2008 del Colegio Mexicano de Reumatología

A las 20:30 horas del 21 de octubre de 2008 se reunieron en el Auditorio «Dr. Aquiles Calles» del Centro Médico Nacional 20 de Noviembre del ISSSTE, sito en Avenida Félix Cuevas 540, 1er Piso Colonia del Valle, Delegación Coyoacán, en la Ciudad de México, los asociados que en la lista de asistencia se detallan a efecto de llevar a cabo la Reunión Mensual Ordinaria del Colegio Mexicano de Reumatología.

Estando presentes 15 socios y no socios 6, no hubo asistentes por videoconferencia (21 total), dio inicio la Sesión Mensual Ordinaria con el siguiente orden del día:

1. Lectura y aprobación del Acta anterior.

Se leyó el Acta de la Sesión Mensual del 30 de septiembre de 2008 del Colegio Mexicano de Reumatología la cual fue aprobada por unanimidad.

Acuerdo: Los asociados del Colegio Mexicano de Reumatología aprueban el Acta de la Sesión de fecha 30 de septiembre de 2008 celebrada en la Ciudad de México en el auditorio «Dr. Aquiles Calles» del Centro Médico Nacional 20 de Noviembre del ISSSTE.

2. Informe de la Mesa Directiva

a. El Día Nacional del Paciente Reumático se organizó en el Distrito Federal y catorce provincias, entre los días 11 y 18 de octubre de 2008, el total de pacientes a este evento fue de 4,113.
b. El Dr. Antonio Rafael Cabral Castañeda, Presidente del Colegio Mexicano de Reumatología, la Dra. Tatiana Sofía Rodríguez Reyna, quien trabaja en el Área de la Esclerodermia y el Dr. Enrique Faugier Fuentes, en Reumatología Pediátrica acudieron a la Octava Conferencia Científica Anual de la Canadian Arthritis Network los días 16-18 de octubre de 2008 en ese país.
c. Se llevó a cabo la segunda fase de la cumbre de expertos sobre tratamientos biológicos, organizado en el Hotel Presidente de Polanco el 17 de octubre del 2008.
d. La Asociación Canadiense de Reumatología enviará a su Residente de Especialidad a este país, su rotación será durante un mes, en el Hospital General de México con el Dr. Rubén Burgos Vargas en el Área de Reumatología Pediátrica.
e. Se informó se enviaría la convocatoria a los Jefes de Servicio para la estancia de dos meses en España de Residentes mexicanos. Los hospitales son:

Hospital	Jefes de Servicio
Hosp. Univ. Valle de Hebrón	Pedro Barceló García
Hosp. Univ. de Bellvitge	Joan Miquel Nolla Solé
Hosp. Univ. 12 de Octubre	Isabel Mateo Bernardo
Hosp. Clínico Univ. San Carlos	Juan Ángel Jover Jover
Hosp. Univ. La Princesa	Pedro Sabando Suárez
Hosp. Univ. Dr. Peset	José A. Román Ivorra
Hosp. General Univ. de Alicante	Eliseo Pascual Gómez
Hosp. Clínico Univ. de Santiago	Juan Jesús Gómez-Reino Carnota
Hosp. Univ. Germans Trias I Pujol	Javier Tena Marsa
Hosp. Univ. Gregorio Marañón	Luis Carreño Pérez
Complexo Hospitalario Da Coruña (CHUC)	Fausto Galdo Fernández
Hosp. Univ. Ramón y Cajal	Antonio Zea Mendoza
Hosp. Univ. Reina Sofía	Eduardo Collantes Estévez
Hosp. Univ. Virgen de la Arrixaca	Alberto Bermúdez Torrente
IMAS Hosp. Univ. de L'Esperança y Hosp. Univ. del Mar	Pere Benito Ruiz

La fecha límite de recepción de documentos es el 30 de enero de 2009. Los documentos deberán ser enviados a la Gerencia Administrativa del Colegio Mexicano de Reumatología.

f. Se recordó se enviarán los casos clínicos para la Sesión Mensual de noviembre del Colegio Mexicano de Reumatología. La fecha límite el 31 de octubre de 2008.

3. *Asuntos generales*

No hubo asuntos generales

4. *Programa académico*

Participa el Dr. Antonio Rafael Cabral Castañeda, como Coordinador de la Sesión Académica.

El Dr. Luis Llorente Peters, Investigador Titular del Departamento de Inmunología/Reumatología del Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, dio una interesante reseña histórica sobre el Laboratorio Cambridge, el laboratorio más productivo en la historia de la ciencia.

Destacó el papel que tuvo el Dr. Max Perutz, descubridor de la estructura molecular de la hemoglobina; ganador del Premio Nobel en Medicina y Director de este Laboratorio, el cual permitió el pensamiento científico en libertad y la comunicación entre sus científicos dando como resultado el trabajo de excelencia de estos hombres de ciencia en ese laboratorio, generando un número importante de Premios Nobel.

La Sesión finalizó a las 22:00 horas.

Dr. Antonio Rafael Cabral Castañeda
Presidente

Algunos Trabajos presentados en el Congreso Anual del Colegio Americano de Reumatología 2008. San Francisco California

439 - Effect of pravastatin plus ezetimibe on carotid intimal-media thickness in patients with Systemic Lupus Erythematosus.

1786 - Clinical, Endoscopic, Manometric, Histologic Findings In The Gastro-esophageal Tract And Prevalence Of *Helicobacter Pylori* In Patients With Systemic Sclerosis.

1257 - Paired Analysis of Autoantibodies, Cytokines and Chemokines in Cerebrospinal Fluid (CSF) of SLE Patients with Central Neuropsychiatric Manifestations (cNPSLE) With and Without Associated Factors.

959 - Defective TGF-b signaling pathway of mononuclear cells in patients with Rheumatoid Arthritis.

1735 - Prevalence of Premature Menopause and Associated Factors in Systemic Lupus Erythematosus (SLE).

1031 - Treatment Compliance During Two Years Of Follow-up In A Cohort Of Early Rheumatoid Arthritis (era) Patients: Associated Factors And Relation With Disease Activity.

1103 - An Open, Observational, Extension Study of a Three-Month, Randomized, Placebo-Controlled Trial to Assess the Long-Term Efficacy and Safety of Infliximab in Juvenile-Onset Spondyloarthritis (Jo-Spa).

1860 - An Endoscopic Proposal to Evaluate Active Nasal Lesions in Wegener Granulomatosis (WG) with High Histopathological Correlation.

522 - The Role Of Socioeconomic Factors In The Clinical Expression Of Spondyloarthritis (SpA).

1485 - Performance Of Different Sets Of Criteria For Clinical Response Evaluation In A Non- Selected Cohort Of Juvenile Idiopathic Arthritis (jia) Patients.

1859 - ANCA Testing in a General Reference Centre: Poor Return and Need for Nomenclature Review.

673 - Assessment of Clinical Efficacy in a Randomized, Double-Blind Study of Etanercept and Sulphasalazine in Patients With Ankylosing Spondylitis.

75 - A Clinical Anatomy Program for Rheumatology Fellows, Mexico, 2007.
Spondyloarthropathies In Iberoamérica, Overview of 2000 Patients: The RESPONDIA Group Juvenile Spondylarthropathies in Latin America.

1213 - The Efficacy and Safety of Abatacept in Methotrexate-naïve Patients with Early Erosive Rheumatoid Arthritis and Poor Prognostic Factors.

1592 - Differences in Inflammatory Arthritis Disease Severity Among Mexican Mestizos and Native American Indians Compared to Caucasians.

1945 - Immunoreactivity and Clinical Response to Pegloticase (PGL): Pooled Data from GOUT1 and GOUT2, PGL Phase 3 Randomized, Double Blind, Placebo-controlled Trials.

22 - Tophus Response to Pegloticase (PGL) Therapy: Pooled Results from GOUT1 and GOUT2, PGL Phase 3 Randomized, Double Blind, Placebo-controlled Trials.

27 - Improvement in Health-related Quality of Life (HRQL) and Disability Index in Treatment Failure Gout (TFG) after Pegloticase (PGL) Therapy: Pooled Results from GOUT1 and GOUT2, Phase 3, Randomized, Double Blind, Placebo (PBO)-Controlled Trials.

34 - Clinical Homogeneity and Syndromic Characteristics of Treatment Failure Gout (TFG) in Four Independent Cohorts.

635 - Efficacy and Safety of Intravenous (IV) Pegloticase (PGL) in Subjects with Treatment Failure Gout (TFG): Phase 3 Results from GOUT1 and GOUT2.

L13 - The Oral Jak Inhibitor CP-690,550 (CP) in Combination with Methotrexate (MTX) is Efficacious, Safe and Well Tolerated in Patients with Active Rheumatoid Arthritis (RA) with an Inadequate Response to Methotrexate Alone.

L14 - Tocilizumab Inhibits Structural Joint Damage in Rheumatoid Arthritis Patients with an Inadequate Response to Methotrexate: The LITHE Study.

L15 - The Efficacy and Safety of Abatacept in SLE: Results of a 12-month Exploratory Study.

1716/438 - Efficacy of Procalcitonin to Determine Infection versus Lupus Flare in patients with Systemic Lupus Erhytematosus.

1859/581 - ANCA Testing in a General Reference Centre: Poor Return and Need for Nomenclature Review.

994/255 - Results of a Phase 2 Randomized, Double-Blind Study of AMG 108 (a Fully Human Monoclonal Antibody to IL-1R type I) in Patients with Rheumatoid Arthritis.

4/4 - Clinical Differences In Late *vs* Early-onset Primary Antiphospholipid Syndrome.

1.

Session: **SLE: Clinical Aspects I**
Sunday, Oct 26, 2008, 9:00 AM - 6:00 PM

Presentation: 439 - Effect of pravastatin plus ezetimibe on carotid intimal-media thickness in patients with Systemic Lupus Erythematosus

Pres. Time: Sunday, Oct 26, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 439
Category: 25. SLE: clinical aspects
Author(s): Olga Vera-Lastra, Arturo Olvera-Acevedo, Gabriela Medina, Pilar Cruz-Dominguez, Luis J. Jara. Instituto Mexicano del Seguro Social, Mexico, City, Mexico

Abstract

Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease associated with accelerated atherosclerosis and increased cardiovascular risk. Statins can reduce inflammation of atherosclerosis, but whether this is due to pleiotropism or cholesterol lowering per se is unclear. The combination of a statin with ezetimibe, acts as a dual inhibiting mechanism against the synthesis and absorption of cholesterol. An indirect estimation of atherosclerosis is the intimal media thickness (IMT) of carotid arteries measured by Doppler sonography. **Purpose:** To investigate the effect of intensive treatment with statin (pravastatin) plus ezetimibe in the carotid IMT in patients with SLE. **Methods:** We studied 22 female SLE patients, the mean age were 41± 5 years, and mean disease evolution 9 ± 5 years. IMT measurements were performed on the right and left common carotid arteries 1.0 cm proximal to the carotid bulb, by B-mode ultrasonography of carotid arteries. We included patients with carotid IMT ≥ 0.8 mm. They received treatment with pravastatin 40 mg/day, and ezetimibe 10 mg/day during six months. The carotid IMT were measured at the start and the end of the study. The levels of lipids (total cholesterol (TC), low-density lipoprotein cholesterol LDL-C, high-density lipoprotein cholesterol (HDL-C) and C- reactive protein (CRP) were also measured. **Results:** 20 patients concluded the study. In average, the basal right and left carotid IMT was > 0.8 ± 14 mm and > 0.8 ± 13, and after six months 0.68 ± 14 mm (p < 0.003) and 0.72 ± 13 mm (p < 0.004). Basal LDL cholesterol levels were 127.76 ± 45 mg/dl and 73.72 ± 28.19 mg/dl at six moths (p < 0.0004); HDL 49.71 ± 17 and 48.94 ± 12 at six months (p NS); CRP levels at start were 3.12 and 2.25 at six months (p < 0.004). **Conclusions:** Intensive treatment with pravastatin and ezetimibe had a significant reduction of the carotid IMT, as well as of the CRP levels and LDL-C wich are indicators of the risk of cardiovascular events.

Research Method: Clinical
Type of Trial: Treatment
Phase: Other
Disclosures: O. Vera-Lastra, None; A. Olvera-Acevedo, None; G. Medina, None; P. Cruz-Dominguez, None; L.J. Jara, None.

2.

Session: **Systemic Sclerosis, Fibrosing Syndromes, and Raynaud's: Clinical Aspects and Therapeutics II**
Tuesday, Oct 28, 2008, 9:00 AM - 6:00 PM

Presentation: 1786 - Clinical, Endoscopic, Manometric, Histologic Findings In The Gastroesophageal Tract And Prevalence Of Helicobacter Pylori In Patients With Systemic Sclerosis

Pres. Time: Tuesday, Oct 28, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 508
Category: 21. Systemic sclerosis, fibrosing syndromes, and Raynaud's: clinical aspects and therapeutics
Author(s): Olga L. Vera-Lastra, Raynaldo Santos-Navarro, Reyna Mendez. Instituto Mexicano del Seguro Social, Mexico, City, Mexico

Abstract

In Systemic Sclerosis (SSc) gastrointestinal manifestations are present up to 90% and the esophagus is the most affected organ. Endoscopy and manometry allow us to evaluate structurally and functionally the esophagic derangements. Altered peristalsis encourage HP infection in patients with SS, few studies has been studied carried out to investigate the frequency of HP. **Purpose:** To investigate clinical, endoscopic, manometric and histologic gastro-esophageal manifestations and prevalence of *Helicobacter pylori* (HP) infection in patients with SSc. Patients and methods: We studies 60 patients with SSc (59 women and 1 man) with mean age of 38 ± 11 years and a mean disease evolution 11 ± 8. An endoscopy of gastro-esophageal tract and their abnormalities were assessed according to Los Angeles Classification (LAC), esophageal manometry was performed and the presence of HP was investigated by gastric biopsy. **Results:** The most frequent clinical manifestations were: dysphagia 80%, pyrosis and regurgitations 68%. Endoscopic findings were: esophagitis 60% (according LAC: Grade A: 35%, grade B: 15%, grade C: 8% and grade D: 2%); hiatal hernia (HH) 65%, loose hiatus 15%; Barrett´s esophagus (BE) 18%. Manometric findings were: hypotensive lower esophageal sphincter (LES) 95% and normal LES 5%. Motility alterations of

the esophageal body were found in 98% with aperistalsis in 41%, slight hypomotility in 30%, severe hypomotility 27% and normal motility in 2%. Gastric disturbances were observed in 80%; of these 40% corresponds to non erosive gastropathy, 30% to erosive gastropathy and 10% to nodular gastropathy. HP was found in 83%. **Conclusion:** The most frequents endoscopic finding were esophagitis and HH, and by manometry were aperistalsis and hypotensive LES. These alterations imply disorders of motility and dysfunction of LES. Barrett´s esophagus was always associated with HH. A high prevalence of HP was found in SS patients.

Research Method: Clinical
Type of Trial: Diagnostic
Disclosures: O.L. Vera-Lastra, None; R. Santos-Navarro, None; R. Mendez, None

3.

