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Summary analysis of the pre-clinical and clinical results of brain tumor patients treated with pritumumab

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Abstract. Pritumumab is a human IgG1 kappa antibody that has been derived from a B-cell isolated from a regional draining lymph node of a patient with cervical carcinoma. Specificity analysis of the antibody with human tissues showed the antigen, altered tumor-associated vimentin, to be highly restricted to various cancers and not normal cells and tissues. In various clinical trials in Japan 249 patients with brain cancer were treated with pritumumab. The overall response rate was between 25–30% with several survivors beyond 5-years post-treatment. The patients were on a low dose regimen of 1mg given twice a week for a course of 24 weeks for a total dose of 48 mgs per course. Pritumumab appears to be a safe and effective therapy in patients with malignant gliomas.

Keywords: Pritumumab, human antibody, clinical trials, glioblastoma, neuroimmunology

1. Introduction

Human antibodies work. So far, the FDA has approved 22 antibodies for therapeutic use and over 200 more are in the clinical pipeline [1]. In addition to these there are many other antibodies in various phases of pre-clinical development so the list will certainly expand with other choices and applications [2].

Pritumumab (also known in the literature as CLNH 11, CLN-IgG, and ACA-11) is a natural human IgG1 kappa antibody that was derived from a B lymphocyte obtained from a regional draining lymph node from a patient with cervical carcinoma through human hybridoma technology [3,4]. Pritumumab has been used to treat 249 patients in several clinical trials of Japanese patients with various brain tumors. The pritumumab antibody used in these trials was purified from the parent human hybridoma, CLNH11 [3,4]. The general properties of pritumumab antibody are listed in Table 1 with their respective reference. This antibody may reflect the natural immune response to cancer antigens [5, 6] and be involved in tumor biology [7,8].

Table 1
Pritumumab general features and characterization

Property	Reference
Clone generation	[3]
Specificity analysis	[3,4,9,16,17,25]
Effector functions	[14–18]
Xenograft model	[17,41]
Antigen characterization	[19,42]

Additional properties for pritumumab are outlined in Table 2. Overall, the hybridoma clone [9–11] as well as the secreted IgG1 antibody have been well characterized [12,13], the antibody shows ADCC and CDCC activity [14–18], the antigen recognized by pritumumab has been characterized [19–22], and an anti-paratactic idiotype antibody has been generated to pritumumab and shown to be a useful clinical reagent and an indi-

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Table 2
Additional properties of pritumumab

Characteristic	Property
Hybridoma	Fusion partner: UC729-6, tetraploid
	HLA A1, A2, A9, A24, B5, B17, Bw4, DR2, DR4, DR7
Antibody	IgG1, kappa; MW 150 K
Effector functions	ADCC ∼36% release CDC ∼60% cytotoxicity
Antigen properties	Non-reduced: MW 226 K
	Reduced: MW 60 K/53 K
	Affinity: $4.5 \times 10^{7}\mathrm{M}^{-1}$

cator of clinical outcome [21–24]. Drug-conjugates of the antibody also demonstrate effectiveness.

Specificity analysis of fresh frozen human tissues has shown that the antigen recognized by pritumumab, altered vimentin, to be restricted to various solid tumors irrespective of the germ layer origin of the tissues [4, 19,25]. The antigen is found on cells of ectodermal (brain), endodermal (colon, pancreas), and mesodermal (reproductive) origin. This is an interesting comment on the natural human immune response to cancer antigens [5,8]. Of particular specificity and interest was the binding of pritumumab to brain tumor tissues [17, 20,26,27].

Glioblastoma multiformes is an astrocytoma with a median survival time of 15 months [28] and after 5-years the survival rate is 3%. The major reason for such an aggressive and difficult to treat tumor is the rapid diffuse infiltration of individual tumor cells into the surrounding brain parenchyma, most often before diagnosis, making surgical debulking difficult. Pritumumab has been used to treat 249 brain cancer patients in various trials in Japan [29–35]. Most of the treated patients have been diagnosed with glioblastomas but others with astrocytomas or neuroblastomas. Of the 249 patients, 175 were evaluated and the results published primarily in the Japanese literature (see references). Patients diagnosed with glioblastomas were chosen for three reasons: (1) the antibody showed strong immunospecificity to malignant cells and tissues of brain origin, (2) the endpoint for glioblastomas is very short (3% survival after 5 years) so improvements in patient's health can be quickly established, and (3) pritumumab readily crosses the blood brain barrier. The half-life of pritumumab in serum was approximately 73 hours [34,35].

