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The Clinical Application of Bispecific Antibodies in Cancer Treatment

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Abstract. Bispecific antibody (bsAb) is a type of human-modified antibody which two or more sites are capable of binding two or more individual antigens. This dual specificity enables bsAbs to have superior application than the monoclonal antibodies as they can eliminate tumour cells via recruiting T cells and also the accessory immune cells in some cases, as well as can simultaneously block two different signalling pathways or different disease mediator. More than 30 technologies have been applied for the development of bsAbs based on heavy chains and light chains heterologous recombination. However, only three bsAbs have been approved and available on the market, whereas over 110 BsAbs are at different clinical or research stages. In this paper, different types of bsAbs will be elaborated as well as the clinical significance of the approved bsAbs.

Keywords: cancer immunotherapy, bispecific antibodies, clinical

1. Introduction

Cancer as the leading cause of death globally has a tremendously high mortality rate that as predicted, 1.9 million cases of cancer will be diagnosed and there will be over six hundred thousand deaths caused by cancer in the United States [1]. With the advanced technology and improved knowledge of the human neoplastic disease, there is an increasing discovery of new drugs to treat cancer and cancer-related diseases. However, the translation of those newly discovered drugs into clinical trial is far slower than people expected as the average time of a single drug to be developed is 13 years. As the clinical practice include the examination of drug toxicity, efficacy, pharmacokinetics and pharmacodynamics [2].

Nowadays, the most common treatments for advanced and metastatic cancer are chemotherapy, surgery and radiation therapy. However, due to the toxic adverse effect, poor patients′ life quality and development of resistance lead to poor clinical response and, many different types of potential therapies are under investigation and clinical trials. In recent years, immunotherapy has become an attractive hot topic as a new treatment for cancer, which mobilizes the immune system to eliminate tumour cells and does not indiscriminately damage cells as conventional therapies do.

Monoclonal antibody (mAb) is a type of immunotherapy that can recognize and target specific proteins on cancer cells. It is considered one of the most effective biotherapeutic drugs in treating several cancer types because of its improved safety and lower toxicity compared to conventional chemotherapy. In 1960, the first concept of human-made antibodies with two different antigen-binding

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sites combined by two different mAbs was described by Nisonoff and co-workers, which is so called bispecific antibody (bsAb). BsAbs are a fast-expanding area of cancer immunotherapy, this innovative concept has evolved into more than 100 different bsAbs over time, but only about a quarter of them has been tested clinically. It has been reported to have great clinical efficacy in some cancer treatments.

BsAbs can function in multiple ways. The typical BsAb application is the redirection and engagement of T cells, in which bsAb synchronously binds to antigens on tumour cells and antigens on T cells. This leads to activation of T cell and contributes to target-dependent tumour cell elimination. In some cases, the involvement of other accessory immune cells to the tumour cells also presents, such as natural killer (NK) cells, dendritic cells (DCs) and macrophages. Some bsAbs function as connectors, which bridge the immune cells to the targeted tumour cells and enable them to act against tumour cells. Some bsAbs are directed to dual target immune checkpoints, enabling the change of the suppressive status of immune cells as well as the release of immune cells. BsAbs can also act by binding two different types of antigens or at different sites on the same antigen and thereby do to maximize therapeutic efficacy [3].

The immunoglobulin antibody consists of two functionally distinguishable segments, which are the constant fragment (Fc) and the antigen binding fragment (Fab). It can be modified in order to simultaneously target different antigens. Three common methods to modify bsAbs include chemical conjugation, quadroma and genetic engineering. Meanwhile, there are also other formats of bsAbs have been created, which act without the presence of Fc region.

The naturally occurring antibodies or conventional human-developed antibodies are directed against only one antigen, whereas BsAbs combine two or multiple specificities into a single polypeptide chain or a single heavy or light chain. Therefore, BsAb is considered to offer more advantages compared to mAbs in the field of cancer immunotherapy. As cancer involves multiple factors and signalling pathways, the dual-targeting concept of BsAb enabled this potential therapy to hold a greater therapeutic promise. However, there are many challenges encountered in the development of bsAbs to treat cancer that can greatly affect the effectiveness of the therapeutic response. For instance, the difference in size and structure of bsAbs in symmetric form compared with natural antibodies [4][5].

