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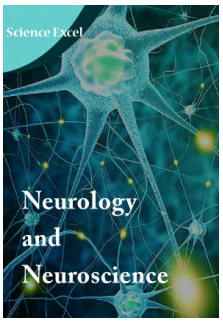

Outcomes in Four Children with Persistent, Recurrent, and Progressive Gangliogliomas Treated in Phase II Studies with Antineoplastons A10 and AS2-1

Burzynski Stanislaw[1], Burzynski Gregory[1], Janicki Tomasz[1], Beenken Samuel[2]

[1]Burzynski Clinic, Houston, Texas, USA

[2]Oncology Writings, Calera, Alabama, USA

*Correspondence

Stanislaw R. Burzynski, MD, PhD

9432 Katy Freeway, Houston, TX 77055, USA

Tel: 713-335-5697

Fax: 713-335-5658

E-mail: srb@Burzynskiclinic.com

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Abstract

Rationale: Gangliogliomas are generally benign tumors and are classified by the World Health Organization (WHO) as grade I or II tumors. However, in 1-5% of cases, gangliogliomas can behave more aggressively (WHO grade III) and have a worse prognosis. Four children with a ganglioglioma are presented to detail and discuss the efficacy of Antineoplastons A10 (Atengenal) and AS2-1 (Astugenal) in the treatment of gangliogliomas. **Objectives:** The children were treated with Antineoplastons A10 and AS2-1 (ANP therapy) at the Burzynski Clinic (BC) according to the phase II Protocols, BT-10 and BT-11. ANP therapy was delivered via subclavian catheter and infusion pump. During ANP therapy, tumor response was determined by comparison of sequential magnetic resonance imaging (MRI) of the brain with a baseline brain MRI. **Findings:** Of the four children treated for gangliogliomas, all had prior surgery but none had radiation therapy (RT) or chemotherapy. Two had recurrent, and progressive tumors with possible high-grade transformation (thalamo-mesencephalic region; temporal lobe with leptomeningeal spread) while two had tumors of the brain stem (persistent multicentric ganglioglioma; persistent and progressive ganglioglioma of the inferior medulla and superior cervical spinal cord), which are more difficult to treat and have a worse prognosis. Physical findings corresponded with the location of each child's tumor. IV ANP therapy continued for 6.4 to 24.8 months. The two children with possible high-grade transformation achieved a partial response (PR) while the two children with brain stem tumors maintained stable disease (SD). Overall survival for these four children ranged from 10.3 to 22.4 years. **Conclusions:** The utilization of ANP therapy in children with gangliogliomas is presented. We conclude that ANP therapy is an attractive therapeutic option for children with gangliogliomas who are ineligible for or refuse surgical resection and/or demonstrate persistent, recurrent, or progressive disease with or without high-grade transformation following surgical resection..

Introduction

In 1930, gangliogliomas were first described by Courville as abnormal growths of tissue that contain neurons and glial cells, specifically astrocytes [1]. With an incidence of 0.4% to 4.3%, ganglioglioma is the most commonly encountered neuronal-glial neoplasm of the central nervous system [2]. Usually seen in children and young adults, this tumor shows no gender preponderance [3]. Gangliogliomas are generally benign tumors and are classified by the World Health Organization (WHO) as a grade I or II tumors. Often arising in the temporal lobe and frequently producing seizures, gangliogliomas are usually benign calcified tumors [4].

However, gangliogliomas behave more aggressively in 1-5% of cases (WHO grade III) and have a worse prognosis. These anaplastic gangliogliomas can develop de novae or after radiotherapy (RT) [5]. In a series of 184 patients with supratentorial gangliogliomas, 1% were found to be anaplastic [6]. The neuronal component of anaplastic gliomas is almost always benign and immunoreactive to synaptophysin and neurofilament [7]. The astrocytic component of grade III gangliogliomas is malignant and immunoreactive to glial fibrillary acidic protein (GFAP) and vimentin while the cell proliferation antigen Ki-67 index is greater than 10% [8].

No specific clinical findings discriminate gangliogliomas from other cerebellar lesions. The signs and symptoms of infratentorial gangliogliomas vary depending on the structures involved by tumor. They include cranial nerve deficits (hearing loss, intractable facial pain, hemifacial seizures), hemiparesis, gait disturbance, and headache [9].

