HuMab-7D8, a monoclonal antibody directed against the membrane-proximal small loop epitope of CD20 can effectively eliminate CD20^{low} expressing tumor cells that resist rituximab- mediated lysis

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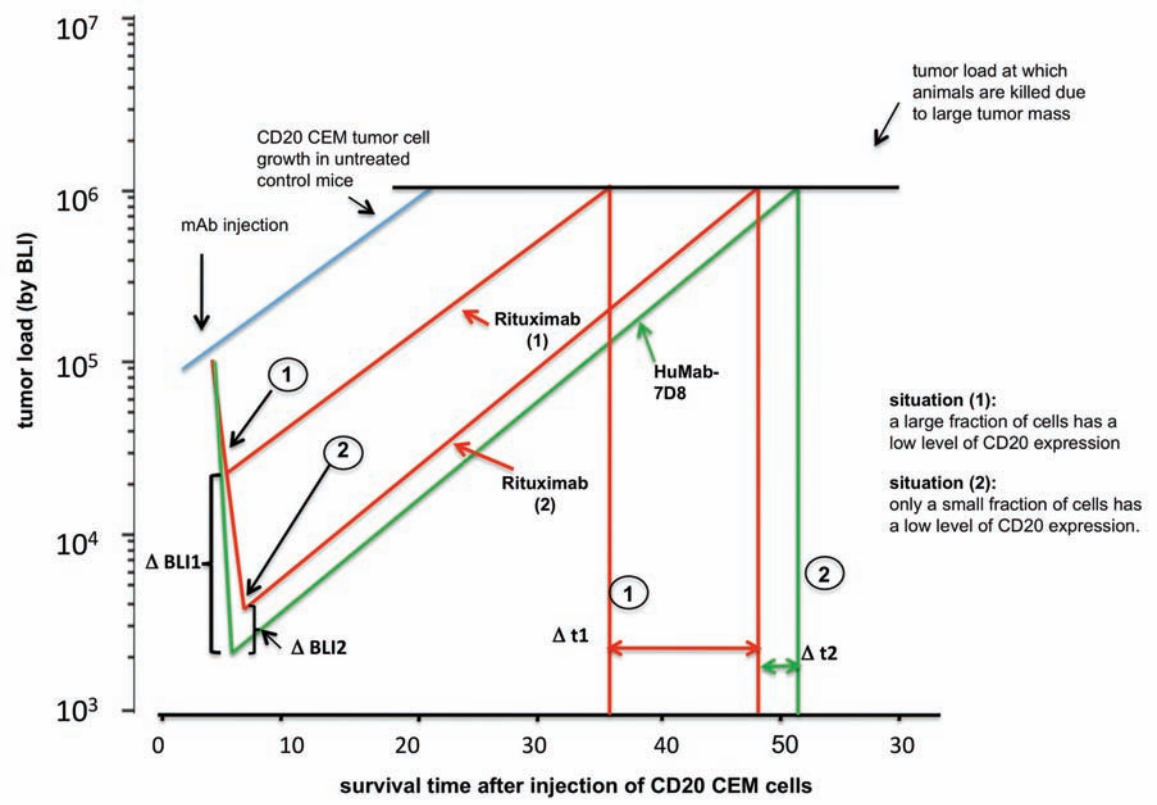

Online Supplementary Figure S1. A schematic model illustrating the effect of CEM-CD20 treatment with rituximab or Humab-7D8 on BLI and survival time. Mice received a polyclonal CD20 transduced cell population with a broad pattern of CD20-expression, from low to high but it also included a small proportion of CD20-negative cells (see for example Figure 2B). The blue line in the figure shows the exponential growth curve of CD20-CEM cells in non-treated control mice (compare BLI curve figure 3B). The green line reflects the maximal estimated 98% cell kill that can be achieved with an antibody that kills all cells, having high or low level of CD20 expression (in this case HuMab-7D8). A small proportion of the cells does not express CD20 (in this example assumed to be 2%, see also Figure 2B) and thus cannot be eliminated. The red lines illustrate: (1) assuming that a large proportion of the cells has a low level of CD20 expression (in the graph 20% is taken as an example) this would have resulted in a large difference in surviving fraction between HuMab-7D8 *versus* rituximab treatment because rituximab less effectively kills the cells with low CD20 expression. Although the negative cells also survive, this nevertheless would have resulted in significant differences in BLI values (ΔBLI1) and survival curves (Δt1); (2) assuming that only a small fraction of cells are CD20^{low}, one would find that HuMab-7D8 still kills all cells except the CD20-negative cells. Rituximab obviously could not kill the negative cells but CD20^{low}-expressing cells would also survive. This difference is, however, small, and estimated to be in the order of 2-fold. The differences in the BLI-derived growth curves (ΔBLI1) and in the survival time (Δt2) are, therefore, small and within the variation of the assay. The latter is what we observed in this study.