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EULAR
LO MEJOR DE REVIEW
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Enfermedades Autoinmunes Sistémicas

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ABSTRACT SESSION:
CLINICAL AND THERAPEUTICAL NEWS IN SYSTEMIC SCLEROSIS
A PHASE 2 STUDY OF SAFETY AND EFFICACY OF ANABASUM (JBT-101) IN SYSTEMIC SCLEROSIS

- Synthetic oral selective cannabinoid receptor II type
- Binds to receptors expressed on activated immune cells and fibroblasts
- Triggers the production of “specialized pro-resolving lipid mediators”
- It works to inhibit inflammation and stop fibrosis without causing immunosuppression
A PHASE 2 STUDY OF SAFETY AND EFFICACY OF ANABASUM (JBT-101) IN SYSTEMIC SCLEROSIS

- Difference in CRISS scores over trial period between Anabasum and placebo groups was significant ($p = 0.044$); Median CRISS score at week 16 reached 33% in JBT-101 group versus 0% in placebo group
- Reduced expression of genes associated with inflammation and fibrosis in skin biopsies
- 12 months extension phase III study
- Anabasum 20mg twice a day
ABSTRACT SESSION:
VASCULITIS CLINICAL AND PATHOGENIC HIGHLIGHTS
MEPOLIZUMAB FOR THE TREATMENT OF PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: A PHASE III RANDOMISED, PLACEBO-CONTROLLED TRIAL (0P0130)

- Monoclonal antibody
- Binds to IL-5 and prevents it from binding to its receptor, on the surface of eosinophil
- Approved for asthma
- The exact mechanism is unknown
MEPOLIZUMAB FOR THE TREATMENT OF PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: A PHASE III RANDOMISED, PLACEBO-CONTROLLED TRIAL

- 136 pts: 68 Mepolizumab, 68 placebo.
- Followed up: 52 weeks.
- **Mepolizumab:**
  - Significantly prolonged remission (OR: 5.9, p<0.001)
  - Significance reduction on steroids dose (0.20, p<0.001)
  - Rates of adverse events: No different between groups
OPTIMAL DOSE OF TOCILIZUMAB FOR THE TREATMENT OF GIANT CELL ARTERITIS: EFFICACY, SAFETY, AND EXPOSURE-EFFICACY ANALYSIS FROM GIACT

- 251 patients RCT
- 1. TCZ weekly. 2. TCZ every other week 3. short term steroids (26 weeks) 4. long term steroids (52 weeks)
- 56% weekly TCZ and 53.1% every other week TCZ achieved sustained remission at 12 months compared to only 14% in the short-course prednisone group (p < 0.0001) and (17.6%) in the long-course prednisone group (p ≤ 0.0002)

Stone J (US)
The median cumulative steroid exposure in both TCZ groups was less than half that of those in the long-course prednisone group.

The incidence of adverse events was similar among the 4 treatment arms.

No deaths and no new vision loss occurred over the period of observation.
OPTIMAL DOSE OF TOCILIZUMAB FOR THE TREATMENT OF GIANT CELL ARTERITIS: CONCLUSIONS

- TCZ weekly plus a 26-week prednisone taper was superior to both short- and long-course prednisone tapers for the achievement of sustained remission at 52 weeks.
- The addition of TCZ to prednisone also led to a substantial reduction in the cumulative prednisone doses required to control GCA.
TOCILIZUMAB IN GIANT CELL ARTERITIS: GIACTA TRIAL vs A SERIES OF PATIENTS FROM CLINICAL PRACTISE

- 119/132 recurrences with conventional treatment

**Results:**
- TCZ was started later than in clinical trial
- Larger number of patients with PR and optic neuritis
- The mean value of ESR
- Higher proportion of pts who received MTX for longer
- Patients characteristics are different

Vegas Revenga Nuria (Spain)
OUTCOME ARE DIFFERENT

TCZ IN GCA

RESULTS

Sustained remission

CLINICAL PRACTICE 27.3%
GIACTA 54.6%

Severe infection

CLINICAL PRACTICE 13.6%
GIACTA 6%
HOT SESSION: VASCULITIS TREATMENT
ANCA-ASSOCIATED VASCULITIS TREATMENT

- Classical treatments
- Tocilizumab trial
- Mepolizumab trial
- EULAR recommendation
ANCA-VASCULITIS TREATMENT

Avacopan (CCX168), an orally administered, selective C5a receptor inhibitor, could replace oral glucocorticoids without compromising efficacy.

Randomized, placebo-controlled trial, adults with newly diagnosed or relapsing vasculitis received placebo plus prednisone starting at 60 mg daily (control group), avacopan (30 mg, twice daily) plus reduced-dose prednisone (20 mg daily), or avacopan (30 mg, twice daily) without prednisone. All patients received cyclophosphamide or rituximab.

The primary efficacy measure was the proportion of patients achieving a $\geq 50\%$ reduction in Birmingham Vasculitis Activity Score by week 12 and no worsening in any body system.
VASCULITIS TREATMENT

- 67 patients
- **Control:**
  - Pred 60mg plus placebo (23)
  - Avacopan 30mg twice/daily plus Prednisolone 30mg (22)
  - Avacopan 30mg twice/daily
- **Results:**
  - Clinical response at week 12 was achieved
  - 70.0% control
  - 86.4% in the avacopan plus reduced-dose prednisone group (P=0.002 for noninferiority),
  - 81.0% in the avacopan without prednisone P=0.01 for noninferiority.
  - No difference in adverse events occurred.
- **Conclusion:**
  - C5a receptor inhibition with avacopan was effective in replacing high-dose glucocorticoids in treating vasculitis
CLINICAL SCIENCE SESSION:
WHICH TARGET/OUTCOME IS MORE RELEVANT IN THE MANAGEMENT OF SLE?
Anifrolumab (ANIFR), a type I IFN receptor antagonist, were assessed in a Phase II, randomized, double-blind, placebo-controlled study in SLE.

