



# Diffuse Intrinsic Pontine Glioma in an 11-Year-Old Female Treated with Antineoplastons: Complete Response and >25 Years Survival

Burzynski Stanislaw<sup>1</sup>, Burzynski Gregory<sup>1</sup>, Janicki Tomasz<sup>1</sup> and Beenken Samuel<sup>2</sup>

<sup>1</sup>Burzynski Clinic, Houston, TX, USA

<sup>2</sup>Oncology Writings, Calera, AL, USA

## Correspondence

Stanislaw R. Burzynski, MD, PhD  
9432 Katy Freeway, Houston, TX 77055, USA  
Tel: +1 713-335-5664  
Fax: +1 713-335-5658  
E-mail: srb@Burzynskclinic.com

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## Keywords

Brain tumor; Diffuse Intrinsic Brainstem Glioma; H3-K27M Diffuse Midline Glioma; Antineoplastons; Phase I and III Studies

## Abbreviations

A-10: Antineoplaston A10 (Atengenal); ANP: Antineoplastons; AS2-1: Antineoplaston AS2-1 (Astugenal); Astugenal: Antineoplaston AS2-1 (AS2-1); Atengenal: Antineoplaston A10 (A10); BC: Burzynski Clinic; BRI: Burzynski Research Institute; CR: Complete response; DIPG: Diffuse intrinsic pontine glioma; DMG: Diffuse midline glioma; FDA: Food and Drug Administration; H3: Histone 3; IND: Investigational new drug application; IRB: Institutional review board; IV: Intravenous; K27M: K27 mutant; MRI: Magnetic resonance imaging; OR: Objective response; OS: Overall survival; PD: Progressive disease; PR: Partial response; RT: Radiation therapy; SD: Stable disease; WHO: World Health Organization

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## Abstract

**Rationale:** Diffuse intrinsic pontine glioma (DIPG), a lethal brain tumor, is the leading cause of brain tumor-related death in children. Over the past few decades clinical trials have shown no improvement in outcome. The purpose of this case study is to detail and discuss the use of Antineoplastons A-10 (Atengenal) and AS2-1 (Astugenal) in the treatment of an eleven-year-old female with a newly diagnosed DIPG.

**Objectives:** The patient described here was enrolled into BT-11, a Phase II protocol utilizing Antineoplastons A-10 and AS2-1 in the treatment of brainstem gliomas. The patient's tumor response to therapy was measured by sequential MRIs of the brain, with and without gadolinium contrast.

**Findings:** At her presentation to the Burzynski Clinic (BC), the patient was alert, and weighed 42.1 Kg. Physical examination showed dysfunction of the 6th and 7th cranial nerves, with lateral movement of the left eye being decreased by approximately 30% and with left-sided facial weakness being present. The patient obtained a baseline MRI, with and without gadolinium. Post-gadolinium T1-weighted axial images showed a 0.80 cm<sup>2</sup> enhancing pontine mass and a 2.70 cm<sup>2</sup> non-enhancing left-sided brainstem mass. Following Antineoplastons (ANP), the patient achieved a complete response (CR) of the enhancing pontine mass. At that time, physical examination, especially neurologic examination, showed no abnormalities. The patient was last seen at the BC on October 15, 2004 and she was in excellent health with no evidence of new/recurrent disease. On August 10, 2021, correspondence with the patient indicated that she continued in excellent health (>25 years survival).

**Conclusions:** ANP is an effective treatment for DIPG and for a variety of low- and high-grade brain tumors. Multiple Phase II protocols utilizing ANP have now been completed and its impact on the treatment of brain tumors has been widely published.

## Introduction

In the 2016 World Health Organization (WHO) classification, histone 3 (H3) K27M-mutant (K27M) diffuse midline glioma (DMG) was recognized as a distinct entity among high-grade gliomas [1]. H3 K27M DMG accounts for approximately 20% of pediatric glioblastomas, and its clinical characteristics have been described in detail in previous studies [2]. The midline locations of DMG tumors at presentation impede complete tumor removal, resulting in a poor survival outcome. Additionally, a previous study reported that H3 K27M DMG showed poorer survival than other grade 4 gliomas that arose at the midline in a pediatric population [3]. Growing understanding of the biology and descriptions of the outcomes of H3 K27M DMG may contribute to improvement of treatment outcomes. DMGs are notable for harboring histone mutations,

including H3F3A K27M, H3F3A G34R, and H3F3A G34V [4,5].