Session: **SLE: Clinical Aspects II**
Monday, Oct 27, 2008, 4:30 PM - 6:00 PM

Presentation: 1257 - Paired Analysis of Autoantibodies, Cytokines and Chemokines in Cerebrospinal Fluid (CSF) of SLE Patients with Central Neuropsychiatric Manifestations (cNPSLE) With and Without Associated Factors

Pres. Time: Monday, Oct 27, 2008, 4:45 PM - 5:00 PM
Location: Room 132
Category: 25. SLE: clinical aspects
Author(s): Hilda E. Fragoso-Loyo[1], Javier Cabiedes[1], Alejandro Orozco-Narvaez[1], Luis Davila-Maldonado[1], Betty Diamond[2], Luis Llorente[1], Jorge Sanchez-Guerrero[1]. [1]Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico, D.F., Mexico; [2]The Feinstein Institute for Medical Research, New York., NY

Abstract

The ACR classifies neuropsychiatric manifestations attributable to SLE as with and without (pure) associated factors. Whether the inflammatory profile between them is different has not been studied. AIM: To compare the inflammatory profile of CSF in SLE patients with cNPSLE manifestations, pure and with associated factors. **Methods:** Thirty-five consecutive SLE patients (ACR), hospitalized because of cNPSLE attributable to SLE, according to the ACR 1999 case definitions, were included. Two rheumatologists and two neurologists, independently classified each cNPSLE manifestation as pure or with associated factors. All the patients were evaluated at hospitalization and six months later according to a standardized protocol, including a CSF sample (35 at hospitalization and 25 six months later). IgG antinuclear antibodies were detected by indirect immunofluorescence; IgG anti-dsDNA, anti-ribosomal P, anticardiolipin, anti-β2 glycoprotein I antibodies were detected by immunoenzymatic assay; IgG anti-NR2 glutamate receptor antibody (NDMAR) were detected by ELISA. Cytokines and chemokines were measured by cytometric bead array kits including cytokines (IL-2, IL-4, IL-6, IL-10, TNFα, and IFNγ) and chemokines (MCP-1, RANTES, IL-8, MIG, and IP-10). **Results:** Seventeen and 18 patients had pure cNPSLE manifestations, and with associated factors, respectively. Clinical manifestations included, 14 seizures, 7 severe refractory headaches, 8 confusional states, 3 cerebrovascular diseases, 2 psychosis, and 1 pseudotumor cerebri. Five males and 30 females, mean age 30.6 ± 11.8 years, and SLE duration 3.6 ± 4.0 years, were included. Clinical and demographic characteristics were similar between groups, except SLEDAI (18.1 ± 8.0 *vs* 11.7 ± 9.7, P = 0.04). Positive abs were detected in patients with pure and with associated factors as follows: P-ribosomal 59 % *vs* 33%, P = 0.12, anti-NMDA 50% *vs* 33%, P = 0.32; neither a difference was seen in ANA, dsDNA, cardiolipin and β-2-GPI antibodies. Six months later, the prevalence and the levels of abs were similar to the baseline values in both groups. The levels of IL-6, IL-8, IP-10, and MCP-1 were elevated in both groups, however, only IP-10 was significantly higher among the patients with pure cNPSLE manifestations (P = 0.009). Six months later, the levels of IP-10 decreased significantly in both groups (P < 0.05), and MCP-1 had a significant decrease only in patients with pure cNPSLE manifestations (P = 0.05). **Conclusion:** Overall, the inflammatory profile in CSF was similar in patients with pure cNPSLE manifestations and with associated factors; however, IP-10 and MCP-1 could be signaling different mechanisms in cNPSLE manifestations.

Research Method: Clinical
Type of Trial: Diagnostic
Disclosures: H.E. Fragoso-Loyo, None; J. Cabiedes, None; A. Orozco-Narvaez, None; L. Davila-Maldonado, None; B. Diamond, None; L. Llorente, None; J. Sanchez-Guerrero, None.

4.

Session: **RA: Human Etiology and Pathogenesis II**
Monday, Oct 27, 2008, 9:00 AM - 6:00 PM

Presentation: 959 - Defective TGF-β signaling pathway of mononuclear cells in patients with Rheumatoid Arthritis

Pres. Time: Monday, Oct 27, 2008, 9:00 AM -11:00 AM

Location: Hall A, Poster Board: 220
Category: 19. RA: human etiology and pathogenesis
Author(s): Daniel X. Xibillé Friedmann[1], Luz M. Mejía Cristóbal[2], Sergio A. Garay Sanchez[2], Ruben Burgos Vargas[3], Miguel Mergold[3], Mariana S. Alvarez Fuentes[4], Jose L. Montiel[2]. [1]Hospital General de Cuernavaca, Cuernavaca, Mexico;[2] Facultad de Farmacia, Universidad Autonoma del Estado de Morelos, Cuernavaca, Mexico; [3]Hospital General de México, México, Mexico; [4]Instituto Nacional de Salud Pública, Cuernavaca, Mexico

Abstract

Purpose: Rheumatoid Arthritis (RA) and Ankylosing Spondylitis (SA) are chronic inflammatory musculoskeletal diseases, characterized by underlying autoimmunity. TGF-β induces a physiological anti-inflammatory response but in patients with RA or SA (RA/SA) higher levels of this cytokine have been seen but seem not to reduce inflammation. We evaluated the expression and functional capacity of TGF-β receptor I and II (TβRI/TβRII) in mononuclear cell from peripheral blood and synovial fluid of RA/SA patients and controls. **Methods:** Peripheral blood and synovial fluid from patients with RA/SA were collected in 2 different hospitals. Control sera was obtained from a blood bank. Mononuclear cells (MNC) were isolated with Ficoll-Paque and fixed with 1% PFA or maintained in RPMI 1640 with 10% SFB at 37°C and 5% CO2. Basal and TGF-β1-activated (R&D) receptor levels were evaluated by flow cytometry employing specific polyclonal antibodies for TβRI and TβRII. Sub-populations of MNC were characterized and analyzed separately. Determination of soluble TGF-β was done with capture ELISA. Determination of baseline of proteins Smad 2/3, phosphorylation, Smad 2/3(Ser433/435) and Smad7 levels was evaluated with FM using specific antibodies. Activation assays of Smad2/3 phosphorylation by TGF-β1 [5 ng/ml] was done with MNC stimulated with Concanavalin A and arrested for 2 h in absence of serum. After adding TGF-β, different incubation times were evaluated by western blot/chemiluminescence and FM. Specificity of the activation assays was done by with TβRI specific inhibitor (HTS466284, TOCRIS). Statistical analysis was done using Student's t and Mann-Whitney's U. **Results:** Sera from 29 patients with RA and 9 with SA, and synovial fluid from 17 RA patients and 12 SA patients were analyzed. Baseline expression of TβRI and TβRII was similar in blood MNC of both patients and controls, but in synovial fluid MNC there was a 50% decrease in their expression in 3 cell populations. We observed a significant TGF-β receptor down-regulation after 48 h. We observed no statistically significant difference in the baseline levels of Smad 2/3 and Smad 7 between MNC of patients and controls, but there was a significant reduction in basal and TGF-β-activated phosphorylation of Smad 2/3 in 66% of MNC cells of RA patients (10/15) suggesting deficient activation of the TGF-β signaling pathway stimulated in blood MNC of patients compared to donors. **Conclusions:** There is a deficient TGF-b-signaling pathway in MNC of RA/SA patients with reduced receptors levels and poor response to in vitro activation accounting for a lack of response to this cytokine in chronic inflammatory arthropathies.

Research Method: Basic
Type of Trial: Correlative
Phase: Phase II
Disclosures: D.X. Xibillé Friedmann, None; L.M. Mejía Cristobal, None; S.A. Garay Sánchez, None; R. Burgos Vargas, None; M. Mergold, None; M.S. Alvarez Fuentes, None; J.L. Montiel, None.

5.

Session: SLE: Clinical Aspects III
Tuesday, Oct 28, 2008, 9:00 AM - 6:00 PM

Presentation: 1735 - Prevalence of Premature Menopause and Associated Factors in Systemic Lupus Erythematosus (SLE)

Pres. Time: Tuesday, Oct 28, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 457
Category: 25. SLE: clinical aspects
Author(s): Juanita Romero-Diaz, Deshire Alpizar-Rodriguez, Evelyn Perez-Trejo, Maria C. Cravioto, Jorge Sanchez-Guerrero. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran, Mexico, D.F., Mexico

Abstract

Although premature menopause in women with SLE is common, the factors associated with it are still undefined. **Aim:** To determine the prevalence and identify factors associated with premature menopause in SLE. **Patients and methods:** SLE patients (≥ 4 ACR criteria), 16-60 years old, were face to face interviewed using a standardized questionnaire. Study variables were grouped as follows: general information (date of birth, years of schooling), smoking habit, gynecobstetric history (age at menarche, hysterectomy, pregnancy, hormonal contraceptives use, and date of last menstrual period). Medical records were reviewed, using a standardized format to gather information about comorbidities, health-related behaviors, treatment, and SLE characteristics. Postmenopausal status was defined as amenorrhea ≥ 12 months in the absence of pregnancy, but in women ≤ 55 year old with history of hysterectomy, postmenopausal status was defined as

FSH level > 35 mU/mL. Age at menopause was defined by the status quo method, and premature menopause was considered when it occurred at age < 40 years. **Statistical analysis:** Descriptive statistic, logistic regression; p value was set at <0.05, two tailed. **Results:** A total of 863 consecutive SLE women attending the outpatient clinic were interviewed. Mean education was 12.5 [4.0] years. The mean age of the population studied was 35.6 [10.7] years, and its distribution was not different from the Mexican general population, p = 0.79. One hundred and sixty five patients [19.1%] were postmenopausal, median age at the interview was 49 years of whom 24 [15%] patients were younger than 40 years. Women with premature and natural menopause had similar frequency of smoking, mean of years of schooling and age at menarche. Women with premature menopause were younger at diagnosis of SLE (23.0 [6.7] *vs* 38.1 [10.5] years, p < 0.001). Length of follow-up was not different between women with premature and natural menopause; 10.3 [6.5] *vs* 12.9 [9.4] years; p = 0.31, respectively. Malar rash (p = 0.03), renal disease (p = 0.001), use of cyclophosphamide (p-0.007), number of SLE criteria (p = 0.048), age at SLE diagnosis (p < 0.001), and number of pregnancies (p < 0.001) were associated with premature menopause. In the multivariate analysis, renal disease (OR 4.4; 95% CI 1.1-16.3; p = 0.028) and age at SLE diagnosis (OR 0.84; 95% CI 0.76-0.90; p < 0.001) were retained. **Conclusions:** In our Center, premature menopause was observed in 2.8 percent of women with SLE. Younger age at diagnosis, and renal disease were found associated.

Research Method: Clinical
Type of Trial: Epidemiologic or Observational
Phase: Other
Disclosures: J. Romero-Diaz, None; D. Alpizar-Rodriguez, None; E. Perez-Trejo, None; M.C. Cravioto, None; J. Sanchez-Guerrero, None.

6.

Session: **RA: Treatment and Pharmacosurveillance**
Monday, Oct 27, 2008, 9:00 AM - 6:00 PM

Presentation: 1031 - Treatment Compliance During Two Years Of Follow-up In A Cohort Of Early Rheumatoid Arthritis (era) Patients: Associated Factors And Relation With Disease Activity

Pres. Time: Monday, Oct 27, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 292
Category: 17. RA: clinical aspects
Author(s): Irazu Contreras-Yañez, Marina Rull-Gabayet, Javier Cabiedes-Contreras, Virginia Pascual-Ramos. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, México City, Mexico

Abstract

Background: Earlier aggressive treatment with disease-modifying anti-rheumatic drugs (DMARDs) plays a major role in improving ERA patient outcomes. Adherence to medications (AM) occurs in only 18-49% of the patients. **Purposes:** 1. To determine non-AM in a cohort of ERA patients over two years of follow-up. 2. To identify associated factors. 3. To investigate the relationship between AM and disease activity. **Methods:** Up to August 2007, charts from a cohort of ERA patients who completed two years of follow-up were retrospectively review by an independent observer with emphasis on treatment prescribed at last visit and its compliance at the follow visit. As part of the standard care provided, every two months patients were evaluated by the same rheumatologist who interview patients regarding treatment adherence, performed tender and swollen joint counts (68/66 joints evaluated) and scored disease activity with the DAS28 (13 consecutive visits). At baseline a complete medical history, socio-demographic data, serologic and disease characteristics were obtained on standardized formats. Comorbidities were recorded at baseline and follow-up evaluations. At last visit, sustained remission was defined as ≥ 3 consecutive two-monthly apart visits with DAS28 < 2.6. Non-AM was defined as any DMARDs and/or corticosteroids noncompliance, including missing or incorrect doses and schedules, for at least one week and was evaluated from the second visit. Descriptive statistics, χ^2 and Mann-Withney U tests were used. **Results:** up to cut-off, charts from 59 patients were review of whom 81.4% were females and 68% had rheumatoid factor. At baseline, they had (mean ± SD) 40.8 ± 14.4 years of age, 10.4 ± 3.9 years of scholarship and 6.1 ± 1.3 of DAS28. During follow-up, 708 visits were reviewed and 71 non-AM notes were identified in 35 (59.3%) patients; Thirty-two non-AM notes during the first year of follow-up and 39 during the second year. Patients with AM (N = 24) had lower age at baseline than non-AM patients (36 ± 13.2 *vs* 44.1 ± 14.1 years, p = 0.03). No other differences were found when socio-demographic characteristics, comorbidities, serological and disease characteristics were analyzed. During follow-up, DMARDs and/or corticosteroids use was similar in both groups, although patients with AM had lower (mean ± SD) DAS28 than non-AM patients (2.5 ± 0.8 *vs* 3.1 ± 0.8, p = 0.002). More patients with AM had sustained remission at last follow-up than non-AM patients (83.3% *vs* 54.3%, p = 0.03). **Conclusions:** non-AM to DMARDs and/or corticosteroids was frequent and progressive in an ERA patients cohort. Patients with AM were younger, had lower disease activity during follow-up and had more frequently sustained remission than patients with non-AM. AM should intentionally be evaluated during patients follow-up as it seems to play a major role in patient outcomes.

Research Method: Observational
Type of Trial: Epidemiologic or Observational

Phase: Other
Disclosures: I. Contreras-Yañez, None; M. Rull-Gabayet, None; J. Cabiedes-Contreras, None; V. Pascual-Ramos, None.

7.

Session: **Spondyloarthritis: Clinical Aspects and Treatment II**
Monday, Oct 27, 2008, 9:00 AM - 6:00 PM

Presentation: 1103 - An Open, Observational, Extension Study of a Three-Month, Randomized, Placebo-Controlled Trial to Assess the Long-Term Efficacy and Safety of Infliximab in Juvenile-Onset Spondyloarthritis (Jo-Spa)

Pres. Time: Monday, Oct 27, 2008, 9:00 AM - 6:00 PM
Location: Hall A, Poster Board: 364
Category: 28. Spondylarthropathies and psoriatic arthritis: clinical aspects and treatment
Author(s): Ruben Burgos-Vargas, Julio C. Casasola-Vargas, Raúl Gutiérrez-Suárez, Janitzia Vázquez-Mellado. Hospital General de México, México, México

Abstract

Background: We have previously shown that infliximab was superior to placebo in controlling disease activity in patients with Jo-SpA who were enrolled in a three-month, double-blind, placebo-controlled, randomized trial (Arthritis Rheuma 2007;56 [suppl]:S319). **Purpose:** To demonstrate sustained efficacy, safety, and tolerability of infliximab at 5 mg/kg over 52 weeks. **Methods:** Patients with JO-SpA (ESSG criteria; ages: onset < 16 years; screening at <18 years) completing the double-blind phase entered the open phase of the trial. In this phase, both the placebo/infliximab (P-Inflix) and the infliximab/infliximab (I-Inflix) groups received infliximab at a dose of 5 mg/kg every six weeks. Patients in the (P-Inflix) had previously received a loading dose of infliximab (weeks 0, 2 and 6). Primary efficacy measure: number of active joints. Secondary outcome measures: number of tender entheses; patient assessment of pain (100 mm NRS); patient/parent assessment of well being (100 mm NRS); investigator assessments of disease activity/health status (100 mm NRS); childhood health assessment questionnaire (CHAQ); and C reactive protein (CRP). Exploratory measures: ACRPed, ASAS, BASDAI, BASFI. **Results:** 26 patients (25 males, median age at onset 15.2 years [9-18]; u-SpA in 21/AS in 5) participated in the double-blind phase; one of those patients in each group withdrew the trial because of protocol violations or lost of followup. Completer analysis demonstrated a significant improvement in the number of active joints as well as in secondary efficacy measures throughout the study (Table). There were no severe adverse events reported in the trial. **Conclusions:** Infliximab induces sustained control of disease activity in patients with JoSpA . Infliximab is safety and well tolerated.

