Learning Goals: Antibody application in clinical oncology

Structure-based mode of action defines treatment modality of antibodies in clinical oncology:

- inhibition of growth factors, e.g. targeting of the HER-2 receptor by Trastuzumab in breast cancer

- internalization of antibodies (directed against tumor-associated antigens) leads to intracellular chemotherapy by toxins or irradiation by radioactive substances directly conjugated to the Fc part of mAbs

- mAbs directed against tumor-associated antigens mediate ADCC, ADCP or CDC by binding of Fc to NK cells, macrophages or the complement system; e.g. targeting of CD20 by Rituximab in B cell cancers (B-NHL, CLL) or CD38 by Daratumumab in Multiple Myeloma

- T cell engaging antibodies:
  - mAbs that inhibit inhibitory immune checkpoint regulators, e.g. by targeting CTLA-4 (Iplimumab) or PD1 (Nivolumab and Pembrolizomab) or PD-L1 (Durvalumab and Atezolizumab) have been clinically approved in different cancer entities
  - bispecific single chain T cell engager (BiTE) antibodies with two binding arms aginst tumor and T cell, e.g. the anti-CD19/CD3 BiTE Blinatumumab for treatment of CD19-positive B cell cancer like CD19+ ALL

- CAR T cells:
  - are autologous T cells containing an that contain an engineered, genetically designed T cell receptor that has been transferred *ex vivo* mostly by lentivirus-based gene shuttling
  - CAR T cell receptors of the second generation are currently under clinical evaluation, these receptors contain an extracellular antigen-binding domain, a linker, a transmembrane domain, a co-stimulatory domain and an intracellular signaling chain
  - CARs directed CD19 in B cell cancer have already been clinically approved