The purpose of this review is to summarize the various findings of pritumumab and to highlight its effectiveness in patients with various brain tumors, in particular glioblastoma. The majority of the clinical data has been published in the Japanese biomedical literature (see references) and may be difficult to obtain in English translations. This review summarizes all of this data on pritumumab, the first human antibody used to treat cancer patients.

2. Materials and methods

2.1. Clone generation

The hybridoma secreting pritumumab was generated in 1982 by the fusion of a B lymphocyte isolated from a regional draining lymph node of a patient with cervical carcinoma with UC-729-6 [3]. The clone was originally called CLNH11 but was also referred to as CLN-IgG, and ACA-11 in the literature. The World Health Organization (WHO) has officially designated this antibody as pritumumab. Pritumumab is a human IgG1, kappa antibody and its general properties are shown in Tables 1 and 2. The affinity of pritumumab for its antigen (as expressed on the human glioblastoma cell line, U-251MG) is 4.5×10^{-7} M.

The growth characteristics of the parent hybridoma have been analyzed and are summarized in Table 1. Subclones were generated for high secretion [3,4] and adapted to optimally grow in serum free media [36–40]. Antibody used for the clinical trials was generated in serum free media [35,37,38] and purified under GMP conditions.

2.2. Specificity analysis

Both cell lines and tissue samples were used to obtain the specificity profile of pritumumab. The overall reactivity with cell lines is shown in Table 3 [3,4,9] and the reactivity with human tissues, both normal and tumor involved, is shown in Table 4 [16,17,25].

2.3. Effector functions

Complement-dependent cytotoxicity (CDC) and antibody-dependent cell mediated cytotoxicity (ADCC) were performed as described [14–18].

Table 3
Enzyme-linked Immunosorbent assay (elisa) – formaldehyde-fixed cells

Cell Line	R.B.A.*	Cell Line	R.B.A.
Cervical Cancer		Gastric Cancer	
Hela	0.94	AGS	0.50
Hela 229	0.86	MKN-1	0.55
ME-180	1.63	MKN-28	1.05
Siha	1.01	MKN-45	1.08
Caski	0.94	MKN-74	1.20
Lung Cancer		KATO-3	0.18
A549	1.00	Hepatoma	
Calu-3	0.41	Alexander cells	1.62
PC-1	1.21	KG-45	1.46
PC-3	0.91	HEP-G2	1.49
PC-6	1.06	Colonic Cancer	
PC-9	0.41	Caco-2	2.19
PC-10	0.61	Bladder Cancer	
PC-13	1.15	HT 1376	0.06
PC-14	0.76	Pancreatic Cancer	
Brain Tumor		Capan-1	0.91
U 87MG	0.81	Renal Cancer	
U138MG	1.03	ACNE	1.06
U251MG	1.08	Neuroblastoma	
U373MG	1.45	PNDW	1.33
Cheng	0.90	Prostate Cancer	
Silberman	1.34	PC-3	0.91
Harman	1.32	Breast Cancer	
Jones	1.12	ZR-75-1	0.47
T-98	1.10	Ovarian Cancer	
Marcus	0.96	SK-OV-3	0.91
Melanoma		Normal Fibroblasts	
G-361	1.31	MRC-9	0.31
SK-MEL-3	1.72	WI-38	0.09
Malme-3M	1.31	Dctroit 551	0.09

*: Relative Binding Affinity to A549.

2.4. Nude mouse xenograft model

Balb/c athymic nude mice were inoculated with 10^6 U251MG cells as described [17,41]. Animals were treated with pritumumab 6 weeks after tumor cell inoculation with either a single 1mg injection or 3 injections of 1mg at 2 week intervals [34,35].

2.5. Drug-pritumumab conjugates

Pritumumab F (ab') 2 fragments were generated by enzymatic digestion. The purified fragments were then reacted with B-mercaptoethanol and subsequently mixed with parachloromercuribenzoic acid (MBA). This complex was then mixed with daunomycin to form drug-antibody conjugates. The daunomycin-pritumumab fragment complex was purified through a Sephadex G-25 column and analyzed by HPLC.

