THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Knowledge that will change your world

Efficacy and safety of anti-IL6 in SLE

DJ Wallace et al, Ann Rheum Disease 2017; 76: 534

- Phase II study (dose ranging)
- Fully human IgG2 that binds and neutralizes IL-6
- Based on a open label Phase I study (N=16)

- Based on Andre's review, what changes in clinical and/or laboratory markers would one expect?

- Lupus disease activity measures
  - Measuring disease activity in adults with systemic lupus erythematosus: the challenges of administrative burden and responsiveness to patient concerns in clinical research.
    - Mikdashi and Nived Arthritis Research & Therapy (2015) 17:183 DOI 10.1186/s13075-015-0702-6

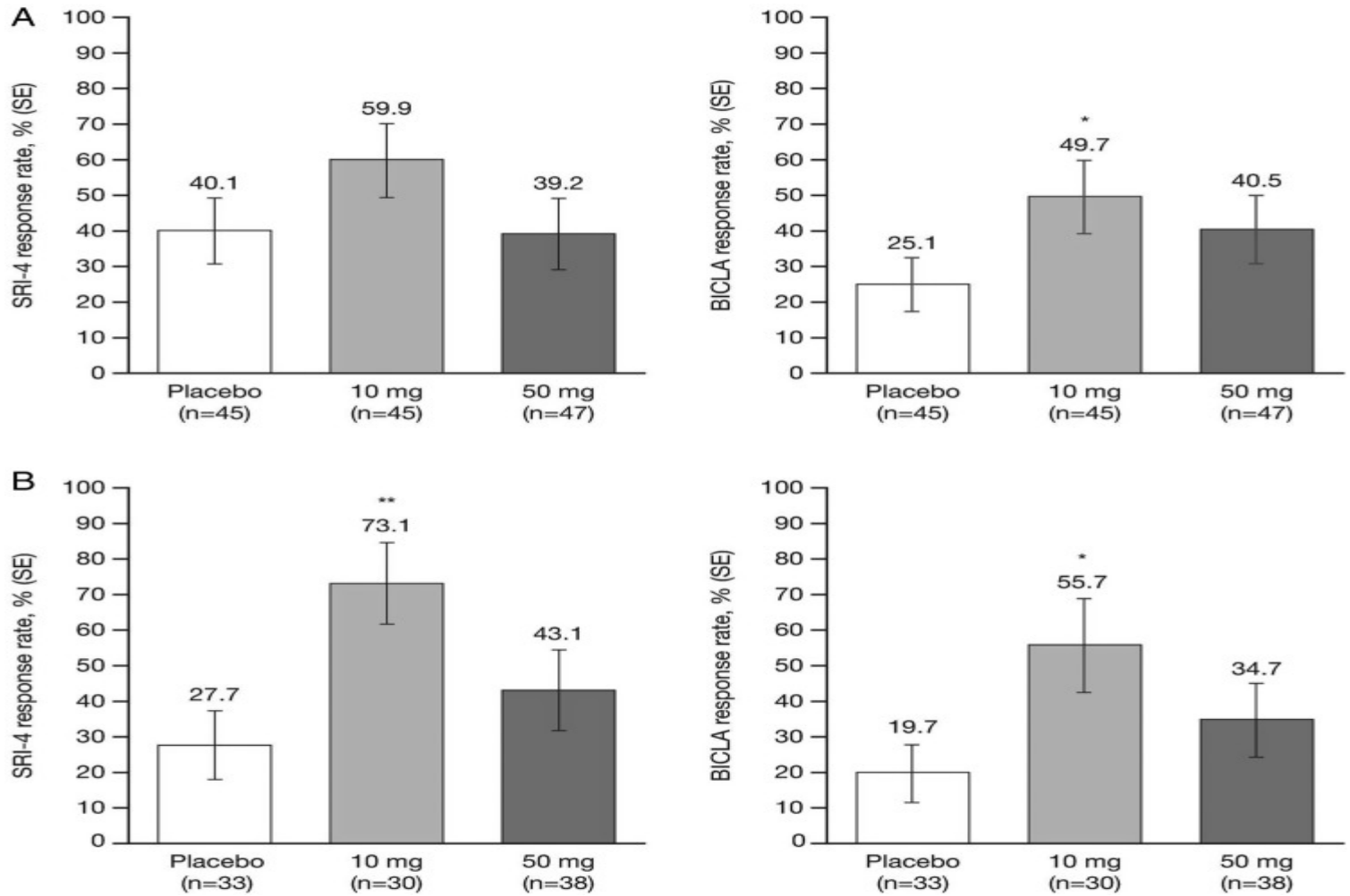
The SLE responder index

The SLE Responder Index (SRI) is a composite outcome that incorporates a modification of SELENA-SLEDAI, BILAG, and a 3-cm visual analog scale of physician rated disease activity (PGA) to determine patient improvement [26]. The SRI was derived following post hoc analysis of data from a phase II belimumab study in SLE to identify subjects with a meaningful clinical improvement in disease activity in response to treatment. The SRI defines a responder as a patient whose disease course fulfils all of the following: (1) at least a 4-point reduction in SELENA-SLEDAI score; (2) no new BILAG A (severe disease activity) or not more than one new BILAG B (moderate disease activity) organ domain score; and (3) no deterioration from baseline in the PGA by at least 0.3 points (or 10 % of 3-point visual analog scale) [27].

The BILAG-Based Composite Lupus Assessment

