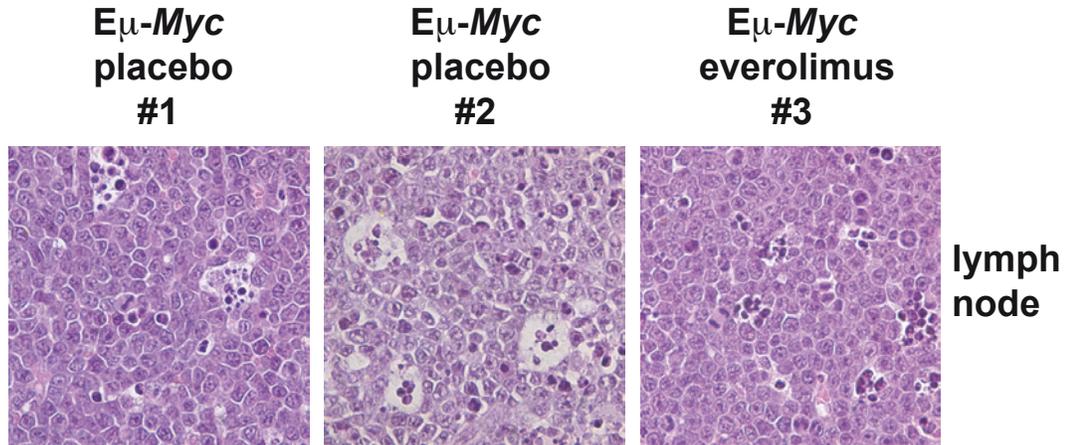
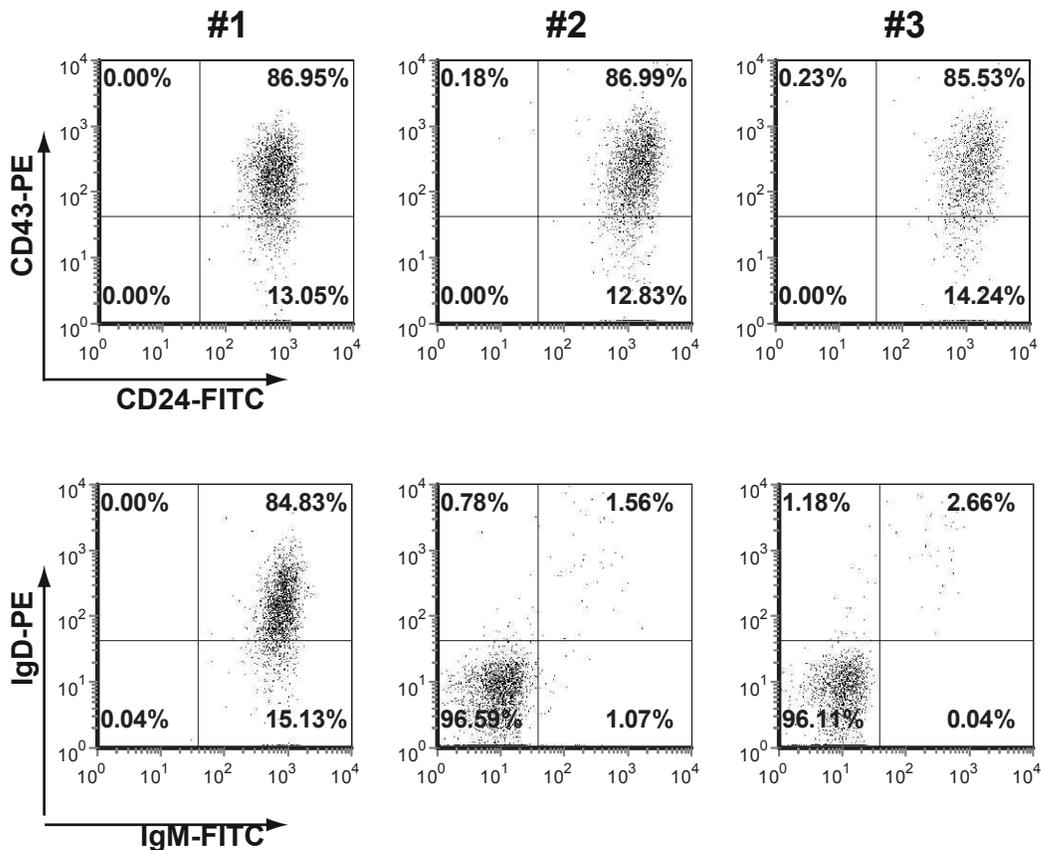


