ENFERMEDADES AUTOINMUNES SISTÉMICAS

Dr. José María Pego Reigosa
Cardiovascular Morbidity and Mortality in Primary Sjögren Syndrome: A Systematic Review and Meta-Analysis
Aurélie Beltai, et al.
Purpose

To investigate the association between pSS and an increase of the cardiovascular morbidity and mortality.

Methods

Systematic review:

- MEDLINE and COCHRANE to January 2017.
- recent abstracts from ACR and EULAR Meetings.

Studies reporting observed cardiovascular morbidity and cardiovascular mortality in pSS and having a comparison group.
Results

457 studies:
- 26 (61254 pSS patients) met the inclusion criteria and were analyzed.
- 10 studies (32907 pSS patients) were included in the meta-analysis.

Patients with pSS, compared to the control population without IMID.

<table>
<thead>
<tr>
<th></th>
<th>RISK</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary morbidity</td>
<td>RR = 1.75</td>
<td>1.36-2.25</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Cerebrovascular morbidity</td>
<td>RR = 1.46</td>
<td>1.43-1.49</td>
<td>p&lt;0.00001</td>
</tr>
<tr>
<td>Heart failure rate</td>
<td>OR = 2.54</td>
<td>1.30-4.97</td>
<td>p&lt;0.007</td>
</tr>
<tr>
<td>Thromboembolic morbidity</td>
<td>RR = 1.78</td>
<td>1.41-2.25</td>
<td>p&lt;0.00001</td>
</tr>
</tbody>
</table>
Conclusion

- Primary Sjögren’s Syndrome is associated with an increased cardiovascular morbidity.
- These patients should also been proposed for a screening of cardiovascular comorbidities and specific preventive interventions.
Abstract Number: 1784

The Novel Anti-CD40 Monoclonal Antibody CFZ533 Shows Beneficial Effects in Patients with Primary Sjögren’s Syndrome: A Phase IIa Double-Blind, Placebo-Controlled Randomized Trial

Benjamin Fisher, et al.
**Purpose**

- Phase IIa Proof of Concept Randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of CFZ533 (anti-CD40 monoclonal antibody) in patients with pSS.

**Methods**

- Clinically active (ESSDAI≥6) pSS patients were randomized:
  - 4 doses of 3 mg/kg s.c. CFZ533 or placebo (2:1, Cohort 1) or
  - 10 mg/kg i.v. CFZ533 or placebo (2:1, Cohort 2)
- over 12 weeks in Period 1.
- Four additional doses of 3 mg/kg s.c. CFZ533 or 10 mg/kg i.v. CFZ533, respectively, in an open label extension (Period 2) for 12 weeks.

**End-points:** safety and efficacy (change in ESSDAI) after 12 weeks.

- In addition: PK/PD of CFZ533, ESSPRI, Multi-dimensional Fatigue Inventory (MFI), PGA, Patient’s Global Assessment, SF-36, and biomarkers of pSS.
Results

44 patients were enrolled.
- Cohort 1: 8 patients received 3 mg/kg s.c. CFZ533 and 4 placebo.
- Cohort 2: 21 received 10 mg/kg i.v. CFZ533 and 11 placebo in Cohort 2.

CFZ533: safe and well tolerated (majority of AEs were mild or moderate).

In Cohort 1:
- ESSDAI improved ~ 2 points from mean baseline scores of ~ 12 in both placebo and 3 mg/kg s.c. groups: no evidence of treatment difference.

In Cohort 2:
- Mean ESSDAI from ~ 11 improved to 6.35 in the 10mg/kg iv group vs. 1.27 in the placebo group: ΔESSDAI=5.64 (95% CI=1.02-10.58) strongly favoring the CFZ533 i.v. treatment.

Improvements in ESSPRI, MFI, PGA and Patient’s Global Assessment and decreases in biomarker CXCL13: observed in the 10mg/kg iv CFZ533 group.
Conclusion

- In this proof of concept study, the anti-CD40 antibody CFZ533 may offer a new treatment modality in clinically active primary Sjögren’s patients.
Treat To Target In Systemic Lupus Erythematosus

- ABSTRACT NUMBER: 1603
- ABSTRACT NUMBER: 1604
- ABSTRACT NUMBER: 1605
- ABSTRACT NUMBER: 1630
- ABSTRACT NUMBER: 1647
Lupus Low Disease Activity State: Can We Relax the Definition and Still Achieve Low Risk of SLE-Related Damage?

