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A phase 1 dose escalation of pritumumab in patients with refractory or recurrent gliomas or brain metastases

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Abstract

Background. This phase 1 (NCT04396717) open-label, multicenter study, evaluated Pritumumab, a IgG1 monoclonal antibody, in patients with gliomas and brain metastases. The primary objective was to evaluate the safety and/or tolerability and to identify a recommended phase 2 dose (RP2D) of Pritumumab.

Methods. Adult patients with recurrent gliomas or brain metastases were enrolled in the dose cohort that was open at the time of their consent. Study treatment consisted of pritumumab administered intravenously weekly on days 1, 8, 15, and 22 in 28-day cycles. Safety, pharmacokinetics (PK), pharmacodynamics (PD), and clinical activity were evaluated.

Results. Fifteen patients received Pritumumab in the recurrent setting. Pritumumab was well tolerated, with no serious adverse events related to Pritumumab reported. The most common drug-related toxicities were constipation and fatigue. There were no dose-limiting toxicities observed, and a maximum tolerable dose was not reached. Thus, the maximum feasible dose and recommended phase 2 dose of Pritumumab was established at 16.2 mg/kg weekly. Out of eleven patients evaluated for efficacy, one patient (9.1%) demonstrated partial response based on response assessment in neuro-oncology criteria, and disease stabilization was seen in 3 patients (27.3%).

Conclusions. Pritumumab was well tolerated with no DLTs observed up to 16.2 mg/kg weekly. Further studies are warranted to determine clinical benefit in patients.

Key Points

1. This phase I study demonstrated promising safety results and laid the groundwork for further clinical development.
2. This study holds promise for improving patient outcomes and fuels further research in brain cancer.

Glioblastoma (GBM) is one of the most common malignant primary tumors of the brain and central nervous system with a poor prognosis. It is the most common type of primary malignant brain tumor in adults, representing approximately 57% of all gliomas and 48% of primary malignant central nervous system tumors, with a 5-year survival rate of less than 10%.[1–3] With the annual worldwide incidence of gliomas in 6 of the 100 000 individuals, there is a 1.6-fold higher likelihood of gliomas occurring in males.[4] Despite aggressive treatments following standard-of-care surgical resection, radiotherapy, and chemotherapy with temozolomide, recurrence is common, and the survival rates remain low for 15–18 months.[5] At recurrence, treatment options become even more limited, and there is a lack of therapies that significantly prolong overall survival. Despite advances in treatment for newly diagnosed glioma patients, essentially all patients will experience disease recurrence. For patients with recurrent disease, conventional chemotherapy is generally ineffective with response rates <20%.[6] Like metastatic cancers to the brain, there is a high frequency of diffuse and leptomeningeal metastases

Importance of Study

The study demonstrates the safety of pritumumab in a phase 1 clinical trial for the treatment of brain cancer. The results from this phase 1 study provide an understanding of the biological insights into pritumumab's mechanism of action, pharmacokinetics, and its interactions with biological systems. The positive safety outcomes open avenues for translational research aimed at exploring combination therapies, biomarkers for patient stratification, and predictive markers of response.

from primary gliomas. Recent genome-wide studies have confirmed that GBM is a heterogeneous group of diseases that makes it difficult to treat everyone the same.[7]

There is a clear need for improved therapeutic strategies for GBM, and likewise, there are many other recurrent primary brain tumors (meningioma, chordomas, gliomas, medulloblastomas, craniopharyngiomas, pituitary tumors, etc.) that also have no effective treatments besides surgery and radiation. In 2016, the World Health Organization (WHO) Classification of Tumors of the Central Nervous System was updated to add a more accurate diagnosis using molecular parameters and histology. This current update breaks the century-old principle of classifying diagnosis by only microscopy.[8] By using phenotypic and genotypic parameters for classification, it leads to greater biologically homogenous diagnostic entities and improved patient management. For example, with the new classification isocitrate dehydrogenase (IDH)-wild type should be considered as a critical biomarker of low-grade gliomas whose characteristics are similar to those of GBM. Analogously, GBMs with mutant IDH are similar to anaplastic astrocytoma. Therefore, the treatment for gliomas should focus on the molecular diagnosis and classification.[9] This phase 1 study with Pritumumab included a wide diagnosis of CNS tumors to assess the clinical, pathological, and molecular diagnosis of the different glioma types, allowing for one to evaluate the data for effective treatment response. This highlights the critical need for novel therapeutic interventions to improve outcomes for patients with gliomas.

Pritumumab, designated by the WHO, is a natural human IgG1 kappa antibody. It was initially developed through human-human hybridoma technology at UC San Diego. This process involved the fusion of a human lymphoblast-like B cell line (UC729-6) with a human lymphocyte (B cell) obtained from a regional lymph node of a patient with cervical carcinoma.[10] Originally, this monoclonal antibody was referred to by various names in early literature, including CLNH-11, CLN-IgG, and ACA-11. However, its official designation is now pritumumab, recognized by the WHO. This antibody holds potential for therapeutic applications in the treatment of certain conditions, owing to its specific properties and origins.

