rhIL-7-hyFc (efineptakin alfa; NT-I7) enhances the anti-tumor response when combined with hIL-2/TCB2c complex

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Abstract

rhIL-7-hyFc (efineptakin alfa; NT-I7) is a potent T cell amplifier, with a homodimeric interleukin-7 (IL-7) fused to the hybridizing IgG1/Fc immunoglobulin domain. Previous work has shown that in mice, NT-I7 dramatically increases tumor-infiltrating CD8+ T cells as well as the expression of granzyme B in the tumor. Here, we investigated the anti-tumor effect of NT-I7 in combination with a T cell activator, SLC-3010 (hIL-2/TCB2c complex), in MC38 tumor-bearing mice. Because TCB2 is an antibody specific for IL-2 that blocks interaction of IL-2 and IL-2R (CD25), SLC-3010 can selectively activate T cells while deactivating Treg activity. Mice were administered a single dose of NT-I7 or SLC-3010 via intramuscular or intravenous injection, respectively. The combination of NT-I7 with SLC-3010 enhanced the anti-tumor response with increased number and frequency of CD8+ T cells as well as granzyme B expression in the tumor. The number of PD-1+ T cells peaked at day 4 and day 7 by SLC-3010 and NT-I7, respectively. The number of Tregs in the tumor was slightly increased by NT-I7 and SLC-3010, but it was not statistically significant. Interestingly, NT-I7, but not SLC-3010, increased the frequency of PD-1+ T cells in the draining lymph node. Meanwhile, SLC-3010 significantly increased the number of PD-1+ CD8+ T cells in the tumor. Our data suggests that NT-I7 can be applied in combination with other immunotherapies such as IL-2 to enhance the anti-tumor response.

PhII-hyFc (efineptakin alfa; NT-I7)

IL-2/TCB2 Complex (SLC-3010)

Schematic Hypothesis

Anti-tumor synergy

NT-I7 and SLC-3010 increase CD8+ T cells in the tumor and TDLN

NT-I7 and SLC-3010 increase PD-1+ CD8+ T cells in the tumor

Cytokine expression in CD8+ T cells

Conclusion

NT-I7 can be applied in combination with other immunotherapies such as IL-2/TCB2c (SLC-3010) to enhance the anti-tumor response.

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