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Recurrent and Progressive Ganglioglioma in an 11-Year-Old Male Treated with Antineoplastons: Partial Response with > than Nine Years and Nine Months Survival and Complete Resolution of Clinical Symptoms/Signs

Burzynski Stanislaw[1], Burzynski Gregory[1], Janicki Tomasz[1] and Beenken Samuel[2]
[1]Burzynski Clinic, Houston, TX, USA
[2]Oncology Writings, Calera, AL, USA

Corresponding Author:
Stanislaw R. Burzynski, MD, PhD
9432 Katy Freeway
Houston, TX 77055
P: 713-335-5664
F: 713-335-5658
Email: srb@Burzynskiclinic.com

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ABSTRACT:

Introduction:

Gangliogliomas constitute approximately 1 percent of all intracranial neoplasms. One to 5% of gangliogliomas are anaplastic and have a poor prognosis. Standard therapy is surgical resection. We present the case of an eleven-year-old male, treated elsewhere with two subtotal resections, whose recurrent and progressive ganglioglioma was treated successfully at the Burzynski Clinic (BC) with Antineoplastons A10 and AS2-1 (ANP therapy).

Materials and Methods:

The patient was seen at the BC on May 3, 2012. Physical exam revealed right hand weakness. He began treatment under Protocol BT-10, "A Phase II Study of Antineoplastons A10 and AS2-1 in Children with Brain Tumors". The patient received increasing doses of intravenous (IV) A10 (Atengenal) and IV AS2-1 (Astugenal), via subclavian catheter and infusion pump, until a maximum tolerated dose of each component was achieved. ANP therapy was continued after an objective response (OR) was achieved.

Results:

Magnetic resonance imaging (MRI) was utilized to determine tumor response to ANP therapy. Baseline MRI of the brain performed on April, 26 2012 revealed a non-enhancing lesion measuring 4.2 x 3.3 cm (13.9 cm^2) and two enhancing lesions with the larger (index) lesion measuring 0.7 x 0.5 cm (0.35 cm^2). On November 5, 2012, MRI of the brain showed the index lesion measuring 0.4 x 0.3 cm (0.12 cm^2), a 66% decrease in two-dimensional size compared to baseline, indicating a partial response (PR). In March 2022, MRI of the brain revealed no change in tumor size and the patient's family confirmed that the patient continued healthy and symptom-free.

Conclusions:

In addition to protocol BT-10, multiple Phase II protocols utilizing ANP therapy in a variety of low- and high-grade brain tumors have been completed and numerous articles have been published. Regarding the case presented here, symptom-free survival of > nine years and nine months suggests that ANP therapy may be an effective therapeutic alternative in recurrent and progressive ganglioglioma.

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INTRODUCTION:

Considering all intracranial neoplasms, only 1% are gangliogliomas, which are more frequent in children and young adults [1]. It is generally a benign tumor and is classified by the World Health Organization (WHO) as a grade I or II tumors. However, in 1-5% of cases, gangliogliomas behave more aggressively, (WHO grade III) and have a poor prognosis. These anaplastic gangliogliomas can develop de novae or after radiotherapy (RT) [2].

Gangliogliomas are usually benign calcified tumors, often arising in the temporal lobe, which frequently produces seizures [3]. In a series of cases reported by Lang and colleagues, the prognosis was favorable with over 93% five-year survival [4] while in a series of 184 supratentorial cases by Luyken and colleagues, there was 98% survival at 7.5 years [5].

Histopathologically, ganglioneuromas are defined by neoplastic astrocytes and neurons [6]. These are classified as WHO grade I or II when the astrocytes appear relatively benign. If a ganglioglioma shows anaplastic features, it is considered WHO grade III (anaplastic glioma). In a series of 184 patients with supratentorial gangliogliomas, 1% were found to be anaplastic [5]. It has been reported that 46% of anaplastic gangliogliomas develop in the temporal lobe compared to 71-80% of grade I and II gangliogliomas [7].

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 GFAP and vimentin while the Ki-67 index is greater than 10%. [8]

When practical, total resection is the standard of care for all grades of ganglioglioma. The efficacy of adjuvant RT and chemotherapy are not well described, but frequently these therapeutic modalities are utilized at the time of the initial diagnosis [4,5,9].