Currently, over 86% of bsAbs were developed for use in cancer treatment. To date, only three have been approved and are available on the market. Two of them are for the treatment of cancer patients, called catumaxomab and blinatumomab. More than 180 bsAbs are under pre-clinical research, also, over 50 are under clinical trials which are mostly in phase I, I/II and II.

2. Immunoglobulin G-link molecules

BsAbs can be classified based on their format and constituent. One major classification is the IgG-like molecules with the presence of fragment crystallizable (Fc) region and the fragment-based molecules that does not have an Fc domain [6].

Fc region is an important immune regulatory receptor that ensures each antibody generates the appropriate immune response. Fc domain receptors result in bsAbs to be capable of triggering common immune response such as macrophages, NK cells, DCs and neutrophil cells. The retaining of Fc region can provide additional support to the aimed depletion via the Fc-mediated functions. The Fc-mediated effector function include antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP) and complement-dependent cytotoxicity (CDC) [7].

The IgG-like bsAbs usually show a greater pharmacokinetic half-life than the fragment-based bsAbs because of their larger size and the neonatal crystallizable fragment receptor (FcRn)-mediated recycling processes which the Fc region would bind to FcRn that is responsible for IgG maintenance [9]. As the reduced serum half-life can result in reduced therapeutic efficacy, IgG-like bsAbs is therefore still in the development. Additionally, the use of Fc region in designing bsAbs benefits the purification, solubility and stability [8].

One main way to produce IgG-like bsAbs is the quadroma technology which is a classic way to construct and produce bsAbs. This technology involves stochastic pairing of heavy chains and light

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chains, meanwhile, nonfunctional antibodies can also be produced. Catumaxomab as an approved trifunctional bsAb was produced by quadroma via using rat and mouse quadroma cell line. [9] In this case, it was found that macrophages, NK cells and DCs can be recruited by the Fc region of catumaxomab and help enhance killing capacity of tumour cells [10].

3. Fragment-based BsAbs

The fragment-based bsAbs would lack the Fc-related effector functions. BsAbs that lack the Fc region are usually smaller than the IgG-like bsAbs, which enables them to have greater tissue penetration. Although they show a relatively short pharmacokinetic half-life because of their small molecular weight, this issue can be tackled by extending the half-life by technologies, such as incorporating a domain to them which binds to the albumin protein which is usually an immobilised serum protein. Moreover, the bsAb that lack an Fc region can rely on their capacity of antigen-binding to exert therapeutic activities.

One of the fragment-based bsAbs is the single-chain variable fragment (scFv), which comprise only the variable domain of light chain and heavy chain connected by a connecter that is usually the $(G_4S)_3$ sequence [11]. The scFv-based bsAbs were suggested to have greater possible clinical application compared to normal IgG molecules because by alternating length of linker or other external factors, they can be dimers, trimers or even tetramers [12].

The tandem scFvs (ta-scFvs) consists of dual scFvs connected by a peptide linker, which is generated to enable dual targeting of different antigens. The long linker enables better binding of different antigen binding sites. The well-known bispecific T cell engager (BiTE) is a type of ta-scFv that can bring T cells from patients to tumour cells. Blinatumomab as one of the approved bsAbs is BiTE can bind to CD3-positive T cells and EpCAM-positive-tumour cells and brings them together to enable tumour cell elimination by patients′ own T cells.

The scFv-based bsAbs also have diabody format, which two linkers connect the variable domains from two individual. Although the increase of linkers can enhance diabody stability, this can impose restriction on flexibility of the antigen-binding sites, resulting in limited antigen binding.

4. Clinical application of BsAbs

Until now, two bsAbs have been approved and applied for treating cancer patients: catumaxomab and blinatumomab. Catumaxomab is a TrioMab that is developed to kill tumour cells via its trifunctional mode of action. Whereas blinatumomab is a BiTEs act by transiently linking two different antigens on two different cells.

