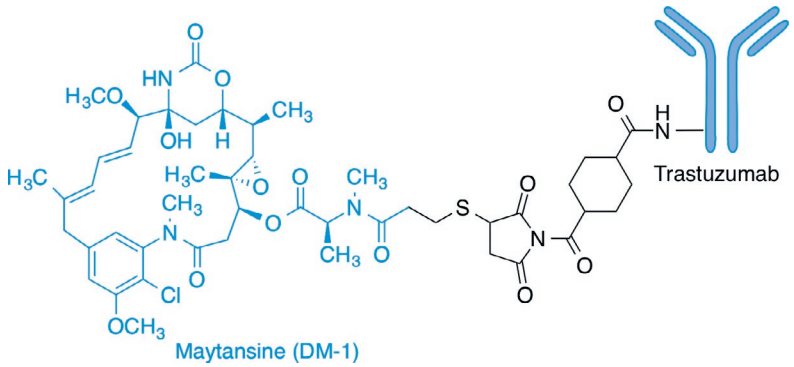
Trastuzumab-DM1, also known as trastuzumab emtansine or ado-trastuzumab emtansine (Kadcyla®), is an ADC that contains the humanized anti-HER-2 MoAb trastuzumab and delivers a thioether-linked to maytansine (DM1), an antimitotic agent that binds tubulin. Because trastuzumab targets the Her-2^+ breast tumor cells, this conjugate was designed to release the drug upon complete degradation of the mAb in the lysosomes of these cells.[73] After a phase III clinical study, this ACD was approved in 2013 specifically for treatment of HER-2^+ metastatic breast cancer in patients who have been treated previously with trastuzumab and a taxane.[74]



Monoclonal antibodies are also employed in nuclear medicine to target radioactive nuclides to specific tumor cells.[75,76] For instance, ibritumomab tiuxetan (Zevalin®) consists of two parts—the murine anti-CD20 ibritumomab, which targets mature B cells, and the EDTA analog tiuxetan, which provides a chelation site for yttrium-90 or indium-111 (Figure 13.36). It was the first targeted radioconjugate agent approved for cancer treatment and is indicated for refractory B-cell non-Hodgkin's lymphoma.

The combination of the antibody tositumomab and its radioactive derivative ^{131}I-tositumomab (Bexxar®) was the basis of an anti-neoplastic radioimmunotherapeutic mAb-based regimen that is indicated for the treatment of patients with CD20 antigen-expressing non-Hodgkin's lymphoma.[77]

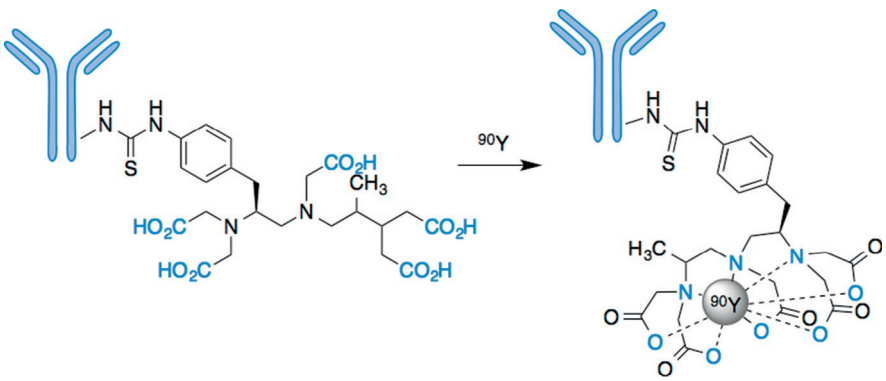


FIGURE 13.36

Structure of ^{90}Y-ibritumomab tiuxetan.