Abstract 68 Figure 1 SM934 restore immune homeostasis in SLE

Technology Major Project New Drug Creation and Manufacturing Program, China (2014Z × 09101002) and National Key Basic Research Programme (973 Programme, 2014CB541906).

Artemisinin analogue SM934 treatment restore immune homeostasis in lupus-prone mice

69

LUPUS IMPACT TRACKER CAN DIFFERENTIATE AMONG TREAT 2 TARGET OUTCOMES IN LUPUS PATIENTS WITH AND WITHOUT CONCURRENT FIBROMYALGIA

¹Meenakshi Jolly, ²Herve Devilliers, ³Iñigo Rua Figueroa, ⁴Javier Narváez-García, ⁵Jaime Calvo Alen, ⁶Maria Galindo Izquierdo, ⁷Francisco Javier López-Longo, ⁸Antonio Fernandez Nebro, ⁹Eva Tomero Muriel, ¹⁰Esther Uriarte Isacelaya, ¹¹Mercedes Freire González*, ¹²Ricardo Blanco Alonso, ¹³Coral Mourinho Rodriguez, ¹⁴José C Rosas-Gómez de Salazar, ¹⁵Gema Bonilla-Hernán, ¹⁶Javier Narváez-García, ¹⁷Eva Salgado-Pérez, ¹⁸Lorena Expósito, ¹Joel Block, ¹³Jose Maria Pego Reigosa. ¹Rush University Medical Center; ²University Hospital of Dijon; ³Hospital De Gran Canaria dr. Negrín; ⁴Hospital de Bellvitge; ⁵Hospital Universitario Araba; ⁶Hospital Universitario 12 De Octubre; ⁷Hospital General Universitario Gregorio Marañón; ⁸UGC de Reumatología, Instituto de Investigación Biomédica de Málaga (IBIMA) Hospital Regional Universitario de Málaga, Spain; ⁹Hospital De La Princesa; ¹⁰Hospital De Donostia; ¹¹Hospital Juan Canalejo A Coruña (CHUAC); ¹²Hospital Marques de Valdecilla; ¹³Complejo hospitalario Universitario Vigo; ¹⁴Hospital De Marina Baixa; ¹⁵Hospital De La Paz; ¹⁶Bellvitge University Hospital, Barcelona; ¹⁷Complejo Hospitalario De Ourense; ¹⁸Hospital Universitario de Canarias

10.1136/lupus-2019-lsm.69

Background Remission and Low Disease activity state (LDAS) are the treat to target (T2T) outcomes used Systemic Lupus Erythematosus (SLE). Lupus Impact Tracker (LIT), a ten item unidimensional patient reported (PRO) tool with good psychometric properties and responsiveness

including to composite response Index (SRI) and T2T outcomes. SLE patients often fibromyalgia (FM). We report discriminant validity of LIT to T2T outcomes in SLE patients stratified by FM from the largest European SLE registry-cohort.

Methods Observational, multi-center data from 1364 adult patients with SLE meeting 1997 ACR criteria were obtained. This included demographics, LIT, disease activity-DA (SLEDAI) and medications. Remission off therapy (ROFT) was defined as SLEDAI=0 without prednisone or Immunosuppressive/s. Remission on-therapy (RONT) was SLEDAI=0 and a prednisone dose 5 mg/day and/or Immunosuppressive/s. LDAS (modified) was SLEDAI 4, prednisone dose 9 mg/day and/or maintenance immunosuppressive/s. Non-optimal (NO) disease status was SLEDAI >4 and/or prednisone dose >9 mg/day and/or immunosuppressive/s in induction dose. LIT values were compared between T2T groups using mixed models among (a) all patients, (b) with and (c) without FM. For Model 1 : RONT and LDAS were combined (given relatively very low DA and lower prevalence of steroid use in LDAS) and compared with NO and ROFT. For model 2, all 4 T2T categories were used.

Results 1232/1364 (90%) were women, and 95% were Caucasian, 76/1364 had FM. Median LIT (Q1, Q3) was 25 (10,46.3). LIT scores were significantly different among T2T categories (table 1). Significant relevant differences were not evident between RONT and LDAS groups: 1) RONT had greater medication use than LDAS (prednisone 5–10 mg/day use of 17.2% vs 8.3%). 2) In LDAS, mean SLEDAI was 2, which can occur without clinical DA. RONT thus fared slightly worse than LDAS in patients evaluation of SLE impact.

