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(54) Title: VARIANT CD3-BINDING DOMAINS AND THEIR USE IN COMBINATION THERAPIES FOR THE TREATMENT OF DISEASE

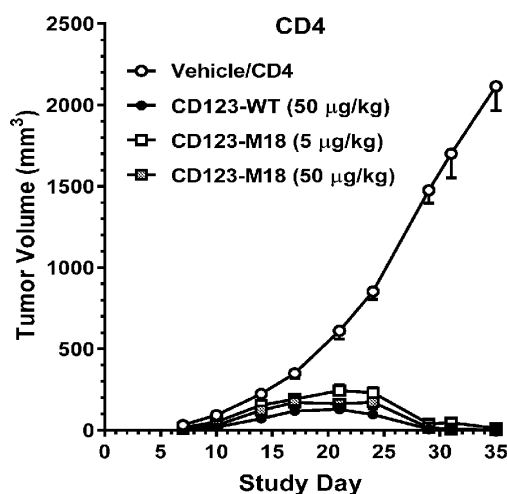


Figure 17A

(57) Abstract: The present invention is directed to DA x CD3 Binding Molecules comprising a vCD3-Binding Domain, which comprises a CDRH1 Domain, a CDRH2 Domain, a CDRH3 Domain, a CDRL1 Domain, a CDRL2 Domain, and a CDRL3 Domain, at least one of which differs in amino acid sequence from the amino acid sequence of the corresponding CDR of a rCD3-Binding Domain, wherein the DA x CD3 Binding Molecule comprising such vCD3-Binding Domain exhibits an altered affinity for CD3, relative to a DA x CD3 Binding Molecule comprising such rCD3-Binding Domain. The invention particularly concerns to such DA x CD3 Binding Molecules comprising a vCD3-Binding Domain which exhibit reduced affinity for CD3 and are capable of mediating redirected killing of target cells expressing a DA and exhibit lower levels of cytokine release relative to a DA x CD3 Binding Molecule comprising a rCD3-Binding Domain. The invention particularly concerns the use of DA x CD3 Binding Molecules comprising a vCD3-Binding

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