We present the case of an eleven-year-old male, treated elsewhere with two subtotal resections, whose recurrent and progressive ganglioglioma was treated successfully at the Burzynski Clinic (BC) with Antineoplaston A10 and AS2-1 (ANP therapy). He had resolution of clinical signs and symptoms, achieved a partial response (PR) by magnetic resonance imaging (MRI), and is living a normal, symptom-free life > 9 years and 9 months after ANP therapy (Photograph 1).

MATERIALS AND METHODS:

In 2001, a 7-month-old male presented to his pediatrician because of seizures and vomiting after eating meals. MRI of the brain, with and without gadolinium, revealed a 1.0 cm tumor arising in the left optic nerve tract, which appeared to be benign. The infant was also found to have a protein deficiency, which prevented the digestion of animal proteins. He was placed on a vegan diet with the resolution of symptoms. Yearly MRIs of the brain, through 2007, showed the left optic tract tumor to be stable. In August 2008, the child developed spasticity in the right hand. MRI of the brain revealed that the tumor had grown to approximately 7 cm in size. In August

2000, the child underwent a subtotal resection in Paris, France. The pathology report from that surgery is not available. In June 2011, an MRI of the brain revealed progression of the tumor at the level of the left optic nerve tract with expansion into the cerebral peduncle, basal ganglia, and temporal lobe. The patient underwent a second subtotal resection in August 2011. The pathology report detailed a ganglioglioma but WHO grading was not performed. However, the progressive nature of the tumor surgery (i.e., two subtotal resections) and proposed RT + chemotherapy in Paris, France strongly suggests a recurrent and progressive ganglioglioma with high-grade transformation. On April 26 2012 MRI of the brain revealed a non-enhancing lesion and two enhancing lesions in the thalamo-mesencephalic area. The patient's parents elected to bring the patient to the Burzynski Clinic (BC) for evaluation and treatment.

This eleven-year-old Caucasian male, from Bucharest, Romania, accompanied by his parents, was seen at the BC on May 3, 2012. He complained of weakness in his right hand. Physical exam revealed a weak right-hand grip while deep tendon reflexes were equal bilaterally with down-going toes bilaterally. Lansky's score was 90%. He began treatment at the BC according to protocol BT-10, "A Phase II Study of Antineoplastons A10 and AS2-1 in Children with Brain Tumors" [10]. Treatment began on May 9, 2012.

Protocol BT-10 was a single-arm, two-stage, phase II trial of ANP therapy 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 [10]. 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 the termination of ANP therapy.

To determine OR, tumor size was measured utilizing sequential MRIs of the brain, with and without gadolinium enhancement. Tumor size was calculated as the product of the two greatest perpendicular diameters as determined by imaging. Response criteria were as follows: a complete response (CR) indicated the complete disappearance of all enhancing tumors while a partial response (PR) indicated a $\geq$ 50% reduction in enhancing tumor size. CR and PR required a confirmatory MRI performed at least four weeks after the initial finding. Progressive disease (PD) indicated a $\geq$ 25 % increase in enhancing tumor size, or new enhancing disease, while stable disease (SD) did not meet the criteria for PR or PD [11]. All MRIs were reviewed by a prominent outside radiologist.

RESULTS:

BT 10 enrolled 34 patients [10]. Thirty patients were evaluable. Of these, 2 patients achieved a CR, 4 patients achieved a PR, 6 patients had SD, and 18 patients had PD. Additional study results are available at ClinicalTrails.gov (NCT00003458). The eleven-year-old patient presented here was one of the 4 patients developing a PR. In his case, a baseline MRI of the brain (April 26, 2012) clearly revealed a non-enhancing lesion in the thalamo-mesencephalic area (Figure 1). The largest enhancing lesion measured 0.7 x 0.5 cm (0.35 cm^2) and served as the index lesion (Figure 1 {arrow}). The patient was treated with ANP therapy under protocol BT-10 and the dosages of A10 and AS2-1 were gradually increased to 15.55 g/kg/d and 0.27 g/kg/d, respectively. On July 2, 2012, an MRI of the brain showed the index lesion measuring 0.5 x 0.4 cm (0.20 cm^2), a 43% decrease in two-dimensional size compared to baseline. On November 5, 2012, an MRI of the brain showed the index lesion measuring 0.4 x 0.3 cm (0.12 cm^2), a 66% decrease in two-dimensional size compared to baseline, indicating a PR (Figure 1 {arrow}). On January 21, 2013, an 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 MRIs of the brain showed no further change in the index lesion. The last post-therapy MRI of the brain performed (July 8, 2019) indicated no further change in the size of the index lesion (Figure1). The patient experienced 4 different adverse events (AEs) that were possibly related to ANP therapy, all of which resolved.