Supplementary Figure S1

A

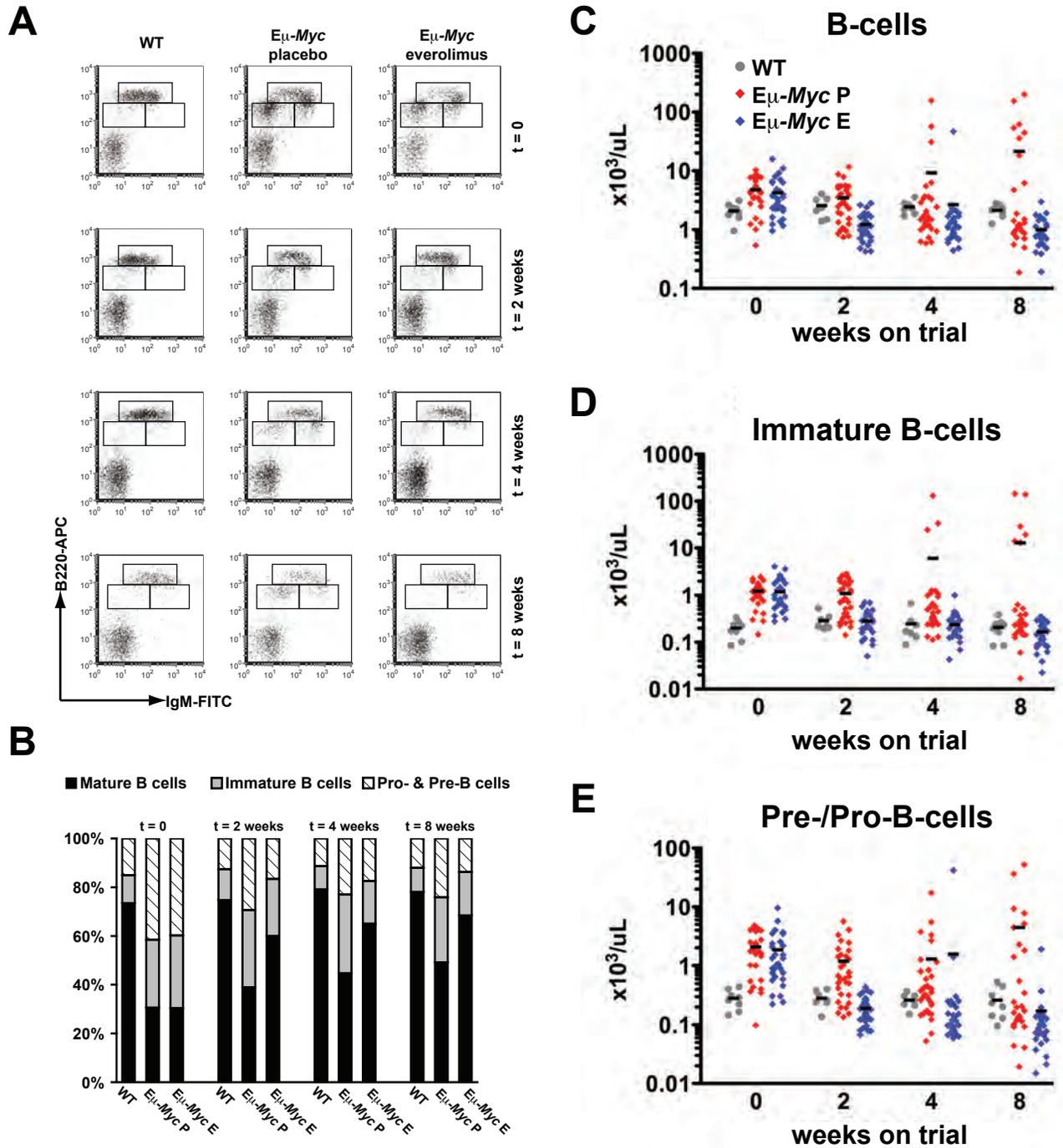


B



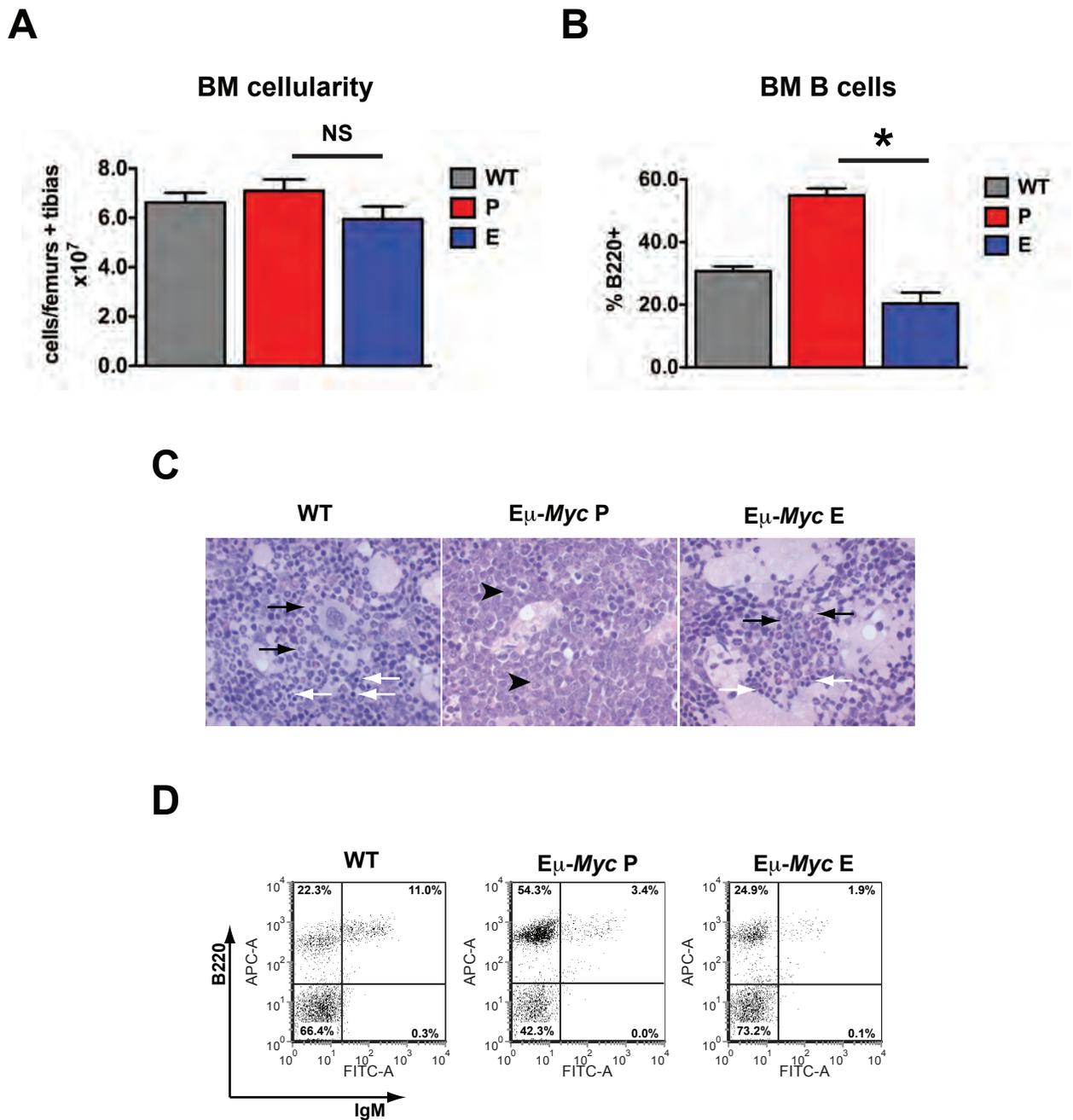
Supplementary Figure S1. Morphology and immunophenotype of tumors arising in placebo and everolimus treated E μ -Myc mice. (A) Representative lymph node morphology of E μ -Myc lymphomas arising in placebo- and everolimus-treated mice. Lymphomas from placebo and everolimus treated mice were similar. Mitotic figures were frequent and tingible-body macrophages were prominent in diseased lymph nodes from mice in both treatment groups. (B) Representative FACS plots showing patterns of surface marker expression in E μ -Myc lymphomas arising in placebo- and everolimus-treated mice. Analysis was performed on B220+ gated lymphocytes. All tumors displayed surface expression of CD24 and CD43. Tumors in placebo mice were IgM+/IgDlo (14/26, 53.8%) e.g. E μ -Myc placebo mouse #1 or IgM/IgD double negative (12/26, 46.2%) e.g. E μ -Myc placebo mouse #2. All tumors arising in everolimus treated mice were IgM/IgD double negative (4/4) e.g. E μ -Myc everolimus mouse #3.