Abstract 69 Table 1 LIT values against T2T outcomes stratified by FM status in SLE

Category	Estimated Mean LIT Score	standard error	P value
ALL (n=1356)			
MODEL 1			
Non Optimal	34.57	0.98	Ref
LDAS/RONT	28.22	0.65	<0.001
ROFT	24.61	1.1	<0.001
MODEL 2			
Non Optimal	34.51	0.98	Ref
RONT	30.43	0.94	0.0007
LDAS	27.18	0.72	<0.001
ROFT	24.55	1.06	<0.001
WITH FM (n=76)			
MODEL 1			
Non Optimal	56.76	4.5	ref
LDAS/RONT	48.43	2.7	<0.001
ROFT	35.95	4.4	<0.001
MODEL 2			
Non Optimal	56.64	4.51	ref
RONT	53.95	5.8	0.64
LDAS	45.77	5.06	0.03
ROFT	35.83	5.84	0.006
WITHOUT FM (n=1280)			
MODEL 1			
Non Optimal	33.4	1	ref
LDAS/RONT	27.1	0.7	<0.001
ROFT	23.8	1.1	<0.001
MODEL 2			
Non Optimal	33.3	0.99	Ref
RONT	29.1	1.22	0.0006
LDAS	26.13	1.04	<0.0001
ROFT	23.76	1.37	<0.0001

LIT was able to differentiate between T2T outcomes, and the scores moved in the anticipated direction. Though LIT scores for RONT were lower than NO in those with FM, they did not reach significance. This could potentially be secondary to small number of FM patients and use of 4 comparator categories.

Conclusions LIT can differentiate between T2T outcomes in SLE patients with and without FM. Given its extensive validation in various languages, regions, measurement equivalence, ease of use, acceptability by patients and physicians, and responsiveness to changes in assessments by physician (SLE-DAI, PGA, SRI, T2T) and patient (HRQOL, SLAQ), the tool is indicated for routine patient care, research and clinical trials.

Funding Source(s): None

70

R848 (RESIQUIMOD), A TLR 7/8 AGONIST, ACCELERATES DISEASE AND CAUSES A FATAL MYELOPROLIFERATIVE DISORDER IN NZM 2410 LUPUS-PRONE MICE

¹Jena Wirth, ²Sheryl Coutermarsh-Ott, ¹Ivan Molano, ³Gary S Gilkeson, ⁴Melissa A Cunningham*. ¹MUSC; ²Department of Biomedical Sciences and Pathobiology, Virginia-Maryland College of Veterinary Medicine; ³Division of Rheumatology and Immunology, Medical University of South Carolina; ⁴Medical University of South Carolina

10.1136/lupus-2019-lsm.70

Background Spontaneous murine models of lupus-like disease are used to study the pathogenesis and genetic causes of SLE. Environmentally-induced lupus models (i.e. pristane-induced) are also valuable to study potential triggers of SLE. Both require extended observation. Some accelerants, (i.e. Type I IFN) are used to trigger earlier disease onset. We used a TLR 7/8 agonist (R848), previously reported to induce lupus-like

Abstract 70 Figure 1 Treatment with Resiquimod (RQ) is associated with a marked proliferation of mononuclear cells consistent with histiocytic sarcoma. In acetone treated mice, the normal lymphoid follicular architecture of the spleen is maintained (top, low mag). In these animals, there are rare, scattered cells within the lymphoid follicles that exhibit strong staining for F4/80, consistent with histiocytic cells (bottom). In animals treated with RQ, there is effacement of the normal lymphoid follicles by a proliferation of mononuclear cells. In these mice, 80-90% of spleen cells exhibit strong punctate to diffuse cytoplasmic staining with F4/80 (bottom) consistent with histiocytic cells. The top images are stained with H&E. The bottom images are stained with an F4/80 antibody using a red chromogen and DAB counterstain. Treatment of lupus prone mice with R848/resiquimod (RQ) is associated with a marked proliferation of mononuclear cells in spleen consistent with histiocytic sarcoma.