Table 4a
Immunoperoxidase staining of pritumumab with malignant and normal tissues

	Malignant	Benign	Normal
Brain*	21/32	2/19	0/8
Tongue	1/1	ND	0/2
Salivary gland	0/1	ND	ND
Thyroid	2/2	ND	ND
Esophagus	1/1	ND	0/2
Lung	3/5	ND	0/2
Stomach	3/5	ND	0/2
Heart	ND	ND	0/2
Renal	1/1	ND	0/3
Adrenal	0/2	ND	0/2
Spleen	0/1	ND	0/4
Liver	0/2	ND	0/3
Pancreas	2/2	ND	0/2
Gall bladder	2/2	ND	0/2
Lymph node	0/17	ND	0/4
Breast	5/15	1/5	0/2
Ovary	6/8	ND	0/2
Uterus	0/8	ND	0/2
Cervical	7/10	ND	0/2
Uterine corpus	2/3	ND	0/2

*see further detail in Table 4b.

Table 4b
Immunoperoxidase staining of various brain tissues with pritumumab

Anaplastic glioma	13/13
Anaplastic astrocytoma	4/4
Astrocytoma	1/5
Medulloblastoma	1/5
Ependymoma	1/2
Oligodendroglioma	1/3
Metastatic tumor	
Adenocarcinoma	3/3
Squamous cell carcinoma	1/2
Craniopharyngioma	2/5
Pituitary adenoma	0/3
Meningioma	0/5
Neurinoma	0/4
Choroids plexus papilloma	0/2
Normal brain (adult)	0/8
Normal brain (fetus)	0/17

2.6. Clinical

2.6.1. Patient recruitment

Patients were placed on study in their respective hospitals and followed all necessary protocols, documentation, ethical guidelines, and requirements according to Japanese laws. Written, informed consents were obtained from each patient or from the patient's family [32].

2.6.2. Treatment protocols

Patients in a Phase 1 trial received pritumumab as described [30,33]. Patients either in an early Phase

Table 5
Summary of pritumumab treatment protocols

Course of treatment*	Total pritumumab dose	# patients treated
1st	48 mgs	249 (100%)
2nd	96 mgs	100 (40%)
3rd	144 mgs	50 (27%)
4th	192 mgs	10 (5%)

*single course of treatment was 1 mg 2x per week for 24 weeks; total = 48 mgs.

Table 6
Various pritumumab treatment protocols used

PROTOCOL	Description
Protocol 1	Phase 1 study to examine toxicity; 10 patients evaluated [30]
Protocol 2	1mg 2x/week for 24 weeks; 10 patients evaluated [33]
Protocol 3	42 patients treated 1mg 1x/week for 24 weeks (7 patients evaluated [31];) 1mg 2x/week for 24 weeks (14 patients evaluated [31];)
Protocol 4	1mg 2x/week for 24 weeks; 69 patients evaluated [34];)
Protocol 5	1mg 2x/week for 24 weeks; 111 patients [35]
Protocol 6	Radioimmunotherapy trial; 7 patients [29]

2 setting or a late Phase 2 setting received pritumumab as shown in Tables 5 and 6 [31,34]. Patients in a radioimmunotherapy trial received pritumumab as described [29].

3. Results

3.1. Pre-Clinical summaries

This data is outlined in Tables 1 and 2. The generated hybridoma is tetraploid with an HLA profile of A1, A2, A9, A24, B5, B17, Bw4, DR2, DR4, and DR7. The hybridoma was adapted to grow in defined serum-free media and subsequently subcloned for high IgG secretion. Monoclonal antibody purified from the hybridoma is an IgG1, kappa. The antibody was purified using standard biochemical procedures of concentration, ammonium sulfate cut, dialysis, ion exchange chromatography, affinity column, followed by gel filtration; purity was $> 98\%$.

Immunoreactivity of pritumumab was analyzed by immunoflourescence, EIA, and immunoperoxidase staining with cell lines (Table 3) and human tissues (Table 4; Figs 1 and 2). Pritumumab primarily reacted with malignant cell lines and cells in human tissues. Normal cell lines and normal tissues were unreactive. Pritumumab has reacted markedly with malignant gliomas, such as glioblastoma, anaplastic astrocytoma, and craniopharyngioma but had not reacted to normal adult or fetal brain tissue or other extraneural tissue in both formalin-fixed and frozen sections.

3.1.1. Effector functions

ADCC cytotoxicity was analyzed by ^{51}Cr release assay with ME-180 target cells. Activity was measured at 36% [20]. CDC analysis using rabbit complement showed an approximate 60% cytotoxicity with primary breast cancer cells. Pritumumab behaves as a typical human IgG1 in its ability to fix complement and augment ADCC activity [14–18].