Pritumumab exhibits specificity in binding to a malignant tumor-associated antigen known as TA226, which is a form of ecto-vimentin. This antigen is expressed across a spectrum of tumor types, including cervical cancer, lung cancer, colorectal cancer, melanoma, stomach cancer, prostate cancer, gallbladder cancer, breast cancer, and various forms of cancer.[10–12] Notably, pritumumab demonstrates heightened reactivity with brain cancer cell lines compared to other cancer types. Importantly, it does not exhibit reactivity with normal neurons, astrocytes, or fetal cerebral cells. This selectivity is crucial for minimizing off-target effects and preserving normal tissue function.

Pritumumab, an immunoglobulin G of isotype 1 with kappa light chains, exerts its antitumor effects primarily through antibody-dependent cellular cytotoxicity (ADCC).[13,14] This mechanism involves the recruitment of immune cells to target and destroy cancer cells bound by the antibody. Studies have demonstrated notable ADCC activity, as well as effective penetration into brain tumors and antitumor activity in nude mouse xenograft models. The binding specificity of pritumumab lies in its interaction with an epitope on the cell surface-expressed vimentin, known as EDV (ectodomain vimentin).[11] Vimentin is a major component of the intermediate filament family of proteins, contributing to cellular integrity and resistance against stress.[15] EDV, being overexpressed on the cell surface of various epithelial cancers, including prostate cancer, gastrointestinal tumors, gliomas, central nervous system tumors, breast cancer, malignant melanoma, and lung cancer, serves as a target for Pritumumab.[10,11]

The overexpression of EDV in cancer is associated with accelerated tumor growth, invasion, and poor prognosis. However, the exact role of EDV in cancer progression remains somewhat unclear, warranting further investigation into its mechanisms and potential therapeutic targeting. Pritumumab's ability to selectively bind to EDV-expressing cancer cells presents a promising avenue for targeted therapy in various cancer types, including those affecting the central nervous system.

The reactivity of pritumumab has been extensively studied, demonstrating efficacy against a wide range of human tumor cell lines in vitro, totaling 30 different lines.[10,11,13] Additionally, its therapeutic potential has been evaluated in vivo using a nude mouse model, where human glioma cell lines were transplanted into athymic mice to mimic tumor growth for 35 days. The brains of euthanized mice were removed, and sliced and various areas were imaged by confocal microscopy (Nikon Eclipse Ti). Findings demonstrate the capacity of pritumumab to cross the blood/tumor barrier in the brain and to concentrate on human tumor xenografts.[16] This is a feature of pritumumab which provides it with an advantage that many other mAbs do not have.[12] In these studies, significant findings were observed regarding the therapeutic effect of pritumumab. Specifically, compared to untreated control animals, those receiving pritumumab exhibited a notable reduction in tumor growth. This effect was evident at various time points post-transplantation, including 10, 15, and 18 days, indicating the sustained antitumor activity of pritumumab

in this experimental setting.[17,18] Thus, this indicates that pritumumab is one of the unique mAbs that is able to cross the blood/tumor barrier in the brain.

These results highlight the potential of pritumumab as a promising therapeutic agent for the treatment of gliomas and potentially other types of tumors. With further investigation and clinical trials warranted to better understand its efficacy, safety profile, and potential for clinical application in cancer therapy, we report the results of a phase I dose-escalation trial of pritumumab administered intravenously in adult patients with brain cancer.

Materials and Methods

This study was conducted at 2 investigational sites in the United States in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization/Good Clinical Practice guidelines. The institutional review boards of all participating sites approved the study, and patients were enrolled following written informed consent. The clinical trial was registered on ClinicalTrials.gov (NCT04396717).

Study Design

This open-label, non-randomized, multicenter, phase 1 sequential 3 + 3 dose-escalation study of pritumumab was designed to evaluate the safety, tolerability, and recommended phase 2 dose (RP2D) of intravenously administered pritumumab in patients with recurrent gliomas or with brain metastases having failed prior therapy. Study treatment consisted of pritumumab administered intravenously weekly on days 1, 8, 15, and 22 in 28-day cycles. Five dosing cohorts were planned.

Eligibility Criteria

Participants considered eligible to participate in the trial were those who met the entire inclusion and exclusion criteria. Key eligibility included those with a histologically confirmed diagnosis of central nervous system cancer, adequate organ function, and at least 28 days from any prior cytotoxic investigational agent. See Supplementary Material date for additional detailed information on the trial eligibility.

Treatment Regimen and Dose Escalation

Pritumumab was administered as an intravenous infusion weekly on days 1, 8, 15, and 22 in 28-day cycles. The dose-escalation levels were 1.6 mg/kg (cohort 1), 4.8 mg/kg (cohort 2), 8.0 mg/kg (cohort 3), 12.0 mg/kg (cohort 4), and 16.2 mg/kg (cohort 5).

