

EULAR
MADRID JUNIO 2017

Con la colaboración de
 **NOVARTIS**

 **Sociedad Española de
Reumatología**

REVIEW
Annual European Congress
of Rheumatology

Enfermedades Autoinmunes Sistémicas. Tratamiento

Dra. M^a José Cuadrado Lozano

EULAR

MADRID JUNIO 2017

Con la colaboración de
 NOVARTIS

 Sociedad Española de
Reumatología

REVIEW

Annual European Congress
of Rheumatology

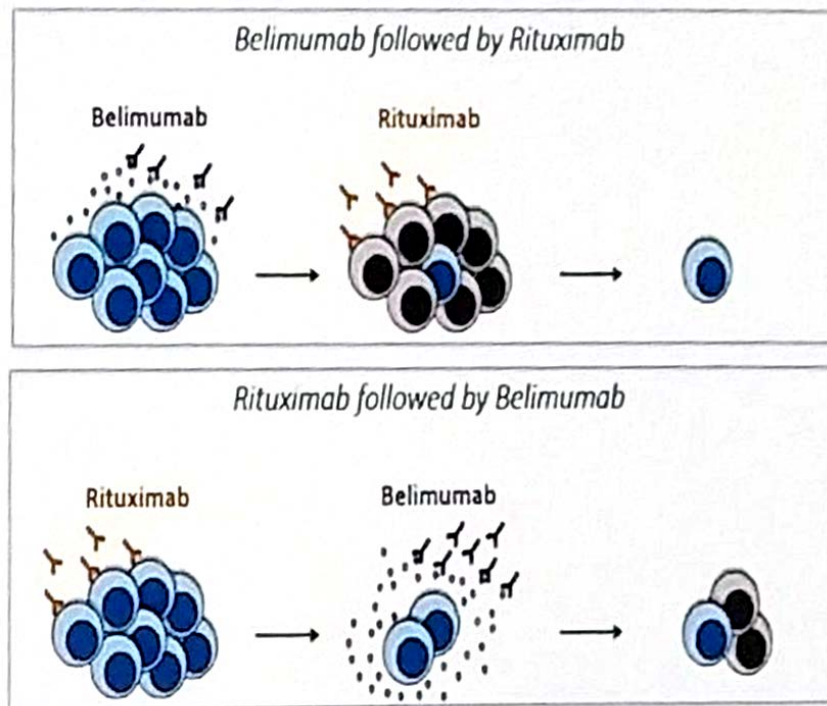
**CLINICAL SCIENCE SESSION:
WHICH TARGET/OUTCOME IS MORE RELEVANT
IN THE MANAGEMENT OF SLE?**

TARGET/OUTCOME 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 ?



TARGET/OUTCOME IN THE MANAGEMENT OF SLE

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 PRECISEASADS
- ▶ 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)

EULAR
MADRID JUNIO 2017

Con la colaboración de
 **NOVARTIS**

 **Sociedad Española de
Reumatología**

REVIEW

Annual European Congress
of Rheumatology

**ABSTRACT SESSION: NEW
TREATMENTS IN SLE, SJÖGREN'S
AND APS**

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.

SLE TREATMENT

CLINICAL AND BIOLOGIC EFFECTS OF ICOSL BLOCKADE BY AMG 557 IN SUBJECTS WITH LUPUS ARTHRITIS (OP0234)

