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OP0162 ABATACEPT TREATMENT FOR PATIENTS WITH EARLY ACTIVE PRIMARY SJÖGREN'S SYNDROME: OPEN-LABEL EXTENSION PHASE OF A RANDOMIZED CONTROLLED PHASE III TRIAL

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Background: Abatacept (CTLA-4-Ig) targets the CD80/CD86:CD28 co-stimulatory pathway required for full T-cell activation and T-cell dependent activation of B-cells. The Abatacept Sjögren Active Patients phase III (ASAPIII) trial is a mono-center, investigator-initiated, placebo controlled study with an open-label extension phase (NCT02067910), which assessed the efficacy and safety of weekly subcutaneous abatacept (125mg) in patients with early active primary Sjögren's syndrome (pSS). Previous analyses of the double blind phase showed no significant effect of abatacept treatment compared to placebo on the primary endpoint, difference in EULAR Sjögren's syndrome disease activity index (ESSDAI) at week 24.[1]

Objectives: To evaluate the efficacy and safety of extended (48 weeks) open label abatacept treatment in pSS patients.

Methods: Included patients had biopsy-proven pSS, fulfilled the AECG and ACR-EULAR criteria, had disease duration ≤7 years (median 2 years), ESSDAI ≥5, and 89% were anti–SSA positive. All 40 patients who received abatacept (ABA) in week 0-24 were subsequently treated with abatacept from week 24-48. Of the 40 patients who received placebo (PLB) in week 0-24, 2 were lost to follow up, and 38 were treated with abatacept from week 24-48. Systemic disease activity (ESSDAI), patient reported symptoms (ESSPRI), serological outcomes (RF and IgG), ocular staining score (OSS) and unstimulated whole salivary flow (UWS) were assessed. We evaluated whether outcomes improved within treatment groups, from week 0 to subsequent visits and from week 24 to subsequent visits:

1. Within ABA→ABA treated patients:
   a. Week 0-48 to assess overall efficacy.
   b. Week 24-48 to assess additional efficacy of long term treatment.
2. Within PLB→ABA treated patients:
   a. Week 0-24 to assess whether a placebo effect occurred.
   b. Week 24-48 to assess short-term efficacy of open label ABA.

GEE modeling was used to test significance of changes over time. Missing data were not imputed.

Results: ESSDAI and ESSPRI were improved within ABA/ABA patients between week 0-48 with additional efficacy after week 24, and within PLB/ABA patients after switching to ABA. Significant decreases in ESSDAI and ESSPRI were also seen within PLB treated patients between week 0-24 (Figure 1). IgG and RF were improved within ABA/ABA patients between week 0-48 with additional efficacy after week 24, and within PLB/ABA patients after switching to ABA. OSS was improved within ABA/ABA treated patients between week 0-48. UWS only showed significant improvement in week 36 within ABA/ABA treated patients. No changes in IgG, RF, OSS or UWS were seen within PLB treated patients. No deaths occurred. One serious adverse event possibly related to intervention occurred during ABA treatment.

Conclusion: ESSDAI and ESSPRI improved significantly during 48-week treatment with abatacept. Placebo treated patients also showed significant improvement in both indices and further improvement occurred after switching to abatacept. Biological activity was decreased by abatacept treatment. 48-week abatacept treatment improved OSS, and might improve UWS. Abatacept was well tolerated by pSS patients.

References:

[1] van Nimwegen et al. Lancet Rheumatol. *Published online 31-01-2020*

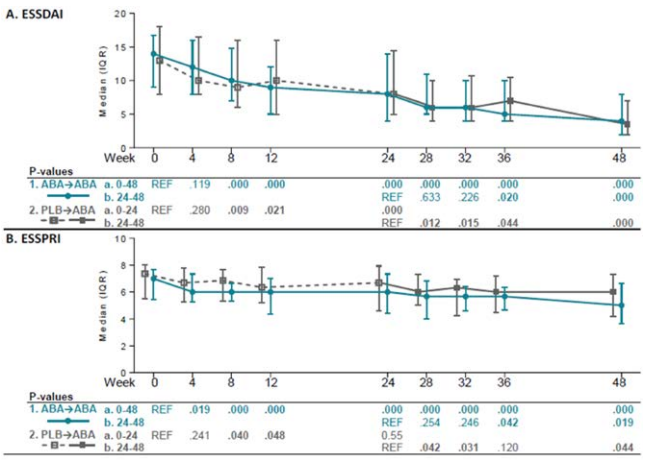

Figure 1. ESSDAI (A) and ESSPRI (B) during ABA/ABA treatment and PLB/ABA treatment in pSS

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OP0163 2019 UPDATE OF THE JOINT EUROPEAN LEAGUE AGAINST RHEUMATISM AND EUROPEAN RENAL ASSOCIATION–EUROPEAN DIALYSIS AND TRANSPLANT ASSOCIATION (EULAR/ERA-EDTA) RECOMMENDATIONS FOR THE MANAGEMENT OF LUPUS NEPHRITIS

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Background: Up to 40% of systemic lupus erythematosus (SLE) patients develop kidney disease, which represents a major cause of morbidity.

Objectives: To update the 2012 EULAR/ERA-EDTA recommendations for the management of lupus nephritis (LN).

Methods: We followed the EULAR standardised operating procedures for the publication of treatment recommendations. Delphi-based methodology led to 15 questions for systematic literature review (SLR), which was undertaken by three fellows.

