Advances in Cancer Prevention
ISSN: 2472-0429
Hsu, Adv Cancer Prev 2023, 7:2
Mini Review
Open Access

Cancer Immunotherapy Regulation by Antibodies

Gerald C Hsu*

Department of Cancer, Aristide Le Dantec Hospital, Dakar, Senegal

Abstract

Radio-immunotherapy with 131I-labelled and 90Y-labelled CD20 conjugates has also shown improved response rates and progression-free survival in patients with NHL. Interestingly, antibody drug or antibody toxin conjugates have been shown to have high potency in haematological malignancies, and there have been two approved by the FDA, gemtuzumab ozogamicin in elderly patients with CD33-positive AML and, more recently, brentuximab vedotin in patients with CD30-positive Hodgkin's lymphoma. These antibody conjugates have provided the first proof-in-principle for antibodies selectively delivering drug payloads to cancer cells, and a similar approach in patients with advanced ERBB2 positive breast cancer with the antibody drug conjugate trastuzumab emtansine.

Keywords: Bio-specific antibody; Glioma; DNA-associated antigens; Immunological pathways; Co-stimulatory molecules; Immunological synapse

Introduction

It should also be noted that outside the United States there are other antibodies that are approved for cancer indications. Catumaxomab, a mouse bio-specific antibody against CD3 and epithelial cell adhesion molecule, is approved in the European Union for use in patients with malignant ascites generated by an EPCAM-positive tumour. Nimotuzumab, a humanized IgG antibody against EGFR, is approved for use in some countries in Asia, South American and Africa for the treatment of head and neck cancer, glioma and nasopharyngeal cancer. Finally, the antibody Vivatuxin, which is an 131I-radiolabelled IgG1κ chimeric mAb against intracellular DNA-associated antigens, is approved by the Chinese drug regulator for the treatment of malignant lung cancer44 [1]. Immune regulation by antibodies Aside from targeting antigens that are involved in cancer cell proliferation and survival, antibodies can also function to either activate or antagonize immunological pathways that are important in cancer immune surveillance. It is now clear that an antigen-specific immune response is the result of a complex dynamic interplay between antigen presenting cells, T lymphocytes and target cells. The recognition of specific antigenic peptides bound to major histocompatibility complex by the T cell receptor is insufficient for T cell activation and just be accompanied by ligation of CD28, a T cell activator, to a member of the B7 family of co-stimulatory molecules [2]. This triggers a series of signalling pathways, resulting in auto-crine interleukin-2 production and T cell activation. At the same time, CTLA4, a molecule that is normally found in intracellular stores, is transported to the immunological synapse, where it serves to down regulate the activated T cell by binding with high avidity to the B7 molecules and stopping the activation signals mediated by CD28.

Discussion

The potential of blocking CTLA4 with an antibody to potentiate T cell activation and responses to targets on tumour cells was first reported in 1996 and provided the scientific foundation for the development of two fully human mAbs that blockCTLA4. A pivotal Phase III trial demonstrated that ipilimumab prolonged overall survival of patients with metastatic melanoma and resulted in the approval of ipilimumab for the treatment of this disease by the FDA, the European Medicines Agency and regulatory agencies from a number of countries [3]. Indeed, ipilimumab was the first treatment to be shown to increase survival in this challenging patient population. CTLA4 blockade does present challenges in terms of toxicity. Given the nonspecific nature of the dis-inhibition of T cells, a series of tissue-specific inflammatory responses, termed immune-related adverse events, have been observed. These are largely confined to the skin and gastrointestinal tract but can FcγRIIa-131H polymorphisms An Fcγ receptor is a protein found on the surface of immune cells that binds the Fc of antibodies, and that facilitates the cytotoxic or phagocytic activity of these cells. Polymorphisms of FcγR genes may result in higher Fc binding in vitro and in vivo, with resulting enhanced cytotoxic activity of antibodies. More rarely, affect the liver and endocrine glands. With early recognition, these events are generally manageable with corticosteroids, which seem not to interfere with the anti-tumour effect of ipilimumab15. The success of immunological checkpoint blockade with ipilimumab has opened the door to other immune-modulating antibodies. The next most advanced product is MDX-1106, a fully human antibody that blocks programmed cell death protein 1, which is a marker of activated or exhausted T cells that can trigger apoptosis when bound by its ligand, PD1 ligand 1 (PDL1; also known as B7H1)45. Interestingly, this ligand is found not only on antigen-presenting cells but also on many tumour cells. PD1 blockade has been shown in early clinical trials to result in durable responses in patients with melanoma, renal cell carcinoma, non-small-cell lung cancer and colorectal cancer [4]. Other antibodies that target PD1 are also in development. Agonistic antibodies are also being explored as immune-modulatory cancer therapies. These include two fully human antibodies to CD137, an activator of T cells, from Pfizer and Bristol Myers Squibb. The BMS antibody has been in Phase I trials, demonstrating anti-tumour efficacy at a wide range of doses, but also severe hepatic toxicity at high doses5. Studies are now reopening using low doses of antibody only.

***Corresponding author:** Gerald C Hsu, Department of Cancer, Aristide Le Dantec Hospital, Dakar, Senegal, E-mail: chsu@hotmail.com

Received: 28-Feb-2023, Manuscript No. ACP-23-91984; **Editor assigned:** 02-Mar-2023, PreQC No. ACP-23-91984(PQ); **Reviewed:** 16-Mar-2023, QC No. ACP-23-91984; **Revised:** 23-Mar-2023, Manuscript No. ACP-23-91984 (R); **Published:** 28-Mar-2023; DOI: 10.4172/2472-0429.1000157

Citation: Hsu GC (2023) Cancer Immunotherapy Regulation by Antibodies. Adv Cancer Prev 7: 157.