DMGs most often form in the brainstem, thalamus, spinal cord, and cerebellum. Brainstem gliomas represent 10 to 20% of primary tumors of the central nervous system and are diagnosed primarily in children with a median age of onset of 6 to 7 years [6]. Gliomas can be low- or high-grade based on histologic criteria and/or MRI findings. The number of children in the USA with brainstem gliomas is approximately 660 [7].

Diffuse intrinsic pontine glioma (DIPG) originates in the pons, an integral part of the brain stem. Individuals suffering from DIPG face a dismal prognosis with a median overall survival of approximately 11 months, and a 2-year survival rate of 10% [8,9]. Due to the location of the tumor, surgical resection is not possible. To date, radiotherapy (RT) remains

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the standard of care at diagnosis, but offers a survival benefit of approximately 3 months [10]. Chemotherapy has not shown to be effective [9]. There is no standard of care for progressive DIPG after RT.

Pontine tumors affect the cranial nerves, causing symptoms such as diplopia (double vision), the inability to fully close the eyelids, drooping of one side of the face, dysphagia (difficulty swallowing), and difficulty with mastication (chewing). These tumors also affect the "long tracks" of the brain, with resultant weakness of the arms and/or legs.

At the time of diagnosis, these tumors are usually confined to the brainstem. When the disease spreads, the spread is usually contiguous. Metastasis via the subarachnoid space has been reported in up to 30% of cases and usually occurs at the same time as local disease relapse. There is no generally applied staging system for childhood brainstem gliomas.

Due to its anatomical location, diagnostic biopsies of brainstem gliomas are difficult to obtain. Diagnosis is frequently based on MRI alone, which identifies five different types of brainstem gliomas: focal, dorsal exophytic, cervicomedullary, and DIPG. However, routine biopsy of children with suspected DIPG has been performed in Europe since 2003 [11]. In a report detailing their experience in 24 children, morbidity was reported in 2 children (cranial nerve palsy, worsening hemiparesis), which was reversible, and there was no mortality. The investigators concluded that the procedure was relatively safe in experienced hands using modern neurosurgical techniques [12]. Given this demonstration of relative safety, there is a movement within the pediatric neuro-oncology community toward routine biopsy of patients with suspected DIPG [12]. As discussed above, most DIPGs belong to the WHO classification of H3 K27M DMGs. However, wild-type H3 K27 DIPGs have not yet been separately designated within this classification and show a similar survival as that of H3-K27M DIPGs [13,14].

A six-week course of conventional RT is standard therapy for DIPG and frequently will result in improvement of signs and symptoms. Unfortunately, the signs and symptoms usually recur after six to nine months, concomitant with rapid disease progression. In children, survival past 14 to 18 months is very uncommon.

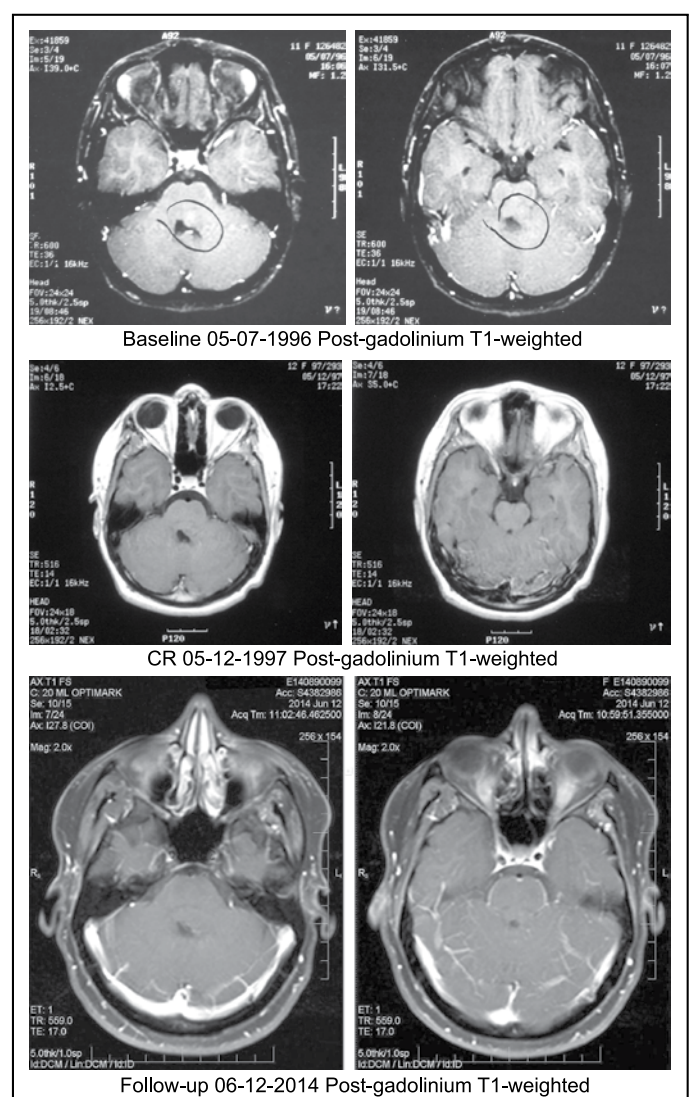
Because of this inevitable disease progression in children with DIPG, at some point during their disease course, many receive adjuvant chemotherapy in an attempt to improve survival, frequently as part of a clinical trial. However, no chemotherapeutic agent has ever demonstrated a significant improvement in outcome beyond that achieved with standard RT alone.

