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Review

Theranostic applications of antibodies in oncology

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ABSTRACT

Targeted therapies, including antibodies, are becoming increasingly important in cancer therapy. Important limitations, however, are that not every patient benefits from a specific antibody therapy and that responses could be short-lived due to acquired resistance. In addition, targeted therapies are quite expensive and are not completely devoid of side-effects. This urges the need for accurate patient selection and response monitoring.
An important step towards personalizing antibody treatment could be the implementation of theranostics. Antibody theranostics combine the diagnostic and therapeutic potential of an antibody, thereby selecting those patients who are most likely to benefit from antibody treatment. This review focuses on the clinical application of theranostic antibodies in oncology. It provides detailed information concerning the suitability of antibodies for theranostics, the different types of theranostic tests available and summarizes the efficacy of theranostic antibodies used in current clinical practice. Advanced theranostic applications, including radiolabeled antibodies for non-invasive functional imagining, are also addressed. Finally, we discuss the importance of theranostics in the emerging field of personalized medicine and critically evaluate recent data to determine the best way to apply antibody theranostics in the future.

1. Introduction

Targeted therapies are becoming increasingly important for the treatment of cancer. These therapies are designed to specifically interfere with aberrant targets or pathways of cancer cells, which is in contrast to the generalized cytotoxic effects of standard chemotherapy (Teng et al., 2013). The two main types of targeted therapy are the monoclonal antibodies

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Table 1 – Registered unconjugated therapeutic antibodies for cancer treatment.

Antibody	Antibody type	Target antigen	Antigen category	FDA-approved indications[a]	Theranostic antibody test
Trastuzumab (Herceptin)	Humanized	HER2	Growth factor	Breast cancer (HER2-positive); as single agent or combined with chemotherapy for adjuvant or palliative treatment Gastric or gastro-oesophageal junction carcinoma (HER2-positive); as first-line treatment in combination with cisplatin and capecitabine or 5-fluorouracil	HER2 IHC[c] (e.g. HercepTest)
Cetuximab[b] (Erbitux)	Chimeric	EGFR	Growth factor	Head and neck cancer; combined with radiation therapy for initial treatment of locally or regionally advanced disease or as single agent for patients who failed prior platinum-based therapy Colorectal cancer (EGFR-positive); palliative treatment of pretreated metastatic disease	Colorectal cancer: EGFR IHC[c] (e.g. EGFR pharmDx kit)
Panitumumab[b] (Vectibix)	Human	EGFR	Growth factor	Colorectal cancer (EGFR-positive); as single agent for pretreated metastatic disease	EGFR IHC[c] (e.g. EGFR pharmDx kit)
Bevacizumab (Avastin)	Humanized	VEGF	Vascular target	Colorectal cancer; for first-line and second-line treatment of metastatic disease, in conjunction with 5-fluorouracil-based chemotherapy Non-small cell lung cancer (NSCLC); first-line treatment of advanced disease, in combination with carboplatin and paclitaxel, in patients who have not yet received chemotherapy Glioblastoma; as single agent in adult patients for second line treatment Renal cell carcinoma (RCC); in conjunction with IFNα to treat metastatic disease	No (under development)
Rituximab (Rituxan)	Chimeric	CD20	Hematopoetic differentiation antigen	Non-Hodgkin's lymphoma (NHL) (CD20-positive); for B cell NHL and maintenance therapy for untreated follicular NHL Chronic lymphocytic leukemia	NHL: CD20 ELISA/ flow cytometry

EGFR: Epidermal Growth Factor Receptor; VEGF: Vascular Endothelial Growth Factor, IHC: immuno-histochemistry, ELISA: enzyme-linked immunosorbent assay.

a Based on cancer.gov (January 2014) and (Scott et al., 2012).

b Not recommended for colorectal cancer patients whose tumors express mutated KRAS.

c In addition to IHC, the predictive value of HER2 and EGFR mRNA expression or gene amplification as measured by polymerase chain reaction (PCR) or fluorescence *in situ* hybridization (FISH) has also been studied in the clinic. Because this review focuses specifically on the theranostic applications of antibodies in oncology, we did not further consider these applications.

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