O 22 Role of CD30 translocation in Hodgkin lymphoma for the mechanism of action of the antibody drug conjugate SGN35/Acetris

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Antibody drug conjugates (ADC) evolved as promising tools in cancer therapy to target cell-damaging drugs to malignant cells while sparing healthy cells. The malignant cells in Hodgkin lymphoma (HL) selectively express CD30 and the CD30-binding tubulin-damaging ADC (SGN-35/Acetris) was evaluated in HL. Although only weakly effective against HL cells in vitro, it had an excellent clinical efficacy. Thus, the precise mechanism of action remains elusive and will be investigated in this proposal. In tumor tissue, the malignant cells communicate with non-malignant stroma cells, which in turn form a tumor-supporting niche and often prevent drug-induced apoptosis. We showed that malignant HL cells shed the CD30 ectodomain (sCD30) and CD30-expressing extracellular vesicles (CD30EVs), which bind to the CD30 ligand (CD30L) on non-malignant cells. We therefore hypothesize that, in addition to its direct cancer cell toxicity, this target antigen translocation may enable ADCs to damage supporter cells. We will compare the impact of CD30EVs and sCD30 in vitro and animal models. This investigation will help to understand the mechanism of SGN-35, contribute to overcome resistance mechanisms and help to select feasible novel targets for future ADCs.

Literature