Magnetic resonance imaging (MRI) features of gangliogliomas generally are non-specific,

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but this tumor can be suspected if it shows one the following features on T1-weighted images: 1) a solid lesion located in the temporal lobes with mild or no edema and homogeneous enhancement; 2) a small cystic lesion with wall enhancement; or 3) a cystic-solid mixed mass with an enhancing nodule [10].

For all grades of ganglioglioma, total resection is the standard of care if technically possible. Adjuvant RT and chemotherapy are frequently utilized at the time of the initial diagnosis, but their efficacy is unknown [6,11,12].

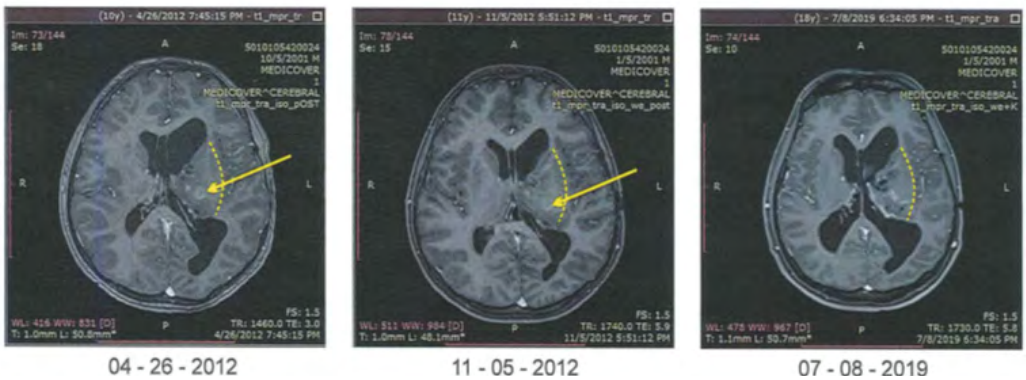
We present four children with childhood ganglioglioma. Two had recurrent, and progressive tumors with possible high-grade transformation (thalamo-mesencephalic region; temporal lobe with leptomeningeal spread) while two had tumors of the brain stem (persistent multicentric ganglioglioma; persistent and progressive ganglioglioma of the inferior medulla and superior cervical spinal cord), which are more difficult to treat and have a worse prognosis. In each case, the child was treated successfully at the Burzynski Clinic (BC) with Antineoplastons A10 and AS2-1 (ANP therapy).

Materials and methods

ANP research began in 1967, when significant deficiencies were noticed in the peptide content of the serum of patients with cancer compared with healthy persons. Initially ANP were isolated from the blood and later from urine [13]. Subsequent studies of the isolated ANP demonstrated that Antineoplaston A-10 and Antineoplaston AS2-1 were the most active ANPs. The chemical name of Antineoplaston A-10 is 3-phenylacetylamino-2,6-piperidinedione. It consists of the cyclic form of L-glutamine connected by a peptide bond to phenylacetyl residue. Its active components are phenylacetylglutamine (PG) and phenylacetylisoglutaminate (isoPG). When given orally, Antineoplaston A10 resists the attack of gastric enzymes. In the small intestine, under alkaline conditions, 30% is digested into phenylacetylglutamine (PG) and phenylacetylisoglutaminate (isoPG) in a ratio of approximately 4:1. The mixture of synthetic PG and isoPG in a 4:1 ratio, dissolved in sterile water constitutes Antineoplaston A10 intravenous (IV) injection. Further metabolism of Antineoplaston A10 results in phenylacetate (PN). Both metabolites PG and PN have anticancer activity. The mixture of PN and PG in a 4:1 ratio, dissolved in sterile water constitutes Antineoplaston AS2-1 IV injection [14].

