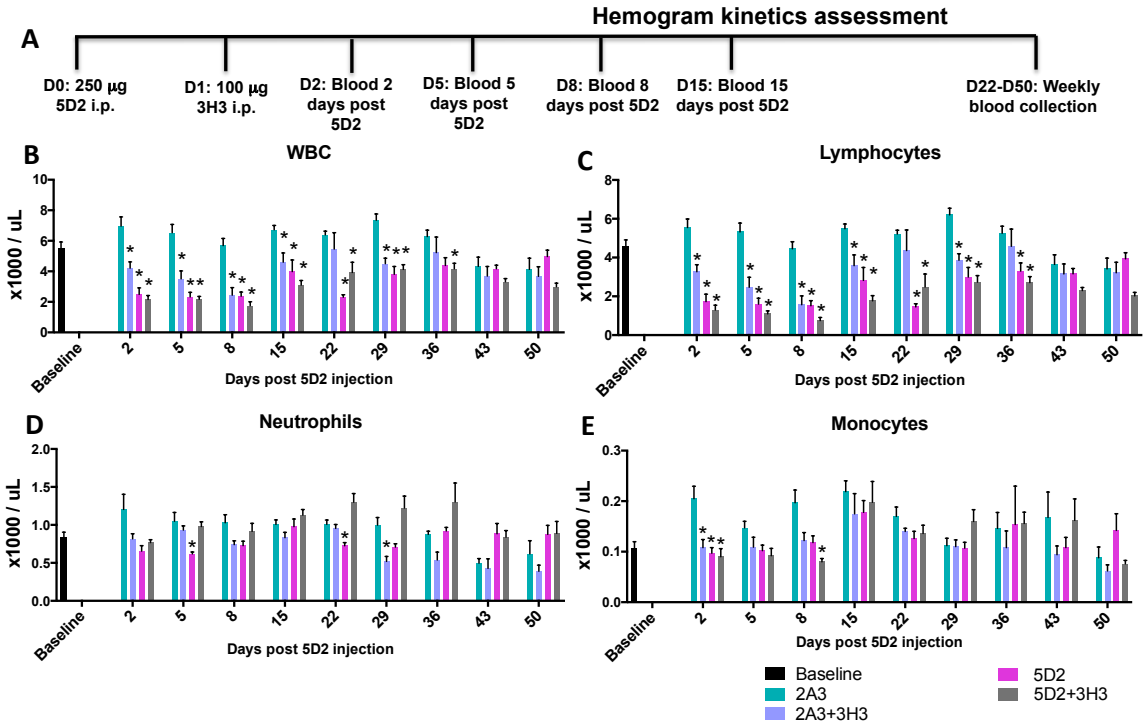
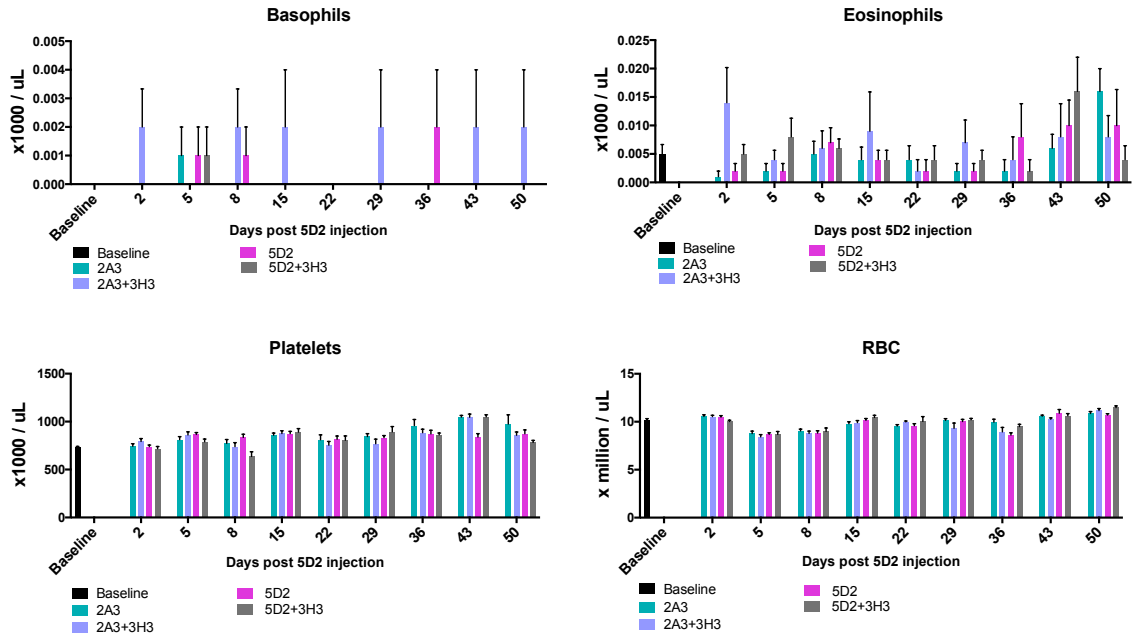
Supplementary Figure 1