Supplementary Figure S2



Supplementary Figure S2. Everolimus restores B-cell development and reduces the expanded pool of circulating B-cell precursors in *Eμ-Myc* mice. Wild-type littermate control mice (WT) (n=8), *Eμ-Myc* mice treated with placebo (P) (n=34) and everolimus (E) (n=33) were bled at 4-5 weeks of age (t=0) and after 2, 4 and 8 weeks. **(A)** Representative FACS plots showing surface expression of B220 and IgM in B-cells from a WT, transgenic placebo- and transgenic everolimus-treated mouse. **(B)** Average percentage of cells gated as mature B-cells (B220^{hi}, IgM⁺), immature B-cells (B220^{lo}, IgM⁺) and pro/pre-B cells (B220^{lo}, IgM⁻) for each group of mice. **(C)** Absolute B-cell numbers in the peripheral blood for individual mice were calculated from the white cell count and the percentage of B220⁺ cells. **(D and E)** Numbers of circulating cells in B-cell subsets for individual mice were calculated from B-cell numbers and the percentage of cells falling into the immature B-cell and Pro-/Pre-B cell gates using flow cytometry. For C-E horizontal bars represent mean values.

Supplementary Figure S3



Supplementary Figure S3. B-cell precursors in the bone marrow of $E\mu$ -Myc mice are reduced by mTORC1 inhibition. 6-7 week old wild-type littermate control mice (WT) (n=5), $E\mu$ -Myc mice treated with placebo (P) for 2 weeks (n=5) and $E\mu$ -Myc mice treated with everolimus (E) for 2 weeks (n=7) were analyzed. **(A)** Average bone marrow (BM) cellularity (P vs E, p=0.10). **(B)** Percent B220+ bone marrow (BM) cells (P vs E, p<0.001). **(C)** H&E stained sternal bone marrow in a representative mouse from each group. White arrows indicate erythroblasts, black arrows indicate granulocytes and arrow-heads indicate lymphoblasts. **(D)** FACS plots showing surface expression of B220 and IgM in bone marrow isolated from a representative mouse from each group. Error bars represent the SEM. p values were generated using a Student's unpaired 2-tailed t-test, *=p<0.05, NS=not significant.