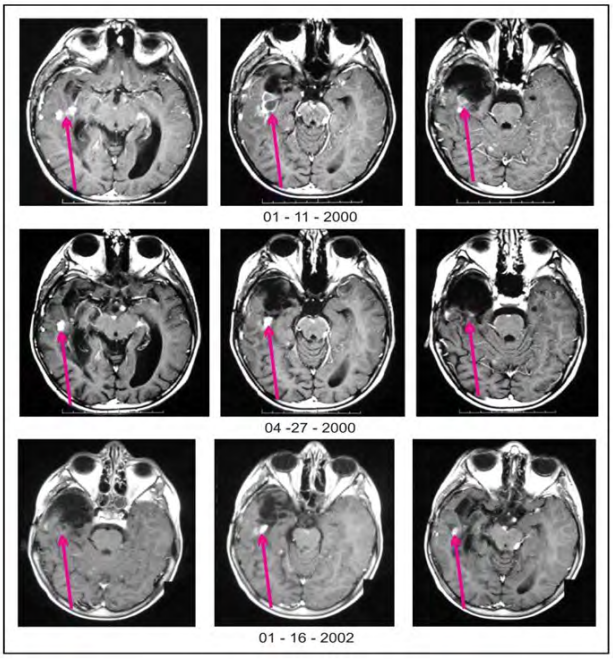
Between 1993 and 2017, four males and one female (n=5), with a median age of 7.6 years (range: two to 16 years), were seen at the BC. A two-year-old male patient with an anaplastic ganglioglioma only had an evaluation at the BC, receiving treatment elsewhere. We present four children, three treated according to Protocol BT-10, "A Phase II Study of Antineoplastons A10 and AS2-1 in Children with Brain Tumors", and one treated according to Protocol BT-11, "A Phase II Study of Antineoplastons A10 and AS2-1 In Patients with Brain Stem Glioma [15,16]. Both Protocols were single arm, two-stage, phase II trials of ANP therapy as treatment in children who were more than 6 months, but less than 18 years of age, with radiologic evidence of persistent, progressive, or recurrent brain tumors despite standard treatment. Additional eligibility criteria included a Lansky/Karnofsky score of 60-100%, and a life expectancy of > 2 months. All study patients and/or their legal guardians read, understood, and signed an Informed Consent Document prior to treatment. Outcome criteria were 1) objective response (OR) and 2) survival. The safety and tolerance of ANP therapy in children with brain tumors were also investigated. Patients received gradually increasing doses of intravenous (IV) A10 and IV AS2-1 via subclavian catheter and infusion pump, until a maximum tolerated dose of each component was achieved. Disease progression, unacceptable toxicity, physician decision, or patient request resulted in termination of ANP therapy.

The four children (three male, one female) described here, came to the BC 1 to 9 months after surgical resection(s) elsewhere. Of the three children with gangliogliomas treated according to Protocol BT-10, one has previously been described [17]. This child (Child #1) presented to the BC on May 3, 2012 at 11 years and four-months-of-age. He had undergone two subtotal resections elsewhere for ganglioglioma of the thalamo-mesencephalic region, which was first-treated when he was seven



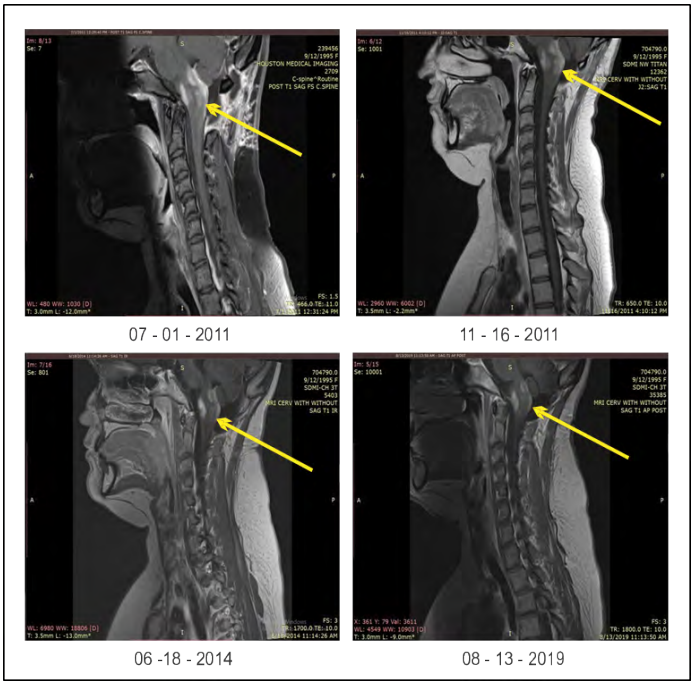
Axial images: April 26, 2012- Baseline MRI of the brain showing measurable enhancing tumor (see arrow) in the right temporal lobe, the suprasellar cistern, and the left ambient cistern with a total volume of 0.35 cm^2. November 5, 2012 - MRI of the brain showing the measurable enhancing tumors (see arrow) with a total volume of 0.12 cm^2, a 66% decrease in total volume when compared to baseline, indicating a PR. July 8, 2019 – Post-therapy MRI of the brain showing no change in the volume of the measurable enhancing tumors (see arrow), confirming a persistent PR. MRI: Magnetic resonance imaging; PR: Partial response.