Primary and main outcome measures at baseline and 52 weeks

	I-Inflix (n = 11) Baseline	week 52	P-Inflix (n = 13) Baseline	week 52
Active joints, n	4.7 (1.7)	0	6.4 (3.8)	0.1 (0.3)
Tender entheses, n	11.9 (10.7)	0	8.8 (5.0)	0.2 (0.6)
Pain, NRS	7.2 (2.0)	1.7 (2.7)	7.7 (1.8)	1.7 (1.4)
CHAQ, score	1.1 (0.5)	1.1 (0.5)	1.3 (0.5)	1.2 (0.3)
CRP, mg/dl	24.8 (10)	1.3 (3.1)	26.8 (17.1)	3.0 (5.7)

*Except for CRP (p = 0.04), there were no differences between groups at week 52

Research Method: Clinical
Type of Trial: Treatment
Phase: Phase II
Disclosures: R. Burgos-Vargas, Roche, Schering-Plough, Abbott, Wyeth, 5; Roche, Schering-Plough, Abbott, Wyeth, 8; J.C. Casasola-Vargas, None; R. Gutiérrez-Suárez, None; J. Vázquez-Mellado, None

8.

Session: **Vasculitis II**
Tuesday, Oct 28, 2008, 9:00 AM - 6:00 PM

Presentation: 1860 - An Endoscopic Proposal to Evaluate Active Nasal Lesions in Wegener Granulomatosis (WG) with High Histopathological Correlation

Pres. Time: Tuesday, Oct 28, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 582
Category: 30. Vasculitis
Author(s): Luis F. Flores-Suárez[1], Olga Beltrán Rodríguez-Cabo[1], Edgardo Reyes[1], Jorge Rojas-Serrano[2]. [1]Instituto Nacional de Ciencias Médicas y Nutrición, Mexico City, Mexico; [2]Instituto Nacional de Enfermedades Respiratorias, Mexico City, Mexico

Abstract

Purpose: Though accessible for tissue sampling, nasal biopsies in WG have poor yield. We present a combined endoscopic and histopathological evaluation of suspected nasal active WG and propose an endoscopic classification. **Methods:** Patients seen

from December 1997-October 2007 (ENT Service) were evaluated. Pre-sampling preparation (nasal washes, gentle crust removal) was done. Six lesions were identified: white submucosal nodules, bloody submucosal patches, polyps (MAJOR); mucosal swelling, vascular submucosal dilatations, ulcers (MINOR). If ≥ 2 major were present they were definitively active; if 1 major plus all minors were present, they were considered endoscopically probably active. 3-4 samples were taken. The histological lesions proposed by Devaney et al[1] were sought (with modifications). Three categories were set: not-diagnostic, probably active (ulcers + mixed infiltration + isolated giant cells) and diagnostic (probable features + microabscess, any vasculitis, collagenous degeneration and geographic necrosis). Histological evaluation went blindly. Two-tailed Fisher exact test to evaluate endoscopic signs and histology. Sensitivities, specificities, predictive values and κ correlations of the composites of endoscopic and histologic activity were determined. P values ≤ 0.05 were significant. **Results:** 18 patients (22 samples). In fifteen cases the ENT specialist suspected active WG (14 definitive, 1 probable). From them, 13 had probable (n = 5, 33%) or definitive (n = 8, 53%) histological WG. The sensitivities, specificities, positive and negative predictive values of the endoscopical evaluation against histological proof for each category (probable or definitive) or its grouping are in the table. The histological diagnostic yield of the macroscopical suspicion of activity (any degree, either probable or definitive) was 87%. Endoscopical lesions correlating with definitive histology: patches (p = 0.0009), submucosal nodules (0.001), mucosal swelling (p = 0.02). **Conclusions:** Careful nasal cavity preparation and observation of the nasal mucosa can guide tissue sampling documenting active WG. This can lead to better histologic yield when definitive proof is needed. The proposed endoscopical grading can increase the positive yield to almost 60% even with stringent macroscopic and microscopic criteria for definitive activity are used, and close to 90% when probable activity is seen in both evaluation grounds. Validation of our findings is necessary.

1 Am J Surg Pathol 1990;14:555-564.

Sensitivities, specificities, predictive and kappa values of endoscopic and histologic parameters

Categories tested	Sensitivity	Specificity	PPV	NPV	p value	k value
Definitive active endoscopy & histology	100%	57%	57%	100%	0.018	0.49
Definitive endoscopy + sum of definitive & probable histology	100%	89%	93%	100%	0.0009	0.9
Sum of definitive & probable endoscopy + definitive histology	100%	50%	53%	100%	0.02	0.42
Sum of any endoscopic + histologic activity	100%	78%	87%	100%	0.0009	0.8

Research Method: Observational
Type of Trial: Diagnostic
Phase: Other, diagnostic methods correlation
Disclosures: L.F. Flores-Suárez, None; O. Beltrán Rodríguez-Cabo, None; E. Reyes, None; J. Rojas-Serrano, None

9.

Session: Spondyloarthritis: Clinical Aspects and Treatment I
Sunday, Oct 26, 2008, 9:00 AM - 6:00 PM

Presentation: 522 - The Role Of Socioeconomic Factors In The Clinical Expression Of Spondyloarthritis (SpA)

Pres. Time: Sunday, Oct 26, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 522
Category: 28. Spondylarthropathies and psoriatic arthritis: clinical aspects and treatment

Author(s): on behalf of RESPONDIA group, Janitzia Vazquez-Mellado[1], Pilar Font[2], Alberto Berman[3], Miguel Gutiérrez[4], Daniel Palleiro[5], José Chavez[6], Ricardo Saenz[7], Ivan Stekman[8], Anabela Barcelós[9], Rómulo Wong[10], Gabriela Huerta[11], Jorge Saavedra[12], José Maldonado-Cocco[13], Diana Flores[14], Carol Pérez[15], Rubén Burgos-Vargas[1], Eduardo Collantes-Estevez[16].
[1]Hospital General de Mexico, Mexico City, Mexico; [2]Reina Sofía University Hospital, Cordoba, Spain; [3]Tucuman College of Medicine, Tucuman, Argentina; [4]Univ Catolica de Chile, Santiago, Chile;[5] Uruguay; [6]Hospital E. Rebagliati, Lima, Peru; [7]Hospital Dr. R.A. Calderón Guardia, San Jose, Costa Rica; [8]Univ Central de Venezuela, Caracas, Venezuela; [9]Unidade de Reumatologia, Lisbon, Portugal; [10]Argentina; [11]Hospital General de México, Mexico City, Mexico; [12]Chile; [13]Instituto Nacional de Rehabilitación, Buenos Aires, Argentina; [14]Hospital Universitario Jose E. Gonzalez, Monterrey, Mexico; [15]Catholic University of Chile, Santiago, Chile; [16]Reina Sofia University Hospital, Córdoba, Spain

Abstract

Geographic and ethnic variations in the clinical expression of SpA appear multifactorial. Iberoamerica comprises nations where socioeconomic disparities influence medical care and perhaps the pattern of certain diseases. RE-

SPONDIA is an Ibero-American (IBA) group of 85 rheumatologists from 9 countries trained to collect SpA demographic and clinical data of since 2006. **Purpose:** To determine the role of socioeconomic levels in the clinical expression of SpA in IBA. **Methods:** This is an observational and cross sectional study of consecutive SpA patients (ESSG criteria) whose demographic, clinical data, and therapeutic data were collected by RESPONDIA members. Data were transmitted on-line and stored in the Spanish SpA Registry (Regisponser) website. The socioeconomic level was determined by using the Graffar scale, whose parameters include educational level, housing conditions, type of actual job, and income source; patients were classified in the high socioeconomic status (high, medium high, and medium Graffar levels) and low (medium-low and low Graffar levels). Statistical analysis: t Student´s test, chi square and logistic regression. **Results:** 902 (with complete socioeconomic evaluation) out of 1,963 were analyzed; 60% of them were males and their means of age at onset, current age, and disease duration (SD) 35 (16) years, 45 (15) years, and 12 (10) years. 52% were HLA-B27. Differences between high level (n = 519, 56%) *vs* low level (n = 383, 41.3%) patients are shown in table. The variables that remain significant in the logistic regression were younger age at onset, tarsitis, limited cervical rotation, high AsQoL, and the diagnosis of ankylosing spondylitis (AS) or undifferentiated SpA (U-SpA). **Conclusions:** The pattern of SpA IBA appears influenced by the socioeconomic level. Thus, patients in the low socioeconomic level were younger at onset and had more often tarsitis, limited cervical mobility, high AsQoL and BASFI scores and are more frequently diagnosed as u-Sp-A. In addition, they are less often treated with anti-TNF agents.

Clinical data	Low socioeconomic level (%)	High socioeconomic level (%)	p	Logistic regression
Age at onset < 18 years	18	13	0.06	0.018
Peripheral arthritis	42	35	0.04	
Enthesitis	46	34	0.000	
Tarsitis	19	12	0.002	0.000
Limited cervical motion	60	47	0.000	0.006
Permanent work disability	16	6	0.000	
Regular exercise	25	39	0.000	
VAS global health ≥ 5	64	51	0.000	
AsQoL ≥ 7	63	42	0.000	0.002
BASFI ≥ 4	56	42	0.000	
AS diagnosis	69	76	0.08	0.010
USpA diagnosis	31	24	0.08	0.010

Clinical characteristics and socioeconomic level

Research Method: Clinical
Type of Trial: Quality of Life or Supportive Care
Phase: Other, Cross-sectional
Disclosures: J. Vazquez-Mellado, None; P. Font, None; A. Berman, None; M. Gutiérrez, None; D. Palleiro, None; J. Chavez, None; R. Saenz, None; I. Stekman, None; A. Barcelós, None; R. Wong, None; G. Huerta, None; J. Saavedra, None; J. Maldonado-Cocco, None; D. Flores, None; C. Pérez, None; R. Burgos-Vargas, Roche, Schering-Plough, Abbott, Wyeth, Pfizer, 5; Roche, Schering-Plough, Abbott, Wyeth, 8; E. Collantes-Estevez, None.

10.

Session: Juvenile Arthritis, Childhood Vasculitis, and Pediatric Bone Health
Tuesday, Oct 28, 2008, 9:00 AM - 6:00 PM

Presentation: 1485 - Performance of Different Sets of Criteria For Clinical Response Evaluation In A Non- Selected Cohort of Juvenile Idiopathic Arthritis (jia) Patients

Pres. Time: Tuesday, Oct 28, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 207

Category: 11. Pediatric rheumatology clinical and therapeutic disease
Author(s): Raúl Gutiérrez, Rubén Burgos Vargas. Hospital General de México, Mexico, Mexico

Abstract

Purpose: To compare the performance and evaluate the usefulness in JIA patients of 4 sets of criteria for clinical response evaluation used in RA. **Methods:** A single center, observational study of a non-selected cohort of JIA patients treated with different DMARD regimens in the out-patient clinic was conducted. Four sets of criteria: DAS, DAS28, CDAI and SDAI were evaluated blindly and compared with the ACR-Ped-30 and the clinician judgment of response (CJR) (100 mm-VAS) as the gold standard to evaluate clinical response in JIA patients. The cut-off values for responders were derived from the EULAR criteria (DAS, DAS28), and from the best threshold obtained from the receiver operating characteristic (ROC) curve analysis (CDAI and SDAI). Performance was assessed by ROC curve properties and other statistics for diagnostic tests. **Results:** 50 JIA patients (female/male ratio: 1.2:1; mean age at diagnosis: 6.4 ± 3.3 years; mean

disease duration: 5.3 ± 2.7 years) were evaluated. The area under the ROC curve (AUC) with 95% confidence interval (95%CI), the likelihood ratio (LR) with 95%CI, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were: 0.842 (0.691-0.994); 6.48 (1.03-40.75); 80.9; 87.5; 97.1; and 46.6; respectively for the CJR in comparison with the ACR-Ped-30 as gold standard. The performance of the DAS in comparison with the CJR was poor. However, the ROC curve properties and other diagnostic test properties were: 0.700 (0.532-0.868); 2.00 (1.05-3.80); 80.0; 60.0; 82.3 56.2; respectively for the DAS28; 0.752 (0.599-0.906); 2.89 (1.23-6.83); 77.1; 73.3; 87.1 57.8; respectively for the SDAI; and 0.705 (0.542-0.868); 2.23 (1.06-4.68); 74.2; 66.6 83.8; 52.6; respectively for the CDAI, when compared with the CJR. In comparison with the ACR-Ped-30 the performance of the four sets of criteria was poor. **Conclusions:** In the daily clinical practice the DAS 28, SDAI and CDAI can be used for the evaluation of clinical response in JIA patients.

Research Method: Observational
Type of Trial: Diagnostic
Phase: Other
Disclosures: R. Gutiérrez, None; R.B. Vargas, None.

11.

Session: **Vasculitis II**
Tuesday, Oct 28, 2008, 9:00 AM - 6:00 PM

Presentation: 1859 - ANCA Testing in a General Reference Centre: Poor Return and Need for Nomenclature Review

Pres. Time: Tuesday, Oct 28, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 581
Category: 30. Vasculitis
Author(s): Luis F. Flores-Suárez, Antonio R. Villa. Instituto Nacional de Ciencias Médicas y Nutrición, Mexico City, Mexico

Abstract

Purpose: ANCA in general practice has poor return. Studies have shown sensitivities of 50% with reports of its positive predictive value (PPV) as low as 0% for ANCA-associated vasculitides (AASV). We report the properties of ANCA testing during a one year period in a reference centre. **Methods:** Samples ran by indirect immunofluorescence (IIF) and/or ELISA against proteinase-3 (PR3-ANCA) and myeloperoxidase (MPO-ANCA) (The Binding Site, UK) between September 2006 and August 2007 were identified. Information on sample procedence, ordering indication, patients' characteristics, data at time of ordering and final clinical diagnosis was retrieved. Two groups were defined: AASV and ANCA-associated intestinal/liver diseases (GI group). The rest had non-ANCA related conditions. For patients with more than one test during the period, only one was randomly selected for analysis. IIF cut-off value was ≥1:40; PR3 and MPO-ANCA > 3.5 and > 9.0 U/mL, respectively. Contingency tables were built for each group (or both) against each method and their combinations, and differences tested. Results: 1049 tests were ordered on 962 individuals; 520 (50%) were from patients attending our centre. When only one test/patient was considered and the information was complete, 410 patients were analyzed. AASV patients = 49, GI group patients = 145, non-ANCA related conditions = 216. IIF was performed on 384, PR3-ANCA on 86 and MPO-ANCA on 92. C-ANCA were positive on 186 (49%), P-ANCA on 53 (14%), atypical (X-ANCA) on 1 (< 0.5%) and double positive on 79 (20.5%); negative IIF was seen in 65 (17%). PR3-ANCA were positive in 21 (24%) and MPO-ANCA in 5 (5%). Most relevant results are shown in the table. Very few patients within the GI group had ELISA ordered so their results are not shown.