The case presented here involves an eleven-year-old female who had not received RT or chemotherapy prior to being seen at the Burzynski Clinic (BC).

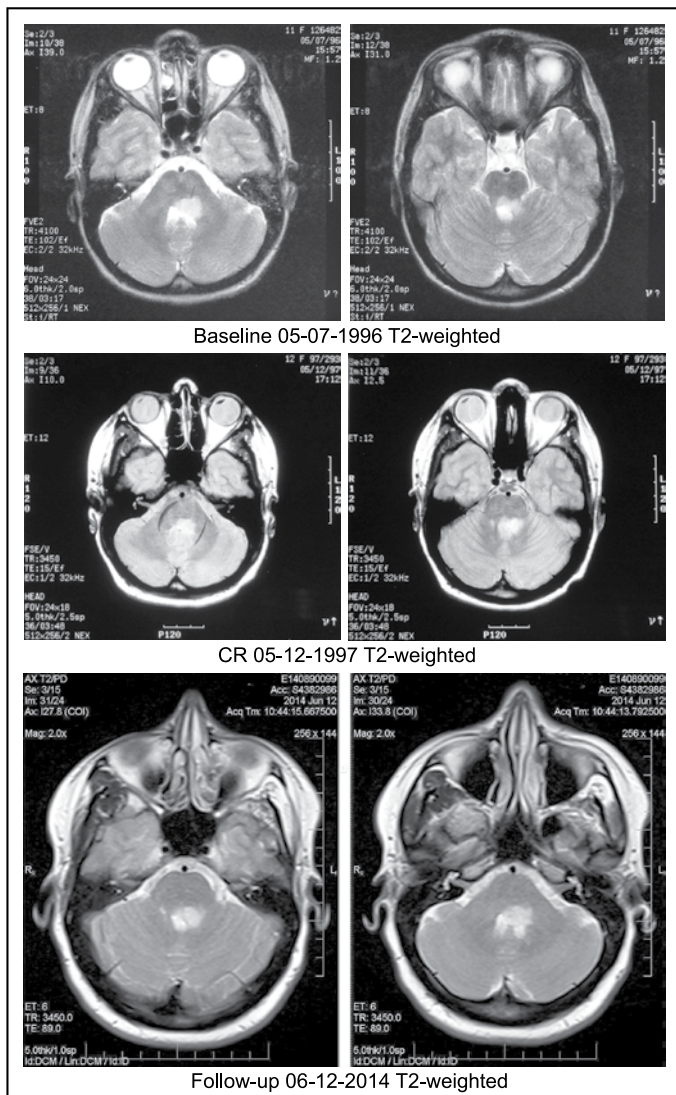
### Materials and methods

An eleven-year-old female (born August 30, 1984) presented to the BC on May 7, 1996 after MRI performed elsewhere had shown a brainstem glioma with significant involvement of the pons. Biopsy had not been performed and histological diagnosis was not available. Even if biopsy had been performed, genomic studies, such as identification of H3-K27M, could not have been performed because the necessary technology was not available at that time. The patient had only received dexamethasone prior to her arrival at the BC as the patient's parents had declined standard RT.