Dose-Limiting Toxicity

A dose-limiting toxicity (DLT) was defined as a clinically significant adverse event (AE) occurring within the first 28 days of starting the study treatment that is considered by the investigator to be possibly, probably, or definitely related to pritumumab. Any grade 3 or 4 toxicity constituted a DLT, including the following toxicity events which must be considered to be clinically relevant (eg, in duration): any grade 3 or 4 non-hematologic toxicity, excluding alopecia or unpremedicated nausea/vomiting, grade 3 nausea, vomiting, or diarrhea lasting >24 hours despite standard prophylaxis and/or treatment, grade 4 diarrhea and vomiting of any duration; grade 3 febrile neutropenia (defined as ANC < 1000/mm^3 with a single temperature of >38.3 °C or a sustained temperature of ≥38.3 °C for more than 1 hour), grade 4 febrile neutropenia of any duration, grade 4 neutropenia lasting >5 days (defined as a neutrophil count of <500/mm^3), grade 4 thrombocytopenia or thrombocytopenia with clinically significant bleeding (i.e. bleeding that requires blood or platelet transfusion or other medical intervention, or that may cause disability or death, such as cerebral hemorrhage), grade 4 anemia of any duration, any clinically significant grade 3 toxicity that precluded administration of the next scheduled dose beyond 14 days was considered a DLT. While the occurrence of DLTs was used to determine whether dose escalation may proceed, dose escalation was also guided by an assessment of all grade toxicities and trends in AEs seen in subsequent dosing cycles when considering future dose escalation and whether an intermediate dose may be warranted.

Additionally, if any of the following events were observed in the current cohort, 2 or more grade 2 AEs that were at least possibly due to Pritumumab, one or more grade 3 AEs deemed at least possibly due to Pritumumab (even if this doesn't meet criteria for a DLT), and a single DLT, dose escalation of subsequent cohorts would be modified to decrease the dose escalation to 50% of the prior dose.

The recommended phase 2 dose (RP2D) was determined at a dose equal to or below the maximum tolerable dose (MTD) upon review of all study data. The final determination also considered any cumulative or delayed toxicity (eg, an AE that occurred later than the DLT observation period).

Dose Modifications

Dose modifications for pritumumab were specified in the protocol and management was detailed for anticipated drug-related toxicities. For toxicities not defined as a DLT, a dose delay of up to 14 days always be considered prior to any dose reduction. For grade 3 non-hematologic toxicities related to study treatment, the first occurrence allowed patients to continue treatment at the current dose level, a second occurrence required a delay in treatment until resolution to grade 1 or baseline. If toxicity resolves within 14 days, patients may resume treatment at the same dose; however, if toxicity resolves after 14 days, treatment is to be resumed at the prior dose level. A third occurrence required a discontinuation from study treatment. Grade 4 non-hematologic toxicities related to study treatment required patients to stop study treatment. All patients were followed up for toxicity from treatment initiation until 30 days after the end of the last investigational product administration. Any event that occurs more than 30 days after the last dose of treatment and is attributed (possibly,

probably, or definitely) to the agent(s) was also reported accordingly.

Safety

Safety evaluations for pritumumab were conducted following a structured schedule to assess hematological, biochemical, and other relevant parameters throughout the treatment regimen. The evaluation schedule included weekly assessments of hematology and chemistry on days 1, 8, 15, and 22 during cycles 1 and 2, followed by biweekly evaluations thereafter. Additionally, coagulation levels were monitored weekly for the first 2 cycles. Physical examinations, assessment of performance status, and neurological exams were conducted at the beginning of each treatment cycle to monitor overall health and any potential treatment-related effects. Vital signs, including blood pressure, heart rate, respiratory rate, and temperature, were measured at every visit to detect any abnormalities. Electrocardiograms (ECGs) were performed at baseline before initiating treatment and at the start of each treatment cycle to assess cardiac function and monitor for any signs of cardiac toxicity. Toxicity assessments were conducted according to the National Cancer Institute Common Toxicity Criteria for AEs (CTCAE) version 5.

Pharmacokinetic Analysis

Pharmacokinetic (PK) data was obtained to guide the optimal dose of pritumumab. Blood samples (in K_2EDTA tubes) were collected pre-dose and at 0.5. 1, 2, and 4 hours (± 30 minutes) after the dosing of pritumumab on days 1, and days 8 or 15 (± 3 days) of cycle 1, and on days 1 or 8 (± 3 days) of cycle 2. Cerebrospinal fluid (CSF) samples (< 10 mL with 1% citric acid added to prevent adsorption loss) were collected via lumbar puncture or from an