3.1.2. Nude mouse xenograft analysis

At one or two weeks post treatment with single 1mg injections of pritumumab the human glioma xenograft growth was temporarily decreased followed by a rapid regrowth that equaled the control group. Those animals treated with multiple injections of pritumumab showed a significant tumor growth inhibition. Histologic examination of the tumor mass after pritumumab treatment showed significant tumor cell necroses with no observed metastasis [17,41]. Pritumumab distributed into tumor tissues 6 hours after administration and was still present at the xenograft 96 hours after treatment [41].

3.1.3. Antigen characterization

Under non-reducing conditions purified pritumumab showed reactivity with a MW 226 K molecule from A549 lung cancer cells. Under reducing conditions purified pritumumab showed reactivity with two chains of MW 60 K and 53 K from A549, Hela, MKN45, and G361 cell lines. Scatchard analysis showed a pritumumab affinity of 4.5×10^{-7} M with the antigen from U-251MG cells. Sequence analysis of purified antigen

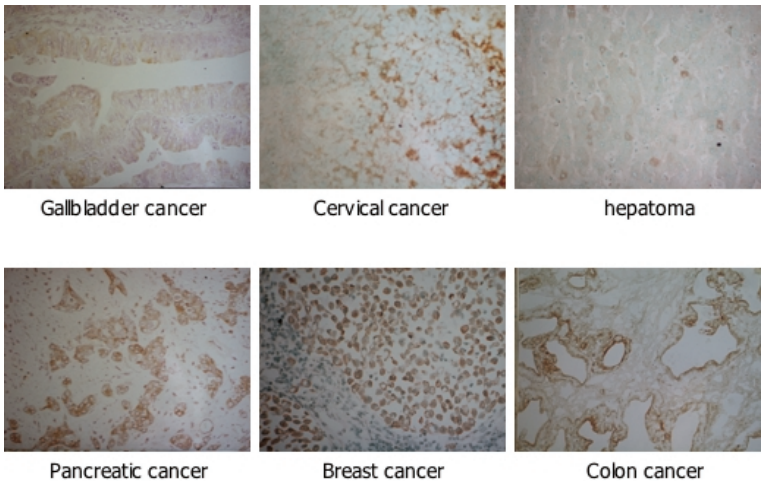

Fig. 1. Immunoperoxidase staining of human tissues with pritumumab. A, gallbladder cancer; B, cervical carcinoma; C, hepatoma; D, pancreatic carcinoma; E, breast cancer; F, colon carcinoma.

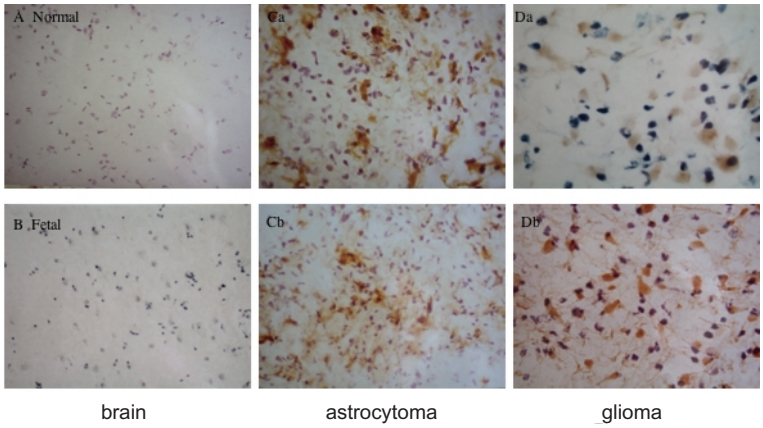

Fig. 2. Immunoperoxidase staining of human brain tissues with pritumumab. A, normal brain; B, fetal brain; C, astrocytoma; D, Glioma.

showed it to be altered vimentin [19,42]. The reactive epitope is located in the c2 (coil 2 of the central rod) domain of vimentin [42]. The antigen was found to be cell bound and not circulating either in the serum or cerebrospinal fluid [32].

3.1.4. Antibody-drug conjugates

The daunomycin-pritumumab fragment complex was purified through a Sephadex G-25 column and analyzed by HPLC; purity was $> 95\%$. The drug-fragment complex showed reactivity with target cell lines, A549 and Hela229 and no reactivity with antigen negative cell lines (Flow-2000 fibroblasts). The cytotoxic effects of the drug conjugate showed a two-log increase in inhibition of cell growth.