4.1. Catumaxomab

Catumaxomab is a monoclonal bispecific trifunctional antibody approved in 2009 for treating patients who are diagnosed of epithelial cell adhesion molecule (EpCAM) positive carcinomas with malignant ascites (MA). The production of catumaxomab involves modification and co-expression of rat IgG2b and mouse IgG2a and is used when standard therapy is not feasible. As the representation of a typically advanced stage of cancer, MA is the accumulation of peritoneal fluid resulting in malignant tumour cells spread into the peritoneal cavity, and it is a condition observed in patients with a variety of epithelial cancers. EpCAM antigen has been considered as a potent target for treating MA as it is strongly expressed in carcinomas of various origins and is a tumor-specific antigen in the peritoneal cavity.

Main way of catumaxomab to eliminate tumour cells is through T-cell mediated lysis, ADCC and phagocytosis. Its variable regions were developed to target CD3 antigen on T cells and EpCAM antigen on tumor cells, which enables the direct recruitment of T cells to eliminate EpCAM positive carcinomas and treat MA. Additionally, as a trifunctional antibody, the Fc region of catumaxomab can selectively bind to typical type of Fcγ receptors on accessory immune cells. Upon binding, these effector cells would be activated and release perforins and granzymes from their granules, which would accelerate tumour cell depletion. Additionally, the anti-tumour activity was found to be assisted

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by cytotoxicity via cytokines secreted by T cells, such as interferon-γ, tumor necrosis factor-α and interleukin-1β. Thus, catumaxomab can stimulate both the innate and the acquired immune systems [13].

4.2. Clinical tial of ctumaxomab

The clinical phase II/III of catumaxomab is one of the pivotal research projects which showed that its intraperitoneal injection in combination with paracentesis showed significantly prolonged puncture-free time, reduced ascites-related symptoms as well as reduced Ep-CAM positive tumour cells in ascites fluid.

In the research, patients diagnosed with ovarian, non-ovarian and gastric cancer were separated into catumaxomab infusion plus paracentesis treatment group or the paracentesis only control group.

It was found that in comparison to the control group, patients who received the combined treatment showed statistically significantly longer median time to the next therapeutic puncture for the relief of ascites symptoms. As shown in figure 1A, it was 71 versus 13 days in ovarian cancer population, 80 versus 15 days in the non-ovarian cancer population, and 118 versus 15 days in the gastric cancer population. The administration of catumaxomab could save approximately 5 punctures, this showed clinical benefit as punctures could lead to cachexia, potential infection and bowel perforation as well as continuous protein loss [14].

After 8 days of the last infusion of catumaxomab in the treatment group or on day 0 in the control group, the ascites symptoms and signs were assessed via subjective interview and objective abdominal examination, respectively. It was found that the treatment group showed six statistically significantly reduced symptoms in comparison to the control. Six reduced symptoms include nausea, anorexia, early satiety, abdominal swelling, abdominal pain and dyspnea. Moreover, a significant difference was determined between the two groups regarding all four tested ascites signs, which are abdominal distension dull to percussion, shifting dullness, fluid thrill and bulging flanks. (Fig. 1B)

Furthermore, tumor cell load in ascites fluid was analyzed by the quantification of EpCAM-positive tumour cells. Results showed a significantly reduced tumour cell load in ascites fluid from patients in the treatment group. After the last catumaxomab infusion, the EpCAM-positive tumour cells were significantly reduced with a median of zero. At the next puncture, researchers observed a significantly lower median tumour cell count in the treatment group in comparison to the control, which is 2,090 tumour cells/10^6 and 18,929 tumour cells/10^6, respectively. (Fig. 1C)

The frequently reported adverse events related to catumaxomab were abdominal pain and cytokine release-related symptoms. But those side effects were considered reversible and acceptable intensity [14].