- ▶ 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

SLE TREATMENT

48 WEEK COMPLETE REMISSION OF ACTIVE LUPUS NEPHRITIS WITH VOCLOSPORIN

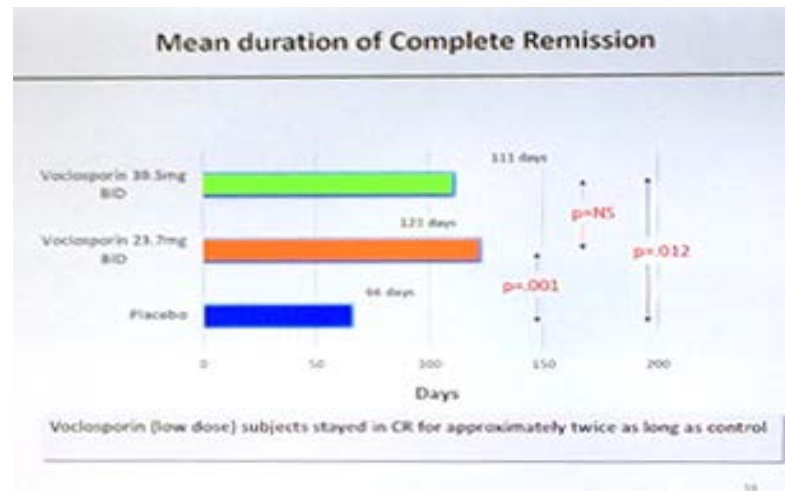
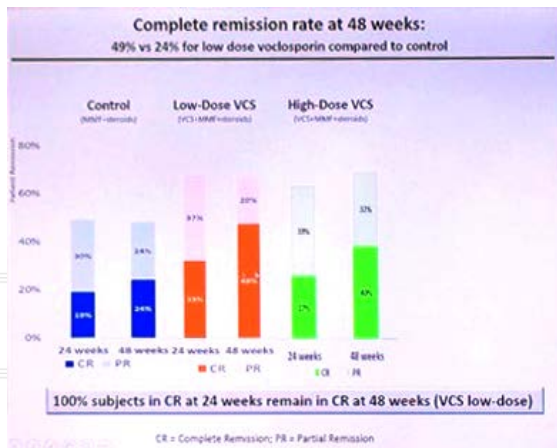
- Low dose Voclosporin showed statistically significant rate of CR and PR at 24 weeks



SLE TREATMENT

48 WEEK COMPLETE REMISSION OF ACTIVE LUPUS NEPHRITIS WITH VOCLOSPORIN

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



SLE TREATMENT

48 WEEK COMPLETE REMISSION OF ACTIVE LUPUS NEPHRITIS WITH VOCLOSPORIN

Conclusion

- 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 allows for faster clinical response to be achieved with less steroid and a safe profile

SIGNIFICANT REDUCTIONS OF PATHOGENIC AUTOANTIBODIES BY SYNERGETIC RITUXIMAB AND BELIMUMAB TREATMENT EFFECTIVELY INHIBITS NEUTROPHIL EXTRACELLULAR TRAPS IN SEVERE, REFRACTORY SLE - THE SYNBIOSE STUDY T.

- **Objectives:** The present study aimed to investigate whether Rituximab (RTX) + Belimumab (BLM) affected pathogenic antibodies in relation to neutrophils extracellular traps (NET) induction in severe refractory SLE
- The study included 10 severe, refractory SLE patients with lupus nephritis and 1 patient with neuropsychiatric lupus.
- Within refractory SLE patients, RTX + BLM resulted in concordant reductions in pathogenic anti-dsDNA antibodies and NET-inducing capacity. This study strongly suggests that NET induction in SLE is mediated by immune complexes, providing a possible explanation underpinning the clinical benefits of RTX+BLM

SJOGREN SYNDROME TREATMENT

LIFITEGRAST OPHTHALMIC SOLUTION 5.0% FOR TREATMENT OF DRY EYE DISEASE: COMBINED EVIDENCE FROM 5 RANDOMIZED CONTROLLED TRIALS.

- 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

EULAR
MADRID JUNIO 2017

Con la colaboración de
 **NOVARTIS**

 **Sociedad Española de
Reumatología**

REVIEW
Annual European Congress
of Rheumatology

**PREGNANCY MEETS RHEUMATIC
PATIENTS**

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 newborn can receive all vaccinations

Flint et al. Rheumatology 2016;1:299.

Skorpen C, et al. Ann Rheum Dis 2016,75:795-810.

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