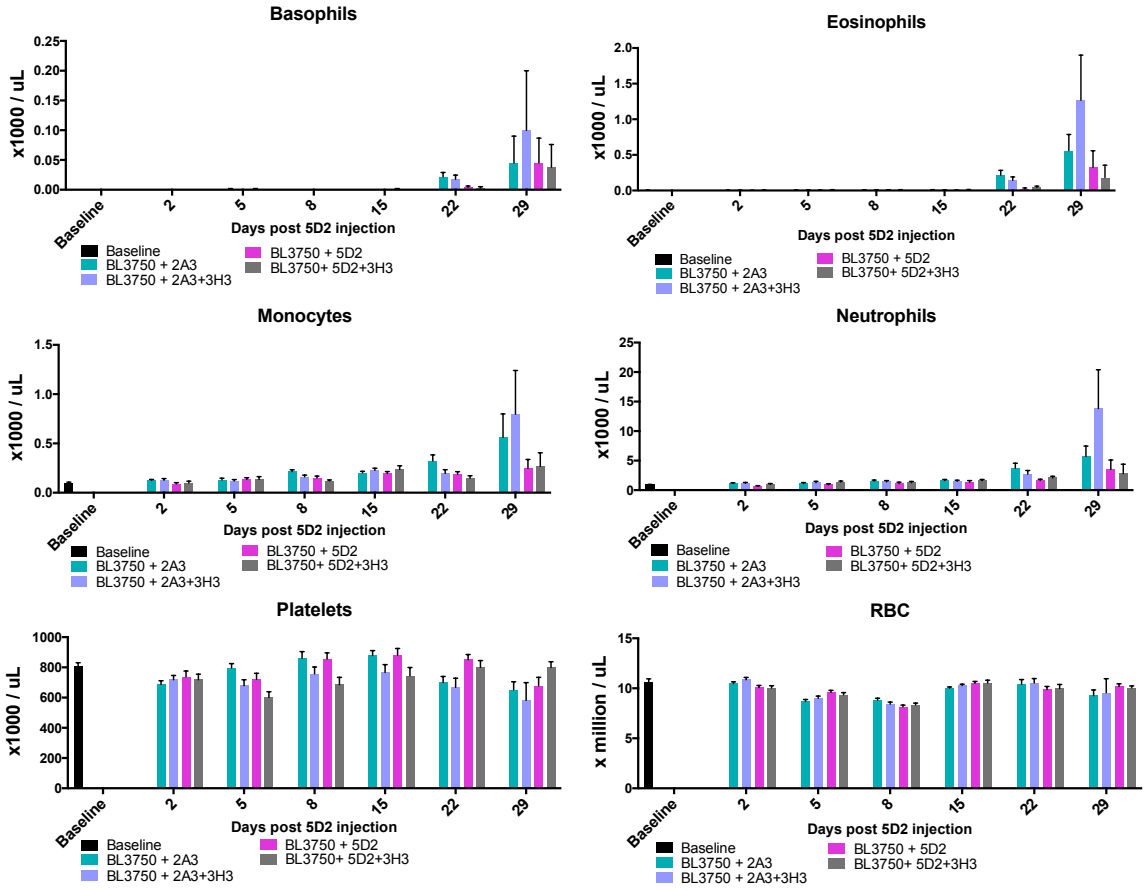
Supplementary Figure 1: Treatment with anti-CD20 and anti-CD137 reduces white blood cell numbers in WT mice without lymphoma. Blood samples were collected for hemogram assessment according to the experimental design proposed in **A**. White blood cell (**B**), lymphocyte (**C**), neutrophil (**D**) and monocyte (**E**) numbers are presented. Data shown is pooled from 2 independent experiments (n (2A3) = 10; n (5D2) = 10; n (3H3) = 10; n (5D2+3H3) = 10). Statistical analysis was calculated using Multiple T tests and a Holm-Sidak Method for multiple comparisons, *P < 0.05 was considered statistically significant.