305 adults with seropositive moderate to severe SLE despite standard of care medication were randomized and received intravenous (iv) ANIFR (300 mg, 1000 mg) or placebo (PBO) every 4 weeks for 48 weeks.

Stratified by IFN gene signature (IFN high vs. IFN low) based on a 4-gene expression assay.

Anifrolumab significantly reduced disease activity compared with PBO across multiple clinical endpoints.

The lack of dose response can be explained by the nearly similar degrees of IFN gene signature inhibition achieved with the two anifrolumab doses.
TARGET/OUTCOME IN THE MANAGEMENT OF SLE

Combining B-cell targeted therapies in SLE?

Belimumab followed by Rituximab

Belimumab

Rituximab

Rituximab followed by Belimumab

Rituximab

Belimumab

Simonetta F. et al. 2016
CONCLUSIONS

- Current understanding of SLE pathogenesis provides a large array of potential targets of therapy.

- Differences exist between SLE individuals in gene module which correlate with disease activity.

- The expression level of 4 induces by type-I INF may allow to select for responders to an anti-IFN targeted approach.

- The identification of an indel variant in BAFF gene may allow to select for anti-BAFF responders.

- B cell target combination has potential for higher efficacy (adverse events need to be carefully evaluated).
SLE TREATMENT
SUSTAINED SAFETY AND EFFICACY OVER 10 YEARS WITH BELIMUMAB (BEL) PLUS STANDARD SLE THERAPY IN PATIENTS WITH SLE (OP0232)

- Of 298 patients in the continuation trial, 131 (44%) remained at Year 10.

- **Conclusions:** Over 10 years BEL + SoC was well tolerated and the rates and nature of AEs were consistent with the known profile of BEL. Efficacy was maintained and prednisone use decreased in those receiving >7.5 mg/day at baseline.
Inducible T-cell co-stimulator ligand (ICOSL) blockade leads to selective inhibition of anti-keyhole limpet haemocyanin (KLH) IgG responses in subjects with systemic lupus erythematosus.

To investigate potential efficacy, safety, and tolerability of AMG 557 in subjects with lupus arthritis withdrawing background therapies to improve interpretability of a small study.

Twenty subjects (19 females) were randomized (10 AMG 557, 10 placebo).

Results from this exploratory placebo-controlled trial in lupus arthritis suggest potential clinical benefit of ICOSL blockade by AMG 557.
SLE TREATMENT
48 WEEK COMPLETE REMISSION OF ACTIVE LUPUS NEPHRITIS WITH VOCLOSPORIN (LB0002)

- Investigational calcineurin inhibitor voclosporin is associated with a significant, threefold-higher rate of complete remission for lupus nephritis (Phase II study)
SLE TREATMENT
48 WEEK COMPLETE REMISSION OF ACTIVE LUPUS NEPHRITIS WITH VOCLOSPORIN (AURA (LV))

**Objective**: Evaluate whether Voclosporine plus SoC speed remission and rate of remission with low dose steroids

- Voclosporina 23.7 mg bd
- Voclosporina 39.5 mg bd
- MMM 2 gr + Steroids
Low dose Voclosporin showed statistically significant rate of CR and PR at 24 weeks

Dobronravov V (Russian)
SLE TREATMENT
48 WEEK COMPLETE REMISSION OF ACTIVE LUPUS NEPHRITIS WITH VOCLOSPORIN

- Voclosporin low dose subjects stayed in CR twice as long as control

Dobronravov V (Russian)
Conclusions

- Voclosporin combined with MMF and steroids leads to increased rates and duration of CR
- AURA is the first study to ever meet all ends points in active LN
- 49.4% CR after 12 months (low dose) higher than other trials
- The multitarget approach allowed for faster clinical response to be achieved with less steroid and a safe profile.
Lifitegrast is an integrin antagonist that decreases T-cell-mediated inflammation associated with dry eye disease (DED)

**Objectives:** To evaluate the combined evidence from 5 clinical trials of lifitegrast ophthalmic solution 5.0% (LIF) in subjects with dry eye disease (DED)

Key measures were inferior corneal staining score (ICSS; 0–4 scale), eye dryness score (EDS)

Visual analogue scale [VAS], 0–100 scale), and visual-related function subscale of a symptom scale (0–4 scale). Pooled safety data (LIF n=1287, PBO n=1177) from all 5 trials were also analyzed

LIF improved signs and symptoms of DED in adults with DED and appeared to be well tolerated with no serious ocular AEs reported
ANTI-TNF AND PREGNANCY

- All anti-TNF seem to be safe for mother and embryo, at the conception time.

- They are safe during the 1st and second trimester but should be stopped at 30 weeks (except IFX at week 20)

CERTOLIZUMAB PEGOL

- It can be used during the whole pregnancy and breastfeeding

- The new born can receive all vaccinations

ANTI-TNF AND BREASTFEEDING

- Ig A is the predominant antibody
- IgG transport to the maternal milk is limited
- Very low levels or not detectable of anti-TNF
- No significative impact in children

RITUXIMAB

- Register including 256 pregnancies (72 prospectives)
- EULAR
  - 22.9% miscarriages
  - -3.6% malformations.
- Stop during 2nd trimester to avoid B depletion in child
- NICE:
  - Should be stop 6 months before conception