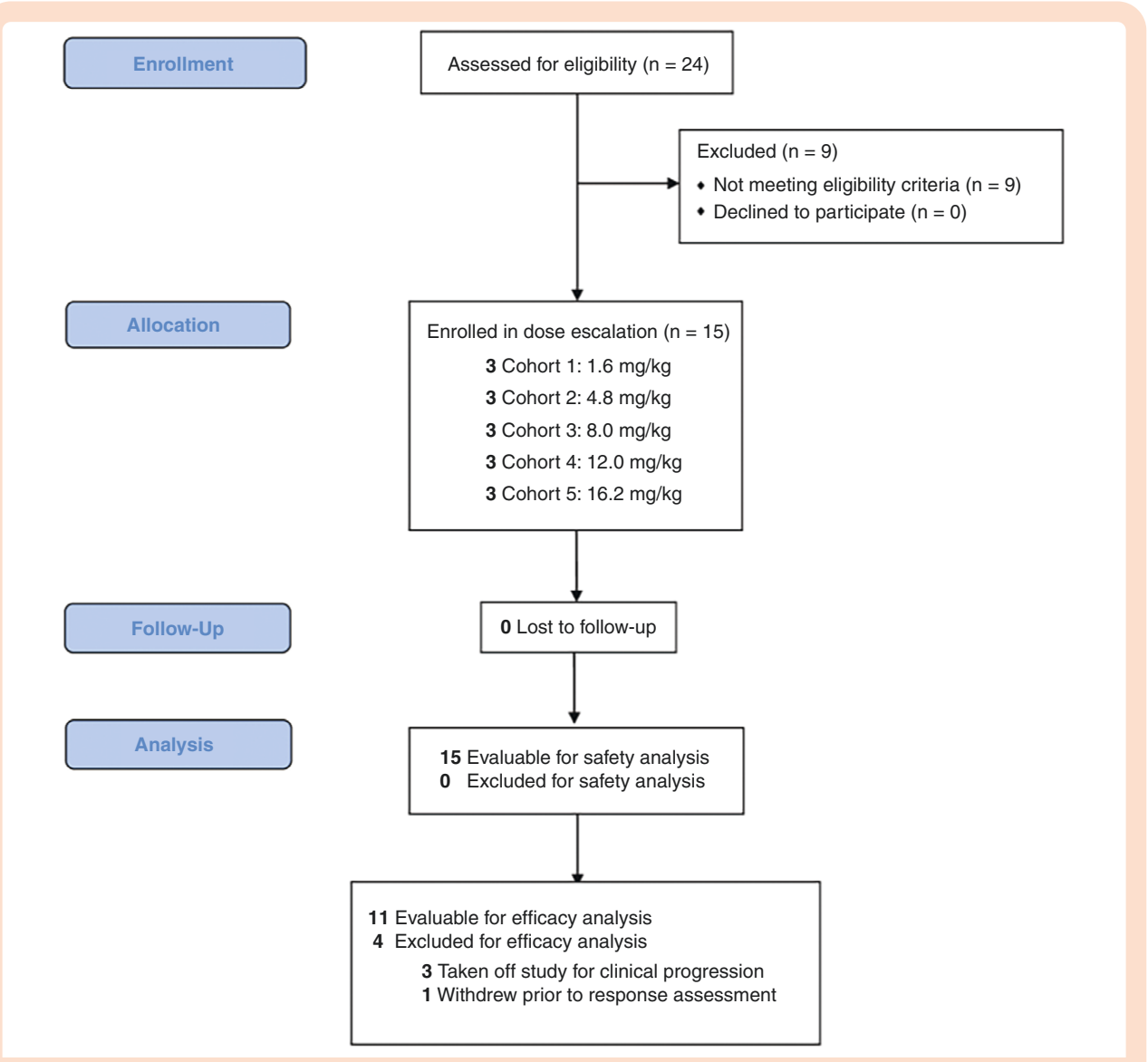

Figure 1. CONSORT flow diagram.

Table 1. Patient Demographics and Clinical Characteristics of All Treated Patients ($N = 15$)

Characteristic	No. of patients	%
Age, years		
Median	58	
Range	40–84	
Gender		
Female	4	27%
Male	11	73%
Racial origin		
White	15	100%
Ethnicity		
Hispanic or Latino	3	20%
Not Hispanic or Latino	12	80%
Pathology		
Glioblastoma, grade IV	12	80%
Anaplastic astrocytoma, grade III	1	7%
Oligodendroglioma, grade III	1	7%
NSCLC with brain metastases	1	7%
Karnofsky performance status		
90	3	20%
80	5	33%
70	6	40%
60	1	7%

Ommaya reservoir to measure pritumumab concentrations 60 minutes (±30 minutes) post-drug administration once during cycle 1, and prior to drug administration once during the first 2 weeks of cycle 2.

Analysis of samples was performed by BioAgilytix, using a method that employed a quantitative sandwich ligand-binding immunoassay format. The mouse IgG1 anti-idiotype (anti-id) antibody (Ab) was used as an antigenic capture and the horseradish peroxidase (HRP) conjugated goat anti-human IgG Ab, multi-species adsorbed (also known as goat anti-human IgG (H + L), multi-species serum proteins adsorbed-HRP or anti-hIgG-HRP) was used as a detection reagent. Wells of the Nunc MaxiSorp® microtiter plate was coated with mouse IgG1 anti-id Ab. After blocking and washing, pritumumab standard, quality control (QC) samples (QCs), and test samples were diluted in Assay Diluent and added to the coated wells. Following incubation and wash steps, the detection of pritumumab was achieved by the addition of anti-hIgG-HRP. After sequential incubation and wash steps, 3,3′,5,5′-Tetramethylbenzidine (TMB) solution was allowed to react with the bound HRP complex. When the signal of the highest standard reached approximately 1.00–1.20 optical density (OD) at 650 nm or after 30 minutes, whichever came first, the plate was quenched with Stop Solution. The color intensity that developed was proportional to the amount of bound pritumumab in the wells. The data were captured using SoftMax Pro 6 version 6.5.1 software program provided by Molecular Devices, with inter-assay calculations done in Excel using unrounded values and reported with 3 significant figures. The OD

Table 2. Number of Patients With Treatment-Related AEs by Dose Level of Pritumumab