Supplementary Figure 2



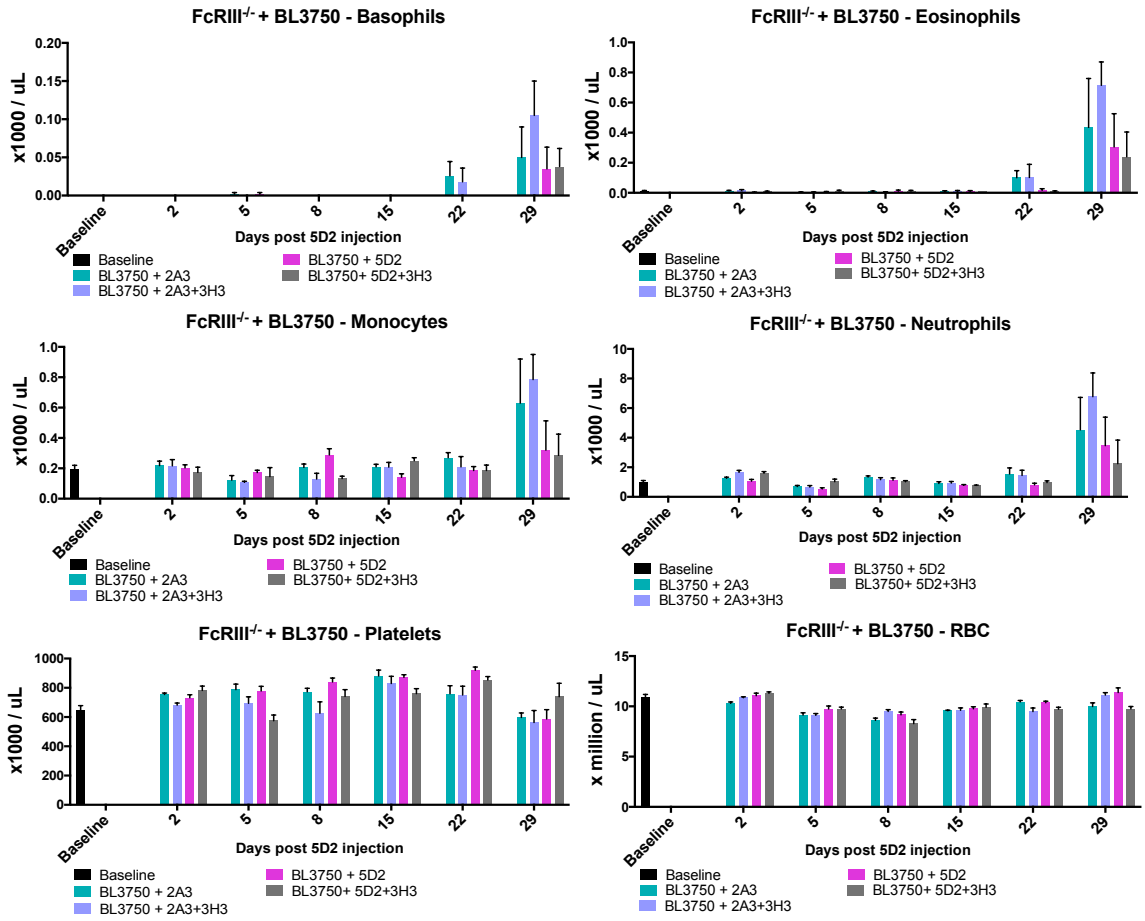
Supplementary Figure 2: Basophils, eosinophils, platelets and red blood cells (RBC) numbers following anti-CD20 and anti-CD137 treatment. Blood samples were collected for hemogram assessment according experimental setting proposed in **Supplementary Figure 1A**. Data shown is pooled from 2 independent experiments (n (2A3) = 10; n (5D2) = 10; n (3H3) = 10; n (5D2+3H3) = 10). Statistical analysis was calculated using Multiple T tests using Holm-Sidak Method for multiple comparisons.