Figure 1. *Child #1. [17]*



Axial images: January 11, 2000 - Baseline MRI of the brain showing measurable enhancing tumor (see arrows) in the right temporal lobe, the suprasellar cistern, and the left ambient cistern with a total volume of 4.56 cm2. April 27, 2000 - MRI of the brain showing the measurable enhancing tumors (see arrows) with a total volume of 1.08 cm2, a 76% decrease in total volume when compared to baseline, indicating a PR. January 16, 2002 – Post-therapy MRI of the brain showing no change in the volume of the measurable enhancing tumors (see arrows), confirming a persistent PR. MRI: Magnetic resonance imaging; PR: Partial response.

Figure 2. *Child #2.*



T1, Sagittal images: July 1, 2011 - Baseline MRI of the brain/spinal cord showed measurable enhancing tumor in the cervical spinal cord and the medulla (see arrow) with a total volume of 9.44 cm2. November 16, 2011 - MRI of the brain/spinal cord showing no change in total tumor volume (see arrow), indicating SD. June 18, 2014 – Post-therapy MRI of the brain/spinal cord showing no change in total tumor volume (see arrow), indicating persistent SD. August 13, 2019 – Post-therapy MRI of the brain/spinal cord showing no change in total tumor volume (see arrow), indicating persistent SD. MRI: Magnetic resonance imaging; SD: Stable disease.

Figure 3. *Child #3.*

years and seven-months-of-age. The pathology report from the second subtotal resection detailed a ganglioglioma but WHO grading was not performed. However, the nature of the tumor surgery and proposed RT + chemotherapy, which were refused by the patient's parents, suggested a recurrent and progressive ganglioglioma with possible high-grade transformation. On April, 26 2012, baseline MRI of the brain revealed a non-enhancing lesion and two enhancing lesions in the thalamo-mesencephalic region, one of which was measurable (> 5mm) with a volume of 0.35 cm^2 (Figure 1). Physical exam at the BC revealed a weak right-hand grip. The child began ANP therapy on May 9, 2012.

Child #2 presented to the BC on January 13, 2000, at eight years and-three-months-of-age. He had undergone two subtotal resections elsewhere for a right temporal lobe ganglioglioma, which was first treated when he was five years and 11-months-of-age. He had leptomeningeal spread of disease. Pathology report from the second subtotal resection detailed a ganglioglioma with some atypia, but not sufficient for a diagnosis of malignancy. However, the nature of the tumor surgery and the presence of leptomeningeal spread suggested a recurrent and progressive ganglioglioma with possible high-grade transformation. On January 11, 2000, baseline MRI of the brain showed measurable enhancing tumor (> 5 mm) in the right temporal lobe, the suprasellar cistern, and the left ambient cistern with a total volume of 4.56 cm^2 (Figure 2). Physical examination revealed strabismus (eyes not looking in the same direction), mydriasis (pupillary enlargement) of the left eye, and loss of peripheral vision. He began ANP therapy on January 18, 2000.

Child #3 presented to the BC on June 28, 2011 at 15 years and nine-months-of-age with persistent low-grade multicentric ganglioglioma, which was first treated when she was 15 years and eight-months-of age. She had undergone partial resection of a cerebellar tumor and biopsies of brain stem, and spinal cord tumors on May 20, 2011. Pathology report detailed a WHO grade I ganglioglioma. RT was suggested, but the patient' parents refused. On July 1, 2011, baseline MRI of the brain at the BC showed measurable enhancing tumor (> 5mm) in the cervical spinal cord and the medulla (Figure 3) with a total volume of 9.44 cm^2. History and physical examination revealed insomnia (difficulty sleeping), fatigue, agitation, headaches, vocal cord paralysis, neck pain, dysphagia (difficulty swallowing), nausea and vomiting, dyspnea (difficulty breathing) and generalized edema. She began ANP therapy, on July 1, 2011, as a Compassion Exception (CE) patient, due to the lack of other protocol treatment options.