In March 2022, more than 9 years and 9 months after ANP therapy, correspondence with the patient's family indicated that the patient was living a normal and symptom-free life (Photograph 1). The family has consented to the use of the radiographs and photographs presented in this publication.

DISCUSSIONS:

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. Protocol BT-10 evaluated the efficacy and safety of ANP therapy in childhood brain tumors. [10].Considering all intracranial neoplasms, only 1% are gangliogliomas, which are more frequent in children and young adults [1].

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. Initially, ANP was isolated from the blood and later from urine. [12] Antineoplastons A10 and AS2-1 are synthetic amino acid derivatives utilized in combination with ANP therapy. A10 (Atengenal) consists of a 4:1 ratio of phenylacetylglutaminate sodium (PG) and phenylacetylisoglutaminate sodium (isoPG). AS2-1 (Astugenal) consists of a 4:1 ratio of phenylacetate sodium (PN) and PG [13]. 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 [14-16].

ANP's mechanism of action differs from that of RT or cytotoxic chemotherapy. The 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" that "turn on" tumor-suppressor genes and "turn off" oncogenes. [17,18] Hence, the antineoplastic action of ANP therapy in DIPG involves restoration of cell cycle control, induction of programmed cell death, and interference with cancer cell metabolism and nuclear transport.

Initially described in 1926, gangliogliomas are composed of both glial cells and cells of neural origin [19]. These tumors occur in all age groups but are most common in the pediatric population [5]. Generally, they behave in a benign manner, but a subset of these tumors, with a higher-grade glial component, is more aggressive [20]. We present here the case of an eleven-year-old boy who was treated at the BC under protocol BT-10 for a recurrent and progressive ganglioglioma with high-grade transformation (anaplastic). Despite the poor prognosis of this tumor, he achieved a PR after 7 months of ANP therapy. Now, more than 9 years and 9 months after ANP therapy, he is healthy and symptom-free. There is a reasonable possibility that the patient has achieved a CR.

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, under the Burzynski Research Institute's (BRI) IND # 43,742. Multiple Phase II protocols have been completed and numerous articles have been published [21-55]. The patient reported here was enrolled in protocol BT-10, "A Phase II Study of Antineoplastons A10 and AS2-1 in Children with Brain Tumors" [10]. His prolonged and symptom-free survival suggests that ANP therapy may be an effective therapeutic alternative in recurrent and progressive ganglioglioma with high-grade progression.

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References

1. DeMarchi R, Abu-Abed S, Munoz D, Macdonald LR (2011) Malignant ganglioglioma: case report and review of literature. Journal of Neuro-oncology 101:311-318.
2. Rumana CS, Valadka AB (1998) Radiation therapy and malignant degeneration of benign supratentorialgangliogliomas.Neurosurgery42:1038–1043.
3. ZenterJ, Wolf HK, Ostertun B, Hufnagel A, Campos MG, Solymosi L, Schramm J (1994) Gangliogliomas: Clinical, radiological, and histopathological findings in 51 patients. J

Neurol Neurosurg Psychiatry 57:1497-1502.