Supplementary Figure 3



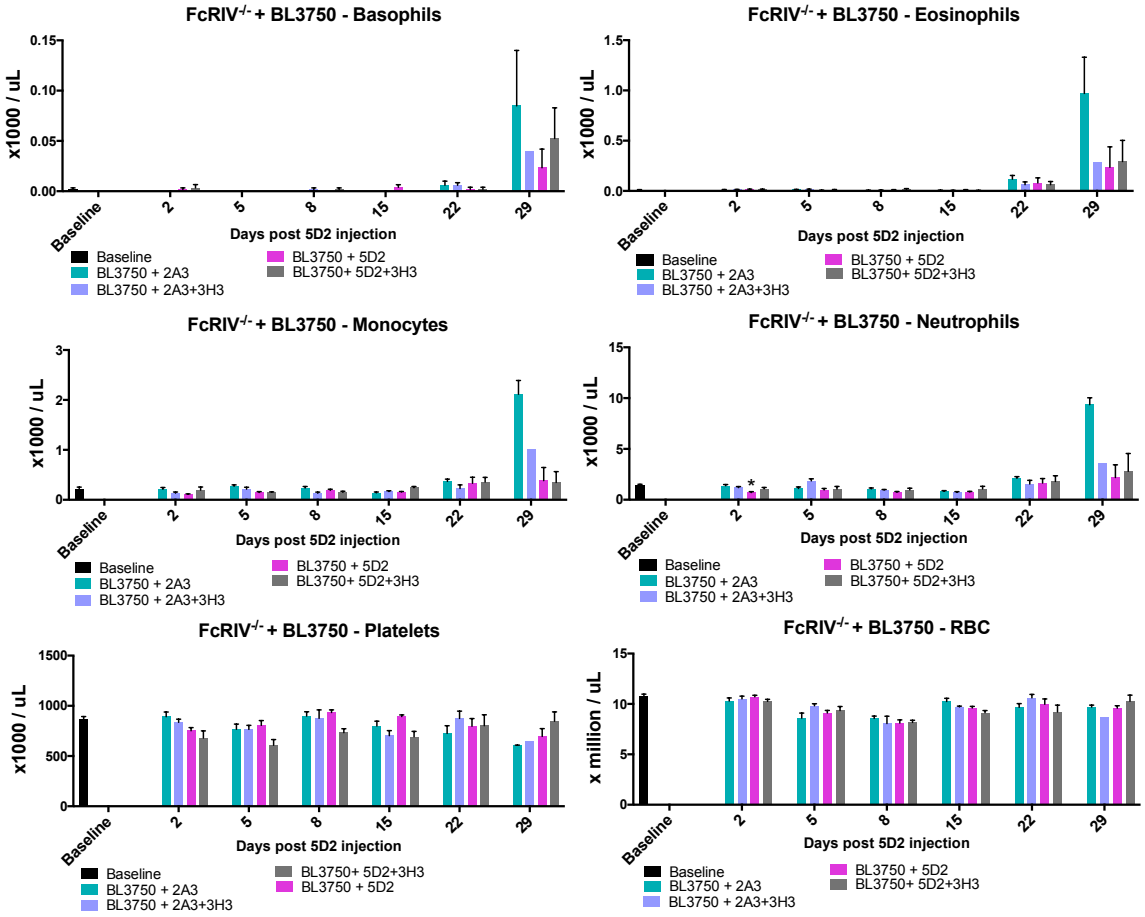
Supplementary Figure 3: Basophils, eosinophils, monocytes, neutrophils, platelets and red blood cells (RBC) numbers following anti-CD20 and anti-CD137 treatment in tumor bearing mice. 1 x 10^5 BL3750 cells were injected i.v. into C57BL/6 wild-type (WT) mice at D0. Control Ig (2A3, 250 µg i.p.) or anti-CD20 (clone 5D2, 250 µg i.p.) was administered on day 4, and anti-CD137 (clone 3H3, 100 µg i.p.) either alone or in combination on day 5. Blood samples were collected for hemogram assessment according to the experimental design proposed in **Figure 2A**. Data shown is pooled from 2 independent experiments (n (2A3) = 10; n (5D2) = 10; n (3H3) = 10; n (5D2+3H3) = 10). Statistical analysis was calculated using Multiple T tests using Holm-Sidak Method for multiple comparisons.

Supplementary Figure 4



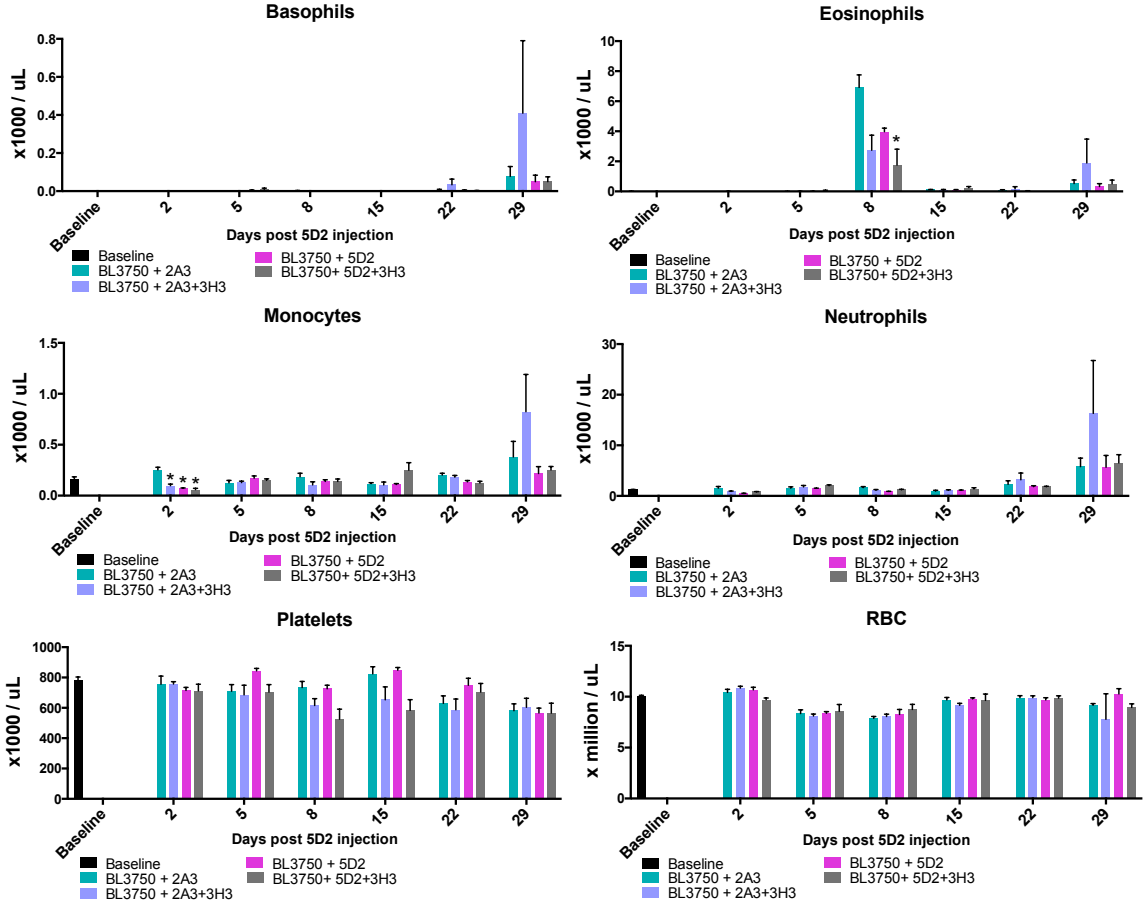
Supplementary Figure 4: Basophils, eosinophils, monocytes, neutrophils, platelets and red blood cells (RBC) numbers following anti-CD20 and anti-CD137 treatment in FcRIII$^{-/-}$ mice. 1 x 10^5 BL3750 cells were injected i.v. into FcRIII$^{-/-}$ mice at D0. Control Ig (2A3, 250 µg i.p.) or anti-CD20 (clone 5D2, 250 µg i.p.) was administered on day 4, and anti-CD137 (clone 3H3, 100 µg i.p.) either alone or in combination on day 5. Blood samples were collected for hemogram assessment according to the experimental design proposed in **Figure 2A**. Results are representative of one experiment, n = 6 each group. Statistical analysis was calculated using Multiple T tests using Holm-Sidak Method for multiple comparisons.

