

Anti-CEACAM6 AFAIKL2 Antibody Fragment/Jack Bean Urease Immunoconjugate L-DOS47

National Cancer Institute

Source

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A lyophilized formulation of DOS47, an immunoconjugate composed of AFAIKL2, a recombinant camelid single-domain antibody which recognizes carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6), and the enzyme urease derived from the plant *Canavalia ensiformis* (Jack bean), with potential antineoplastic activity. Upon intravenous administration, the AFAIKL2 antibody fragment moiety of L-DOS47 specifically targets and binds to CEACAM6 expressed on certain tumor cells. In turn, the urease moiety of L-DOS47 catalyzes the hydrolysis of urea into ammonia, which is further hydrolyzed to produce hydroxyl ions, and causes a locally increased concentration of the toxic waste product ammonia, which under normal conditions is converted into the nontoxic substance urea via the urea cycle. This increases the pH of the tumor microenvironment and alkalinizes the highly acidic environment that is needed for cancer cell survival and proliferation. In addition, the ammonia diffuses into cancer cells and exerts a cytotoxic effect. Altogether, this leads to cell death of CEACAM6-expressing cancer cells. The naturally-occurring enzyme urease catalyzes the hydrolysis of urea into ammonia and carbon dioxide. CEACAM6, a tumor-associated antigen and CEA family member, is overexpressed in a variety of tumor cells and plays a key role in tumor initiation, progression, metastasis and survival.