	CTCAE grade																
	1.6 mg/kg ($n = 3$)			4.8 mg/kg ($n = 3$)			8.0 mg/kg ($n = 3$)			12.0 mg/kg ($n = 3$)			16.2 mg/kg ($n = 3$)			Total patients ($n = 15$)	
	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	No.	%
Gastrointestinal disorders																	
Constipation	1						1	1			1		1			**5**	**33.3%**
Nausea							1									**1**	**6.7%**
General disorders																	
Dehydration				1												**1**	**6.7%**
Fatigue				1			2	1			2		1	1		**8**	**53.3%**
Investigations																	
Hypomagnesemia							1									**1**	**6.7%**
MCHC Low													1			**1**	**6.7%**
Musculoskeletal and connective tissue disorders																	
Muscle weakness (lower extremities)													1			**1**	**6.7%**
Muscle weakness (upper extremities)													1			**1**	**6.7%**
Exacerbation of joint tenderness	1															**1**	**6.7%**
Neuropathy										1						**1**	**6.7%**
Psychiatric disorders																	
Depression													1			**1**	**6.7%**
Skin and subcutaneous tissue disorders																	
Dry Skin (Face)										1						**1**	**6.7%**
Pruritus	1															**1**	**6.7%**
Scalp Dryness							1									**1**	**6.7%**

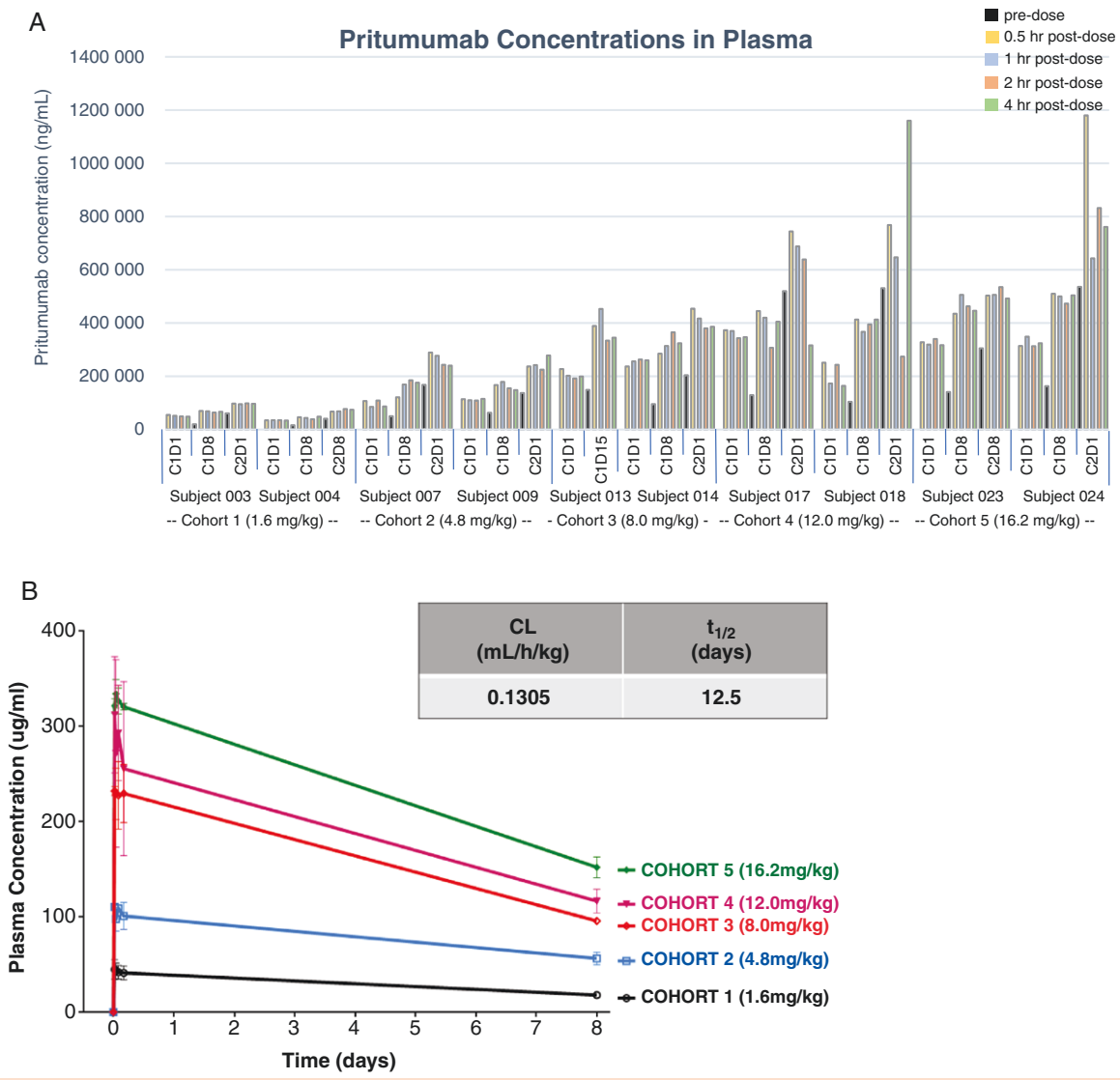

Figure 2. Pritumumab concentration. (A) Concentration of pritumumab (ng/mL) in blood at indicated time points. (B) Plasma concentration per cohort.

response generated was directly proportional to the amount of analyte detected in the well. Back-calculated concentrations of analyte were generated using a 4PL fit model.