Supplementary Figure 5



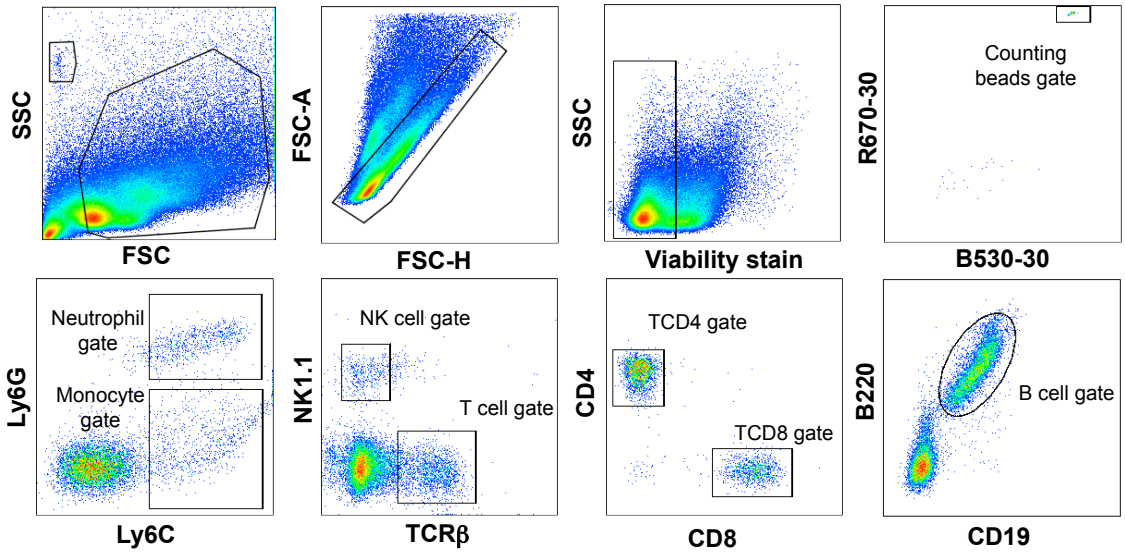
Supplementary Figure 5: Basophils, eosinophils, monocytes, neutrophils, platelets and red blood cells (RBC) numbers following anti-CD20 and anti-CD137 treatment in FcRIV$^{-/-}$ mice. 1 x 10^5 BL3750 cells were injected i.v. into FcRIV$^{-/-}$ mice at D0. Control Ig (2A3, 250 μg i.p.) or anti-CD20 (clone 5D2, 250 μg i.p.) was administered on day 4, and anti-CD137 (clone 3H3, 100 μg i.p.) either alone or in combination on day 5. Blood samples were collected for hemogram assessment according to the experimental design proposed in **Figure 2A**. Results are representative of one experiment, n = 6 each group. Statistical analysis was calculated using Multiple T tests using Holm-Sidak Method for multiple comparisons.