Table. ANCA testing properties in a general referral centre

Method	Group tested	Sensitivity	Specificity	PPV	NPV
IIF[a]	AASV	86%	18%	13%	89%
ELISA[b]	AASV	54%	82%	64%	69%
IIF + ELISA[c]	AASV	86%	23%	14%	92%
IIF[a]	GI group	90%	21%	41%	77%
IIF + ELISA[c]	Both groups	87%	31%	54%	72.5%

a) any pattern; b) reactivity against any antigen; c) C- or P-ANCA plus any reactivity

46% of IIF were false positive, which explains why combining both methods decreased minimally this rate. ELISA testing had the best yield. Several reasons explain our results (setting, ordering departments, test indications, possible IIF lecture discrepancy). Nevertheless, a suboptimal use of ANCA was found, especially IIF. **Conclusions:** There is a need to establish stringent cut-off values and propose ordering indications to avoid misuse of ANCA in reference centres. We think in accordance with some experts that the term ANCA needs redefinition, possibly limiting it to those recognizing MPO and PR-3 as antigens (small-vessel vasculitides related). Those found in other diseases might be better termed neutrophil specific (NSA) or neutrophil recognizing antibodies (NERA). Reporting under such definitions could also influence on better performance of true ANCA testing, increas-

ing PPV and specificity. Also, ANCA standardization is urgently needed.

Research Method: Other
Type of Trial: Diagnostic
Phase: Other, non-applicable
Disclosures: L.F. Flores-Suárez, None; A.R. Villa, None.

12.

Session: **Spondyloarthritis: Treatment**
Sunday, Oct 26, 2008, 2:30 PM - 4:00 PM

Presentation: 673 - Assessment of Clinical Efficacy in a Randomized, Double-Blind Study of Etanercept and Sulphasalazine in Patients With Ankylosing Spondylitis

Pres. Time: Sunday, Oct 26, 2008, 3:15 PM - 3:30 PM
Location: Room 300
Category: 28. Spondylarthropathies and psoriatic arthritis: clinical aspects and treatment

Author(s): J. Braun[1], F. Huang[2], R. Burgos-Vargas[3], I. E. van der Horst-Bruinsma[4], B. Freundlich[5], B. Vlahos[5], A. S. Koenig[5]. [1]Rheumatology Medical Center, Ruhrgebeit, Herne, Ruhr-University, Bochum, Germany; [2]Department of Rheumatology, Chinese PLA General Hospital, Beijing, China; [3]Hospital General de México and Universidad Nacional Autónoma de México, Mexico City, Mexico; [4]VU University Medical Center, Department of Rheumatology, Amsterdam, Netherlands; [5]Wyeth Research, Collegeville, PA

Abstract

Purpose: Ankylosing spondylitis (AS) is a form of chronic inflammatory arthritis that affects the spine. Etanercept (ETN) is a fully human tumor necrosis factor soluble receptor that is effective in the treatment of AS. Patients have historically been treated with non-biologic DMARDs, such as sulphasalazine (SSZ), despite limited data to support use in the spine. Clinical benefit of SSZ may be seen as early as 4 weeks or as late as 12 weeks.1 This study compared efficacy of ETN with SSZ in patients with AS. **Methods:** This was a randomized, double-blind study. Patients with AS (N = 566) were treated for 16 weeks with ETN 50 mg once weekly (N = 379) or SSZ 3 g daily (N = 187). Eligible patients had active AS based on 1) BASDAI VAS ≥ 30; 2) morning stiffness VAS ≥ 30; 3) VAS ≥ 30 for two of the following: patient global assessment of disease activity; pain; BASFI; and be a candidate for treatment with SSZ (eg, presence of peripheral joint symptoms) and ETN. All patients had failed > 1 NSAIDs for > 3 months. Main exclusion criteria: complete ankylosis of the spine; previous ETN treatment; and SSZ treatment within 6 months of screening. Primary endpoint: proportion of patients achieving 20% improvement from baseline in Assessment of AS (ASAS 20) at 16 weeks. LOCF was used for imputation of missing values on the modified intention-to-treat population. **Results:** Overall, mean age was 41 y, 74% were male, and average disease duration was 7.5 y. The proportion of patients who achieved ASAS 20 was greater (P < 0.001) in the ETN group *v* the SSZ group from Week 2. At Week 16, 75.5% ETN-treated patients achieved an ASAS 20 response *v* 51.3% SSZ-treated patients. ASAS 40, ASAS 5/6, partial remission for AS, BASFI, BASDAI, BASMI, nocturnal back pain, and Modified Schobers responses were all higher (P < 0.001) in the ETN group compared with the SSZ group at all time points. In the ETN group, 7 subjects (1.8%) reported serious adverse events compared with 4 subjects (2.1%) in the SSZ group (P = NS). There were no new safety signals. **Conclusions:** In this study, etanercept was significantly more effective than SSZ at improving the clinical symptoms of AS as early as Week 2. These results support a role for etanercept therapy in patients with this chronic disorder. [1]http://www.pfizer.com/files/products/uspi_azulfidine_en.pdf

Week 16 (LOCF)		
	ETN Number (% improvement)	SSZ Number (% improvement)
ASAS40	229/379(60.4)	61/187(32.6)
ASAS5/6	164/375(43.7)	38/185(20.5)
Partial Remission	124/379(32.7)	29/187(15.5)
	Mean (% improvement)	Mean (% improvement)
BASFI	32.7(48.3)	45.6(27.0)
BASDAI	26.0(55.5)	39.5(31.0)
BASMI	2.8(25.0)	3.3(7.0)
Nocturnal Back Pain	25.4(60.0)	41.2(34.8)
Modified Schobers	4.4(19.6)	4.1(6.0)

Research Method: Clinical
Type of Trial: Treatment
Phase: Phase IV
Disclosures: J. Braun, Abbott, 2; Centoor, 2; Shering-Plough, 2; Pfizer, 2; Wyeth, 2; Abbott, 8; Centoor, 8; Shering-Plough,8; Pfizer, 8; Wyeth, 8; F. Huang, None; R. Burgos-Vargas, Schering-Plough, 8; Wyeth, 8; Abbott, 8; Roche, 5; Schering-Plough, 5; Wyeth, 5; Abbott, 5; Roche, 8; I.E. van der Horst-Bruinsma, None; B. Freundlich, Wyeth, 3;

B. Vlahos, Wyeth, 1; Wyeth, 1; Wyeth, 3; A.S. Koenig, Wyeth, 1; Wyeth, 1; Wyeth, 3.

13.

Session: **Education**
Sunday, Oct 26, 2008, 9:00 AM - 6:00 PM

Presentation: 75 - A Clinical Anatomy Program for Rheumatology Fellows, Mexico, 2007

Pres. Time: Sunday, Oct 26, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 75
Category: 34. Education
Author(s): J. J. Canoso[1], C. Abud-Mendoza[2], L. Barile-Fabris[3], R. Burgos-Vargas[3], I. García-De la Torre[4], M. Garza-Elizondo[5], S. Gutiérrez-Ureña[4], F. Irazoque-Palazuelos[3], L. Lino-Pérez[6], J. Miranda-Limón[3], C. Ramos-Remus[4], M. Robles San Román[7], R. A. Kalish[8]. [1]Centro Médico ABC, Mexico City, Mexico; [2]UASLP, San Luis Potosí, Mexico; [3]UNAM, Mexico City, Mexico; [4]UDG, Guadalajara, Mexico; [5]UANL, Monterrey, Mexico; [6]Consejo Mexicano de Reumatología, Mexico City, Mexico; [7]Colegio Mexicano de Reumatología, Mexico City, Mexico; [8]Tufts University, Boston, MA

Abstract

Purpose: Musculoskeletal clinical anatomy workshops (MCAW) for rheumatologists and fellows held both locally and abroad have indicated a need for and interest in improving anatomy skills. We therefore offered a MCAW to all 1st and 2nd year rheumatology fellows from our 12 university programs to determine their baseline knowledge in clinical anatomy, increase their knowledge of clinical anatomy, identify potential instructors for future MCAW, and compile qualitative evaluations of the MCAW. Staff were invited to attend as observers. **Methods:** A single instructor held seven MCAW within a 3 month time period, each with 4 to 10 fellows (median 6). A pre-MCAW evaluation of fellow knowledge was administered to two balanced fellow groups (A, n = 23 and B, n = 24) with each receiving a unique set of 20 practical questions (e.g.: «show in my hand where the transverse carpal ligament is», «could you identify the tibialis posterior tendon in my inverted foot?). The MCAW lasted 4.5 h including a 30 min break; it consisted of the presentation of 27 vignettes encompassing all regions of the musculoskeletal system, a list of relevant anatomic structures for each region, and a hands-on identification of each structure in the participants' bodies. At the conclusion of the MCAW we surveyed participants interest in becoming a MCAW instructor. Three months later we asked the participants for a qualitative assessment of the MCAW. **Results:** Forty-seven of 51 (92%) fellows participated in the MCAW. Group A and B median (range) correct answers to the pre-MCAW practical questions were 10 of 20 (2 to 14) and 8.5 of 20 (3 to 14), respectively; 1st and 2nd year fellows median (range) correct answers were 9.5 (2 to 14) and 9 (5 to 14), respectively. Two 1st year fellows and 2 junior staff expressed an interest in becoming instructors. Early results of the qualitative assessment of the MCAW are encouraging with most responders perceiving meaningful knowledge gain and better appreciation for clinical anatomy. **Conclusions:** We found deficiency in knowledge of clinical anatomy in our 1st and 2nd year fellows similar to our experience from previous workshops. However these selected for individuals specifically interested rather than all fellows. Four individuals will be trained to become MSCAW instructors and yearly workshops are planned for all 1st year fellows under the aegis of our College of Rheumatology. Clinical anatomy must be emphasized in training programs if rheumatologists are to be experts not only in the major rheumatic diseases but also in regional rheumatic syndromes.

Research Method: Other, Clinical anatomy workshop
Type of Trial: Other, Knowledge assessment, demonstration and qualitative impact assessment
Phase: Other, does not apply
Disclosures: J.J. Canoso, None; C. Abud-Mendoza, None; L. Barile-Fabris, None; R. Burgos-Vargas, Speaker or advisory board, Roche, Schering Plough, Abbott, Wyeth, Pfizer, 9; I. García-de la Torre, None; M. Garza-Elizondo, None; S. Gutiérrez-Ureña, None; F. Irazoque-Palazuelos, None; L. Lino-Pérez, None; J. Miranda-Limón, None; C. Ramos-Remus, None; M. Robles San Román, None; R.A. Kalish, None.

14.

Session: **Spondyloarthropathies In Iberoamérica, Overview of 2000 Patients: The RESPONDIA Group**
Monday, Oct 27, 2008, 6:15 PM - 7:30 PM

Presentation: Overview of Spondylarthropaties in Latin America: the RESPONDIA Group

Presenter: Janitzia Vazquez-Mellado, MD, PhD; Hospital General de Mexico; Mexico City, Mexico
Pres. Time: Monday, Oct 27, 2008, 6:15 PM - 6:25 PM
Location: Room 132

15.

Session: **Spondyloarthropathies In Iberoamérica, Overview of 2000 Patients: The RESPONDIA Group**

Monday, Oct 27, 2008, 6:15 PM - 7:30 PM

Presentation: Juvenile Spondylarthropathies in Latin America

Presenter: Ruben Burgos-Vargas, MD; Hospital General de Mexico; Mexico City, Mexico
Pres. Time: Monday, Oct 27, 2008, 6:25 PM - 6:50 PM
Location: Room 132

16.

Session: RA Treatment: Biologic Efficacy RCT's
Monday, Oct 27, 2008, 2:30 PM - 4:00 PM

Presentation: 1213 - The Efficacy and Safety of Abatacept in Methotrexate-naïve Patients with Early Erosive Rheumatoid Arthritis and Poor Prognostic Factors

Pres. Time: Monday, Oct 27, 2008, 3:45 PM - 4:00 PM
Location: Room 307
Category: 18. RA treatment: small molecules
Author(s): R. Westhovens[1], M. Robles[2], S. Nayiager[3], J. Wollenhaupt[4], P. Durez[5], J. Gomez-Reino[6], W. Grassi[7], B. Haraoui[8], W. Shergy[9], SH. Park[10], H. Genant[11], C. Peterfy[12], J-C. Becker[13], A. Covucci[13], R. Helfrick[13], J. Bathon[14]. [1]UZ Gasthuisberg, KU Leuven, Belgium; [2]Centro Medico Toluca, Metepec, Mexico; [3]St Augustine's Hospital, Durban, South Africa; [4]Klinikum Eilbek, Hamburg, Germany; [5]Univ Catholique de Louvain, Brussels, Belgium; [6]Hospital Clinico Univ De Santiago, A Coruna, Spain; [7]Univ Politecnica delle Marche, Ancona, Italy; [8]Institut de Rhumatolgie de Montreal, Montreal, QC, Canada; [9]Univ of Alabama, Huntsville, AL; [10]Kangnam St Mary's Hospital, Seoul, Republic of Korea; [11]Univ of California, San Francisco, CA; [12]Synarc, Inc., San Francisco, CA; [13]Bristol-Myers Squibb, Princeton, NJ; [14]Johns Hopkins Univ School of Medicine, Baltimore, MD

Abstract

Background: In early RA, erosions and seropositivity (RF/anti-CCP) are indicators of poor prognosis. Here we present 1-yr results from a 2-yr study of abatacept (ABA) in seropositive MTX-naïve patients with early erosive RA. **Methods:** In this Phase IIIb, double-blind study, patients with RA for ≤ 2 yrs were randomized (1:1) to receive ABA + MTX or placebo + MTX. Patients were MTX naïve, RF/anti-CCP positive and had evidence of erosions (hands, wrists or feet). ABA was administered at ~10 mg/kg according to weight range; MTX was initiated at 7.5 mg/wk and titrated to 20 mg/wk by Wk 8. Primary endpoints were: DAS28 (CRP)-defined remission (< 2.6) and joint damage progression (Genant-modified Sharp total score [TS]1) at Yr 1. Other efficacy measures included ACR responses. Safety was monitored throughout. **Results:** Patients had high baseline disease activity with short disease duration (Table), and were positive for RF (96.5%), anti-CCP (89.0%) or both (89.0%). Of the 256 and 253 patients treated with ABA + MTX or MTX alone, 90.6 and 89.7% completed Yr 1, respectively. Fewer patients in the ABA + MTX vs MTX group discontinued due to lack of efficacy (0 *vs* 3.2%) or AEs (3.5 *vs* 4.3%). Significant efficacy was observed at Yr 1 (Table).