Validation of Remission and Lupus Low Disease Activity State As Predictors of Organ Damage in SLE

Lupus Low Disease Activity State Protects Against Most Subtypes of Organ Damage in SLE

Achievement of Lupus Low Disease Activity State (LLDAS) in the Early Phase of Systemic Lupus Erythematosus Prevent Damage Accrual

A Lupus Low Disease Activity State Is Associated with Reduced Flare, Lower Organ Damage Accrual, and Better Quality of Life in Patients with SLE
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Remission
Lupus Low Disease Activity State (Lldas)

- Remission and Lupus Low Disease Activity State are two useful therapeutic objectives that are associated with lower damage accrual.
ABSTRACT NUMBER: 1587 POSTER
ABSTRACT NUMBER: 1588 POSTER
ABSTRACT NUMBER: 1612
ABSTRACT NUMBER: 2619 POSTER
Mycobacterial Infection in SLE: Clinical Significance and Associated Factors. Data from the Registry of Patients of the Spanish Society of Rheumatology (RELESSER). Ana Lois et al.

Neoplasia in Patients with SLE in Spain: RELESSER Registry Data. Ana Urruticoechea et al.

Primary Respiratory Disease in Patients with SLE: Data from the Spanish Rheumatology Society Lupus Registry (RELESSER) Cohort. Javier Narváez et al.

Hemophagocytic Syndrome in Patients from SLE Registry from the Spanish Society of Rheumatology (RELESSER). Ana Lois et al.
ABSTRACT NUMBER: 2983

Predictors for Disease Worsening Defined By Organ Failure in Diffuse Systemic Sclerosis: A European Scleroderma Trials and Research (EUSTAR) Analysis

Mike Oliver Becker, et al.
Purpose
- To identify predictive factors of organ failure in patients with diffuse SSc from the large EUSTAR group database.

Methods
- Inclusion criteria: diagnosis of diffuse SSc and a F-U after 12 ± 3 months.
- Disease worsening/organ progression:
  - new renal crisis,
  - decrease in forced vital capacity ≥10%,
  - new left ventricular ejection fraction (LVEF) <45% or decrease in LVEF by >10% for patients with baseline LVEF <50%,
  - new pulmonary (arterial) hypertension on echocardiography,
  - or death.
Results

- 1451 patients met the inclusion criteria, 706 had complete data available on all parameters for disease worsening.

- 228/706 (32.3%) had disease progression within the F-U (12±3 months).
  - decrease in FVC (103 patients, 14.6%),
  - or death (92 patients, 13.0%)

- Of the 42 clinical parameters introduced into the model as outcome predictors, 8 remained in the final regression model (Table 1).
### Table 1: Predictive factors in the final LASSO regression model.

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>SE</th>
<th>p-value</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Intercept)</td>
<td>-2.74</td>
<td>0.405</td>
<td>&lt;0.0001</td>
<td>0.06</td>
<td>0.03–0.14</td>
</tr>
<tr>
<td>Age (per 1 year)</td>
<td>0.02</td>
<td>0.007</td>
<td>0.001</td>
<td>1.02</td>
<td>1.01–1.04</td>
</tr>
<tr>
<td>Active digital ulcers</td>
<td>0.50</td>
<td>0.222</td>
<td>0.026</td>
<td>1.64</td>
<td>1.06–2.54</td>
</tr>
<tr>
<td>C-reactive protein elevation</td>
<td>0.59</td>
<td>0.194</td>
<td>0.002</td>
<td>1.80</td>
<td>1.23–2.63</td>
</tr>
<tr>
<td>Significant dyspnea</td>
<td>0.18</td>
<td>0.261</td>
<td>0.491</td>
<td>1.20</td>
<td>0.72–2.00</td>
</tr>
<tr>
<td>Lung fibrosis</td>
<td>0.79</td>
<td>0.221</td>
<td>0.0004</td>
<td>2.21</td>
<td>1.43–3.41</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>0.50</td>
<td>0.204</td>
<td>0.015</td>
<td>1.64</td>
<td>1.10–2.45</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>0.50</td>
<td>0.301</td>
<td>0.098</td>
<td>1.65</td>
<td>0.91–2.97</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>0.56</td>
<td>0.301</td>
<td>0.064</td>
<td>1.75</td>
<td>0.97–3.16</td>
</tr>
</tbody>
</table>

CI, confidence interval; OR, odds ratio; SE, standard error
Conclusion

- The identification of the predictive factors for SS worsening / organ failure could enable cohort enrichment with patients at risk for overall disease worsening in observational studies and/or clinical trials.
Abstract Number: 1845

Comparison of Magnetic Resonance Angiography (MRA) and 18f-Fluorodeoxyglucose Positron Emission Tomography (PET) in Large Vessel Vasculitis.