In brief summary, catumaxomab significantly prolonged the need of paracentesis which decreased the potential of patients getting other adverse events from paracentesis. Also, it can significantly reduce ascites symptoms and signs, which would help improve patients′ life quality. Moreover, adverse events caused by catumaxomab were generally manageable and reversible, indicating a good safety profile. Therefore, the treatment of catumaxomab infusion combined with paracentesis showed effective anti-EpCAM-positive-tumour cell activity, and demonstrated clinically relevant benefits in patients with MA caused by carcinomas from different origins.

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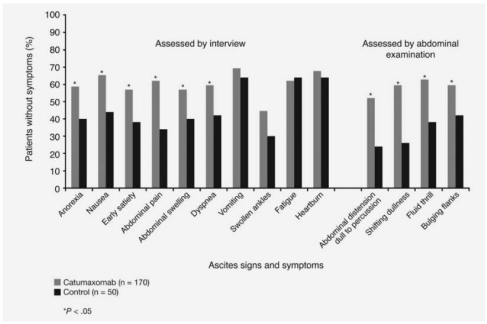
A

	Pooled population (n = 258)		Ovarian cancer (n = 129)		Nonovarian cancer (n = 129)		Gastric cancer (n = 66)	
	C + P (n = 170)	P (n = 88)	C + P (n = 85)	P (n = 44)	C + P (n = 85)	P (n = 44)	C + P (n = 46)	P (n = 20)
Puncture-free survival (days)								
Median (95% CI)	46 (35–53)	11 (9–16)	52 (38–62)	11 (9–20)	37 (27–49)	14 (8–17)	44 (27–69)	15 (8–21)
Factor of prolongation	4.2		4.7		2.6		2.9	
p-value[1]	<0.0001		<0.0001		<0.0001		<0.0001	
HR, estimate (95% CI)	0.254 (0.185–0.350)		0.205 (0.129–0.327)		0.309 (0.199–0.482)		0.289 (0.151–0.554)	
Time to next paracentesis (days)								
Median (95% CI)	77 (62–104)	13 (9–17)	71 (52–104)	11 (9–20)	80 (64–135)	15 (8–19)	118 (64–147)	15 (8–24)
Factor of prolongation	5.9		6.4		5.3		7.9	
p-value[1]	<0.0001		<0.0001		<0.0001		<0.0001	
HR, estimate (95% CI)	0.169 (0.114–0.251)		0.152 (0.088–0.260)		0.183 (0.101–0.331)		0.143 (0.057–0.359)	
Overall survival (days)								
Median (95% CI)	72 (61–98)	68 (49–81)	110 (70–164)	81 (68–134)	52 (44–74)	49 (33–68)	71 (50–98)	44 (28–68)
p-value[1]	0.0846		0.1543		0.4226		0.0313	
HR, estimate (95% CI)	0.723 (0.498–1.048)		0.650 (0.357–1.183)		0.825 (0.514–1.324)		0.469 (0.232–0.951)	

[1]Log-rank test.

B



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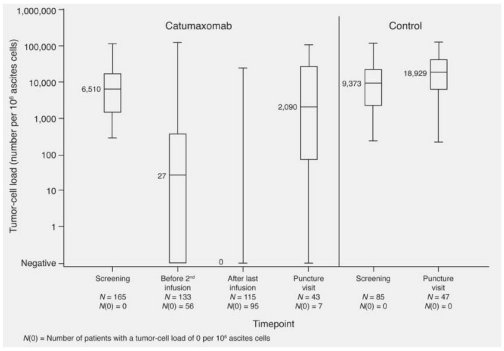

Figure 1. linical response of experimental group and control group.

4.3. Blinatumomab

Blinatumomab is the first bispecific monoclonal antibody being tested under clinical trials and have been approved in 2018. It is used to treat patients who achieved first or second complete remission of B-cell precursor acute lymphoblastic leukemia (BCP ALL) but with minimal residual disease (MRD). In the past, by using intensive chemotherapy, there was a high rate of BCP ALL patients achieved complete remission (CR) but experienced relapse, which was assumed to be caused by MRD. It was reported that MRD is the riskiest factor for ALL patients regarding the relapse-free survival (RFS) and overall survival (OS). [15] Blinatumomab is designed to target CD3-positive T cells and CD19-positive B lymphomas. The CD19 antigen was found to be expressed at the early stage of B cell development as well as in 95% of patients with BCP ALL. Blinatumomab functions by activating cytotoxic T cells from patients, and linking those cells to the CD19-positive malignant B lymphomas, enabling the elimination of tumor cells in both the resting and proliferating phase. The T cell activation triggered by blinatumomab involves proliferation of T cell and production of cytokine [16].