Supplementary Figure 6



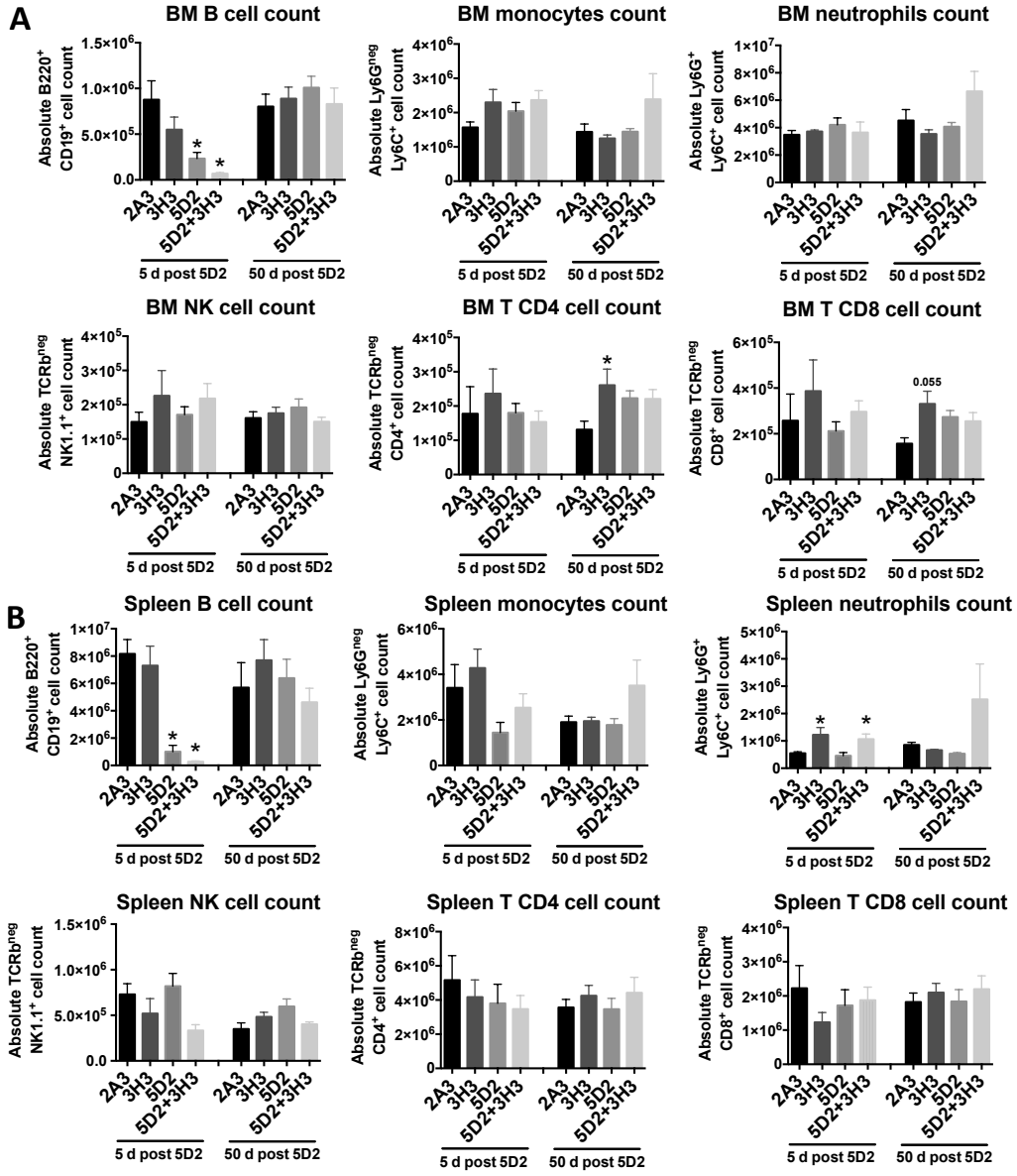
Supplementary Figure 6: Basophils, eosinophils, monocytes, neutrophils, platelets and red blood cells (RBC) kinetics after following anti-CD20 and anti-CD137 treatment in FcγR $^{-/-}$ mice. 1 x 10^5 BL3750 cells were injected i.v. into FcγR $^{-/-}$ mice at D0. Control Ig (2A3, 250 µg i.p.) or anti-CD20 (clone 5D2, 250 µg i.p.) was administered on day 4, and anti-CD137 (clone 3H3, 100 µg i.p.) either alone or in combination on day 5. Blood samples were collected for hemogram assessment according to the experimental design proposed in **Figure 2A**. Results are representative of one experiment, n = 6 each group. Statistical analysis was calculated using Multiple T tests using Holm-Sidak Method for multiple comparisons.

