depletion (BCD) and to explore the dynamics of repopulation of the PC pool, the mice were killed at different time points after the treatment, and PC and B cells subsets were characterised by FACS and ELISPOT.

Results Our results showed that after depleting short and long-lived PC with bortezomib these cells, including the autoreactive ones, were early regenerated. These results confirmed the hypothesis that new autoreactive PC can be generated from chronically activated B cells. Therefore, the authors treated NZB/W mice with bortezomib in combination with a murine anti-CD20 antibody. The group treated with the combination-therapy showed a heterogeneous grade of BCD more efficient in lymph nodes and spleen respect to BM. The mature, transitional and follicular B cells were efficiently depleted instead marginal zone, germinal center and prepro B cells were particularly resistant. Moreover, although in the mice treated with the combination therapy the repopulation of the PC pool was slower respect to bortezomib-treatment, the supply of newly generated autoreactive PC from hyperreactive-B cells was not completely suppressed.

Conclusions Our data showed that PC are regenerated early after bortezomib mediated depletion. Moreover, anti-CD20 therapy was not able to completely prevent the differentiation of autoreactive B cells in long-lived autoreactive PC after depletion, maybe due to the incomplete BCD in NZB/W mice. These results shed new light on the dynamics and relationship between PC and B cells and emphasise a rationale for developing a combination therapy able to efficiently target both the compartment in autoimmune diseases.

4 TARGETING AUTOACTIVE PLASMA CELLS IN AUTOIMMUNITY: A NEW TREATMENT APPROACH COMBINING PLASMA CELL AND B CELL DEPLETION

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Background and objectives Systemic lupus erythematosus (SLE) is a prototypic systemic autoimmune disease. Compelling evidence suggests that autoreactive memory plasma cells (PC) contribute to the maintenance of autoimmunity and inflammatory processes secreting pathogenic autoantibodies. These cells reside in specific survival niches in the bone marrow (BM) and inflamed tissues where they are resistant to immunosuppression and cytotoxic drugs. In this study the authors tested a new treatment approach aimed at depleting PC and, at the same time, preventing the generation of new autoreactive plasmablasts/PC that results from B cell-hyperactivity. To this aimed the authors combined the PC-depleting drug bortezomib with an anti-CD20 antibody and analysed the PC-B cells dynamics in BM and spleen.

Materials and methods Lupus-prone NZB/W mice were treated or not with a murine anti-CD20 antibody. After 1 week the mice were injected twice with bortezomib to deplete short- and long-lived PC. To assess the grade of PC and B cell