cell checkpoints and aberrant plasmablast development in SLE has not been previously characterised. Iberdomide (a cereblon modulator) known to induce the degradation of transcription factors IKZF1 and IKZF3 is being explored as a therapeutic target for SLE. The aim of this study was to utilise iberdomide to evaluate the effect of inhibition of IKZF1 and IKZF3 on transcriptional programmes underlying B cell differentiation, gene expression and immunoglobulin production in SLE B cells.

Methods CD19⁺B cells were isolated from peripheral blood of 25 SLE patients and stimulated with IL-2, IL-10, IL-15, CD40L and TLR7 ligand Resiquimod for 5 days to induce plasmablast differentiation. In separate studies, B cells were treated from the outset with iberdomide (10 nM) or vehicle and subsequently differentiated, or differentiated plasmablasts (day 4) were treated with iberdomide or vehicle for 18 hour. Treated plasmablasts underwent fluorescence-activated cell sorting (FACS), and IgG/IgM secretion analysed with ELISA. FACS-sorted CD27-IgD⁺naïve B cells and CD20^{low}CD27⁺CD38⁺plasmablasts were subjected to bulk ultra-low input RNA-seq along with matched baseline B cells. Unsupervised clustering, differential gene expression and pathway analysis were performed on transcriptome data.

Results Day 0 iberdomide (n=9), but not day 4 iberdomide (n=16), significantly reduced the CD20^{low}CD27⁺CD38⁺plasmablast numbers following cell culture (p=0.03). Similarly, Day 0 iberdomide significantly decreased supernatant IgG/IgM concentrations (p=0.050 and 0.017, respectively), but not day 4 iberdomide. RNA-seq of sorted naïve B cells and plasmablasts cultured with day 4 iberdomide demonstrated significant differential gene expression in both populations (400 and 461 differentially modulated genes in naïve B cells and plasmablasts, FDR-adjusted p<0.05). Pathway analysis showed that IKZF1/IKZF3 inhibition resulted in downregulation of JAK-STAT signalling downstream of IL12 (FDR=7.92E-04), IL12 signalling (FDR=0.0014), and p53 signalling regulation of cell death (FDR=0.0043) and showed a trend to upregulation of RUNX1 signalling and Rho GTPase cycle.

Conclusions Iberdomide exposure significantly blocked SLE B cell differentiation into plasmablasts, but did not alter fully differentiated plasmablast viability, confirming the role of IKZF1 and IKZF3 in the process of B cell differentiation into aberrant plasmablasts in SLE. Our study demonstrates that IKZF1 and IKZF3 inhibition results in differential expression of key B cell development transcriptional gene modules in both SLE naïve B cells and plasmablasts.

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UNDERSTANDING SYSTEMIC LUPUS ERYTHEMATOSUS. A QUALITATIVE STUDY OF WOMEN WITH INACTIVE DISEASE

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Background Systemic lupus erythematosus (SLE) is a chronic and cyclic disease with an autoimmune characteristic caused by a combination of environmental, hereditary, stress or congenital predispositions. The acute period of the disease is experienced by the patients as debilitating and of adaptive

psychological changes. In the period of remission of the clinical symptoms of the disease, other adaptive psychological components are used as a way of dealing with the limitations imposed by the disease. Objective: To verify how people with systemic lupus erythematosus use adaptive psychological resources to deal with the disease in this asymptomatic period.

Methods This qualitative study was used to study 9 selected women after the application of SLEDAI (Systemic Lupus Erythematosus Systemic Activity Index) in the post-consultation period with scores equal to or less than 3. Subsequently, the first author's psychologist The qualitative research studies proposed the understanding of the phenomena observed in the scientific environment. The data collected through the recording of participants' speeches were analyzed through content analysis, using the theoretical framework of health psychology. The intention is always to understand the manifestation of something in a group, without the causal intention, only then to give visibility to new strategies both for therapeutic interventions and for new generalizable scientific studies. University Hospital of Southeastern Brazil. In this qualitative study, the strategy of saturation was used to calculate sample size and the number of individuals was held when we verified similarity in responses.

Results 9 female participants were selected. In the speeches of participants, the following topics were identified: Do not think about the existence of the disease; The return to daily activities; Living with other people; The perception of the current body.

Conclusions The perception of the possibility of reactivation of the disease, allows these participants a constant vigil of occasional symptoms that arise. It is such a way to have emotional control over the occasional symptoms that arise. Reviving in anticipation all the trajectory of a possible aggravation of the disease. It is the fear and rationalization of the possibility of reactivation of Systemic Lupus Erythematosus, which allows these participants to have adherence to the continuous treatment in this period.

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CELL BOUND COMPLEMENT ACTIVATION PRODUCTS IN COMBINATION WITH LOW COMPLEMENT C3 OR C4 HAVE HIGH DIAGNOSTIC YIELD IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Cell Bound Complement Activation Products (CB-CAPs), are stable form of classical complement activation, *ex-vivo*, and sensitive and specific marker of SLE. In the present study, we sought to compare the performances of CB-CAPs to gold standard low complement C3 or C4.