Table. Baseline characteristics and clinical efficacy at Year 1, by treatment group

	ABA + MTX (N = 256)	MTX (N = 253)	Estimate of difference for ABA + MTX *vs* MTX
Baseline characteristics			
Mean tender joints, n (SD)	31.3 (14.8)	30.8 (14.0)	-
Mean swollen joints, n (SD)	22.9 (11.3)	21.9 (10.1)	-
Disease duration, months	6.2 (7.5)	6.7 (7.1)	-
MTX dose and clinical efficacy at Year 1			
Mean MTX dose	18 mg	19 mg	
Patients achieving DAS28 (CRP)-defined remission, % (95% CI)	41.4 (35.4, 47.4)	23.3 (18.1, 28.5)	18.1* (9.6, 26.6)
ACR 50 responders, % (95% CI)	57.4 (51.4, 63.5)	42.3 (36.2, 48.4)	15.1* (6.0, 24.2)
ACR 70 responders, % (95% CI)	42.6 (36.5, 48.6)	27.3 (21.8, 32.8)	15.3* (6.6, 24.0)
MCR (ACR 70 for 6 consecutive months), % (95% CI)	27.3 (21.9, 32.8)	11.9 (7.9, 15.8)	15.5* (8.2, 22.8)
Mean change from baseline in TS, n (SD)	0.63†‡ (1.74)	1.06‡ (2.45)	-

*p < 0.001 and †p = 0.04 for ABA + MTX *vs* MTX alone; ‡ N = 242

AEs and SAEs occurred in 84.8 *vs* 83.4% and 7.8 *vs* 7.9% of patients in the ABA + MTX *vs* MTX groups, respectively. Serious infections occurred in 2 (0.8%) *vs* 4 (1.6%) and autoimmune disorders occurred in 6 (2.3%) *vs* 5 (2.0%) ABA + MTX- *vs* MTX-treated patients, respectively; no malignancies were reported. Acute infusion reactions (mostly mild/moderate), occurred in 16 (6.3%) *vs* 5 (2.0%) of ABA + MTX- *vs* MTX-

treated patients. **Conclusions:** Abatacept + MTX provided significantly better efficacy and favorable safety compared with MTX alone in an MTX-naïve population with early erosive RA and poor prognostic factors.

References

1. Genant H, et al. Ann Rheum Dis 2007; doi:10.1136/ard.2007.085084

Presentation:
Research Clinical
Method:

Disclosures: R. Westhovens, Bristol Myers Squibb, 5; Schering Plough, 5; Bristol Myers Squibb, 8; M. Robles, None; S. Nayiager, None; J. Wollenhaupt, None; P. Durez, None; J. Gomez-Reino, Bristol Myers Squibb, 5; Schering Plough, 5; Wyett, 5; Roche Farma, 5; UCB, 5; Bristol Myers Squibb, 8; Wyett, 8; Schering Plough, 8; Roche Farma, 8; W. Grassi, None; B. Haraoui, Amgen/Wyeth Canada, 2; Abbott Canada, 2; Bristol Myer Squibb Canada, 2; Abbott Canada, 5; Amgen/Wyeth Canada, 5; Bristol Myers Squibb Canada, 5; Roche Canada, 5; Schering Canada, 5; UCB Canada, 5; Abbott, 8; Wyeth, 8; Bristol Myers Squibb, 8; Roche, 8; W. Shergy, Amgen, 2; Abbott, 2; Bristol Myers Squibb, 2; Centocor, 2; Wyeth, 2; Genentech, 2; Amgen, 8; Abbott, 8; Centocor, 8; Bristol Myers Squibb, 8; Genentech, 8; Pfizer, 8; S. Park, None; H. Genant, Merck, 2; GSK, 2; Amgen, 2; Wyeth, 2; Roche, 2; Servier, 2; Pfizer, 2; Novartis, 2; Lilly, 2; Synarc, 3; Merck, 5; GSK, 5; Amgen, 5; Wyeth, 5; Roche, 5; Servier, 5; Pfizer, 5; Novartis, 5; Lilly, 5; BMS, 5; ONO, 5; Synarc, 6; BOD, 6; Merck, 8; GSK, 8; Amgen, 8; Wyeth, 8; Roche, 8; Servier, 8; Pfizer, 8; Novartis, 8; Lilly, 8; BMS, 8; ONO, 8; C. Peterfy, Synarc Inc, 1; Synarc Inc, 3; Synarc Inc, 4; J. Becker, Bristol Myers Squibb, 1; Bristol Myers Squibb, 1; Bristol Myers Squibb, 3; A. Covucci, Bristol Myers Squibb, 3; R. Helfrick, Bristol Myers Squibb, 1; Full Time BMS, 3; J. Bathon, Johns Hopkins University, 3; Abbott, 5; Amgen, 5; Centocor, 5; Novartis, 5; Research support: Amgen, 9; Research support: Biogen-Idec, 9; Research support: Bristol-Myers Squibb, 9.

17.

Session: **RA: Assessment of Disease Activity and Outcomes**
Tuesday, Oct 28, 2008, 9:00 AM - 6:00 PM

Presentation: 1592 - Differences in Inflammatory Arthritis Disease Severity Among Mexican Mestizos and Native American Indians Compared to Caucasians

Pres. Time: Tuesday, Oct 28, 2008, 9:00 AM -11:00 AM

Location: Hall A, Poster Board: 314
Category: 17. RA: clinical aspects

Author(s): Carol A. Hitchon[1], Christine A. Peschken[1], Mariana Alvarez[2], David Robinson[1], Hani S. El-Gabalawy[1], Daniel Xibille-Friedmann[3]. [1]University of Manitoba, Winnipeg, MB, Canada; [2]Instituto Nacional de Salud Pública, Cuernavaca, Mexico; [3]Hospital General de Cuernavaca, Cuernavaca Morelos, Mexico

Abstract

Purpose: Ethnic differences are reported in inflammatory arthritis (IA). Native American Indians are known to have early onset severe disease. We sought to compare the presenting features and clinical outcomes of IA in three ethnic groups: Mexican Mestizos (MM), Native American Indians (NAI) and Canadian Caucasians (CC) looking at early and established disease. **Methods:** Patients with early inflammatory arthritis (EIA) of less than 12 months symptom duration ((Rheumatoid arthritis (RA) =126; undifferentiated arthritis (UA) n = 63; MM n = 52, NAI n = 23, CC n = 114) were followed in outpatient clinics in Canada and Mexico and compared to patients with Late Rheumatoid arthritis (LRA) having their first clinic visit after Jan 2000 (MM = 121, NAI = 120, CC = 295). Clinical features, treatment, and patient global assessments were assessed at the initial visit and at one year. Disease remission was defined as DAS3ESR < 2.6. Associations were tested using non-parametric tests and binary logistic regression. **Results:** MM and NAI with EIA were younger than CC at their initial clinic visit (39 and 36 vs 51 years $p < 0.0001$) and had higher baseline patient global scores (EIA 58 vs 36 and 39 $p < 0.0001$). MM were more likely to have been receiving steroids (prednisone or equivalent) prescribed by other physicians and had more aggressive treatment started on the first clinic visit with a greater use of combination DMARDS (mostly methotrexate (MTX) with anti-malarials). However, the use of DMARDs over the first year (none vs anti-malarials vs methotrexate (MTX) or sulfasalazine (SSZ)) was similar across groups. At one year, MM and NAI were less likely to achieve remission than CC (MM 1/19(5%); NAI 3/15(20%); CC 54/93 (58%) $p < 0.001$). In a comparison group of LRA, MM and NAI were also younger at initial visit (46 and 46 vs 55 years $p < 0.0001$) with higher patient global scores (50 *vs* 43 *vs* 40 $p = 0.03$). Despite a longer follow-up duration of LRA for NAI and CC than MM, the groups were equally likely to receive MTX or SSZ and combination therapy although CC tended to use fewer total numbers of DMARDs than MM or NAI ((1.9 *vs* 2.7 and 2.6 $p = 0.05$). At one year, MM and NAI with LRA were also less likely to achieve remission than CC ($p < 0.001$). Logistic regression models to predict remission at one year in EIA included ethnicity (MM vs NAI vs CC), baseline DAS3ESR, and DMARD treatment (MTX or SSZ

vs anti-malarials vs none over the first year). Ethnicity and baseline DAS predicted remission at one year in EIA ($p < 0.0001$). **Conclusions:** MM and NAI have an early age of onset of IA and are less likely to achieve remission at one year despite receiving more aggressive therapy. These poor prognostic ethnic groups tend to be more socially disadvantaged. Factors leading to this aggressive disease, genetic or environmental need to be explored.

Research Method: Observational
Type of Trial: Epidemiologic or Observational
Disclosures: C.A. Hitchon, None; C.A. Peschken, None; M. Alvarez, None; D. Robinson, None; H.S. El-Gabalawy, None; D. Xibille-Friedmann, None.

18.

Session: Crystal Associated Arthropathies
Tuesday, Oct 28, 2008, 2:30 PM - 4:00 PM

Presentation: 1945 - Immunoreactivity and Clinical Response to Pegloticase (PGL): Pooled Data from GOUT1 and GOUT2, PGL Phase 3 Randomized, Double Blind, Placebo-controlled Trials.

Pres. Time: Tuesday, Oct 28, 2008, 3:30 PM - 3:45 PM
Location: Room 104
Category: 14. Metabolic and crystal arthropathies
Author(s): M. A. Becker[1], E. L. Treadwell[2], H. S. Baraf[3], N. L. Edwards4, S. R. Gutierrez-Urena[5], J. S. Sundy[6], J. Vazquez-Mellado[7], R. A. Yood[8], Z. Horowitz9, B. Huang9, A. Maroli9, R. Waltrip[9], D. Wright[9]. [1]University of Chicago, Chicago, IL; [2]East Carolina University, Greenville, NC; [3]Center for Rheumatology & Bone Research, Wheaton, MD; [4]University of Florida, Gainesville, FL; [5]Hospital Civil de Guadalajara, Guadalajara, Mexico; [6]Duke University Medical Center, Durham, NC; [7]Hospital General de Mexico, Mexico City, Mexico; [8]Fallon Clinic, Worcester, MA; [9]Savient Pharmaceuticals, Inc., East Brunswick, NJ.

Abstract

Purpose: To characterize the relationships between plasma uric acid (PUA) response and infusion reactions (IRs) and immunoreactivity to PGL (PEGylated recombinant mammalian uricase) in PGL-treated subjects. **Methods:** Subjects in the GOUT1 and GOUT2 trials were treated with PGL q2w or q4w or placebo. PUA response was defined as PUA < 6.0 mg/dl for ≥ 80% of the time in months 3 and 6. A validated ELISA was used for periodic measurement of anti-PGL antibodies (Abs) and anti-polyethylene (PEG) Abs. Ab titers were defined as: low (≤ 1:810), moderate (1:2430 or 7290), high (> 1:7290), or no increase. Subjects who were Ab negative at BL and at months 3 or 6, and subjects who were Ab positive at BL but had no increase in titer at months 3 or 6 were defined as having no increase in Ab titer. Relationships of immunoreactivity to PUA response and IRs were assessed throughout the 6 month trial. Pooled data from the 2 trials are reported. **Results:** 75/85 and 78/84 subjects in the q2w and q4w groups, respectively, had Month 3 and 6 samples for Ab analyses. Of these, 36/75 (48%) and 32/78 (41%) in q2w and q4w, respectively, were PUA responders. High anti-PGL titer was negatively correlated with responder status for both PGL groups ($P < 0.001$). High titer anti-PGL was found in 1/68 (1%) of responders and 51/85 (60%) of nonresponders ($P < 0.001$). IRs were experienced by 18/75 (24%) q2w subjects and 30/78 (38%) q4w subjects. High anti-PGL titer was positively related to IRs: among subjects with high anti-PGL titer, 13/25 (52%) in the q2w and 18/27 (67%) in the q4w had IRs. There was no relationship between anti-PGL titer and IR severity. 28 PGL-treated subjects were anti-PGL positive at BL; 7/28 (25%) experienced IRs compared with 41/125 (33%) subjects who were anti-PGL negative at BL ($P = 0.50$). All anti-PEG positive subjects were also anti-PGL positive. 27/28 (96%) q2w subjects and 24/25 (96%) q4w subjects with any anti-PEG titer were nonresponders. 14/28 (50%) q2w subjects and 19/25 (76%) q4w subjects with any anti-PEG titer had IRs. Treatment emergent low titer anti-PGL IgE in 17 subjects did not predict IRs. No PGL neutralizing Ab was found. **Conclusion:** High anti-PGL titer and any anti-PEG titer were positively associated with PUA nonresponder status, indicating PGL inhibition with presence of these Abs. Anti-PGL Abs are non-neutralizing. IRs were also associated with anti-PEG and high anti-PGL titers.

Research Method: Interventional
Type of Trial: Treatment
Phase: Phase III
Disclosures: M.A. Becker, Takeda Pharmaceuticals, 5; Novartis, 5; Regeneron, 5; Savient Pharmaceuticals, Inc., 5; Procter & Gamble Pharmaceuticals, 5; E.L. Treadwell, Savient Pharmaceuticals, Inc., 2; H.S. Baraf, Savient Pharmaceuticals, Inc., 2; Savient Pharmaceuticals, Inc., 5; N.L. Edwards, Savient Pharmaceuticals, Inc., 2; Savient Pharmaceuticals, Inc., 5; S.R. Gutierrez-Urena, Savient Pharmaceuticals, Inc., 2; J.S. Sundy, Savient Pharmaceuticals, Inc., 2; J. Vazquez-Mellado, Savient Pharmaceuticals, Inc., 2; R.A. Yood, Savient Pharmaceuticals, Inc., 2; Z. Horowitz, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; B. Huang, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; A. Maroli, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; R. Waltrip, Savient Pharmaceuti-

cals, Inc., 1; Savient Pharmaceuticals, Inc., 3; D. Wright, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3.

19.

Session: **Crystal Associated Arthropathies**
Sunday, Oct 26, 2008, 9:00 AM - 6:00 PM

Presentation: 22 - Tophus Response to Pegloticase (PGL) Therapy: Pooled Results from GOUT1 and GOUT2, PGL Phase 3 Randomized, Double Blind, Placebo-controlled Trials

Pres. Time: Sunday, Oct 26, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 22
Category: 14. Metabolic and crystal arthropathies
Author(s): H. S. Baraf[1], M. A. Becker[2], N. L. Edwards[3], S. R. Gutierrez-Urena[4], J. S. Sundy[5], E. L. Treadwell[6], J. Vazquez-Mellado[7], R. A. Yood[8], Z. Horowitz[9], B. Huang[9], A. Maroli[9], R. Waltrip[9]. [1]Center for Rheumatology & Bone Research, Wheaton, MD;[2] University of Chicago, Chicago, IL;[3] University of Florida, Gainesville, FL; [4]Hospital Civil de Guadalajara, Guadalajara, Mexico; [5]Duke University Medical Center, Durham, NC; [6]East Carolina University, Greenville, NC; [7]Hospital General de Mexico, Mexico City, Mexico; [8]Fallon Clinic, Worcester, MA; [9]Savient Pharmaceuticals, Inc., East Brunswick, NJ

Abstract

Purpose: To evaluate reduction in tophus size in treatment failure gout (TFG) subjects participating in a 6 month placebo (PBO)-controlled trial of PGL (8 mg q2w or 8 mg q4w). **Methods:** Computer-assisted photographic analysis (CAPA) was used to assess tophi. CAPA is a validated assessment of soft tissue mass lesions using standardized serial photographs scored by central readers blinded to study treatment. Photographs of the hands and feet and up to 2 other tophus sites were taken at baseline (BL) and at weeks 13, 19, and 25. Central readers assessed up to 7 tophi (5 measurable and 2 unmeasurable). Measurable tophi had to be ≥ 5 mm in the longest dimension with distinguishable borders at BL. Unmeasurable tophi (because of location, shape, or other factors) had to be ≥ 10 mm for inclusion. Endpoints included an overall tophus response, tophus resolution, and the time to tophus resolution. Tophus response to therapy for each subject was based on best response among all tophi and was defined on an ordinal scale [complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD)]. CR was defined as complete resolution of ≥ 1 tophus without increase in size in any other tophus or appearance of new tophi. Tophus response was analyzed by PGL responder *vs* nonresponder status (responders were defined as subjects maintaining PUA <6 mg/dL for at least 80% of the time during months 3 and 6 of the treatment period). **Results:** At BL, 73% (154 of 212 dosed) of subjects had at least 1 tophus. At final visit, 106/154 subjects had CAPA evaluable tophi. A higher percent of subjects had achieved CR in the q2w *vs* PBO group (Table, 41% *vs* 7%, P = 0.002). CR in the q4w *vs* PBO group was not significant (24% *vs* 7%, P = 0.2). A numerically higher percent of PGL responders showed CR of tophi than nonresponders (q2w, 62% *vs* 26%; q4w, 41% *vs* 11%).