Supplementary Figure 7



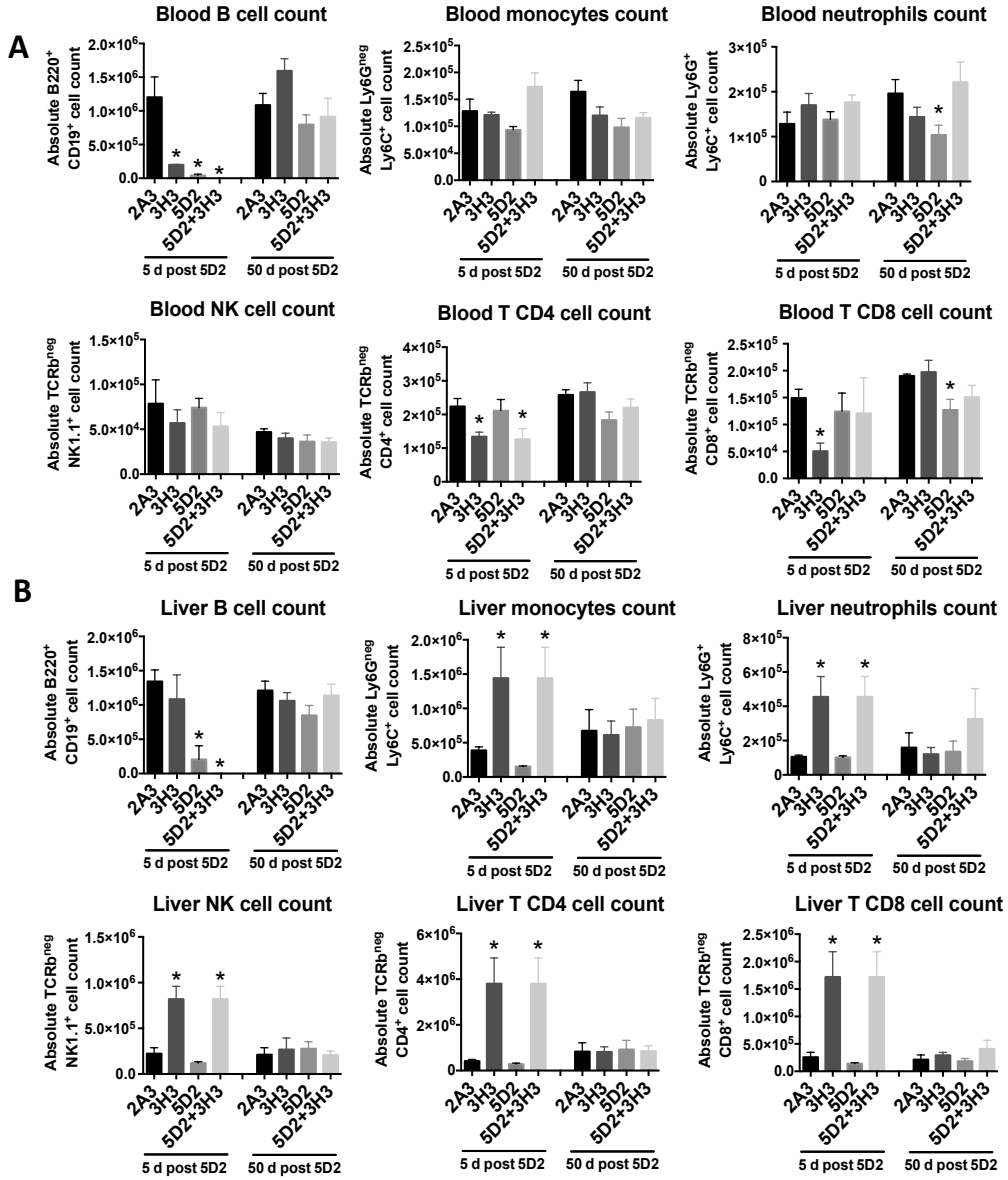
Supplementary Figure 7: Gating strategy for leucocyte counting assays. Dot plots are representative from a spleen homogenate.