4.4. Clinical trial of blinatumomab

A multi-institutional phase III trial was performed on patients who were heavily pretreated for BCP ALL to compare the clinical response of using blinatumomab and chemotherapy. The overall results suggested the superiority use of blinatumomab over standard chemotherapy for treating BCP ALL relapsed patients. Patients were randomly assigned to blinatumomab or standard chemotherapy group in a 2:1 ratio. Blinatumomab were administered in a 6-week cycle which includes 4 weeks of treatment and 2 weeks of no treatment.A statistical significantly longer median OS was observed in the blinatumomab group, which was 7.7 months, whereas the median OS of chemotherapy group was only 4 months. The curves of OS for two groups began to be separated within three months and then converged around 16 to 17 months. (Fig. 2A) Following the elimination of patients that have had allogenic stem-cell transplantation in the past, the median OS was found to be 6.9 months in blinatumomab group and 3.9 months in chemotherapy group. (Fig. 2B) Which also showed a

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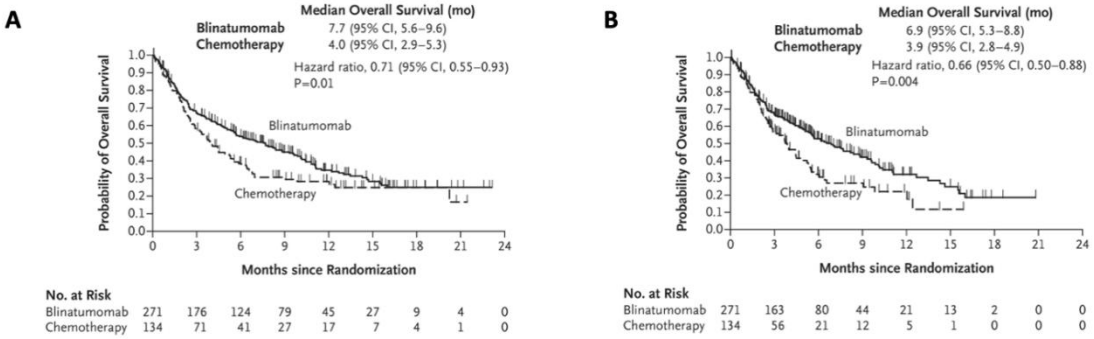
statistical significantly longer median OS in blinatumomab group. Noticeably, the curves of the two groups did not converge again when stem-cell transplanted patients were censored [17].

The research also demonstrated a consistently significantly higher remission rates in the blinatumomab group within 12 weeks. In regard to the full hematologic recovery, it was 34% in blinatumomab group and 16 % in chemotherapy group. With respect to full, partial or incomplete hematologic recovery, it was 44% and 25% in blinatumomab and chemotherapy group, respectively. (Fig. 2C) [17]



C

Response Category	Blinatumomab Group (N=271)		Chemotherapy Group (N=134)		Treatment Difference (95% CI)	P Value†
	no.	*% (95% CI)*	*no.*	*% (95% CI)*	*percentage points*	
Complete remission with full hematologic recovery	91	33.6 (28.0–39.5)	21	15.7 (10.0–23.0)	17.9 (9.6–26.2)	<0.001
Complete remission with full, partial, or incomplete hematologic recovery	119	43.9 (37.9–50.0)	33	24.6 (17.6–32.8)	19.3 (9.9–28.7)	<0.001
Complete remission with partial hematologic recovery	24	8.9 (5.8–12.9)	6	4.5 (1.7–9.5)		
Complete remission with incomplete hematologic recovery	4	1.5 (0.4–3.7)	6	4.5 (1.7–9.5)		

Figure 2. Clinical data of experimental group treated with blinatumomab and control group treated with standard chemotherapy.