At the time of her presentation at the BC the patient was alert, and weighed 42.1 kg. Vital signs were stable. Physical examination showed dysfunction of the 6th and 7th cranial nerves, with lateral gaze of the left eye being decreased by approximately 30% and with the presence of left-sided facial weakness. The patient obtained a baseline MRI, with and without gadolinium (see Figure 1- and 2-Baseline). The pontine lesion appeared to occupy less than 50% of the pons. If biopsy had been taken and the pontine tumor was pathologically grade 3 or 4, the diagnosis of DIPG would be assured. However, no biopsy was taken. There was incomplete data for making a definitive diagnosis. Because the enhancing lesion was confined to the pons and the pontine lesion initially progressed before responding to ANP, we have classified this tumor as a DIPG, with extension to the midbrain.



**Figure 1. Post-gadolinium T1-weighted axial images.** Baseline images of 05-07-1996 show an enhancing pontine mass measuring 0.80 cm<sup>2</sup> and a non-enhancing brainstem mass measuring 2.70 cm<sup>2</sup>. CR images of 05-12-1997 show no enhancing pontine mass (complete response) and a non-enhancing brainstem mass measuring 2.04 cm<sup>2</sup>. Follow-up images of 6-12-2014 show no enhancing pontine mass (continuation of complete response) and a non-enhancing brainstem mass measuring 2.08 cm<sup>2</sup>.



**Figure 2. T2-weighted axial images.** Baseline images of 05-07-1996 show a low intensity signal pontine mass measuring 0.80 cm<sup>2</sup> and a high signal intensity brainstem mass measuring 2.70 cm<sup>2</sup>. CR images of 05-12-1997 show no pontine mass (complete response) and a high signal intensity brainstem mass measuring 2.04 cm<sup>2</sup>. Follow-up images of 6-12-2014 show no pontine mass (continuation of complete response) and a high signal intensity brainstem mass measuring 2.08 cm<sup>2</sup>.

The patient was considered a candidate for protocol BT-11, “A Phase II study of Antineoplastons A-10 and AS2-1 in Patients with Brainstem Gliomas”. [15] Before being administered Antineoplastons (ANP) in BT-11, the patient met the following eligibility criteria i) The presence of an incurable brain stem glioma; ii) No prior standard therapy; iii) A life expectancy of at least two months; iv) A signed informed consent document indicating that the patient/parents were aware of the investigational nature of ANP, the unpredictable nature of the patient’s response to ANP, and the possibility of worsening disease while receiving ANP.

The specifics of therapy and measurement of response under BT-11 have previously been reported [15]. The method of delivery of A-10 and AS2-1 was via a subclavian catheter and infusion pump. A minimum of six months of treatment was necessary for a patient to be evaluable. Patients were removed



**Photograph 1.** The patient, tumor-free, with two children.

from treatment secondary to progressive disease, unacceptable toxicity, or patient request.

A-10 and AS2-1 were initiated on May 8, 1996 and the dosage was gradually increased to 11.64 g/kg/d and 0.38 g/kg/d, respectively. MRIs were performed every one to two months. The patient was on IV ANP from May 8, 1996 until March 24, 1998. She began oral ANP on March 25, 1998 and continued it until February 16, 1999, when it was discontinued.

**Results**

The patient experienced no severe adverse events during the time she received her IV ANP, May 8, 1996 until March 24, 1998. Of the adverse events experienced, only two episodes of nausea, one being grade one and the other being grade two, were designated as being due ANP.

Response to ANP was measured by MRIs with and without gadolinium enhancement. Tumor size was calculated as the product of the two greatest perpendicular diameters as determined by imaging. The response criteria were as follows: a complete response (CR) indicated complete disappearance of all enhancing tumor while a partial response (PR) indicated a > 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 >25 % increase in enhancing tumor size, or new enhancing disease, while stable disease (SD) did not meet the criteria for PR or PD. All MRIs were reviewed by a prominent outside radiologist.

