US-FDA Approved Antibody-Drug Conjugates (ADCs) For Cancer Therapy

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Introduction: Antibody drug conjugates (ADCs) were developed to enhance the specificity and selectivity of anti-cancer therapeutics as potential alternatives to conventional cancer treatments. They are typically composed of an antibody, a linker, and a cytotoxic agent. This review focuses on FDA approved ADCs, what antigen each ADC targets, and the use of specific cytotoxic agents.

Methods: The databases PubMed and MEDLINE were searched to identify studies that included information on FDA approved antibody drug conjugates. Some inclusion criteria include randomized controlled trials and non-randomized controlled clinical trials. The data collected includes the pharmacodynamics, presence of a specific antigen, advantages and disadvantages, clinical trials as well as challenges for ADCs.

Results: Ozogamicin is a cytotoxic agent conjugated with one of the two antibodies (inotuzumab and gemtuzumab). Inotuzumab targets CD22 and Gemtuzumab targets CD33. Upon binding to the targets, the cytotoxic agent is internalized and it causes cell death by DNA strand scission.Vedotin, also known as monomethyl auristatin E (MMAE), is a synthetic antineoplastic agent. Brentuximab vedotin, polatuzumab vedotin, and enfortumab vedotin target CD30, CD79b, and Nectin-4, respectively on cells, and cause the ADC to be internalized via endocytosis. As the vesicle fuses with a lysosome, the linker that binds MMAE to the antibody is cleaved to release MMAE. MMAE in turn binds to microtubules within the cell to inhibit their assembly, and ultimately cause cell arrest. Lutathera utilizes a radioisotope link via a chelating molecule that target somatostatin receptors on cancer cells and is taken up into the cell. Ionizing radiation is released from the radionuclide to cause breaks in the DNA of the tumor cells.

Conclusion: ADCs could be used to target antigens such as CD22, CD33, CD20, CD30, CD79b, and Nectin-4 resulting in decrease in the progression of different types of cancers ultimately leading to favorable survival rates in cancer patients.