4. Lang FF, Epstein FJ, Ransohoff J, Allen JC, Wisoff J, Abbott IR,Miller DC (1993) Central nervous system gangliogliomas. Part 2.Clinical outcome. J Neurosurg 79:867–873.
5. Luyken C, Blumcke I, Fimmers R, Urbach H, Wiestler OD, Schramm J (2004) Supratentorial gangliogliomas: histopathological grading and tumor recurrence in 184 patients with a median follow-up of 8 years. Cancer 101:146-155.
6. Nelson JS, Burger JM, Wiestler OD, VandenBerg SR (2000)Ganglioglioma and gangliocytoma. In: Kleihues P, Cavenee WK (eds) World Health Organization Classification of Tumors. Pathology and genetics of tumors of the nervous system. IARC Press, Lyon, pp 96-98.
7. Blumcke I, Wiestler OD (2002) Gangliogliomas: an intriguing tumor entity associated with focal epilepsies. J Neuropathol Exp Neurol 61:575-584.
8. Schittenhelm J, Reifenberger G, Ritz R, Nagele T, Weller M, Pantazis G, Capper D, Beschorner R, Meyermann R, Mittlebronn M (2008) Primary anaplastic ganglioglioma with a small-cell glioblastoma component. Clin Neuropathol 27:91-95.
9. Liauw SL, Byer JE, Yachnis AT, Amdur RJ, Mendenhall WM (2007) Radiotherpay after subtotally resected or recurrent ganglioglioma. Int J Radiat Oncol Biol Phys 67:244-247.
10. Burzynski SR, Janicki TJ, Burzynski GS, Marszalek A (2017) A phase II study of Antineoplastons A10 and AS2-1 in children with brain tumors. Final report (Protocol BT-10). J Cancer Ther 8:173-187.
11. Wen, PK, Macdonald DR, Reardon DA, et al. (2010) Updated response criteria for high-grade gliomas: Response Assessment in Neuro-Oncology (RANO) working group. J Clin Oncol, 28(11): 1963-1972.
12. Burzynski SR. Antineoplastons: Biochemical defense against cancer. (1976) Physiol Chem Phys. 1976; 8:275-279.
13. Burzynski SR. Synthetic antineoplastons and analogs. Drugs of the Future. 1986; 11:679-688.
14. Burzynski, S.R. (2004) The Present State of Antineoplaston Research (1). Integrative Cancer Therapies, 3, 47-58.doi.org/10.1177/1534735403261964
15. Burzynski, S.R., Weaver, R.A., Janicki, T., Szymkowski, B., Jurida, G., Khan, M., et al. (2005) Long-Term Survival of High-Risk Pediatric Patients with Primitive Neuroectodermal Tumors Treated with Antineoplastons A10 and AS2-1. Integrative Cancer Therapies, 4, 168-177. doi.org/10.1177/1534735405276835
16. Burzynski, S.R. (2006) Treatments for Astrocytic Tumors in Children: Current and Emerging Strategies. Pediatric Drugs, 8, 167-168. doi.org/10.2165/00148581-200608030-00003
17. Burzynski SR, Patil S. (2014) The effect of Antineoplaston A10 and AS2-1 and metabolites of sodium phenylbutyrate on gene expression in glioblastoma multiforme. J Cancer Ther 5:929-945

18. Burzynski SR, Janicki T, Burzynski G. (2005) Comprehensive genomic profiling of recurrent classic glioblastoma in a patient surviving eleven years following antineoplaston therapy. Cancer Clin Oncol 4(2):41-52.
19. Perkins, O.C. (1926) Gangliogliomas. Archives of Pathology & Laboratory Medicine 2, 11-17.
20. Matsumoto, K., Tamiya, T., Ono, Y., Furuta, T., Asari, S. and Ohmoto, T. (1999) Cerebral Gangliogliomas: Clinical Characteristics, CT and MRI. Acta Neurochirurgica 141, 135-141. doi.org/10.1007/s007010050277
21. Burzynski SR, Weaver RA, Bestak M, Lewy RI, Janicki TJ, Jurida, GF, Paszkowiak JK, Szymkowski BG, Khan MI. (2003) Phase II study of Antineoplastons A10 and AS2-1 (ANP) in children with recurrent and progressive multicentric glioma. A preliminary report. Neuro-Oncol 5:358.
22. Burzynski SR, Lewy RI, Weaver R, Janicki T, Jurida G, Khan M, Larisma CB, Paszkowiak J, Szymkowski B. (2004) Long-term survival and complete response of a patient with recurrent diffuse intrinsic brain stem glioblastoma multiforme. Integ Cancer Ther 3:257-261. doi: 10.1177/1534735404267748
23. Burzynski SR, Weaver R, Lewy R, Janicki T, Jurida G, Szymkowski B, Khan M, Bestak M. (2004) Phase II study of antineoplaston A10 and AS2-1 in children with recurrent and progressive multicentric glioma. A Preliminary Report. Drugs R&D 5(6):315-326.
24. Burzynski SR, Weaver R, Bestak M, Janicki T, Jurida G., Szymkowski B, Khan M, Dolgopolov V. (2004) Phase II studies of antineoplastons A10 and AS2-1 (ANP) in children with atypical teratoid/rhabdoid tumors (AT/RT) of the central nervous system. A preliminary report. Neuro-Oncol 6:427.
25. Burzynski SR, Weaver R, Bestak M, Janicki T, Szymkowski B, Jurida G, Khan M, Dolgopolov, V. (2004) Treatment of primitive neuroectodermal tumors (PNET) with antineoplastons A10 and AS2-1 (ANP). Preliminary results of phase II studies. Neuro-Oncol 6:428.
26. Burzynski SR. Targeted Therapy for Brain Tumors. (2006) In: Yang AV, ed. Brain Cancer Therapy and Surgical Interventions. New York Nova Science Publishers, Inc.
27. Burzynski SR, Janicki, TJ, Weaver RA, Burzynski B. (2006) Targeted therapy with Antineoplastons A10 and AS2-1 of high grade, recurrent, and progressive brainstem glioma. Integ Cancer Ther5(1):40-47. doi: 10.1177/1534735405285380
28. Burzynski SR. (2007) Recent clinical trials in diffuse intrinsic brainstem glioma. Cancer Ther5:379- 390.
29. Burzynski S, Janicki T, Burzynski G, Marszalek A. (2014) Long-term survival (>13 years) in a child with recurrent diffuse pontine gliosarcoma: A case report. J Ped Hematol Oncol 36(7):e433-9. doi: 10.1097/MPH.0000000000000020
30. Burzynski SR, Janicki TJ, Burzynski GS, Marszalek A. (2014) A phase II study of antineoplastons A10 and AS2-1 in children with high-grade glioma. Final report (Protocol BT-06) and review of recent trials. J Cancer Ther 5:565-577. doi.org/10.4236/jct.2014.56065