Determination of a response by RANO criteria relies on post-gadolinium T1-weighted MRI images of enhancing disease. [16] In the case presented here, MRI performed on May 12, 1997 (see Figure 1-CR) demonstrated a CR of the enhancing pontine lesion, while the patient was receiving IV ANP. The corresponding T2-weighted image is seen in Figure 2-CR. Follow-up MRI on June 12, 2014 demonstrated maintenance of this CR (see Figure 1-Follow-up). The corresponding T2-weighted image is seen in Figure 2- Follow-up.

At the time of her CR (see Figure 1- and Figure 2- CR), the patient's physical examination, especially the neurologic examination, showed no abnormality. The patient was last seen at the BC on October 15, 2004. She was in excellent health with no evidence of new/recurrent disease. Correspondence with the patient on August 10, 2021 indicated that she continued in excellent health (>25 years survival). She is happily married, with two children (Photograph 1). On 9/16/2021, we received a Consent Release from the patient allowing us to utilize her medical information, MRI images, and photographs in a manuscript for publication.

## Discussion

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 [17]. Subsequent studies of the isolated ANP demonstrated that Antineoplaston A-10 and Antineoplaston AS2-1 were the most active ANP. The chemical name of Antineoplaston A-10 is 3-phenylacetyl-amino-2,6-piperidinedione. It consists of the cyclic form of L- glutamine connected by a peptide bond to phenylacetyl residue. 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 phenylacetylglutamate (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 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 [18].

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. [19,20] 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.

Successful completion of Phase I and early Phase II clinical studies led to multiple Phase II clinical studies of Antineoplastons A-10 and AS2-1 in a variety of low- and high-grade brain tumors, under the Burzynski Research Institute's (BRI) IND # 43,742. The patient reported here was enrolled in protocol BT-11, "A Phase II study of Antineoplastons -10 and AS2-1 in patients with Brainstem Gliomas. [15] Multiple Phase II protocols have been completed and numerous articles have been published [21-54].

In 2014, an unpublished review of 168 DIPG patients treated with Antineoplastons A-10 and AS2-1 in six different Phase II protocols at BRI, under IND # 43,742, was conducted. An ~13% overall survival (OS) rate was seen in patients  $\geq 3$  to  $\leq 21$  years of age compared to ~ 7% for RT. Based on this information, we collaborated with the FDA to develop BRI-BT-52, "A Randomized Phase 3 Study of Combination Antineoplaston Therapy [Antineoplastons A10 (Atengenal) and AS2-1

(Astugenal)] Plus Radiation Therapy vs. Radiation Therapy Only in Subjects with Newly Diagnosed Diffuse, Intrinsic Brainstem Glioma", which is IRB approved. Subsequent collaboration with the FDA resulted in "A Phase 2 Study of Atengenal (A-10) and Astugenal (AS2-1) in Diffuse, Intrinsic, Brainstem Glioma (DIPG)", which has received IRB approval and will be opened for patient accrual in the near future.

## Conclusion

We have presented here the case of an eleven-year-old female who obtained a CR, clearance of physical signs, and long-term survival (> 25 years) following therapy with Antineoplastons A-10 and AS2-1 for DIPG. Antineoplastons A-10 and AS2-1 are an attractive therapeutic option for those patients with a DIPG (or other high-grade astrocytoma) who are ineligible for or refuse RT, and/or demonstrate PD following RT or chemotherapy. In collaboration with the FDA confirmatory Phase II and Phase III studies have been developed.

