Anti-mesothelin-Pseudomonas Exotoxin 24 Cytolytic Fusion Protein LMB-100

National Cancer Institute

Source

National Cancer Institute. Anti-mesothelin-Pseudomonas Exotoxin 24 Cytolytic Fusion Protein LMB-100. NCI Thesaurus. Code C121653.

An anti-mesothelin (MSLN) recombinant cytolytic fusion protein (cFP) composed of a humanized Fab fragment of anti-MSLN monoclonal antibody SS1 linked to a truncated and de-immunized 24 kDa fragment of the Pseudomonas exotoxin (PE) (PE24), with potential antineoplastic activity. Upon intravenous administration of anti-MSLN-PE24 cFP LMB-100, the anti-MSLN moiety targets and binds to MSLN-expressing tumor cells. Upon binding and internalization through endocytosis, the toxin moiety ADP-ribosylates and inactivates eukaryotic elongation factor 2 (eEF2), preventing the elongation step of protein synthesis and leading to both an inhibition of protein synthesis and an induction of MSLN-expressing tumor cell apoptosis. MSLN, a tumor-associated antigen overexpressed in a variety of cancer cell types, plays a key role in tumor cell proliferation and migration. The engineered PE24 portion of LMB-100 does contain the targeting domain and furin cleavage site, which are needed for cytotoxicity, but most of the translocation domain II is deleted and the catalytic domain III contains point mutations, which result in the deletion and silencing of most T- and B-cell epitopes; therefore, the immunogenicity and toxicity is reduced compared to non-engineered PE toxin, which allows for the administration of larger doses of LMB-100.