31. Burzynski SR, Janicki TJ, Burzynski GS. (2014) A phase II study of antineoplastons A10 and AS2-1 in adult patients with recurrent glioblastoma multiforme: Final report (Protocol BT-21). J Cancer Ther 5:946-956. doi.org/10.4236/jct.2014.510100
32. Burzynski SR, Burzynski GS, Janicki TJ. (2014) Recurrent glioblastoma multiforme—A strategy for long-term survival. J Cancer Ther 5:957-976. doi.org/10.4236/jct.2014.510101
33. Burzynski SR, Janicki TJ, Burzynski, GS, Marszalek A, Brookman S. (2014) A phase II study of antineoplastons A10 and AS2-1 in children with recurrent, refractory or progressive primary brain tumors—Final report (Protocol BT-22). J Cancer Ther 5:977-988. doi.org/10.4236/jct.2014.510102
34. Burzynski SR, Janicki TJ, Burzynski GS, Brookman S. (2014) Preliminary findings on the use of targeted therapy with pazopanib and other agents in combination with sodium phenylbutyrate in the treatment of glioblastoma multiforme. J Cancer Ther 5:1423-1437.
35. Burzynski GS, Janicki TJ, Marszalek A. (2014) Long-term survival (>20 years) of a child with brainstem glioma treated with antineoplastons A10 and AS2-1: a case report. Neuro-Oncol11;16.
36. Burzynski SR, Janicki TJ, Burzynski GS, Marszalek A. (2014) The response and survival of children with recurrent diffuse intrinsic pontine glioma based on phase II study of antineoplastons A10 and AS2-1 in patients with brainstem glioma. Childs Nerv Syst 30:2051-2061. doi.org/10.1007/s00381- 014-2401-z
37. Burzynski SR, Burzynski G, Janicki J, Marszalek A. (2015) Complete response and Long-term survival (>20 years) of a child with tectal glioma: A case report. Pediatr Neurosurg50(2):99-103. doi: 10.1159/000369907
38. Burzynski SR, Janicki TJ, Burzynski G. (2015) A phase II study of Antineoplastons A10 and AS2-1 injections in adult patients with recurrent anaplastic astrocytoma - Final report (Protocol BT-15). Cancer Clin Oncol 442:13-23.
39. Burzynski SR, Janicki TJ, Burzynski GS, Marszalek A. (2015) A Phase II Study of Antineoplastons A10 and AS2-1 in adult patients with Newly-Diagnosed Anaplastic Astrocytoma Final Report (Protocol BT-08). Cancer Clin Oncol 4:28-38.
40. Burzynski SR, Burzynski GS, Marszalek A, Janicki J, Martinez-Canca J. (2015) Long-term survival (over 20 years), complete response and normal childhood development in medulloblastoma treated with Antineoplastons A10 and AS2-1. J Neurol Stroke 2(3):00054.
41. Burzynski SR, Burzynski GS, Marszalek A, Janicki TJ, Martinez-Canca JF. (2015) Long-term survival over 21 years and pathologically confirmed complete response in pediatric anaplastic astrocytoma: A case report. J Neurol Stroke 2(6):00072.
42. Burzynski SR, Burzynski GS, Brookman S. (2015) A Case of Sustained Objective Response of Recurrent/Progressive Diffuse Intrinsic Pontine Glioma with Phenylbutyrate and Targeted Agents. J Cancer Ther 6:40-44. doi: 10.4236/jct.2015.61006
43. Burzynski SR, Janicki, T, Burzynski G, Marszalek A. (2015) A phase II study of antineoplastons A10 and AS2-1 in patients with brainstem gliomas. The report on non-