Determination of Response

Tumor response was assessed by MRI after every 2 treatment cycles, or earlier if clinically indicated, according to the response assessment in neuro-oncology criteria.

Results

Patients and Treatment

Between February 2021 and January 2022, 24 patients with brain cancer consented to the study; 9 were screen failures and 15 were enrolled (Figure 1). A descriptive analysis of baseline patient characteristics is summarized in Table 1. At study entry, the median age was 58 (range 40–84), 73% of patients were male, 12 patients had glioblastoma, 1 had anaplastic astrocytoma grade III, 1 had oligodendroglioma grade III, and one had non-small cell lung cancer with brain metastases. Referrals for brain metastases were limited due to rapid changes in available treatment modalities including radiosurgery and new drugs with brain penetrance. Patients were administered pritumumab in sequential dose cohorts of 1.6 mg/kg (cohort 1), 4.8 mg/kg (cohort 2), 8.0 mg/kg (cohort 3), 12.0 mg/kg (cohort 4), and 16.2 mg/kg (cohort 5) at on days 1, 8, 15, and 22 of each cycle.

Safety and Tolerability

The most common AEs possibly attributed to pritumumab in patients were constipation (5 patients, 33.3%) and fatigue (8 patients, 53.3%). The remaining AEs occurred at a frequency of 1 patient (6.7%) which included nausea, joint

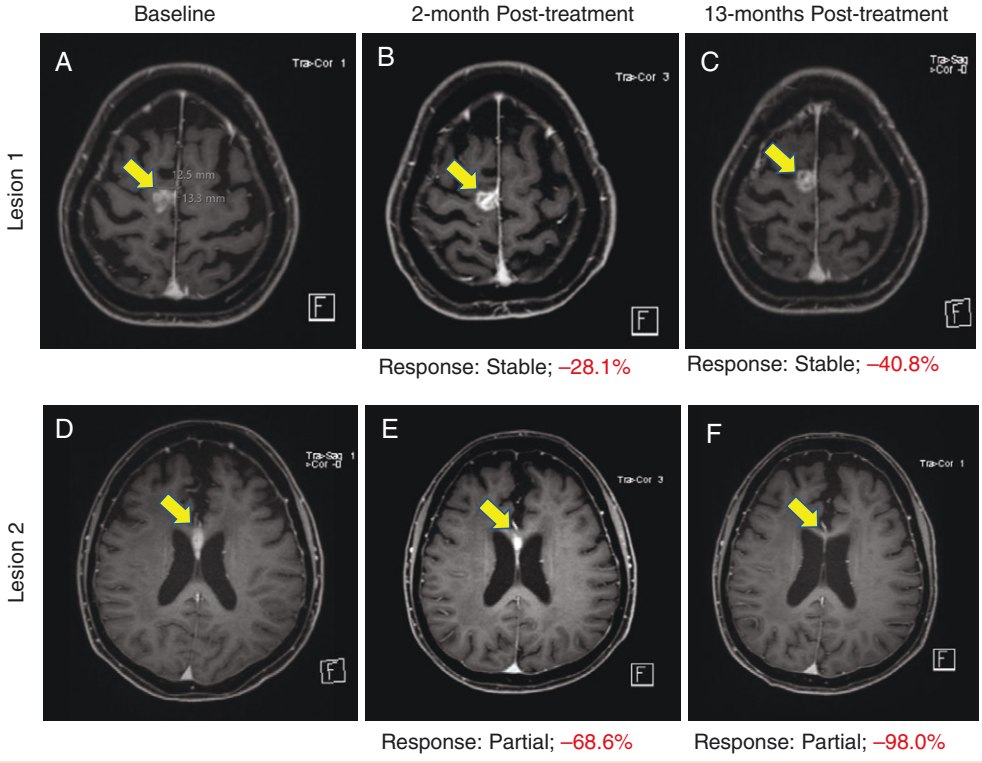

Figure 3. MRI brain. Post-contrast MRI of patient with glioblastoma **(A,D)** lesion 1 and 2 before starting pritumumab 1.6 mg/kg, **(B,E)** lesion 1 and 2, 2 months post-treatment and **(C,F)** lesion 1 and 2, 13 months post-treatment

tenderness dehydration, muscle weakness in upper extremities, muscle weakness in lower extremities, low mean corpuscular hemoglobin concentration, hypomagnesemia, neuropathy, pruritus, scalp dryness, dry skin of the face, and depression. There were no dose-limiting toxicities attributable to pritumumab. Although there were 12 patients (80.0%) with grade 3 to 4 treatment-emergent AEs, none were related to the study drug, and there were no grade 3, 4, or 5 AEs which were attributable to pritumumab. Table 2 summarizes the number of patients with possible treatment-related toxicities by dose level and CTCAE grade. There were no serious AEs (SAEs) considered to be at least possibly related to pritumumab. In the absence of an MTD and reviewing safety data from all cohorts, the maximum feasible dose for phase 2 dose was defined as 16.2 mg/kg every 7 days.