Although blinatumomab showed greater treatment efficacy, severe adverse events occurred to patients in blinatumomab group were 62%, whereas it was 45% in chemotherapy group. However, there was a lower rate of adverse events graded 3 or higher in the blinatumomab group, which was 87% compared to 92% in chemotherapy group. The incidence of neurologic event that occurred in two groups was similar, which was 9.4 & and 8.3% in blinatumomab and chemotherapy groups, respectively. The blinatumomab group showed the incidence of cytokine release syndrome, but was considered no need to disrupt the blinatumomab treatment.

In short conclusion, this study demonstrated a significantly longer OS and greater remission rate by using blinatumomab to treat relapsed or refractory BCP ALL patients. It shows a significant clinical benefit of the use of blinatumomab over standard chemotherapy for treatment of BCP ALL patients. Blinatumomab as the immune-based cancer therapy showed greater depth and efficacy than standard chemotherapy.

5. Conclusion

In overall, the potential application of bsAbs in treating cancer or cancer-related disease is noticeable. Different types of bsAbs showed their own advantages and limitations, meanwhile, technologies can be utilised to tackle the limitations and enable the design and development of different bsAbs. Due to the ability of dual targeting, bsAbs are superior to other antibodies as T cells can be brought into close proximity with tumour cells. Also, with the presence of Fc region, additional cancer elimination mechanism can be triggered, such as ADCC, ADCP and CDC. The success of catumaxomab and blinatumomab has drew the attention of pharmaceutical industries that diverse formats of bsAbs are currently under development. Despite the application in fighting against cancer or cancer-related

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disease, bsAbs can also synchronously block different pathogenic mediators and showed alternative treatment options regarding the autoimmune diseases and inflammatory diseases. However, several hurdles still remain regarding the development of various form of bsAbs resulting in limited numbers of bsAbs have been moved into clinical stages. The purity of products as well as the large-scale production that is time- and money-consuming are still the main issues that have trapped the discovery and production of bsAbs. Also, the identification of potential bsAbs with synergistic effects still faces the challenge. Moreover, as the immunotherapy, adverse events are common in the application of bsAbs, such as cytokine release syndrome and infusion-related reactions. However, the reported adverse events are usually manageable and reversible. With the development, there is great potential of the application of bsAbs in therapies.

References

[1] Zhang, Zhe et al. "Overcoming Cancer Therapeutic Bottleneck By Drug Repurposing". Signal Transduction And Targeted Therapy, vol 5, no. 1, 2020. Springer Science And Business Media LLC, doi:10.1038/s41392-020-00213-8. Accessed 10 Sept 2022.

[2] Siegel, Rebecca L. et al. "Cancer Statistics, 2022". CA: A Cancer Journal For Clinicians, vol 72, no. 1, 2022, pp. 7-33. Wiley, doi:10.3322/caac.21708. Accessed 10 Sept 2022.

[3] Wu, Yuze et al. "Recent Advances And Challenges Of Bispecific Antibodies In Solid Tumors". Experimental Hematology &Amp; Oncology, vol 10, no. 1, 2021. Springer Science And Business Media LLC, doi:10.1186/s40164-021-00250-1. Accessed 10 Sept 2022.

[4] Labrijn, Aran F. et al. "Bispecific Antibodies: A Mechanistic Review Of The Pipeline". Nature Reviews Drug Discovery, vol 18, no. 8, 2019, pp. 585-608. Springer Science And Business Media LLC, doi:10.1038/s41573-019-0028-1. Accessed 10 Sept 2022.

[5] Ma, Jiabing et al. "Bispecific Antibodies: From Research To Clinical Application". Frontiers In Immunology, vol 12, 2021. Frontiers Media SA, doi:10.3389/fimmu.2021.626616. Accessed 10 Sept 2022.