diffuse intrinsic pontine glioma (Protocol BT-11). J Cancer Ther 6:334-344. doi: 10.4236/jct.2017.82015

44. Burzynski SR, Janicki T, Burzynski G. (2015) A phase II study of Antineoplastons A10 and AS2-1 in adult patients with primary brain tumors. Final Report (Protocol BT-09). J Cancer Ther 6:1063-1074. doi.org/10.4236/jct.2015.612116
45. Burzynski SR, Janicki TJ, Burzynski GS. (2016) Primary CNS tumors and Leptomeningeal, Disseminated and/or Multicentric disease in children treated in Phase II studies with Antineoplastons A10 and AS2-1. Cancer Clin Oncol 5(2):38-48.
46. Burzynski SR, Janicki TJ, Burzynski GS. (2016) A phase II study of antineoplastons A10 and AS2-1 in children with low-grade astrocytomas–Final report (Protocol BT-13). J Cancer Ther 7(12):837-850.
47. Burzynski SR, Janicki TJ, Burzynski GS. (2017) Antineoplastons A10 and AS2-1 in the Treatment of children with optic pathway glioma: Final Report for protocol BT-23. Cancer Clin Oncol6(1):25-35.
48. Burzynski SR, Janicki TJ, Burzynski GS, Marszalek A. (2017) A phase II study of Antineoplastons A10 and AS2-1 in children with brain tumors. Final Report (Protocol BT-10). J Cancer Ther 8:173-187.
49. Burzynski SR, Janicki T, Beenken, S. (2019) Treatment of recurrent glioblastoma multiforme (rGBM) with Antineoplaston AS2-1 in combination with targeted therapy. Cancer Clin Oncol, 8, 1-15.
50. Burzynski, SR, Janicki, T, Burzynski, GS, Beenken, S. (2021) Long-term survival (27.7 years) following IV Antineoplaston Therapy (ANP) in a 36-year-old-female with a progressive diffuse intrinsic pontine glioma (DIPG). Int J Radiol Imaging Technol, 7, 073-078. doi:10.23937/2572-3235.1510073
51. Burzynski, SR, Burzynski, GS, Janicki, T, Beenken S. (2021) Long-term survival (23 years) in a 26-year-old male after Antineoplaston therapy for a progressive, diffuse intrinsic pontine glioma: A case report. Int J Brain Disord Treat, 6, 038-044. doi.org/10.23937/2469-5866/
52. Burzynski, SR, Janicki T, Burzynski GS, Beenken S. (2021) Resolution of clinical signs, a complete response, and long-term survival (>23 Years) in a 3 and ½ month female with a newly diagnosed diffuse intrinsic pontine glioma treated with antineoplastons. Biomed Res Clin Prac, 6:1-6. doi: 10.15761/BRCP.1000220.
53. Burzynski, SR, Janicki T, Burzynski GS, Beenken S. (2022) A 25-year-female with diffuse intrinsic pontine glioma surviving for more than nine years following treatment with antineoplastons. Int J Clin Oncol Cancer Res, 7(1):1-7. doi:10.11648/j.ijcocr.20220701.11
54. Burzynski SR, Burzynski GS, Janicki T, Beenken, S. (2022) Twenty-two-year survival in a 15-year-old female with a recurrent posterior fossa ependymoma treated with antineoplastons Oncol Clin Res 3(1) 99-105.
55. Burzynski, SR, Janicki T, Burzynski GS, Beenken S. (2022) Diffuse intrinsic pontine glioma in an 11-year-old female treated with antineoplastons: Complete response and > 25-year survival. Ped Neonatal Med (In Press).