Pharmacokinetics of Pritumumab

Following intravenous administration of pritumumab, plasma samples for subjects were sent for analysis. The pharmacokinetics of Pritumumab were analyzed using data from cohorts 1–5 with at least 14 days of pharmacokinetic data. The data from cohort 1 ($n = 2$), cohort 2 ($n = 2$), cohort 3 ($n = 2$), cohort 2 ($n = 2$), and cohort 5 ($n = 2$) was used to generate a PK profile for Pritumumab. The maximum serum concentration (Cmax), the time to reach Cmax (Tmax), and the area under the curve (AUC) for dosing from 0.5 to 4 hours are presented in Figure 2A. The clearance (CL), which describes the relationship between the concentration of a drug and the rate of elimination of the drug from the body, of pritumumab derived from AUC is approximately 0.13 mL/h/kg (Figure 2B). Increasing the concentration of the drug results in a proportional increase in concentration removed from the body. Pritumumab PK appears to be linear with no observed sink effect. The projected half-life (T1/2) for this antibody was calculated to be 12.5 days. The collection of CSF was optional and only at per principal investigator's discretion if it did not pose a safety risk to the patient for collection. Due to the collection of only one cerebrospinal fluid sample in this study, it was insufficient for inclusion in the data analysis.

Antitumor Activity

Response assessment was evaluated for 11 patients out of 15. One patient withdrew from the study prior to a response assessment for reasons other than disease progression and 3 patients were taken off the study by the principal investigator for clinical disease progression. Partial response was observed in 1 patient (6.7%), one who had glioblastoma in cohort 1. Figure 3 shows the subject's response in 2 lesions. Disease stabilization was seen in 3 patients (20%), all who had glioblastoma. Seven exhibited progressive disease. Overall, the median progression-free survival was 1.6 months. Median overall survival was 10.8 months (95% CI; Figure 4).

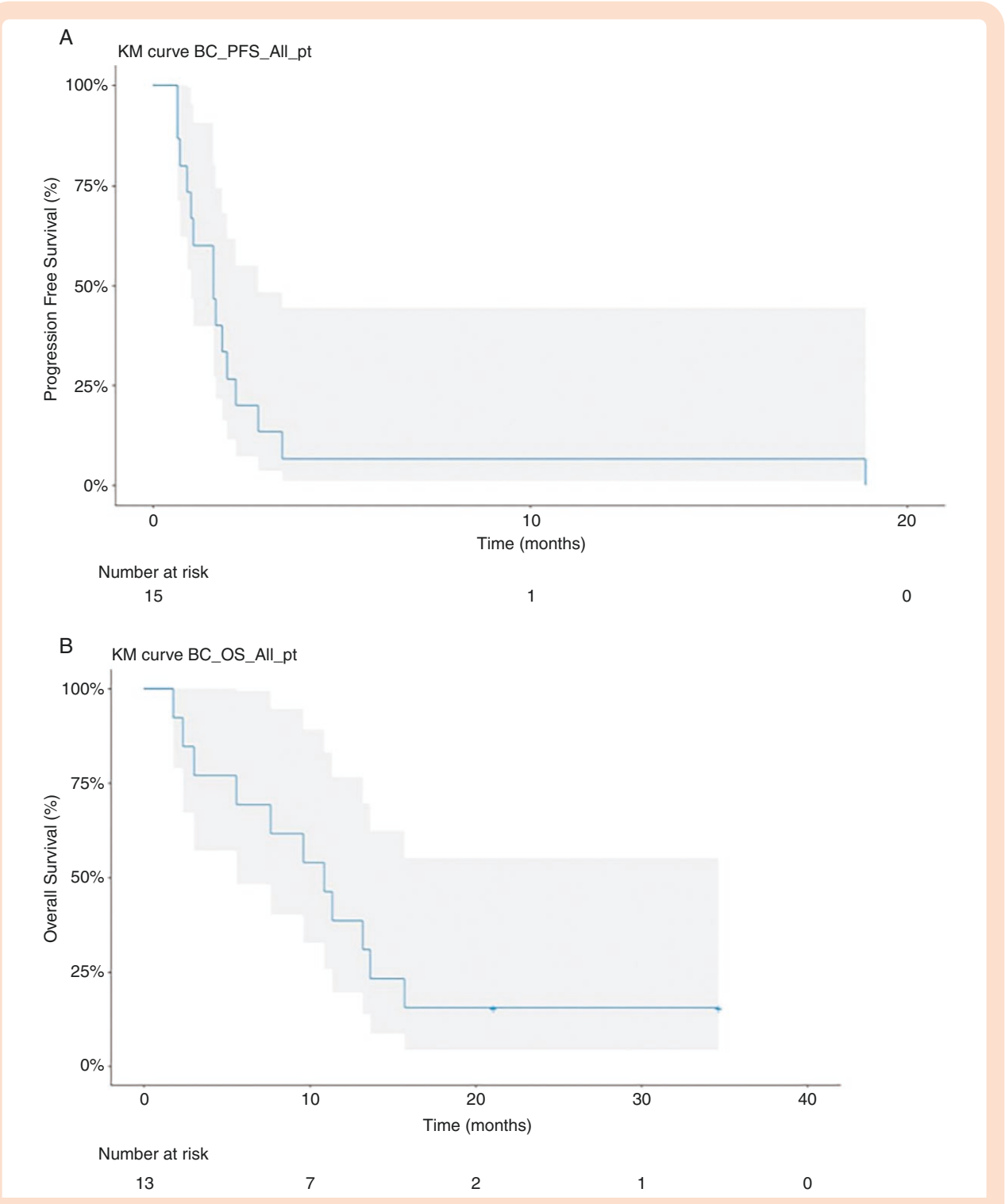

Figure 4. Analysis of efficacy. **(A)** Kaplan–Meier plot of median progression-free survival among patients treated with pritumumab, with confidence interval. **(B)** Kaplan–Meier plot of overall survival among patients treated with pritumumab, with confidence interval.

