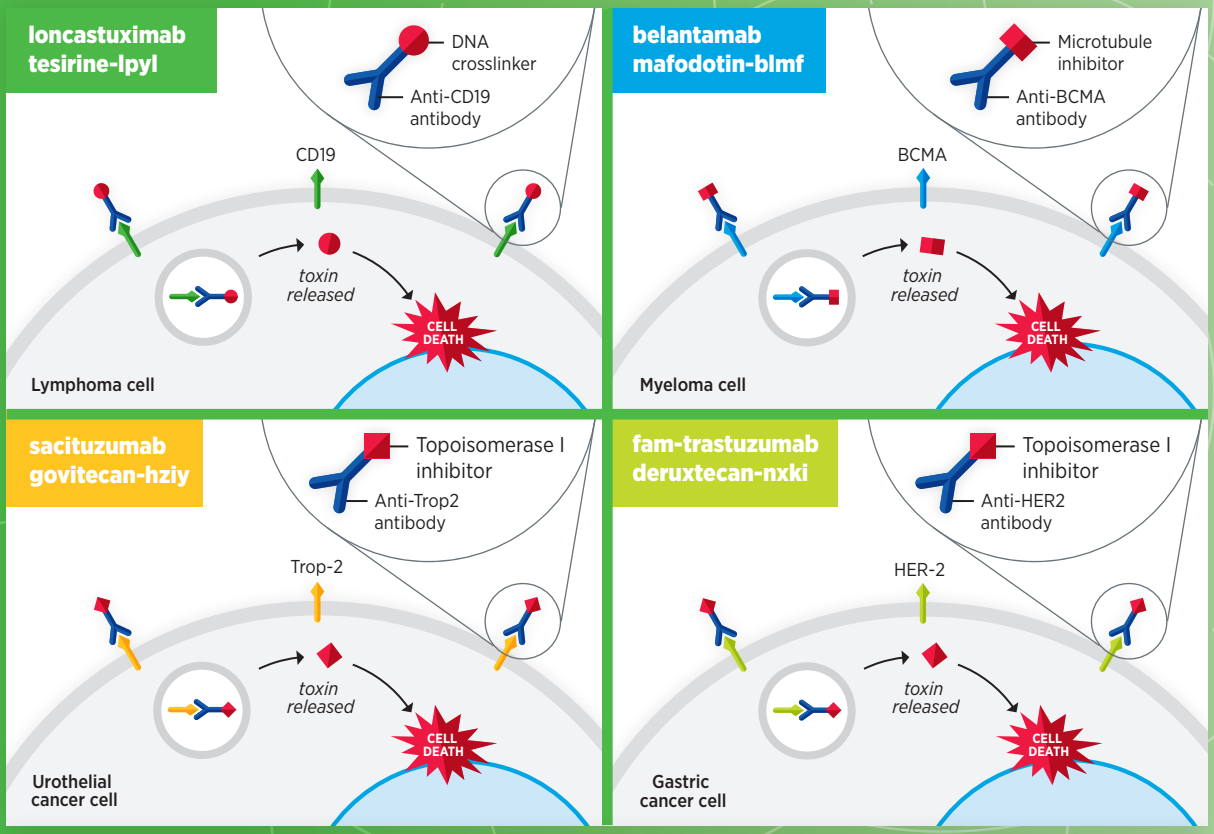
FIGURE 22

DELIVERING CYTOTOXIC AGENTS PRECISELY TO CANCER CELLS



Between August 1, 2020 and July 31, 2021, FDA approved two new antibody-drug conjugates (ADCs), belantamab mafodotin-blmf (Blenrep) and loncastuximab tesirine-lpyl (Zynlonta), to treat multiple myeloma and large B-cell lymphoma, respectively. The approval of another ADC, fam-trastuzumab deruxtecan-nxki (Enhertu)—first approved by FDA in 2019 to treat HER2-positive metastatic breast cancer—was expanded to treat HER2-positive gastric or gastroesophageal junction (GEJ) cancers, increasing the targeted therapy options for gastric cancer patients. The FDA also expanded the use of sacituzumab govitecan-hziy (Trodelvy), an ADC previously approved to treat locally advanced or metastatic triple-negative breast cancer for the treatment of certain patients with bladder cancer.

The antibody portion of belantamab mafodotin-blmf recognizes the B-cell maturation antigen (BCMA), a protein that is present in abundance on the surface of multiple myeloma cells. The antibody is attached to a cytotoxic agent that blocks microtubules, the structural proteins that are necessary for cell multiplication. Once internalized, the cytotoxic drug is released inside the cell, where it inhibits microtubules and blocks cell division.

In case of loncastuximab tesirine-lpyl, the antibody is directed against CD19, a protein located on the surface of normal B cells and lymphoma cells, and is attached to a cytotoxic agent that irreversibly binds to DNA and prevents cells from dividing.

Fam-trastuzumab deruxtecan-nxki binds to the HER2 protein present on the surface of tumor cells for certain types of breast and gastric cancer and delivers a cytotoxic agent that kills cancer cells by blocking a protein necessary for DNA duplication, an essential process for cell multiplication.

Sacituzumab govitecan-hziy carries an inhibitor against the same protein targeted by fam-trastuzumab deruxtecan-nxki, but the antibody portion of the ADC attaches to a different protein, called Trop-2, which is commonly found on the surface of breast and urothelial cancer cells.