Kaitlin A. Quinn, et al.
Purpose

To assess agreement between MRA and PET for disease activity and disease extent and to determine MRA features associated with PET activity.

Methods

Prospective, observational cohort of patients with GCA or Takayasu’s arteritis. Comparator group: patients with vasculopathy or healthy controls.

Clinical assessment, MRA, and PET within 24 hours. Imaging and clinical assessments blinded. MRA and PET evaluated for evidence of active vasculitis.

To evaluate extent: aorta and branches divided in 15 vascular territories. Vascular involvement defined:

- MRI: presence of wall thickness, edema, stenosis, occlusion, or aneurysm.
- PET: visual FDG uptake in each arterial territory > liver.

Agreement was assessed. Multivariable logistic regression: factors on MRA associated with PET interpretation of disease activity.
Results

- n = 68 (GCA=26; TAK=24; Comparator=18), 115 paired PET/MRA studies.
- 1398 vascular territories were evaluated.
- Active disease in 76 PETs and 77 MRAs.
- 80 studies showed agreement (70%, K=0.32). 35 studies with disagreement: PET showed disease activity in 17 studies and MRA in 18 (McNemar’s p=1.00).
- Clinical disease status was associated with PET scan interpretation (p=0.01) but not MRA interpretation (p=0.52).
- More comparators showed active vasculitis by MRA vs PET (50% vs 11%, p=0.03).
- 782 territories showed agreement PET/MRA (56%, K=0.17) for disease extent.
- 608 territories with disagreement: MRA showed disease in more territories than PET (513 vs 95, McNemar’s p<0.01).
- Territories with PET disease activity: positively associated with edema (OR=1.36, p<0.01) and wall thickness (OR=1.17, p=0.04) but not with stenosis (OR=0.07, p=0.33).
Conclusion

- Fair agreement in the interpretation of PET/MRA for disease activity.
- PET, and not MRA interpretation: associated with clinical assessment.
- MRA detects disease activity and damage, thus identifying a greater extent of vascular involvement compared to PET.
- Thus, PET and MRA provide complementary information in LVV.
Abstract Number: 1884

Mepolizumab for the Treatment of Patients with Eosinophilic Granulomatosis with Polyangiitis: Post-Hoc Results of a Phase III Randomized, Placebo-Controlled Trial.

Jonathan Steinfeld, et al.
Purpose

- To investigate post-hoc the benefit in terms of not only remission, but
  - oral corticosteroid reduction,
  - and/or relapses.
Methods

- Phase III, randomized, placebo-controlled, double-blind, parallel-group, multi-center study in patients with EGPA and a history of relapsing or refractory disease on stable therapy with PRDL/PRD $\geq 7.5 - \leq 50$ mg/day with or without additional IS therapy for $\geq 4$ weeks.

- Randomized 1:1
  - mepolizumab 300mg or placebo s.c. + SoC, for 52 weeks.

- Remission: BVAS=0 and GC$\leq 4$mg/d + EULAR definition (BVAS=0, GC$\leq 7.5$mg/d).

- Oral GC reduction: $\geq 50\%$ reduction from baseline in average PRDL/PRD dose during Weeks 48-52.

- Benefit in relapse: relapse free throughout the 52 week treatment period.
Results

- 136 patients.
- Mepolizumab n=68, placebo n=68.
- 53 (78%) subjects in the mepolizumab group vs. 22 (32%) in the PBO group:
  - clinical benefit in terms of remission and/or 50% reduction in oral GC dose and/or having no relapses during the study treatment period.
- 59 (87%) subjects in the mepolizumab group vs. 36 (53%) in the PBO group:
  - clinical benefit for the EULAR definition of remission.
Conclusion

- Mepolizumab compared to placebo is significantly better in:
  - remission,
  - absence of relapse,
  - and/or steroid reduction.