This highlights an important aspect of antibody therapeutics. Although higher doses of a blocking antibody may yield improved efficacy, low doses of agonistic antibodies may provide a better risk benefit profile compared with higher doses. Other pathways of interest for agonistic antibodies include those of CD40, for which favourable preclinical and clinical results have been noted, particularly in pancreatic cancer46, and the glucocorticoid-induced TNF receptor. Antibody therapeutics might also have a role in the generation of de novo immune responses to the antigen targeted by the antibody through promoting anti-gen presentation to Fc receptor-bearing cells. Such responses may allow for the effects of therapeutic antibodies to persist after the dosing is completed. There are multiple mechanisms by which antibody treatment of patients with malignant tumours may not achieve a therapeutic effect [5]. These include the heterogeneity of target antigen expression in the tumour, physical properties and pharmacokinetics of anti-bodies that have an impact on uniform penetrance into a tumour and intra-tumoural microenvironment. Antibody dose and concentration in the tumour and possible receptor saturation kinetics can also affect therapeutic impact, as can signalling pathway promiscuity, as well as immune escape through ineffective FcγR binding and immune suppression. Although the physical properties of antibodies are highly relevant to their efficient penetration of the tumour and concentration achieved in vivo, detailed information on intra-tumoural concentration achievable in the clinic is lacking for most clinically approved antibodies49. In addition, although it is known that tumour expression of the target antigen or receptor is also crucial for antibody efficacy, heterogeneity in expression between primary and metastatic lesions, and between individual metastatic lesions, is common [6]. Intriguingly, although high receptor expression is known to be associated with response to trastuzumab, it is not necessarily predictive of response, and it can be down regulated as part of the development of resistance. Moreover, expression of EGFR in archived samples of colorectal cancer has not been shown to be predictive of response to cetuximab or panitumumab, indicating that target receptor expression is only one part of the complex interplay between binding of the antibody to the tumour and the therapeutic response. ADCC has been demonstrated to have a major role in antibody efficacy, and there is evidence that FcγRIIa-131H polymorphisms have a favourable effect on response rates for cetuximab in colorectal cancer, trastuzumab in breast cancer and rituximab in follicular lymphoma [7]. The abrogation of signalling pathways is known to be a principle mechanism for antibody-based tumour killing, and the development of resistance to therapy may be due to multiple inherent and acquired mechanisms [8]. Primary resistance may be attributable to gene mutations 36–38 or to promiscuous signalling because of interactions between cell surface receptors [9]. Signalling attenuation, which may occur as a result of alterations in receptor internalization and degradation, might also have an impact on the effectiveness of signalling blockade with antibodies. The development of resistance to antibody therapy, through over-activation of alternative signalling pathways, may also play a major part in the lack of tumour response to treatment. An understanding of the complexity of signalling pathways in different tumours may assist in selecting patients who are suited to a specific antibody treatment and might also provide insight into combinations of therapies that may have efficacy in selected patients [10]. The use of mAbs for the therapy of cancer is one of the great success stories of the past decade. This success builds on a long history of scientific investigation that aimed to understand the complexities of antibody serology, target selection, antibody receptor function and immune regulation of tumour growth. The future promise of antibody therapeutics in cancer is dependent on having a better understanding of the lessons learned from laboratory studies and clinical trials, on applying innovative approaches to target and antibody selection and on early phase clinical trials that will guide appropriate development strategies, leading to clinical benefit in cancer patients.

Conclusion

Nonetheless, even cancers impervious to the new drugs could be treated if those malignancies have the right error-riddled DNA signature. In its refined version, the genome of a common bacteriophage and synthetic strands that were designed to fold up its DNA are encapsulated and do not encode any proteins or do any of the normal DNA functions. Potentially, the technique should work on most any form of drug-resistant cancer.

Acknowledgement

None

Conflict of Interest

None

References

1. Rovner MH (2005) Likely consequences of increased patient choice. Health Expect US 8: 1-3.
2. Marc EL, Chris B, Arul C, David F, Adrian H, et al. (2005) Consensus statement: Expedition Inspiration 2004 Breast Cancer Symposium : Breast Cancer – the Development and Validation of New Therapeutics. Breast Cancer Res Treat EU 90: 1-3.
3. Casamayou MH (2001) The politics of breast cancer. GUP US 1-208.
4. Baralt L,Weitz TA (2012) The Komen–planned parenthood controversy: Bringing the politics of breast cancer advocacy to the forefront. WHI EU 22: 509-512.
5. Kline KN (1999) Reading and Reforming Breast Self-Examination Discourse: Claiming Missed Opportunities for Empowerment, J Health Commun UK 119-141.
6. Keller C (1994) The Breast, the Apocalypse, and the Colonial Journey. J Fem Stud Relig USA 10: 53-72.
7. Berwick DM (1998) Developing and Testing Changes in Delivery of Care. Ann Intern Med US 128: 651-656.
8. Connor BO (2000) Conceptions of the body in complementary and alternative medicine. Routledge UK 1-279.
9. Lynch K (2019) The Man within the Breast and the Kingdom of Apollo. Society 56: 550-554.
10. Saarinen R (2006) Weakness of will in the Renaissance and the Reformation. OSO UK 29-257.