	Number of CR (% of subjects)			
Treatment Group	Week 13	Week 19	Week 25	Any Visit
Q2 Week	10/49 (20.4)	16/46 (34.8)	18/43 (41.8)	21/51 (41.2)
Q4 Week	4/50 (8.0)	12/44 (27.3)	11/44 (25.0)	12/51 (23.5)
PBO	0/24 (0)	2/26 (7.7)	2/25 (8.0)	2/27 (7.4)

Conclusion: In TFG subjects, PGL q2w reduced tophus burden in 40%. Complete resolution was seen in 20% of q2w subjects within the first 13 weeks of treatment.

Research Method: Interventional
Type of Trial: Treatment
Phase: Phase III
Disclosures: H.S. Baraf, Savient Pharmaceuticals, Inc., 2; Savient Pharmaceuticals, Inc., 5; M.A. Becker, Savient Pharmaceuticals, Inc., 5; N.L. Edwards, Savient Pharmaceuticals, Inc., 2; Savient Pharmaceuticals, Inc., 5; S.R. Gutierrez-Urena, Savient Pharmaceuticals, Inc., 2; J.S. Sundy, Savient Pharmaceuticals, Inc., 2; E.L. Treadwell, Savient Pharmaceuticals, Inc., 2; J. Vazquez-Mellado, Savient Pharmaceuticals, Inc., 2; R.A. Yood, Savient Pharmaceuticals, Inc., 2; Z. Horowitz, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; B. Huang, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; A. Maroli, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; R. Waltrip, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3.

20.

Session: **Crystal Associated Arthropathies**
Sunday, Oct 26, 2008, 9:00 AM - 6:00 PM

Presentation: 27 - Improvement in Health-related Quality of Life (HRQL) and Disability Index in Treatment Failure Gout (TFG) after Pegloticase (PGL) Therapy: Pooled Results from GOUT1 and GOUT2,

Phase 3, Randomized, Double Blind, Placebo (PBO)-Controlled Trials

Pres. Time: Sunday, Oct 26, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 27
Category: 14. Metabolic and crystal arthropathies
Author(s): N. L. Edwards[1], H. S. Baraf[2], M. A. Becker[3], S. R. Gutierrez-Urena[4], J. S. Sundy[5], E. L. Treadwell[6], J. Vazquez-Mellado[7], R. A. Yood[8], A. K. Kawata[9], K. L. Benjamin[9], Z. Horowitz[10], B. Huang[10], A. Maroli[10], R. Waltrip[10]. [1]University of Florida, Gainesville, FL; [2]Center for Rheumatology & Bone Research, Wheaton, MD; [3]University of Chicago, Chicago, IL; [4]Hospital Civil de Guadalajara, Guadalajara, Mexico; [5]Duke University Medical Center, Durham, NC; [6]East Carolina University, Greenville, NC; [7]Hospital General de Mexico, Mexico City, Mexico; [8]Fallon Clinic, Worcester, MA; [9]United BioSource Corp., Bethesda, MD; [10]Savient Pharmaceuticals, Inc., East Brunswick, NJ

Abstract

Purpose: TFG is characterized by chronic pain and disability associated with flares, tender joints and tophi with impact on functioning and HRQL. We assessed change in HRQL and disability associated with PGL (PEGylated recombinant mammalian uricase) treatment. **Methods:** Subjects in the GOUT1 and GOUT2 trials were treated with either q2w or q4w PGL (or PBO). SF-36 and HAQ-DI were completed at weeks 1 (baseline), 13, 19, and 25. The Arthritis-Specific Health Index (ASHI) was computed from SF-36 scores, and Standard Disability Index (SDI) score for HAQ-DI. Physical and Mental composite scores (PCS, MCS) were computed from the SF-36. Differences in treatment and PBO group were evaluated by independent-groups t-tests. **Results:** Of 212 patients enrolled, 157 (74.1%) completed the study. Most patients were male (81.6%) and Caucasian (67.5%). Mean age was 55.4 years (SD = 14.01, range: 23-89). Mean baseline plasma uric acid was 9.7 mg/dL. Average number of self-reported acute flares in past 18 months was 9.8 (SD = 12.13; range: 0-100). At Week 25, PGL-treated subjects reported greater improvements in HRQL and lessened disability relative to PBO (Table). The q2w group reported significantly greater improvements in SF-36 bodily pain ($p < 0.001$), general health ($p<0.05$), physical functioning ($p < 0.05$), role-physical ($p < 0.01$), vitality ($p < 0.05$), PCS ($p < 0.001$), and ASHI ($p < 0.001$). The q4w group showed improvements in bodily pain ($p < 0.001$), physical functioning ($p < 0.05$), PCS ($p < .001$), and ASHI ($p < 0.001$). Compared to PBO, there was less disability ($p < 0.001$), less pain (q2w: $p < 0.001$; q4w: $p < 0.05$) and better global health (q2w: $p < 0.001$; q4w: $p < 0.01$). There were no significant differences in SF-36 mental health, role-emotional, or social functioning. **Conclusions:** Treatment with PGL was associated with improvements in HRQL (particularly domains related to bodily pain and physical functioning) and decreased disability over time. Subjects treated with PGL q2w had greater improvement than those treated with the q4w dose.

Change in Baseline to Final SF-36 Summary Scores for ITT Population

	Q2wk	Q4wk	Placebo
PCS	4.38 (9.42, $p < 0.001$)	4.94 (8.49, $p < 0.001$)	-0.3 (8.966, $p = 0.83$)
MCS	2.13 (10.8, $p = 0.088$)	0.08 (10.23, $p = 0.94$)	2.36 (9.64, $p = 0.12$)
ASHI	16.5 (28.8, $p < 0.001$)	15.0 (25.1, $p < 0.001$)	0.93 (22.8, $p = 0.79$)

Research Method: Interventional
Type of Trial: Treatment
Phase: Phase III
Disclosures: N.L. Edwards, Savient Pharmaceuticals, Inc., 2; Savient Pharmaceuticals, Inc., 5; H.S. Baraf, Savient Pharmaceutical Inc., 2; Savient Pharmaceutical Inc., 5; M.A. Becker, Savient Pharmaceuticals, Inc., 5; S.R. Gutierrez-Urena, Savient Pharmaceuticals, Inc., 2; J.S. Sundy, Savient Pharmaceuticals, Inc., 2; E.L. Treadwell, Savient Pharmaceuticals, Inc., 2; J. Vazquez-Mellado, Savient Pharmaceuticals, Inc., 2; R.A. Yood, Savient Pharmaceuticals, Inc., 2; A.K. Kawata, Savient Pharmaceuticals, Inc., 5; K.L. Benjamin, Savient Pharmaceuticals, Inc., 5; Z. Horowitz, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; B. Huang, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; A. Maroli, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; R. Waltrip, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3.

21.

Session: **Crystal Associated Arthropathies**
Sunday, Oct 26, 2008, 9:00 AM - 6:00 PM

Presentation: 34 - Clinical Homogeneity and Syndromic Characteristics of Treatment Failure Gout (TFG) in Four Independent Cohorts

Pres. Time: Sunday, Oct 26, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 34
Category: 14. Metabolic and crystal arthropathies
Author(s): R. A. Yood[1], H. S. Baraf[2], M. A. Becker[3], N. L.

Edwards[4], S. R. Gutierrez-Urena[5], J. S. Sundy[6], E. L. Treadwell[7], J. Vazquez-Mellado[8], Z. Horowitz[9], B. Huang[10], A. Maroli[10], R. Waltrip[10]. [1]Fallon Clinic, Worcester, MA; [2]Center for Rheumatology & Bone Research, Wheaton, MD; [3]University of Chicago, Chicago, IL; [4]University of Florida, Gainesville, FL; [5]Hospital Civil de Guadalajara, Guadalajara, Mexico; [6]Duke University Medical Center, Durham, NC; [7]East Carolina University, Greenville, NC; [8]Hospital General de Mexico, Mexico city, Mexico; [9]Savient Pharmaceutical, Inc., East Brunswick, NJ; [10]Savient Pharmaceuticals, Inc., East Brunswick, NJ

Abstract

Purpose: To study the baseline clinical characteristics, clinical history, quality of life (QOL), and functional status in 4 independent samples of TFG subjects. **Methods:** This analysis includes 4 studies of TFG subjects: a 12 month natural history study (NHS) that evaluated gout disease severity and progression; a phase 2 and two phase 3 (GOUT1 and GOUT2) studies that examined the safety and efficacy of pegloticase (PGL, PEGylated recombinant mammalian uricase) in TFG. NHS inclusion criteria: ≥ 3 gout flares/year, or chronic synovitis/arthropathy, or presence of tophi, or uric acid nephrolithiasis/nephropathy. All subjects had serum urate (SUA) > 6 mg/dL. Phase 2 and 3 studies inclusion criteria: symptomatic gout (≥ 3 flares in previous 18 months, or ≥ 1 tophus, or gouty arthropathy). All subjects had SUA ≥ 8 mg/dL. In all 4 studies, subjects had either failed or had contraindication to currently available urate lowering therapy (ULT). Baseline (BL) evaluations included history (self-reported gout flares), physical exam (tophi and STJ count), SUA, QOL by SF-36, and disease-related disability by HAQ-DI. **Results:** BL demographic and disease characteristics were similar across studies (Table). Mean SF-36 PCS scores showed substantial impairment compared to the general population score of 50 while mean MCS scores were less impaired. Mean HAQ-DI was similar to that reported for OA/RA patients (0.8-1.2), but higher than the population norm of 0.49. Flares and tophi correlated with greater functional and QOL impairment. **Conclusion:** Entry criteria in all 4 studies were based on sustained symptomatic gout and failure to respond to ULT. TFG subjects were found to have severe gout (high flare frequency, chronic STJ, tophi, functional and QOL impairment), features of metabolic syndrome, and a common pattern of medical comorbidities. These results suggest that TFG is a coherent clinical syndrome characterized by sustained arthritis symptoms, functional impairment, and reduced QOL comparable to that seen in RA and OA. TFG is a clinical concept denoting the most severe syndrome in the spectrum of gout, one that warrants consideration for aggressive use of new therapeutic options.

	NHS N = 110	Phase 2 N = 41	GOUT1 N = 104	GOUT2 N = 108
Age, *y*	59	58	57	54
Male, %	82	85	77	86
BMI	32	32	34	32
SUA, *mg/dL*	7.8	10.3	10.2	9.94
Acute flares, *mean per 12 m*	7	8	7	5
Chronic arthropathy/ synovitis, %	52	ND	61	56
Tophi, %	70	71	71	75
Total tender joints, *mean*	5	ND	13	11
Total swollen joints, *mean*	6	ND	11	10
SF-36, *mean*				
MCS	49	ND	46	49
PCS	34	ND	33	34
HAQ-DI, *mean*	0.97	ND	1.3	1.0
Disease duration, *y*	> 5 y: 35%	14.4	15	15
Co-morbidities, %				
Hypertension	71	68	72	70
OA	42	17	38	27
Renal conditions*	44	10	38	22
CVD	15	17	41	20
Diabetes mellitus	14	24	23	21
Hyperlipidemia	5	15	24	15

ND = not determined; *renal dysfunction or insufficiency or chronic kidney disease.

Research Method: Observational

Type of Trial: Epidemiologic or Observational

Phase: Other, Observational

Disclosures: R.A. Yood, Savient Pharmaceuticals, Inc., 2; H.S. Baraf, Savient Pharmaceuticals, Inc., 2; Savient Pharmaceuticals, Inc., 5; M.A. Becker, Savient Pharmaceuticals, Inc., 5; N.L. Edwards, Savient Pharmaceuticals, Inc., 2; Savient Pharmaceuticals, Inc., 5; S.R. Gutierrez-Urena, Savient Pharmaceuticals, Inc., 2; J.S. Sundy, Savient Pharmaceuticals, Inc., 2; E.L. Treadwell, Savient Pharmaceuticals, Inc., 2; J. Vazquez-Mellado, Savient Pharmaceuticals, Inc., 2; Z. Horowitz, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; B. Huang, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; A. Maroli, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; R. Waltrip, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3.

22.

Session: Discovery 2008: Innovations in Rheumatic Disease

Sunday, Oct 26, 2008, 11:00 AM -12:30 PM

Presentation: 635 - Efficacy and Safety of Intravenous (IV) Pegloticase (PGL) in Subjects with Treatment Failure Gout (TFG): Phase 3 Results from GOUT1 and GOUT2

Pres. Time: Sunday, Oct 26, 2008, 11:15 AM -11:30 AM
Location: Hall C
Category: 14. Metabolic and crystal arthropathies

Author(s): J. S. Sundy[1], H. S. Baraf[2], M. A. Becker[3], N. L. Edwards[4], S. R. Gutierrez-Urena[5], E. L. Treadwell[6], J. Vázquez-Mellado[7], R. A. Yood[8], Z. Horowitz[9], B. Huang[9], A. Maroli[9], R. Waltrip[9]. [1]Duke University Medical Center, Durham, NC; [2]Center for Rheumatology & Bone Research, Wheaton, MD; [3]University of Chicago, Chicago, IL; [4]University of Florida, Gainesville, FL; [5]Hospital Civil de Guadalajara, Guadalajara, Mexico; [6]East Carolina University, Greenville, NC; [7]Hospital General de México, Mexico City, Mexico; [8]Fallon Clinic, Worcester, MA; [9]Savient Pharmaceuticals, Inc., East Brunswick, NJ

Abstract

Purpose: To assess the efficacy and safety of PGL (PEGylated recombinant mammalian uricase) in the management of TFG. Methods: TFG subjects (212) were treated with IV PGL or placebo (PBO) in replicate 6 month randomized, double blind, studies, Gout Outcome and Urate Therapy (GOUT1 and GOUT2). Subjects were randomized to PGL 8 mg q2w (n = 85), 8 mg q4w (n = 84), or PBO (n = 43). TFG was defined as: ≥ 3 flares in the previous 18 months, or ≥ 1 tophus, or gouty arthropathy; serum urate > 8.0 mg/dL; and prior failure of maximum medically appropriate dose of allopurinol or contraindication to allopurinol. Subjects with plasma uric acid (PUA) < 6.0 mg/dL 80% of the time in months 3 and 6 met the primary endpoint in the ITT analysis. Data were pooled for secondary endpoints: reduction of tophus size, gout flare incidence, swollen joints (SJ), tender joints (TJ), quality of life by SF-36, disability by HAQ-DI, and safety. **Results:** Subjects at baseline were: 82% male; mean age 55 years; and with a high degree of comorbidity: hypertension (71%), chronic kidney disease (43%), cardiovascular disease (31%), and diabetes (22%). Both PGL groups were significantly superior to PBO for the primary efficacy endpoint in both studies (table).