One of the children presented here (Child #4) was treated according to Protocol BT-11: "A Phase II Study of Antineoplastons A10 and AS2-1 In Patients with Brain Stem Glioma [16], as described above. Child #4 presented to the BC on December 9, 2002, at 15 years and ten-months-of-age with a progressive ganglioglioma involving the inferior medulla and the upper cervical spinal cord, which was initially treated when he was 13 years and 4-months-of-age. He had undergone surgery elsewhere on three occasions: 1) on June 19, 2000 a partial resection of the spinal cord tumor was performed; 2) on July 5, 2002, partial resection of the spinal cord tumor with laminectomies was performed; and 3) on October 2, 2002, another partial resection of the spinal cord tumor was performed. Pathology report detailed a WHO grade I ganglioglioma on each occasion. On December 11, 2002, MRI of the brain at the BC showed measurable enhancing tumor (> 5mm) in the cervical spine and the medulla with a total volume of 4.60 cm^2. The child's history and physical examination revealed facial edema, neck pain, abdominal distention, upper extremity weakness with paresthesia (numbness and tingling) of the fingers, and spasticity, clonus (involuntary muscle contractions), and foot drop of the right lower extremity, which caused instability with a need for assistance when walking and standing. He began ANP therapy on December 12, 2002, as a Compassion Exception (CE), due to poor performance status.

Results

In all cases, response to ANP therapy was measured by serial brain MRIs, with and without gadolinium contrast. Tumor volume was calculated as the sum of the volume of all measurable lesions (> 5mm diameter) with volume being calculated as the product of the two greatest perpendicular diameters as determined by imaging. The response criteria were as follows: a CR indicated complete disappearance of all enhancing tumor while a partial response (PR) indicated a 50% or greater reduction in total enhancing tumor volume. CR and PR required a confirmatory brain MRI performed at least four weeks after the initial finding. PD indicated a 25 % or greater increase in enhancing tumor volume, or new enhancing disease, while stable disease (SD) did not meet the criteria for PR or PD [30]. All brain MRIs were reviewed by a prominent outside radiologist. Consent was obtained from each child's parents/guardians for publication of the brain MRIs presented in this report.

For Child #1, baseline MRI of the brain (April, 26 2012) showed a non-enhancing lesion in the thalamo-mesencephalic region and an enhancing lesion measuring 0.7 x 0.5 cm with a volume of 0.35 cm^2 (Figure 1), as previously described. The dosages of A10 and AS2-1 were gradually increased to a maximum of 15.55 g/kg/d and 0.27 g/kg/d, respectively (BT-10). On November 5, 2012, MRI of the brain showed a 66% decrease in the volume of the enhancing lesion (0.12 cm^2) compared to baseline, indicating a PR (Figure 1). On January 21, 2013, MRI of the brain showed no change in the size of the index lesion, confirming the PR. ANP therapy was discontinued on June 11, 2013 when serial brain MRIs showed no significant change in the volume of the enhancing tumor, indicating a persistent PR. Post-therapy MRI of the brain performed on July 8, 2019 and again showed no significant change in the volume of the measurable enhancing tumor (Figure 1). The patient's weak right-hand grip has resolved. He experienced four different grade 1 and 2 adverse events (AEs) that were possibly related to ANP therapy, all of which have resolved. Based on recent correspondence, overall survival (OS) is now 10.3 years.

For Child #2, baseline MRI of the brain (January 11, 2000) showed measurable enhancing tumor in the right temporal lobe, the suprasellar cistern, and the left ambient cistern (Figure 2) with a total volume of 4.56 cm^2, as previously described. The dosages of A10 and AS2-1 were gradually increased to a maximum of 13.14 g/kg/d and 0.37 g/kg/d, respectively (BT-10). On April 27, 2000, MRI of the brain showed the total volume of measurable enhancing tumor to be 1.08 cm^2, a 76% decrease in total volume when compared to baseline, indicating a PR (Figure 2). On June 26, 2000, MRI of the brain showed a 53% decrease in the total volume of the measurable enhancing tumors, when compared to baseline, confirming the PR. ANP therapy was discontinued on January 4, 2002 when serial brain MRIs indicated no further change in the volume of the measurable enhancing tumors. Post-therapy MRI of the brain, performed on January 16, 2002 again showed no change in the volume of the measurable