3.2. Clinical

3.2.1. GMP antibody production and manufacturing

Pritumumab was isolated and purified from mass cultures of the parent hybridoma grown under serum-free conditions using conventional techniques under GMP manufacturing protocols. The antibody was provided as a lyophilized powder that was subsequently reconstituted prior to injection.

3.2.2. Patient recruitment

Patients who have gone on any of the various pritumumab studies were clinically diagnosed with brain tumor. These patients received conventional surgery (where applicable), chemotherapy, and, if necessary, radiation treatments. Prior to dosing with pritumumab

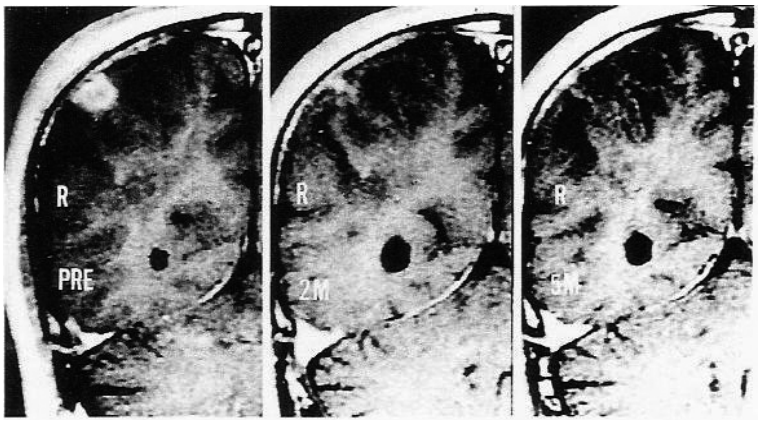

Fig. 3. Image analysis of patients with brain cancer treated with pritumumab (33). Malignant astrocytoma of the right parietal lobe before (a), and after (b,c) pritumumab therapy. (a), Gadolinium-enhanced magnetic resonance image shows a small tumor of the right parietal lobe. The same tumor at 2 months (b) and at 5 months (c) after pritumumab therapy. Gd-enhanced MR images show that the tumor lesion decreased in size and finally disappeared.

the patients were kept off any treatments for at least 4 weeks to allow a "washing" period to remove any effects of previous treatment protocols thereby reducing unwanted side effects.

3.2.3. Treatment protocols

From a total of 249 patients treated with pritumumab 175 were evaluated (see Tables 5 and 6; refs 29–35). Of these, one group received doses under a Phase 1 setting to determine the safety of the antibody [30,33]. As reported, "adverse reaction and abnormal laboratory data was not found" [33] in any of the treated patients. A single course of pritumumab treatment consisted of 1mg given twice per week for 24 weeks making the total dose per course of 48mgs. All of the patients were given a single course of treatment. A second course was given to approximately 40% of these patients, a third course given to 27% of the patients and a fourth course given to 5% of the patients (Table 5). The majority of the observed partial (PR) and complete responses (CR) were observed with patients receiving 3 to 4 courses of pritumumab treatments.

Under different Phase 2 settings one group of 10 patients treated with pritumumab [33] reported that one patient with a malignant astrocytoma showed a total regression, 3 patients (one glioblastoma multiforme and two with astrocytomas) showed a reduction in tumor size and an improvement in the neurological symptoms and overall status, one patient showed (another case of glioblastoma multiforme) stable disease (which had progressed rapidly and presented deteriorating neurological symptoms. This overall decline was stabilized for 15 months with continuous iv therapy with pritumumab; the patient ultimately died of pneumonia), and the remaining 5 cases showed progressive disease, unaffected by the therapy protocol.

The injected antibody had a biphasic half life in patients [31,35]. The first phase half-life was 0.63 hrs and the second phase half-life was 73 hrs.

3.2.4. Patient analysis

Patient images

The images shown in Figures 3–6 are brain scans of individual patients who have been successfully treated with pritumumab. In Fig. 3 are images of a patient with malignant astrocytoma of the right parietal lobe. After 5 months post treatment the tumor was unable to be imaged suggesting a complete response in this patient. In Fig. 4 are images of a patient with pontine glioma (protoplasmic astrocytoma) and peritumoral edema to the right of the pons who has been successfully treated with pritumumab. Six months after treatment the tumor mass has been significantly reduced and the markedly deviated IVth ventricle has been corrected. In Fig. 5 are images of a patient with glioblastoma multiformes of the left frontal lobe with severe peritumoral edema. After 10 months post treatment there was a significant decrease in tumor size, diminishing of the peritumoral edema, and enlargement of the leteral ventricles. In Fig. 6 are images of a patient with a right occipital glioblastoma. After 1.5 years post pritumumab treatment the patient shows dramatic reduction of the tumor mass.