Supplementary Figure 8



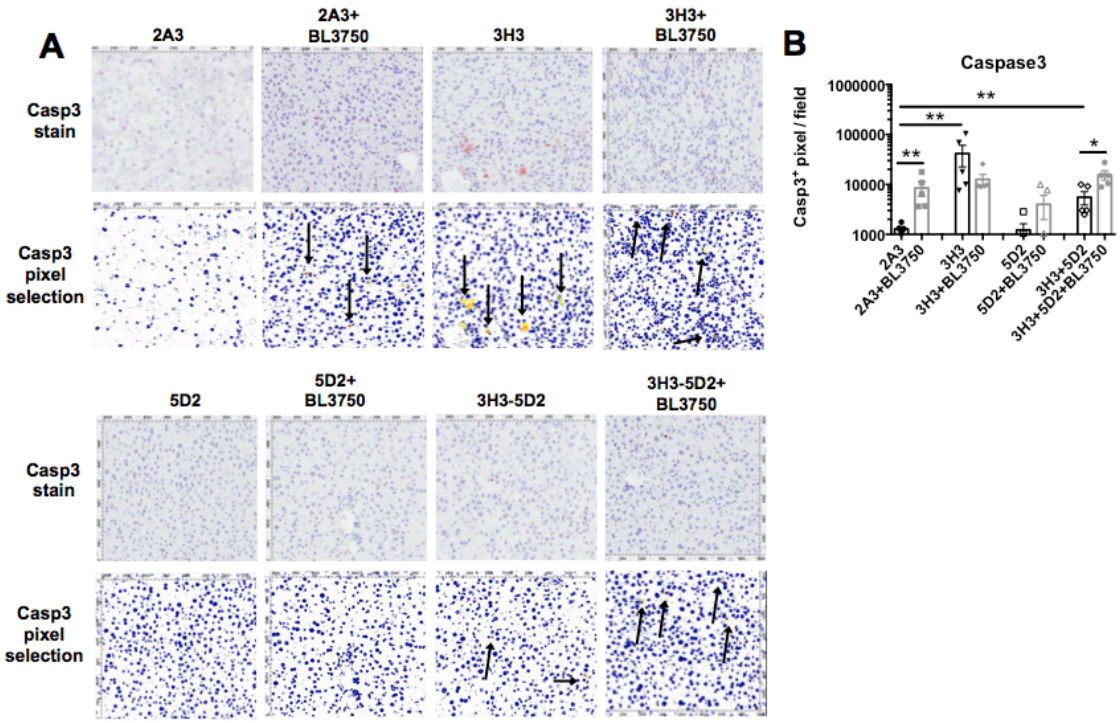
Supplementary Figure 8. Treatment with anti-CD20 and anti-CD137 mAbs reduces B cell numbers in bone marrow (BM) and spleen compartments. Leukocyte quantification from BM (**A**), and spleen (**B**), after anti-CD20 (clone 5D2, 250 μg i.p.) or isotype control antibody (clone 2A3 250 μg i.p.) on day 4, and anti-CD137 (clone 3H3, 100 μg i.p.) treatment either alone or in combination on day 5 in naive C57BL/6J mice treated according to **Figure 1A**. Blood and organs were collected for leukocyte assessment 5 and 50 days post 5D2 treatment. Bead-based absolute counting was utilized to quantify monocytes/macrophages ($Ly6G^{neg}Ly6C^{+}$), neutrophils ($Ly6G^{+}Ly6C^{+}$) NK cells, ($TCR\beta^{neg}NK1.1^{+}$), $CD4^{+}$ T cells ($TCR\beta^{+}CD4^{+}$), $CD8^{+}$ T cells ($TCR\beta^{+}CD8^{+}$). Results are representative of one experiment n = 5 each group. *P < 0.05 was considered statistically significant by Mann-Whitney test.

Supplementary Figure 9



Supplementary Figure 9. Treatment with anti-CD20 and anti–CD137 mAbs reduces B cell numbers in peripheral blood (blood) and liver compartments. Leukocyte quantification from blood (**A**), and liver (**B**), after anti-CD20 (clone 5D2, 250 μg i.p.) or isotype control antibody (clone 2A3 250 μg i.p.) on day 4, and anti-CD137 (clone 3H3, 100 μg i.p.) treatment either alone or in combination on day 5 in naive C57BL/6J mice treated according to **Figure 1A**. Blood and organs were collected for leukocyte assessment 5 and 50 days post 5D2 treatment. Bead-based absolute counting was utilized to quantify monocytes/macrophages ($Ly6G^{neg}Ly6C^{+}$), neutrophils ($Ly6G^{+}Ly6C^{+}$) NK cells, ($TCR\beta^{neg}NK1.1^{+}$), $CD4^{+}$ T cells ($TCR\beta^{+}CD4^{+}$), $CD8^{+}$ T cells ($TCR\beta^{+}CD8^{+}$). Results are representative of one experiment n = 5 each group. *$P < 0.05$ was considered statistically significant by Mann-Whitney test.

Supplementary Figure 10



Supplementary Figure 10: Greater tissue Caspase-3 levels indicate enhanced liver injury in anti-CD137 and anti-CD137/CD20 treated mice. Caspase 3 immunohistochemistry was performed in liver formalin-fixed sections. Slides were scanned using an Aperio XT slide scanner using 40x scan magnification. **A**: The Aperio Algorithm: Positive Pixel Count V9 was used to quantify positive pixels. A Hue Value = 0.1 was set up to select DAB (Caspase 3) staining and quantify the respectively pixels (selected as yellow by the image analysis) from different groups. Representative Caspase 3 IHC images from liver are shown in the first line according the treatment group, pixel selection by image analysis is represented in the line below. **B**: DAB (Caspase 3)-positive pixel quantification from one field/liver/group is represented. Statistical analysis was performed using Mann-Whitney test, $^{**}P < 0.01$; $n = 5$.