Case #	Sex	Age at first Tx	1st TX	Recurrence Interval (Months)	2nd Tx	Time Between Last Tx and Beginning of ANP Therapy (Months)	Ganglioglioma Pathology after last Tx	Symptoms/Signs on Initial Evaluation at the BC	Age at Initial Evaluation at the BC	Treated According to Protocol	Duration of ANP therapy (Months)	Best Response on ANP Therapy	Overall Survival from Start of Tx at BC (Years)	Status of Signs/ Symptoms at Last Follow-up
1	Male	7 Years and 7 Months	S	36	S	8.8	Thalamo-mesencephalic; Possible high-grade transformation	Weak right-hand grip	11 Years and 4 Months	BT-10	13.0 (IV)	Partial Response	10.3*	Resolved
2	Male	5 Years and 11 Months	S	26	S	1.5	Temporal lobe; Possible high-grade transformation	Strabismus, Mydriasis, Loss of peripheral vision	8 Years and 3 Months	BT-10	23.5 (IV)	Partial Response	22.4*	Diminished; Patient is employed
3	Female	15 Years and 8 Months	S + Bx	-	-	1.3	Brain stem and spinal cord; Low grade	Insomnia, Fatigue, Agitation, Headaches, Vocal cord paralysis, Neck pain, Dysphagia, Nausea and vomiting, Dyspnea, and Generalized edema	15 Years and 9 Months	BT-10 (CE)	24.8 (IV)	Stable Disease	11.0*	Resolved
4	Male	13 Years and 4 Months	P	27	S	2.3	Brain stem and spinal cord; Low grade	Neck pain, Abdominal distention, Upper extremity weakness with paresthesia of the fingers, Spasticity and clonus and foot drop of the right lower extremity, which caused instability with a need for assistance when walking and standing	15 Years and 10 Months	BT-11 (CE)	6.4 (IV) and 13.0 (Oral)	Stable Disease	19.5*	Excellent cognitive skills; College graduate; Persistent upper extremity weakness and dysfunction of the right lower extremity

ANP therapy: Antineoplastons A10 and AS2-1; BC: Burzynski Clinic; Bx: Biopsy; Clonus: Involuntary muscle contractions; CE: Compassionate Exception; Dysphagia: Difficulty swallowing; Dyspnea: Difficulty breathing; Insomnia: Difficulty sleeping; IV: Intravenous; Mydriasis: Pupillary enlargement; P: Partial resection; Paresthesia: Numbness and tingling; S: Subtotal resection; Strabismus: Eyes not looking in the same direction; Tx: Treatment; * All patients are currently alive with no evidence of tumor

Table 1. *Characteristics, Treatments, Symptoms/Signs, Best Response to ANP Therapy, Overall Survival and Current Status of Four Patients with Gangliogliomas*

enhancing tumors (Figure 2), indicating a persistent PR. The patient's strabismus, mydriasis, and loss of peripheral vision have improved. He experienced four different grade 1 and 2 AEs that were possibly related to ANP therapy, all of which resolved. Based on recent correspondence, overall survival is now 22.4 years.

For Child #3, baseline MRI of the brain/spinal cord (July 1, 2011) showed measurable enhancing tumor in the cervical spinal cord and the medulla (Figure 3) with a total volume of 9.44 cm^2, as previously described. The dosages of A10 and AS2-1 were gradually increased to a maximum of 11.67 g/kg/d and 0.31 g/kg/d, respectively (BT-10). On November 16, 2011, MRI of the brain/spinal cord showed no significant change in total tumor volume, indicating SD (Figure 3). ANP therapy was discontinued on July 23, 2013. Post-therapy MRIs of the brain/spinal cord, including those performed on June 18, 2014 (Figure 3) and August 13, 2019 (Figure 3), showed no significant change in volume of the measurable enhancing tumors, indicating persistent SD. The patient's insomnia, fatigue, agitation, headaches, vocal cord paralysis, neck pain, dysphagia, nausea and vomiting, dyspnea, and generalized edema have resolved. She experienced one grade 2 AE that was possibly related to ANP therapy, which has resolved. Based on recent correspondence, overall survival is now 11.0 years.

For Child #4, baseline MRI of the brain (December 11, 2002) showed measurable enhancing tumor in the cervical spinal cord and the medulla with a total volume of 4.60 cm^2, as previously described. The dosages of A10 and AS2-1 were gradually increased to a maximum of 10.91 g/kg/d and 0.35 g/kg/d, respectively (BT-11). IV ANP therapy was discontinued after 6.4 months when serial brain/spinal cord MRIs showed no significant change in the total volume of measurable enhancing tumor, indicating persistent SD. The patient continued on oral ANP therapy for an additional 13 months. MRI of the brain/spinal cord performed on August 25, 2004, showed no significant change in total tumor volume, indicating persistent SD. The patient is a college graduate and has excellent cognitive skills. He has persistent upper extremity weakness and dysfunction of the right lower extremity. He experienced two different grade 1 and 2 AEs that were possibly related to ANP therapy, both of which have resolved. Based on recent correspondence, overall survival is now 19.5 years.