Phase 1

In a Phase 1 setting [30] two groups of 5 patients each were treated with pritumumab. Group 1 consisted of

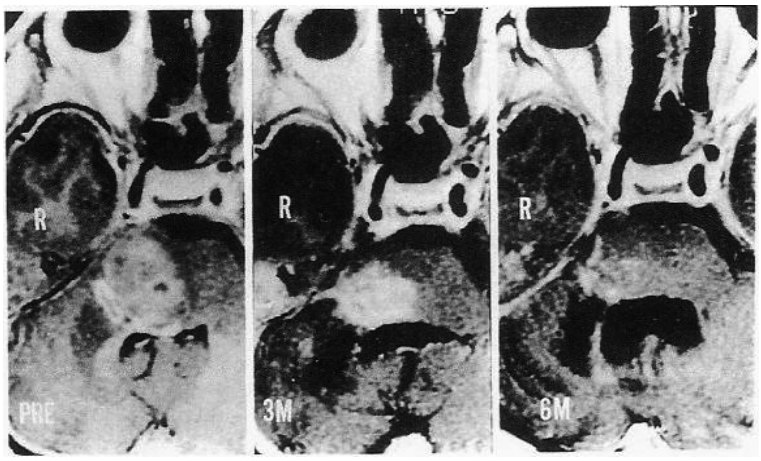

Fig. 4. Results of a case of a pontine glioma (protoplasmic astrocytoma) before (a) and after (b,c) pritumumab therapy (33). (a),Gd-enhanced MR image shows an irregularly enhanced tumor with peritumoral edema to the right of the pons and a markedly deviated IVth ventricle. The same tumor after 3 months (b) and after 6 months (c) of pritumumab therapy. The Gd-enhanced MR images show that the tumor has decreased in size and that the deviation of the IVth ventricle has been corrected.

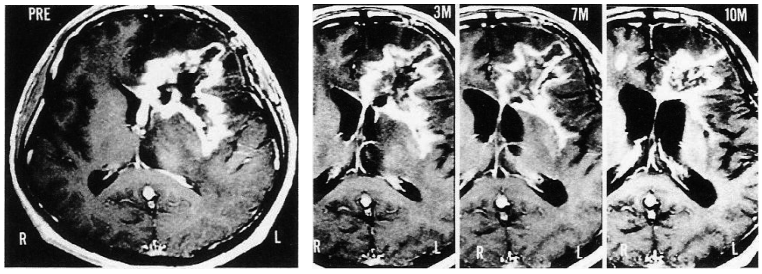

Fig. 5. A, a glioblastoma multiforme of the left frontal lobe prior to therapy (33). Gd-enhanced MR imaging shows an irregularly enhanced tumor manifesting severe peritumoral edema of the left frontal lobe. B, Findings after the start of pritumumab therapy at 3 months (a), at 7 months (b), and at 10 months (c). These Gd-enhanced MR images show a decrease in tumor size, mass effect and peritumoral edema. These images also show the gradual enlargement of the leteral ventricles.

5 glioblastoma patients and were treated with 1mg per week for 4 weeks (4mgs total dose). Group 2 consisted of 5 anaplastic astrocytoma patients and were given 1mg twice per week for 4 weeks (8mg total dose). No toxicities were observed. One patient responded at that dose.

Early Phase 2

In an early Phase 2 setting [31] two groups were treated. Group 1 received 1mg per week for 24 weeks and their response rate was 14%. Group 2 received 1mg twice per week for 24 weeks and their response rate was 50%; making the overall response rate in this study of 38%. In Group 2 there were one CR (4.8%) and 6 PR (33%) responses. Of these, one out of two glioma patients responded (50%), 3 out of 8 anaplastic astrocytoma patients responded (37.5%) and 4 out of 11 glioblastoma patients responded (36%).

Late Phase 2

In a late Phase 2 setting [34] each patient received 1mg twice per week for 24 weeks. The astrocytoma response was 40%, the anaplastic astrocytoma response was 39%, the glioblastoma response rate was 5.6%, the brainstem glioma response was 100%, and the medulloblastoma response rate was 0%, making the overall average of 27% response.

Overall response rates

Based on the data shown in Fig. 7 the 5-year survival of a group of 66 glioblastoma patients treated under a late Phase 2 setting with pritumumab had an overall aggregate survival of almost 25%. Focusing on those patients that either had a partial or complete response the survival after 5-years was over 70%. Typical 5-year survival of these patients with traditional treatments is 3%.