Discussion

The phase 1 dose-escalation study conducted with Pritumumab in patients with gliomas and brain metastases was aimed to evaluate the safety, tolerability, pharmacokinetics, and preliminary efficacy of the antibody in this patient population. The primary objectives of the study were to establish the safety profile of Pritumumab, determine its pharmacokinetic properties, and identify any dose-limiting toxicities. Secondary objectives included assessing preliminary efficacy endpoints such as

tumor response rate, progression-free survival, and overall survival.

Weekly dosing of pritumumab was generally well tolerated. The most common AEs related to the study drug were grade 1 or 2 constipation and fatigue. There were no treatment-related AEs greater than a grade 2, no serious AEs attributed to pritumumab, and no dose-limiting toxicities. Plasma concentrations show the steady state of pritumumab in plasma increases with higher doses. Dosing at 16.2 mg/kg allows for an increase in therapeutic efficacy without toxicity. Therefore, the maximum tolerated dose was not achieved, and the maximum feasible dose was determined to be 16.2 mg/kg. For the phase 2 study being planned, data based on the T1/2 show that a dosing schedule of 7–14 days is appropriate for this antibody depending on dose and combinations in the future.

There was one partial response in subject 003 who had recurrence after 3 years post-surgery/radiation/chemotherapy while on observation. This patient had 2 lesions: one lesion continued to remain stable (maximum reduction of 40.83% from baseline), while the other showed partial response (maximum reduction of 98.01% from baseline) for nearly 17 cycles (Figure 2). Molecular profiling of this patient done by Caris Life Sciences showed the following biomarkers: MGMT promoter hypermethylation detected, BRCA1 mutated, CDKN2A expressed copy number loss, EGFR was amplified, LZTR1 biologically relevant somatic variant, PD-1 was positive, 2-5/HPF, PD-L1 was positive, 2+, 100%, TOPO1 was 2+, 100%, TS was positive, 2+, 25%, and tumor mutational burden was Intermediate at 11 mut/Mb. While this is one case and

In summary, this phase 1 study established the maximum feasible dose of pritumumab and identified a phase 2 recommended dose of 16.2 mg/kg every 7 days. A phase 2 study is being planned with a larger population to look at the efficacy of pritumumab. It will focus on enrolling patients who are newly diagnosed with glioblastoma or who have glioblastoma whose tumors have recurred or progressed following initial treatment with surgery, radiation, and/or chemotherapy. Arm A will have 2 cohorts with 1:1 randomization, aiming to determine the efficacy and safety profile of pritumumab as a single agent and in combination with temozolomide in patients with recurrent glioblastoma. A subcohort of up to 6 patients who require surgical resection, will be allowed to receive up to 2 doses of Pritumumab prior to surgery, and subjects will then resume study as per protocol. Arm B of the study will enroll patients who are newly diagnosed glioblastoma who have not previously received any local or systemic therapy and pritumumab will be added to chemoradiation.

Supplementary Material

Supplementary material is available online at *Neuro-Oncology Advances* (https://academic.oup.com/noa).

Keywords

brain cancer | glioblastoma | monoclonal antibody | pritumumab

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Conflict of interest statement

S.K. reports research funding to institution from AADI, Aivita Biomedical, Inc., Bavarian Nordic, Bayer, Biocept, Blue Earth Diagnostics, Caris MPI, CNS Pharmaceuticals, EpicentRx, Incyte, Lilly, Oblato, Orbus Therapeutics, and Stemedica Cell Technologies; reports stock or other ownership interests in xCures; reports receiving honoraria from Jubilant Biosys and Pyramid Biosciences; and is a consultant/advisory board member for Curtana Pharmaceuticals, Nascent Biotech, Biocept, iCAD, and xCures; JC reports research funding to institution from Nascent Biotech. IB reports consulting fees and stock options from Nascent Biotech. S.C. is employed by Nascent Biotech. All other authors declare no competing interests.

Authorship statement

Conception and design: S.K.. Collection and assembly of data: All authors. Data analysis and interpretation: J.M.G., S.K., and N.N.. Plasma PK analyses were done by I.B. and D.S.. Manuscript writing: J.M.G. and S.K.. Final approval of manuscript: All authors.

Data availability

Patient clinical data generated which is de-identified in this study is available upon reasonable request from the corresponding author. The genetic sequencing data as part of standard-of-care is not publicly available due to patient privacy requirements. Derived data supporting the findings of this study are available from the corresponding author upon reasonable request.

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