Table 1 presents features of the four patients presented. It allows for visual comparison of the four cases and highlights the prolonged overall survival (OS) and marked improvement in signs/symptoms without a radiologic CR (see Discussion).

Discussion

Despite dramatic progress over the last 50 years in the treatment of many childhood cancers, primary brain tumors remain the leading cause of death in pediatric oncology. With an incidence of 0.4% to 4.3%, ganglioglioma is the most commonly encountered neuronal-glial neoplasm of the central nervous system [2]. For WHO grade I gangliogliomas, surgical resection is standard therapy. When there is gross total resection of the ganglioglioma, symptoms improve, especially any seizure activity that was present [18]. Children may have a better response to therapy [18, 19]. Gangliogliomas situated in the temporal lobe also have a better prognosis after gross total resection, with a 97% recurrence free survival rate after 7.5 years [6, 20]. The children we present here, with supra- and infra-tentorial tumors treated with ANP therapy, and with current SD or a PR, have a median OS of 15.3 years (range: 10.3 to 22.4 years). All patients are currently alive with no evidence of tumor progression.

If residual tumor exists after partial or sub-total surgical resection, recurrences can occur, either presenting with the same WHO grade, or as a grade III tumor (anaplastic) [21]. For gangliogliomas located in the brain stem, there is a 3.5- to 5-fold increased risk of recurrence compared to those which have a supratentorial location [22]. Two of the children presented here had brain stem involvement.

As previously described, antineoplaston research began in 1967, when significant deficiencies were noticed in the peptide content of the serum of patients with cancer compared with healthy persons [13]. Research activities stemming from this observation led to the development of Antineoplastons A10 and AS2-1, which are synthetic amino acid derivatives utilized in combination as ANP therapy. Initial clinical responses to ANP therapy in the treatment of pediatric brain tumors led to the design and implementation of a series of clinical studies to evaluate the safety and efficacy of ANP [23-25].

ANP's mechanism of action differs from that of RT or cytotoxic chemotherapy. Growth of normal cells is controlled by cell cycle progression genes (oncogenes) and by cell cycle arrest genes (tumor suppressor genes). In cancer, alteration of these control genes in malignant cells favors aggressive cell proliferation. Evidence suggests that ANP affects 112 genes in the tumor genome and functions as "molecular switches" which "turn on" tumor-suppressor genes and "turn off" oncogenes. [26,27] Hence, the antineoplastic action of ANP therapy in gangliogliomas involves restoration of cell cycle control, induction of programmed cell death, and interference with cancer cell metabolism and nuclear transport.

We present four children with childhood ganglioglioma. Two had recurrent, and progressive tumors with possible high-grade transformation (thalamo-mesencephalic region; temporal lobe with leptomeningeal spread) while two had tumors of the brain stem (persistent multicentric ganglioglioma; persistent and progressive ganglioglioma of the inferior medulla and superior cervical spinal cord), which are more difficult to treat and have a worse prognosis. In each case the children were treated successfully at the Burzynski Clinic (BC) with Antineoplastons A10 and AS2-1 (ANP therapy), two maintaining SD and two achieving a PR. Each patient had improvement in their initial sign/symptoms, and prolonged OS (Table 1), suggesting that, in addition to standard radiological evaluation, improvement in symptoms and OS may be important endpoints in determining the efficacy of ANP therapy.

Conclusions

Successful completion of Phase I and early Phase II clinical studies led to multiple Phase II clinical studies of ANP therapy in a variety of low- and high-grade brain tumors, including gangliogliomas, under the Burzynski Research Institute's (BRI) IND # 43,742. Multiple Phase II protocols have been completed and numerous articles have been published [28-76]. The children reported here received ANP therapy for persistent, recurrent, and progressive gangliogliomas with or without high-grade transformation. Their radiological and clinical responses to ANP therapy, along with prolonged OS suggest that it may be an effective therapeutic alternative in persistent, recurrent and progressive gangliogliomas with or without high-grade transformation occurring in both the supra- and infra-tentorial regions of the brain.

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Clinical Trials Registry

Clinical Trials.gov

BT-10 (NCT00003458)

BT-11 (NCT00003459)

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