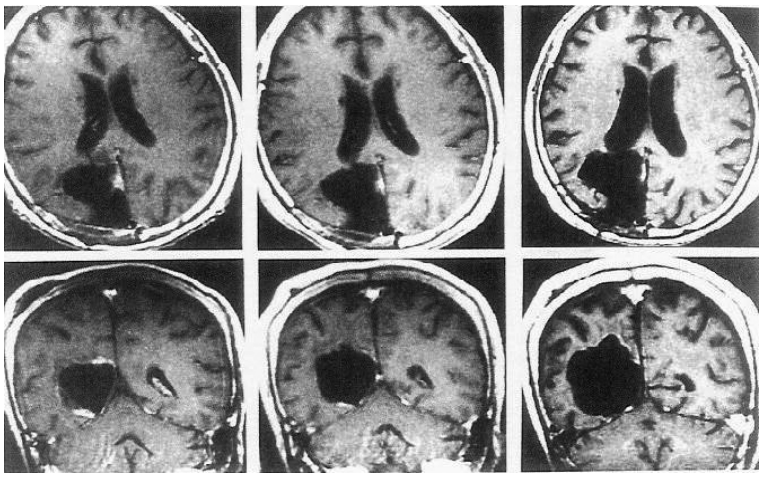

Fig. 6. Serial computed tomography (CT) scan of a 66-year old female with right occipital glioblastoma (23). (a), image taken immediately prior to pritumumab therapy; (b) image taken 2.5 months after the start of pritumumab therapy; (c) image taken 1.5 years after the start of pritumumab therapy.

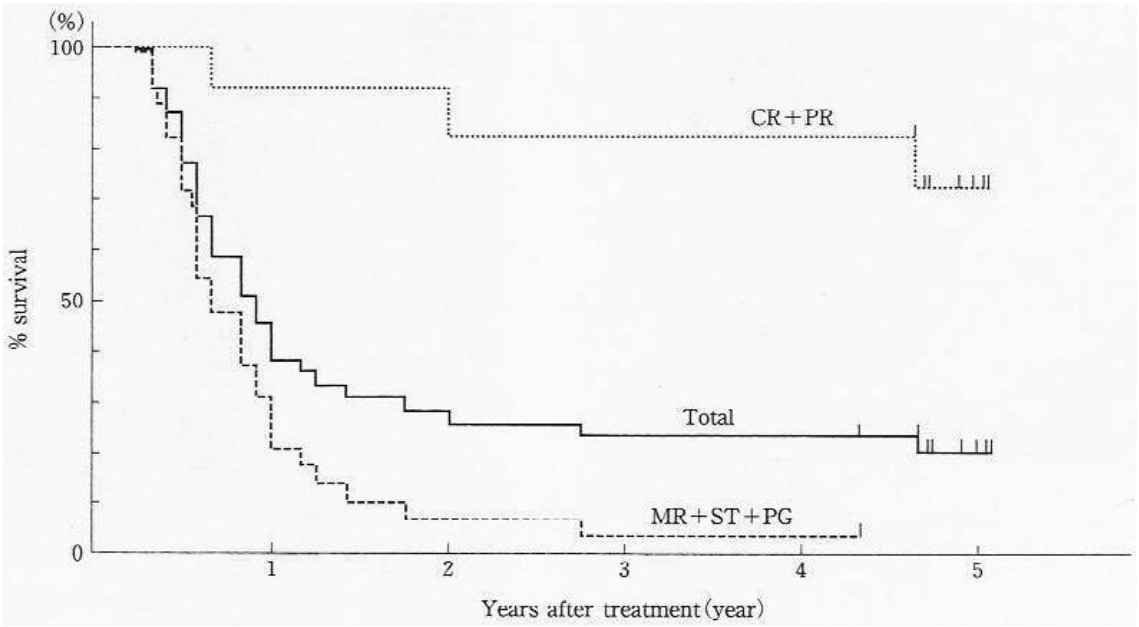

Fig. 7. 5-year survival data of 66 glioblastoma patients treated with pritumumab (35). CR, complete response; PR, partial response; MR, moderate response; ST, stable disease; PG, progressive disease. (see ref 35).