	Subjects (%) with PUA < 6.0 mg/dL		
	Pegloticase q2w	Pegloticase q4w	Placebo
GOUT1 N = 104	47 (P < 0.001)	20 (P = 0.044)	0
GOUT2 N = 108	38 (P = 0.001)	49 (P = 0.001)	0

Complete resolution of ³ 1 tophus occurred in 21/52 q2w, 11/52 q4w, and 2/29 PBO subjects (P = 0.002 q2w *vs* PBO). SF-36 physical component summary score and HAQ-DI for physical functioning improved significantly in both PGL groups. Subjects on PGL had significantly greater reductions in TJs, but not SJs, *vs* PBO [q2w: -7.4 ± 12.0 (P = 0.008), q4w: -6.1 ± 10.6 (P = 0.024), PBO: -1.2 ± 12.3). Gout flares and infusion reactions (IRs) were the most common adverse events (AEs). The number of gout flares in the PGL groups did not differ significantly from PBO. IRs occurred in 26% q2w, 40% q4w, and 5% PBO subjects and were the most common reason for study withdrawal. Serious AEs occurred in 24% q2w, 23% q4w, and 12% PBO subjects. **Conclusion:** In subjects who have failed available treatment, PGL achieved the primary endpoint for reduction in PUA in ~ 40% of subjects. Improvement in clinical outcomes was observed in a significant proportion of subjects. The most frequent AEs were gout flares and IRs.

Research Method: Clinical
Type of Trial: Treatment
Phase: Phase III
Disclosures: J.S. Sundy, Savient Pharmaceuticals, Inc, 2; H.S. Baraf, Savient Pharmaceuticals, Inc., 2; Savient Pharmaceuticals, Inc, 5; M.A. Becker, Savient Pharmaceuticals, Inc., 5; N.L. Edwards, Savient Pharmaceuticals, Inc., 2; Savient Pharmaceuticals, Inc., 5; S.R. Gutierrez-Urena, Savient Pharmaceuticals, Inc., 2; E.L. Treadwell, Savient Pharmaceuticals, Inc., 2; J. Vázquez-Mellado, Savient Pharmaceuticals Inc., 2; R.A. Yood, Savient Pharmaceuticals, Inc., 2; Z. Horowitz, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc, 3; B. Huang, Savient Pharmaceuticals, Inc., 3; Savient Pharmaceuticals, Inc., 1; A. Maroli, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3; R. Waltrip, Savient Pharmaceuticals, Inc., 1; Savient Pharmaceuticals, Inc., 3.

23.

Session: ACR Business Meeting and Late-Breaking Abstracts

Tuesday, Oct 28, 2008, 2:00 PM - 4:00 PM

Presentation: L13 - The Oral Jak Inhibitor CP-690,550 (CP) in Combination with Methotrexate (MTX) is Efficacious, Safe and Well Tolerated in Patients with Active Rheumatoid Arthiritis (RA) with an Inadequate Response to Methotrexate Alone

Pres. Time: Tuesday, Oct 28, 2008, 3:00 PM - 3:15 PM
Location: Room 307
Category: 18. RA treatment: small molecules
Author(s): J. Kremer[1], S. Cohen[2], B. Wilkinson[3], C. Conell[3], J. French[3], J. Gomez Reino[4], D. Gruben[3], K. Kanik[3], S. Krishnaswami[3], V. Pascual-Ramos[5], G. Wallenstein[3], S. Zwillich[3]. [1]Albany Medical College, Albany, NY; [2]Metroplex Clinical Research Center, Dallas, TX; [3]Pfizer Inc, New London, CT; [4]Hospital Clínico Universitario, Santiago de Compostela, Spain; [5]Instituto Nacional de Ciencias, Mexico City, Mexico

Abstract

Purpose: To compare the efficacy, safety and tolerability of 6 dose levels of oral CP *vs* placebo for the treatment of RA in patients (pts) with active RA on stable background MTX, who had an inadequate response to MTX alone; to characterize the dose-response profile of CP. **Methods:** In this 6-month, double-blind, placebo-controlled Phase 2B study, pts with active disease (≥ 6 tender joints, ≥ 6 swollen joints and CRP > 7 mg/dL or ESR > ULN) were randomized equally to 1, 3, 5, 10, 15 mg BID, or 20 mg QD, of CP or placebo. Pts receiving CP 1 mg, 3 mg BID, 20 mg QD, or placebo who did not achieve ≥ 20% reduction from baseline in swollen and tender joint counts at Wk 12 were reassigned to CP 5 mg BID for the remainder of the study. The primary outcome was ACR response rate at Wk-12. Efficacy and safety assessments were carried out at Wks 2, 4, 6, 8, 12, 16, 20, and 24. Data are presented from an interim analysis at Wk-12; efficacy data are through Wk-12 (or early termination), safety data are through Wk-24. **Results:** 509 pts (80% women) were randomized. Mean ages across dose groups were 50.8-56.1 years (range 18-81 years). Mean disease duration ranged from 7.1-11.7 years; 69%-89% were rheumatoid factor positive. At baseline, mean tender joint counts ranged from 21.49-24.71, swollen joint counts from 14.04-16.52 and HAQ-DI from 1.20-1.57. Mean baseline DAS28-3 (CRP) scores ranged from 5.14-5.49. The most frequently reported treatment-emergent AEs (all causality) were: nausea 2.4%; headache 2.2% and increased ALT 2.0%. Serious AEs ranged from 1-8% in the CP dose groups with none in the placebo arm. 5 serious infections were reported, with no dose-related pattern. Minor dose-related changes in hemoglobin (Hb) were seen; only 2 pts experienced Hb drops > 3 g/dL below baseline (1 pt each on placebo and CP 10 mg BID) and no pts' neutrophil count fell below 500/μl. Dose-dependent increases in LDL, HDL and total cholesterol were observed, which appeared to plateau between Wks 6 and 12. Reversible ALT increases of > 3 x the ULN were seen in 5 pts receiving CP 15 mg BID and in one pt in each of CP 10 mg BID, 20 mg QD and placebo. **Conclusions:** Doses of CP 3 mg BID and higher were efficacious *vs* placebo. Tolerability, AEs and some changes in laboratory values were dose dependent. A range of doses appears suitable to evaluate further in Phase 3 studies table.

CP treatment group (n)	%responders at Week 12							
	ACR 20[3]	ACR 50[3]	ACR 70[3]	HAQ-DI response[1]	DAS 28 remission[2]	Lack of efficacy	AE	Any reason
1 mg BID (71)	49.3	23.9	7.0	62.5*	6.9	2 (2.8)	3 (4.2)	10 (14.1)
3 mg BID (68)	58.8*	30.9	22.1*	62.1*	32.1*	0	1 (1.5)	9 (13.2)
5 mg BID (71)	60.6*	36.6*	18.3*	67.7*	17.5	1 (1.4)	3 (4.2)	13 (18.3)
10 mg BID (75)	60.0*	30.7	13.3	68.2*	30.2*	0	5 (6.7)	9 (12.0)
15 mg BID (75)	58.7*	46.7**	25.3*	64.6*	37.7**	0	7 (9.3)	12 (16.0)
20 mg QD (80)	60.0*	36.3*	23.8*	69.1*	24.6*	1 (1.3)	4 (5.0)	12 (15.0)
Placebo 69	37.7	17.4	5.8	40.7	8.8	4 (5.8)	3 (4.3)	14 (20.3)

*p ≤ 0.05, **p ≤ 0.0001 *vs* placebo
AE, treatment-emergent AE (all causality)
[1]HAQ-DI response: ≥ 0.22 unit improvement from baseline
[2]DAS28 remission: based on DAS28-3 (CRP) achieving < 2.6 having been ≥ 2.6 at baseline
[3]Missing data were imputed by LOCF

Research Method: Clinical
Type of Trial: Treatment
Phase: Phase II
Disclosures: J. Kremer, Abbott, Amgen, BMS, Centocor, Genentech, Roche, 2; Abbott, Amgen, BMS, Centocor, Genentech, Roche, 5; Wyeth, 8; S. Cohen, Pfizer Inc, 1; Pfizer, 2; Amgen, 2; Wyeth, 2; Proctor and Gamble, 2; Genentech, 2; Biogen-Idec, 2; Roche, 2; Genentech, 5; Biogen-Idec, 5; Amgen, 5; Roche, 5; B. Wilkinson, Pfizer Inc, 3; C. Conell, Pfizer Inc, 3; J. French, Pfizer Inc, 1; Pfizer Inc, 3; J. Gomez Reino, Wyeth, 5; Schering Plough, 5; BMS, 5; Roche, 5; D. Gruben, Pfizer Inc, 3; K. Kanik, Pfizer Inc, 3; S. Krishnaswami, Pfizer Inc, 3; V. Pascual-Ramos, None; G. Wallenstein, Pfizer Inc, 1; Pfizer Inc, 3; S. Zwillich, Pfizer Inc, 3.

24.

Session: **ACR Business Meeting and Late-Breaking Abstracts**
Tuesday, Oct 28, 2008, 2:00 PM - 4:00 PM

Presentation: L14 - Tocilizumab Inhibits Structural Joint Damage in Rheumatoid Arthritis Patients with an Inadequate Response to Methotrexate: The LITHE Study

Pres. Time: Tuesday, Oct 28, 2008, 3:15 PM - 3:30 PM
Location: Room 307
Category: 18. RA treatment: small molecules

Author(s): Joel M. Kremer[1], Roy M. Fleischmann[2], Anne-Marie Halland[3], Jan Brzezicki[4], Thasia Woodworth[5], Elena Fisheleva[5], Emma Alecock[5], Ruben Burgos-Vargas[6]. [1]Albany Medical College, Albany, NY; [2]Metroplex Clinical Research Center, Dallas, TX; [3]Arthritis Research Center, Panorama Hospital, Panorama, Cape Town, South Africa; [4]Wojewódzki Szpital Zespolony, Oddzia[3] Reumatologiczny, Elbl[1]g, Poland; [5]Roche, Welwyn, United Kingdom; [6]Hospital General de Mexico, Mexico City, Mexico

Abstract

Purpose: Tocilizumab (TCZ), an anti-interleukin-6 (IL-6) monoclonal antibody, improves the signs and symptoms of RA in patients with inadequate response (IR) to DMARDs, including methotrexate (MTX). The efficacy of TCZ plus MTX in preventing structural joint damage in MTX-IR patients and improving patient function was investigated in a planned 12-month analysis of a 2-year study. **Methods:** Phase 3, randomized, double-blind, placebo-controlled trial. MTX-IR patients with moderate-to-severe active RA received MTX once weekly (10-25 mg oral or parenterally) plus TCZ 4 or 8 mg/kg, or placebo (control) IV every 4 weeks for 1 year. A switch to blinded rescue treatment was available at Weeks 16 and 28, if required. Primary endpoints included changes from baseline in Genant-modified Sharp score (linear extrapolation) and the area under the curve (AUC) in the Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 52. **Results:** he analysis population (ITT) included 1190 randomized patients (TCZ 8 mg/kg n = 398, TCZ 4 mg/kg n = 399, control n = 393). Mean joint erosion, joint space narrowing, and total Genant-modified Sharp scores showed significant inhibition of radiographic progression from baseline in both TCZ groups compared with control (Table). The mean change from baseline in HAQ-DI significantly decreased in TCZ-treated patients compared with control. DAS28 remission rates were significantly higher in the TCZ 8 mg/kg group compared with control, and low disease activity rates were significantly higher with both TCZ groups compared with control (Table). The safety profile was consistent with previous studies and did not change from 6 to 12 months. The most common serious adverse events were serious infections (TCZ 8 mg/kg 3.0%, TCZ 4 mg/kg 2.5%, control 1.5%). Medically significant infusion events were reported in the TCZ 4 mg/kg group only (4 anaphylactic reaction, 2 hypersensitivity). **Conclusion:** Significantly improved DAS remission rates were achieved with TCZ treatment, suggesting an important role for IL-6 blockade in MTX-IR patients with RA. TCZ therapy significantly inhibited the progression of structural joint damage, improved function (HAQ-DI), and the signs and symptoms of RA significantly more than control, with an acceptable safety profile.

Table. Disposition (all randomized ITT patients) and efficacy at week 52.

	TCZ 8 mg/kg +MTX (n = 398)	TCZ 4 mg/kg +MTX (n = 399)	Control (n = 393)
Disposition, % (n)			
Completed 52 weeks	86 (342)	86 (344)	85 (334)
Remaining on randomized treatment	73 (292)	65 (260)	41 (161)
Received rescue therapy	15 (59)	24 (95)	50 (195)
Total genant-modified sharp score, mean (SD)			
Baseline score	29.1 (28.5)	29.5 (28.7)	28.8 (32.4)
Change from baseline	0.3 (1.3)*	0.3 (1.5)*	1.1 (3.0)
Annualized progression rate	0.2 (1.1)	0.3 (1.0)	0.8 (1.9)
Joint erosion score change from baseline, mean (SD)	0.2 (0.9)*	0.2 (0.9)*	0.7 (1.9)
Joint space narrowing score change from baseline, mean (SD)	0.1 (0.6)**	0.1 (0.7)**	0.4 (1.7)
No progression in joint erosion, % (n)	87 (302)	83 (280)	70 (203)
No progression in joint space narrowing, % (n)	91 (315)	91 (307)	85 (245)
No progression in total genant-modified sharp score, % (n)	85 (294)	81 (273)	67 (195)
HAQ-DI			
Baseline score, mean (SD)	1.5 (0.6)	1.5 (0.6)	1.5 (0.6)
AUC change from baseline, adjusted mean	-144.1	-128.4	-58.1
Treatment difference *vs* control (95% CI)	-86.0 (-112.7, -59.2)*	-70.3 (-97.0, -43.6)*	–
ACR20, % (n)	56 (222)*	47 (186)	25 (97)
ACR50, % (n)	36 (145)*	29 (116)	10 (39)
ACR70, % (n)	20 (80)*	16 (65)	4 (15)
DAS28 clinical remission (< 2.6), % (n)	47 (127)*	30 (70)	8(12)
Low disease activity (≤ 3.2), % (n)	64 (171)*	45 (105)*	19 (28)

* $p \leq 0.0001$; ** $p < 0.01$ *versus* control

Research Method: Clinical
Type of Trial: Treatment
Phase: Phase III
Disclosures: J.M. Kremer, Abbott, Amgen, BMS, Centocor, Genentech, Roche, 2; Abbott, Amgen, BMS, Centocor, Genentech, Roche, UCB, 5; R.M. Fleischmann, Abbott, Astra-Zeneca, Proctor and Gamble, 1; Abbott, Amgen, Wyeth, Centocor, Roche, Genentech, BiogenIdec, UCB, Pfizer. Array, Regeneron, Lilly, XDx, Pozen, 2; Abbott, Amgen, Wyeth, Centocor, Roche, Genentech, BiogenIdec, UCB, Pfizer. Lilly, 5; Abbott, Amgen, Wyeth, Genetech, 8; A. Halland, Roche Advisory Board for Actemra South Africa, 6; J. Brzezicki, None; T. Woodworth, Roche, 3; E. Fisheleva, Roche, 3; E. Alecock, Roche, 3; R. Burgos-Vargas, Abbott, Pfizer, Roche, Schering-Plough, Wyeth, 5; Abbott, Pfizer, Roche, Schering-Plough, Wyeth, 8.

25.