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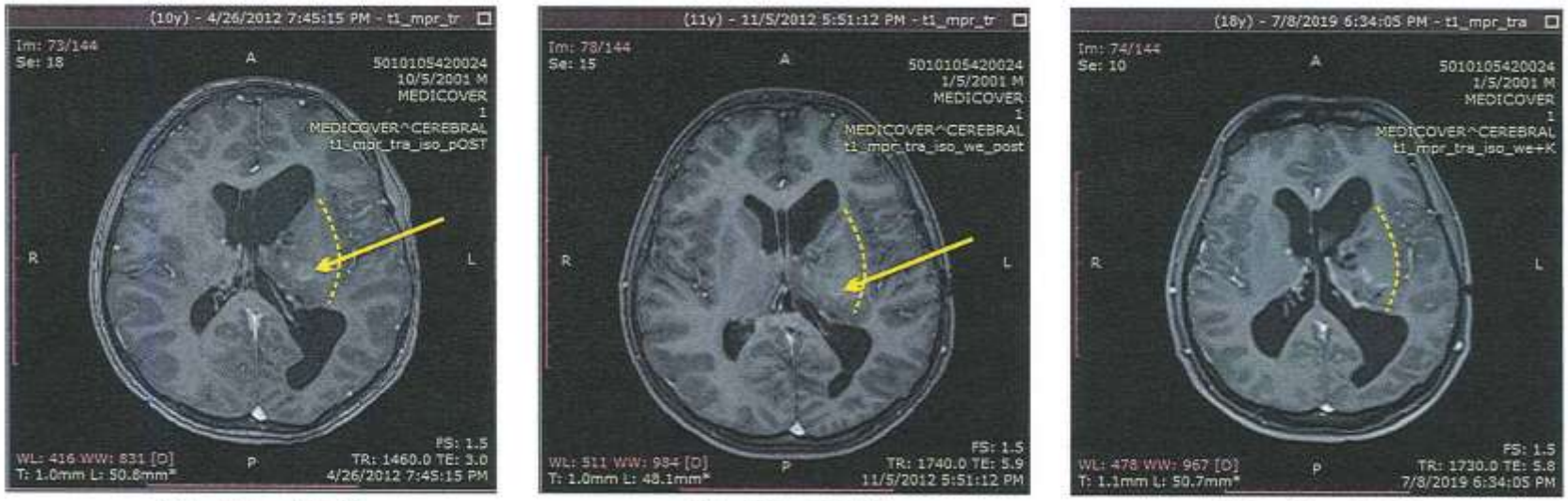

FIGURE 1.

T1, Axial images: April 4, 2012 - Baseline MRI of the brain showing a non-enhancing lesion, confirmed on T2 and FLAIR images (dotted line) and two enhancing lesions, in the thalamo-mesencephalic area - the largest enhancing lesion (arrow) measured 0.7 x 0.5 cm (0.35 cm^2) and served as the index lesion. **November 5, 2012 -** MRI of the brain showing the index lesion (arrow) as measuring 0.4 x 0.3 cm (0.12 cm^2), a 66% decrease in two-dimensional size compared to baseline, and indicating a PR – the non-enhancing lesion (dotted line) remained unchanged, as confirmed by T2 and FLAIR images. **July 8, 2019 –**The last post-therapy MRI of the brain showing no change in the size of the index lesion with continuation of the PR – the non-enhancing lesion (dotted line) remained unchanged, as confirmed by T2 and FLAIR images. FLAIR=Fluid attenuated inversion recovery; MRI=magnetic resonance imaging; PR=Partial response.

PHOTOGRAPH 1.
Post-treatment, symptom-free patient at 18 years of age.

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ABBREVIATIONS

A10	Antineoplaston A10, Atengenal
AS2-1	Antineoplaston AS2-1, Astugenal
ANP therapy	Antineoplastons A10 and AS2-1
CR	Complete response
BC	Burzynski Clinic
BRI	Burzynski Research Institute
FDA	Food and Drug Administration
GFAP	Glial fibrillary acidic protein
isoPG	Phenylacetylisoglutaminate sodium
IV	Intravenous
Ki-67	Cell proliferation antigen Ki-67
MRI	Magnetic resonance imaging
OR	Objective response
PD	Progressive disease
PG	Phenylacetylglutaminate sodium
PN	Phenylacetate sodium
PR	Partial response
RT	Radiation therapy
SD	Stable disease
WHO	World Health Organization