3.2.5. Radioimmunotherapy

In a study [29], 7 patients with recurrent malignant glioma were treated with 131-I labeled pritumumab (2.5 mg, 2.5 mCi) intra-tumorally through Ommaya reservoir, a plastic container placed in the subgaleal space that is connected to the lateral ventricle by tubing. The patients were monitored with external scintigraphy. From the gamma image, specific incorporation of the radiolabeled pritumumab was observed with 70.5% of the radioactivity distributed in the area of tumor tissue and perifocal region. The interstitial irradiation dose was calculated as 15Gy in 8 days. Neither adverse side effects nor antibody toxicity were observed in these patients. Those patients receiving either two or three repeated radioimmunotherapy treatments showed the best benefit of surviving with two patients showing partial remission and three patients as no change over the 9–15 month observation period after therapy [29].

4. Discussion

Pritumumab has been shown to be a safe and effective therapy for patients with brain cancer. One study [35] reported 5-year survival data of 66 glioblastoma patients treated with pritumumab with an overall response rate of approximately 25%. By combining only the 3 CR patients with the 13 PR patients in this study the response rate was about 73% (see Fig. 7). Note, in this study the patients received a total dose of 48mgs of pritumumab; a small amount compared to the hundreds of milligrams of standard therapy of other approved antibodies [1].

Individual doses of pritumumab treatments were limited to one milligram due to the levels of DNA ($\sim$8pg/dose) in the preparations (pritumumab was isolated from mass cultures of the parent hybridoma and not a recombinant cell line). The limit of 10pg of DNA per dose is required according to the FDA guidelines for biotechnology products. Since the injected dose of 1mg was low no toxicities were observed in the treated patients. Even with such a low 1mg dose there was a significant response rate from the treated patients; the highest observed combined response rate in one study [34] was 40% with astrocytoma patients. An even higher dose may be more beneficial to patient's clinical outcomes so additional trials at a higher dose will be investigated. Also, at higher doses there may be toxicities but these will need to be determined, if any, with additional clinical trials.

Another study reported [33] that 40% of the treated patients (10 total) responded to the pritumumab therapy so it appears the relative immune health of the treated patients may play a role in antibody immunotherapy. A higher dose may overcome this deficiency resulting in a higher response rate, though this remains to be tested. A study of 21 cases [31] showed that those treated with 1mg per week had a response rate of 14.2% whereas those receiving 1mg twice per week had a response rate of 50%; overall response rate was 38% (8/21). This suggests that the dose of the antibody is critical for long term benefit. Also, as shown in Table 5, those patients who received multiple courses of pritumumab over long periods of time benefited the most from this treatment. Also, patients who developed an anti-idiotypic response to pritumumab showed a better clinical outcome than those patients who did not develop an anti-idiotype response [23].

The antigen recognized by pritumumab is a "vimentin-like" protein [19,42]. The sequence of the antigen is in homology with the vimentin gene but the neo-epitope recognized by pritumumab is novel in that it is expressed on the cell surface [42] and does not match the specificity of commercially available anti-vimentin antibodies. It was speculated that the natural human immune response recognized the vimentin-like neo-epitope when it became expressed on the surface of malignant epithelial cells. Also, the neo-epitope had to have been in high enough concentration on the membrane to actually stimulate an immune response. The altered vimentin antigen drove the immune response to recognize it as foreign.

Based upon the novel specificity of pritumumab it is tempting to speculate that this antibody may reflect an aspect of the natural human anti-cancer immune response [5,7,43]. Since the antibody was derived from a sentinel lymph node [3,7] this lends more credence to that aspect of human cancer biology. Patients do generate a humoral immune response to their own tumor antigens [1,5,8] and pritumumab appears to be one of these antibodies. Since tumors do grow this questions either the immune efficiency of the generated antibody response or perhaps the tumor cells outgrow the speed of the amount of antibodies generated by cancer patients necessary to eradicate their cancer cells. Histological examination of many tumor masses frequently does show areas of necrosis. One interpretation may be this is a reflection of an active anti-cancer immune response whereby antibodies (along with a cellular response) are killing tumor cells. Since there may not be enough generated effective antibody(ies) by the patients not all tumor cells are killed thereby allowing either escape mutants to proliferate or the tumor mass in general to grow unchecked. Further clinical trials will be conducted to address the overall effectiveness of pritumumab antibody therapy.

5. Conclusion

Pritumumab, a natural human antibody and not a genetically engineered Mab, has shown promise in the cancer clinic. Patients treated with pritumumab have benefited from the therapy. The recognized antigen, an altered tumor-associated vimentin, may represent a class of altered normal antigens identified by the intelligence of the natural human immune response that can be exploited in cancer immunotherapy.

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