The BILAG-Based Composite Lupus Assessment (BICLA) is a composite index that was originally derived by expert consensus of disease activity indices [33]. The BICLA response was the primary endpoint in the EMBLEM (Study of Epratuzumab in Serologically-positive Systemic Lupus Erythematosus (SLE) Patients With Active Disease) (NCT00624351), a 12 -week multicenter, phase IIb randomized double-blind placebo-controlled trial that assessed the efficacy and safety of epratuzumab in patients with moderate-to-severe SLE disease activity. Requirement for the BICLA response were: (1) BILAG-2004 improvement (all A scores at baseline improved to B/C/D, and all B scores improved to C or D); (2) no worsening in disease activity (no new BILAG A or more than one new BILAG B score); (3) no worsening of total SLEDAI-2 K score from baseline; (4) no significant deterioration (<10 % worsening) in physician's global assessment; and (5) no treatment failure (initiation of non-protocol treatment) [34].

- What was seen?
  - No significant change in SRI-4
  - Modest change in BICLA


A
SRI-4 response rate, % (SE)
100
90
80
70
60
50
40
30
20
10
0
40.1
59.9
39.2
Placebo (n=45)
10 mg (n=45)
50 mg (n=47)
BICLA response rate, % (SE)
25.1
*
49.7
40.5
Placebo (n=45)
10 mg (n=45)
50 mg (n=47)
B
SRI-4 response rate, % (SE)
27.7
**
73.1
43.1
Placebo (n=33)
10 mg (n=30)
50 mg (n=38)
BICLA response rate, % (SE)
19.7
*
55.7
34.7
Placebo (n=33)
10 mg (n=30)
50 mg (n=38)

“The incidence of severe flares was significantly reduced with 10 mg (n=0) and 50 mg (n=2) combined versus placebo (n=8; p<0.01).”

Patients with disease flares, n/N (%) (from Table 2)

Severe BILAG flares (new BILAG A or two new BILAG B organ domain scores)	5/45 (11.1)	2/43 (4.7)	0/44 (0.0)
Severe SFI flares	8/45 (17.8)	0/43 (0.0)†	2/44 (4.5)†

- Serious Adverse reactions
  - Pulmonary embolism

- You’re sitting on the Pfizer scientific board,
  - What would you do next?

Questions | Discussion

205.934.7442

ccts@uab.edu

www.uab.edu/ccts

PCAMS -1924 7th Ave. South

@cctsnetwork

Search: cctsnetwork