[6] Brinkmann, Ulrich, and Roland E. Kontermann. "The Making Of Bispecific Antibodies". Mabs, vol 9, no. 2, 2017, pp. 182-212. Informa UK Limited, doi:10.1080/19420862.2016.1268307. Accessed 10 Sept 2022.

[7] Spiess, Christoph et al. "Alternative Molecular Formats And Therapeutic Applications For Bispecific Antibodies". Molecular Immunology, vol 67, no. 2, 2015, pp. 95-106. Elsevier BV, doi:10.1016/j.molimm.2015.01.003. Accessed 10 Sept 2022.

[8] Kontermann, Roland E., and Ulrich Brinkmann. "Bispecific Antibodies". Drug Discovery Today, vol 20, no. 7, 2015, pp. 838-847. Elsevier BV, doi:10.1016/j.drudis.2015.02.008. Accessed 10 Sept 2022.

[9] Fan, Gaowei et al. "Bispecific Antibodies And Their Applications". Journal Of Hematology &Amp; Oncology, vol 8, no. 1, 2015. Springer Science And Business Media LLC, doi:10.1186/s13045-015-0227-0. Accessed 10 Sept 2022.

[10] Zeidler, R et al. "The Fc-Region Of A New Class Of Intact Bispecific Antibody Mediates Activation Of Accessory Cells And NK Cells And Induces Direct Phagocytosis Of Tumour Cells". British Journal Of Cancer, vol 83, no. 2, 2000, pp. 261-266. Springer Science And Business Media LLC, doi:10.1054/bjoc.2000.1237. Accessed 10 Sept 2022.

[11] Ahamadi-Fesharaki, Raoufeh et al. "Single-Chain Variable Fragment-Based Bispecific Antibodies: Hitting Two Targets With One Sophisticated Arrow". Molecular Therapy - Oncolytics, vol 14, 2019, pp. 38-56. Elsevier BV, doi:10.1016/j.omto.2019.02.004. Accessed 10 Sept 2022.

[12] Le Gall, Fabrice et al. "Di-, Tri- And Tetrameric Single Chain Fv Antibody Fragments Against Human CD19: Effect Of Valency On Cell Binding". FEBS Letters, vol 453, no. 1-2, 1999, pp. 164-168. Wiley, doi:10.1016/s0014-5793(99)00713-9. Accessed 10 Sept 2022.

[13] Seimetz, Diane. "Novel Monoclonal Antibodies For Cancer Treatment: The Trifunctional

DOI: 10.54254/2753-8818/3/20220395

Antibody Catumaxomab (Removab®)". Journal Of Cancer, vol 2, 2011, pp. 309-316. Ivyspring International Publisher, doi:10.7150/jca.2.309.

[14] Heiss, Markus M. et al. "The Trifunctional Antibody Catumaxomab For The Treatment Of Malignant Ascites Due To Epithelial Cancer: Results Of A Prospective Randomized Phase II/III Trial". International Journal Of Cancer, vol 127, no. 9, 2010, pp. 2209-2221. Wiley, doi:10.1002/ijc.25423.

[15] Jen, Emily Y. et al. "FDA Approval: Blinatumomab For Patients With B-Cell Precursor Acute Lymphoblastic Leukemia In Morphologic Remission With Minimal Residual Disease". Clinical Cancer Research, vol 25, no. 2, 2019, pp. 473-477. American Association For Cancer Research (AACR), doi:10.1158/1078-0432.ccr-18-2337.

[16] May, Megan Brafford, and Ashley Glode. "Blinatumomab: A Novel, Bispecific, T-Cell Engaging Antibody". American Journal Of Health-System Pharmacy, vol 73, no. 1, 2016, pp. e6-e13. Oxford University Press (OUP), doi:10.2146/ajhp150134. Accessed 11 Aug 2022.

[17] Kantarjian, Hagop et al. "Blinatumomab Versus Chemotherapy For Advanced Acute Lymphoblastic Leukemia". New England Journal Of Medicine, vol 376, no. 9, 2017, pp. 836-847. Massachusetts Medical Society, doi:10.1056/nejmoa1609783.