Results: The changes include recommendations for treatment targets, use of glucocorticoids and calcineurin inhibitors (CNI), and management of

end-stage-kidney-disease (ESKD). The target of therapy is complete response (proteinuria <0.5-0.7gr/24h with [near-]normal glomerular filtration rate) by 12 months, but this can be extended in patients with baseline nephrotic-range proteinuria. Hydroxychloroquine is recommended with regular ophthalmological monitoring. In active proliferative LN, initial (induction) treatment with mycophenolate mofetil (MMF 2-3g/day, or mycophenolic acid at equivalent dose) or low-dose intravenous cyclophosphamide (CY; 500mg x6 biweekly doses), both combined with glucocorticoids (pulses of intravenous methylprednisolone, then oral prednisone 0.3-0.5mg/kg/day) is recommended. MMF/CNI (especially tacrolimus) combination and high-dose CY are alternatives, for patients with nephrotic-range proteinuria and adverse prognostic factors. Subsequent long-term maintenance treatment with MMF or azathioprine should follow, with no or low-dose (<7.5 mg/day) glucocorticoids. The choice of agent depends on the initial regimen and plans for pregnancy. In non-responding disease, switch of induction regimens or rituximab are recommended. In pure membranous LN with nephrotic-range proteinuria or proteinuria >1g/24h despite renin-angiotensin-aldosterone blockade, MMF in combination with glucocorticoids is preferred. Assessment for kidney and extra-renal disease activity, and management of comorbidities is lifelong with repeat kidney biopsy in cases of incomplete response or nephritic flares. In ESKD, transplantation is the preferred kidney replacement option with immunosuppression guided by transplant protocols and/or extra-renal manifestations.

Conclusion: The updated recommendations intend to inform rheumatologists, nephrologists, patients, national professional societies, hospital officials, social security agencies and regulators about the treatment of LN based on most recent evidence.

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OP0164

BLISS-LN: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 TRIAL OF INTRAVENOUS BELIMUMAB IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS

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Background: Lupus nephritis (LN), a serious manifestation of systemic lupus erythematosus (SLE), affects nearly 70% of patients (pts) in high-risk groups. To preserve renal function, LN requires fast and effective treatment. Despite medical advances, progression rates at 15 years to end-stage renal disease (ESRD) remain >40% for pts with diffuse proliferative LN. Belimumab (BEL), approved in pts aged ≥5 years with active SLE, improved renal parameters in pts with baseline renal involvement in a *post hoc* analysis of Phase 3 trials data.

Objectives: To assess efficacy and safety of intravenous (IV) BEL vs placebo (PBO), plus standard therapy (ST), in pts with active LN.

Methods: BLISS-LN is a Phase 3, randomised, double-blind, PBO-controlled, 104-week study (GSK Study BEL114054, NCT01639339). Adults with SLE and biopsy-proven LN (class III, IV, and/or V) were randomised (1:1) to monthly BEL 10 mg/kg IV or PBO, plus ST. Primary endpoint: Primary Efficacy Renal Response (PERR); defined as urine protein creatinine ratio [uPCR] ≤0.7; estimated glomerular filtration rate [eGFR] within 20% of the pre-flare value or ≥60 ml/min/1.73m^2; no rescue therapy) at Week (Wk) 104. Key secondary endpoints: Complete Renal Response (CRR; defined as uPCR <0.5; eGFR within 10% of the pre-flare value or ≥90 ml/min/1.73m^2; no rescue therapy) at Wk 104; PERR at Wk 52; time to renal-related event (defined as ESRD/doubling of serum creatinine/renal worsening/renal disease-related treatment failure) or death. Other endpoints: time to PERR/CRR sustained through Wk 104; SLEDAI-S2K score <4 points at Wk 104; safety.

Results: Overall, 448 pts were randomised (efficacy: 223/group; safety: 224/group). Significantly more BEL (43%) than PBO (32.3%) pts achieved PERR at Wk 104 (OR 1.55, 95% CI 1.04, 2.32; p=0.0311). More BEL than PBO pts achieved key secondary and other efficacy endpoints (Table).

Overall, 214 (95.5%) BEL and 211 (94.2%) PBO pts had ≥1 adverse event (AE); 58 (25.9%) BEL and 67 (29.9%) PBO pts had ≥1 serious AE; 29 (12.9%) pts in each group had ≥1 AE resulting in study treatment discontinuation; 4 (1.8%) BEL and 3 (1.3%) PBO pts developed on-treatment fatal AEs.

Conclusion: In the largest LN study to date, data from BLISS-LN demonstrate that BEL plus ST significantly improves LN renal responses compared with ST alone with a favourable safety profile.

Study funding: GSK.

Table.

Endpoint, n (%)	PBO (n=223)	BEL (n=223)	OR/HR (95% CI) vs PBO	p-value
CRR at Wk 104*	44 (19.7)	67 (30.0)	OR 1.74 (1.11, 2.74)	0.0167
PERR at Wk 52*	79 (35.4)	104 (46.6)	OR 1.59 (1.06, 2.38)	0.0245
Time to PERR through Wk 104†	72 (32.3)	96 (43.0)	HR 1.46 (1.07, 1.98)	0.0157
Time to CRR through Wk 104†	44 (19.7)	67 (30.0)	HR 1.58 (1.08, 2.31)	0.0189
Time to renal-related event or death†	63 (28.3)	35 (15.7)	HR 0.51 (0.34, 0.77)	0.0014
SLEDAI-S2K score <4 points at Wk 104*	41 (18.4)	62 (27.8)	OR 1.76 (1.11, 2.78)	0.0164

*PBO and BEL columns represent the n (%) responders

†Data presented as n (cumulative incidence)

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