Session: **ACR Business Meeting and Late-Breaking Abstracts**
Tuesday, Oct 28, 2008, 2:00 PM - 4:00 PM

Presentation: L15 - The Efficacy and Safety of Abatacept in SLE: Results of a 12-month Exploratory Study

Pres. Time: Tuesday, Oct 28, 2008, 3:30 PM - 3:45 PM
Location: Room 307
Category: 25. SLE: clinical aspects
Author(s): JT Merrill[1], R. Burgos-Vargas[2], R. Westhovens[3], A. Chalmers[4], D. D'Cruz[5], D. Wallace[6], SC Bae[7], L. Sigal[8], J-C Becker[8], S. Kelly[8], K. Raghupathi[9], Y. Peng[9], M. Kinaszczuk[8], P. Nash[10]. [1]Univ of Oklahoma, Oklahoma City, OK; [2]Hosp General de Mexico, Mexico City, Mexico; [3]Univ Hospitals KU, Leuven, Belgium; [4]Univ of British Columbia, Vancouver, BC, Canada; [5]The Rayne Institute, London, United Kingdom; [6]UCLA, Los Angeles, CA; [7]Hanyang Univ, Seoul, Republic of Korea; [8]Bristol-Myers Squibb, Priceton, NJ; [9]Bristol-Myers Squibb, Pennington, NJ; [10]Univ of Queensland, Brisbane, Australia

Abstract

Purpose: To assess the safety and efficacy of abatacept in SLE patients with flare of polyarthritis, serositis or discoid lesions. **Methods:** In a 1-yr, exploratory, Phase II trial, patients with SLE and active polyarthritis, serositis or discoid lesions were randomized 2:1 to abatacept (~10 mg/kg) or placebo (PBO) by IV infusion on Days 1, 15, 29, then every 4 wks. Prednisone (30 mg/day or equivalent) was given for 1 mth then tapered according to protocol. The primary endpoint was the proportion of patients with new SLE flare (adjudicated BILAG A or B) after the start of steroid taper over 1 yr. Secondary BILAG endpoints, physician-assessed flare, patient-reported outcomes (PRO), anti-dsDNA (Farr RIA) and safety were assessed over 1 yr. **Results:** 118 abatacept and 57 PBO patients were evaluated: baseline characteristics were similar. Primary manifestations at entry were discoid rash (34.3%), polyarthritis (54.3%) and serositis (11.4%). The proportion of patients with new adjudicated BILAG A or B flare over 1 yr (95% CI) was 79.7% (72.4, 86.9) for abatacept vs 82.5% (72.6, 92.3) for PBO. Results for secondary BILAG endpoints were similar. In post-hoc analyses, the proportion of patients with flare over 1 yr rated by treating physicians (95% CI) was 63.6% (54.9, 72.2) for abatacept *vs* 82.5% (72.6, 92.3) for PBO; the difference was greatest in the polyarthritis subgroup (57.1% [44.9, 69.4] *vs* 84.4% [71.8, 97.0]). The proportion of patients on ≤ 7.5 mg prednisone and rated to have no flare during Mths 10-12 was 49.2% (40.1, 58.2) *vs* 28.1% (16.4, 39.7) for abatacept vs PBO. In pre-specified exploratory analyses, PROs were significantly better (treatment difference [95% CI]) in the SF-36 physical component summary (3.9 [1.2, 6.6]), fatigue VAS 100 mm (-9.5 [-17.7, -1.3]), and MOS-sleep (-7.6 [-12.3, -2.9]) for abatacept vs PBO. The median (Q1, Q3) change from baseline in anti-dsDNA antibody titre (IU/ml) was -0.3 (-5.1, 0.5) vs -0.1 (-1.6, -0.6) for abatacept vs PBO. AEs were comparable (90.9% for abatacept *vs* 91.5% for PBO). SAEs were higher for abatacept (19.8%) *vs* PBO (6.8%); most were single events, appeared related to underlying disease, and occurred during or shortly after steroid taper with no discernible pattern across organ class. **Conclusions:** In this Phase II study in patients with moderate to severe SLE, the adjudicated BILAG-based primary and secondary endpoints were not met. In post-hoc and exploratory analyses, other clinical measures and biomarker data suggest abatacept activity, supporting its continued assessment in lupus.

Research Method: Clinical
Type of Trial: Treatment
Phase: Phase II
Disclosures: J. Merrill, Bristol-Myers Squibb, 2; Bristol-Myers Squibb, 5; Bristol-Myers Squibb, Medical Advisory Boards, 9; R. Burgos-Vargas, Abbott, 5; Roche, 5; Schering-Plough, 5; Wyeth, 5; Abbott, 8; Roche, 8; Schering-Plough, 8; R. Westhovens, UCB, 2; Bristol-Myers Squibb, 5; Schering-Plough, 5; Bristol-Myers Squibb, 8; A. Chalmers, Hoffman La Roche, 2; Bristol-Myers Squibb, 2; D. D'Cruz, Aspreva, 2; Bristol-Myers Squibb, 5; Aspreva, 5; Aspreva, 8; D. Wallace, None; S. Bae, None; L. Sigal, Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 3; J. Becker, Bristol-Myers Squibb, 1;

Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 3; S. Kelly, Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 3; K. Raghupathi, Bristol-Myers Squibb, 1; Pharmaceutical Product Development, Inc., 1; Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 3; Y. Peng, Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 3; M. Kinaszczuk, Bristol-Myers Squibb, 1; Johnson and Johnson, 1; Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 3; P. Nash, Centocor, 2; Centocor, 5; Schering-Plough, 8.

Session: Antiphospholipid Syndrome
Sunday, Oct 26, 2008, 9:00 AM - 6:00 PM

Presentation: 4 - Clinical Differences In Late *vs* Early-onset Primary Antiphospholipid Syndrome

Pres. Time: Sunday, Oct 26, 2008, 9:00 AM -11:00 AM
Location: Hall A, Poster Board: 4
Category: 24. Antiphospholipid syndrome
Author(s): Gabriela Medina, Olga Vera Lastra, Luis J. Jara. Hospital de Especialidades Centro Médico «La Raza», IMSS, Mexico City, Mexico

Abstract

Background: Clinical course of patients with late-onset *vs* early-onset in systemic lupus erythematosus and rheumatoid arthritis suggest differences according to age. This aspect has not been analyzed in primary antiphospholipid syndrome patients (PAPS). **Purpose:** To evaluate clinical differences in PAPS patients with late *vs* early onset. **Methods:** We studied 60 PAPS patients (47 female) (Sapporo criteria, 1999) divided into 2 groups: Group I, late-onset, arbitrarily defined as age at the time of diagnosis ≥ 45 years and Group II, early-onset with age at the time of diagnosis < 45 years. We reviewed clinical charts to determine clinical characteristics, organ damage (permanent loss of the normal function of an organ system due to a clinical manifestation of APS) and functional impairment (inability to perform everyday activities). For the statistical analysis we used descriptive statistics, T Student2 s test and Chi square test. **Results:** We found 15 patients with disease of late-onset and 45 of early-onset. Mean age at onset in group I was 51.8 ± 6 *vs* Group II, 30.4 ± 6.9 years (p = 0.001); disease evolution was 7.9 ± 6.1 *vs* 7.9 ± 4.9 (p = NS); delay in diagnosis was 2.5 ± 5.2 *vs* 2.9 ± 3.9 years (p = NS) respectively. The most frequent clinical manifestations at disease onset were stroke and deep venous thrombosis (DVT) and the subsequent manifestations were pulmonary embolism and DVT. Coincident with initial symptoms, 73% of late-onset patients had one or more cardiovascular risk factors (CRF), in contrast only 31% in early-onset group had CRF (p = 0.006). In group I organ damage was observed only in 1 patient due to mesenteric thrombosis (MT), and functional impairment was observed in 5 patients due to: mild pulmonary hypertension (PH):3, chronic skin ulceration (CSU) and postphlebitic sequela (PS): 1, body lateropulsion:1. In early-onset (Group II) organ damage was observed in 5 patients due to MT:1, loss of a limb:2, myocardial infarction :1, blindness in one eye:1. Functional impairment was observed in 14 patients due to PS:3, CSU:4, central facial palsy:3, hemiparesis:2, paraparesis:1, moderate PH:1. Despite of CRF, the prevalence of stroke was similar in both groups (Group I, 5/15 *vs* Group II, 15/45, p = NS). **Conclusions:** This study suggests that PAPS patients with early-onset had more organ damage regardless of the disease evolution. Late-onset PAPS patients had more CRF at the time of diagnosis; however cardiovascular complications were similar in both groups. Early-onset PAPS seems to have a more aggressive course.

Reference

Erkan D, Yazici Y, Sobel R, Lockshin MD. Primary antiphospholipid syndrome: functional outcome after 10 years. J Rheumatol. 2000;27:2817-21.

Research Method: Clinical
Type of Trial: Epidemiologic or Observational
Disclosures: G. Medina, None; O. Vera Lastra, None; L.J. Jara, None

Annual slide competition 2008. Honorific mention
Clinical & pathologic images of unusual rheumatic diseases

DIFFUSE AND FOCAL PULMONARY COCCIDIOIDOMYCOSIS: RADIOLOGIC AND HISTOPATHOLOGIC FINDINGS IN VERTEBRAL AND PULMONARY COCCIDIOIDOMYCOSIS

- Computed tomography demonstrates bone erosions in vertebral body (T10).
- A chest radiograph shows thin walled cavity in the upper right lung.
- Coccidioides immitis spherule releasing endospores (40x10X),
- Coccidioidal GRANULOMA WITH MULTINUCLEATED GIANT CELL engulfing a spherule, surrounded BY MACROPHAGES, EPITHELIAL CELLS AND LYMPHOCYTES. (HE hematoxylin eosin stain). (Photomicrograph). 10x10X

References

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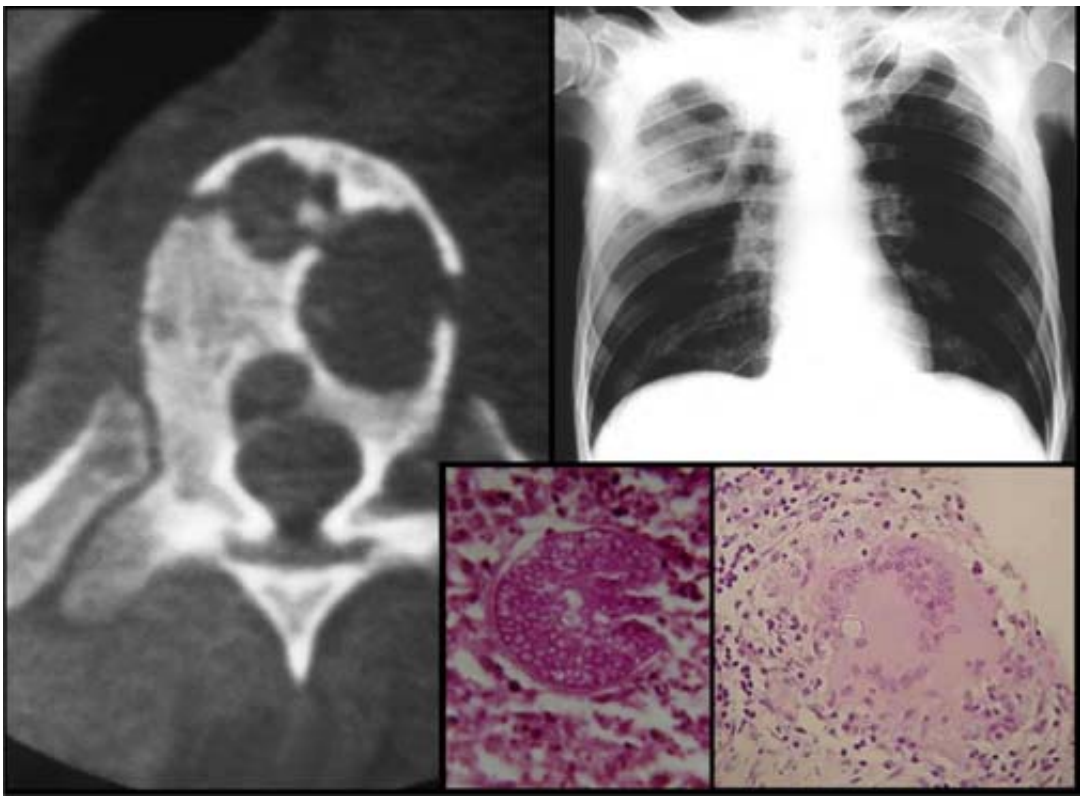
2. Galgiani JN, Ampell NM, Blair A, et al. Coccidioidomycosis. Clin Infect Dis 2005; 41: 1217.
3. Saubolle MA, McKellar PP, Sussland D. Epidemiologic, clinical, and diagnostic aspects of coccidioidomycosis. J Clin Microbiol 2007; 45: 26.

Juan Elmer Olguín Redes, MD.



ACR News and Information

- Search for Next Editor, *Arthritis & Rheumatism* (2010–2015 Term)
- Enter your CME for the 2008 Annual Scientific Meeting
- ACR Session Select is Now Available!
- Arthritis Act Is Still Alive!
- **Congratulations to the 2008 Slide Competition Winners!**
- Nurse Practitioner and Physician Assistant Postgraduate Rheumatology Training Program Opens December 1, 2008
- New Denial Code: No NPI Means No Payment
- The ACR/AMA Physician Practice Information Survey Is Underway – Rheumatologists Need to Respond!
- CARE 2008 – Online Self Assessment - Now Available
- Welcome to the newest ACR and ARHP members
- Funding Opportunities for Rheumatoid Arthritis Researchers
- Postponement of the 2009 Competitive Acquisition Program

Annual Slide Competition Winners 2008

Congratulations to the following individuals for their outstanding submissions to the 2008 ACR Slide Competition:

*****Overall Winner*****
Atypical Mycobacterial Scleritis in a Spondylitis Patient Treated with a TNF-Antagonist
Submitted by: Daniel Schaffer, MPS & Kevin Moder, MD
Rochester, MN

Still Image – First Place Winner
Gastric Antral Vascular Ectasia (watermelon stomach) in Systemic Sclerosis
Submitted by: Tamar Brionez, MD
Houston, TX

Case Study – First Place Winner
Primary Hypertrophic Osteoarthropathy
Submitted by: Jaejoon Lee, MD
Seoul, Republic of Korea

Honorable Mention
Ankylosing Spondylitis: Gas in the L1 Vertebral Body Following Collapse (Kummel Disease)
Submitted by: Arezou Khosroshahi, MD
Boston, MA

Honorable Mention
Disabling Pansclerotic Morphea
Submitted by: Carl Gauthier, Jr., MD
Hammond, LA

Honorable Mention
Giant Cell Tumor of Tendon Sheath
Submitted by: Lester Miller, MD
Santa Cruz, CA

Honorable Mention
Juvenile Dermatomyositis
Submitted by: Jay Adams
Richfield, MN

Honorable Mention
«Kissing-Hugging» Osteophyetes
Submitted by: Eddys Disla, MD
New York, NY

Honorable Mention
Ochronosis: Resected Femoral Head and Knee Synovial Fluid and Urine after Sun Exposure
Submitted by: Lester Miller, MD
Santa Cruz, CA

Honorable Mention
Radiographic Evaluation of Possible Spondyloarthritis
Submitted by: Marc Miller, MD
Portland, ME

Honorable Mention
Systemic AL Amyloidosis: Papular Periorbital Deposition and Pinch Purpura
Submitted by: Rohit Aggarwal, MD
Chicago, IL

Honorable Mention
Disseminated Coccidioidomycosis with Vertebral Involvement
Submitted by: Juan Elmer Olguin-Redes, MD
Hermosillo, Sonora, Mexico

Mensaje Navideño 2008

Feliz Navidad y exitoso 2009

Estimado amigo y colega Reumatólogo:

Recibe mis felicitaciones y parabienes en esta Navidad y al igual que cada año, tus anhelos y deseos se vean realizados.

Que la noche del 24 de diciembre compartiendo el tibio hogar junto a tu familia, eleves una oración para agradecer las bendiciones recibidas en este año y que el augurio de un 2009, lleno de expectativas, se vea colmado de satisfacciones, éxito y buenos propósitos. Un abrazo cordial para cada uno de ustedes y de sus familiares.

Dr. Juan Elmer Olguín Redes
Editor en Jefe del Boletín Mexicano de Reumatología