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## References

- Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. *Acta Neuropathol.* 2016;131:803–20.
- Gielen GH, Gessi M, Hammes J, Kramm CM, Waha A, Pietsch T. H3F3A K27M mutation in pediatric CNS tumors: a marker for diffuse high-grade astrocytomas. *Am J Clin Pathol.* 2013;139:345–9.
- Karremann M, Gielen GH, Hoffmann M, et al. Diffuse high-grade gliomas with H3 K27M mutations carry a dismal prognosis independent of tumor location. *Neuro Oncol.* 2018;20:123–31.
- Mackay A, Burford A, Carvalho D, et al. Integrated molecular meta-analysis of 1,000 pediatric high-grade and diffuse intrinsic pontine glioma. *Cancer Cell.* 2017;32:520–37.
- Schwartzentruber J, Korshunov A, Liu XY, et al. Driver mutations in histone H3.3 and chromatin remodeling genes in pediatric glioblastoma. *Nature.* 2012; 482:226–31.
- Smith MA, Freidlin B, Ries LA, Simon R. Trends in reported incidence of primary malignant brain tumors in children in the United States. *J Natl Cancer Inst.* 1998;90:1269-77.
- Central Brain Tumor Registry of the United States (CBTRUS) statistical report: Primary brain and other central nervous system tumors diagnosed in the United States in 2013-2017.
- Hoffman LM, Veldhuijzen van Zanten SEM, Colditz N, et al. Clinical, radiologic, pathologic, and molecular characteristics of long-term survivors of diffuse intrinsic pontine glioma (DIPG): A Collaborative Report from the International and European Society for Pediatric Oncology DIPG Registries. *J Clin Oncol.* 2018;36(19):1963–1972.
- Jansen MH, Veldhuijzen van Zanten SE, Sanchez Aliaga E, et al. Survival prediction model of children with diffuse intrinsic pontine glioma based on clinical and radiological criteria. *Neuro Oncol.* 2015; 17(1):160–166.
- Langmoen IA, Lundar T, Storm-Mathisen I, Lie SO, Hovind KH. Management of pediatric pontine gliomas. *Childs Nerv Syst.* 1991;7(1):13–15.
- Roujeau T, Machado G, Garnett M, et al. Stereotactic biopsy of

- diffuse pontine lesions in children. *J. Neurosurg.* 2007;107:1–4.
12. Cage TA, Samagh SP, Mueller S, et al. Feasibility, safety, and indications for surgical biopsy of intrinsic brainstem tumors in children. *Nerv Syst.* 2013; 29(8):1313-9.
  13. Castel D, Philippe C, Calmon R, et al. Histone H3F3A and HIST1H3B K27M mutations define two subgroups of diffuse intrinsic pontine gliomas with different prognosis and phenotypes. *Acta Neuropathol.* 2015;130(6):815–827.
  14. von Bueren AO, Karremann M, Gielen GH, et al. A suggestion to introduce the diagnosis of “diffuse midline glioma of the pons, H3 K27 wildtype (WHO grade IV)”. *Acta Neuropathol.* 2018; 36(1):171– 173.
  15. Burzynski SR, Janicki, T, Burzynski G, Marszalek A. 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.* 2015;6:334-344.
  16. Wen PY, Macdonald DR, Reardon DA, et al. Updated response assessment criteria for high-grade gliomas: response assessment in Neuro-Oncology Working Group. *J Clin Oncol.* 2010; 28(11):1963- 1972.
  17. Burzynski SR. Antineoplastons: Biochemical defense against cancer. *Physiol Chem Phys.* 1976;8:275- 279.
  18. Burzynski SR. Synthetic antineoplastons and analogs. *Drugs of the Future.* 1986;11:679-688.
  19. Burzynski SR, Patil S. The effect of Antineoplaston A10 and AS2-1 and metabolites of sodium phenylbutyrate on gene expression in glioblastoma multiforme. *J Cancer Ther.* 2014;5:929-945
  20. Burzynski SR, Janicki T, Burzynski G. Comprehensive genomic profiling of recurrent classic glioblastoma in a patient surviving eleven years following antineoplaston therapy. *Cancer Clin Oncol.* 2015;4(2):41-52.
  21. Burzynski SR, Weaver RA, Bestak M, et al. Phase II study of Antineoplastons A10 and AS2-1 (ANP) in children with recurrent and progressive multicentric glioma. A preliminary report. *Neuro-Oncol.* 2003;5:358.
  22. Burzynski SR, Lewy RI, Weaver R, et al. Long-term survival and complete response of a patient with recurrent diffuse intrinsic brain stem glioblastoma multiforme. *Integ Cancer Ther.* 2004;3:257-261.
  23. Burzynski SR, Weaver R, Lewy R, et al. Phase II study of antineoplaston A10 and AS2-1 in children with recurrent and progressive multicentric glioma. A Preliminary Report. *Drugs R&D.* 2004;5(6):315-326.
  24. Burzynski SR, Weaver R, Bestak M, et al. 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.* 2004; 6:427.
  25. Burzynski SR, Weaver R, Bestak M, et al. Treatment of primitive neuroectodermal tumors (PNET) with antineoplastons A10 and AS2-1 (ANP). Preliminary results of phase II studies. *Neuro-Oncol.* 2004; 6:428.
  26. Burzynski SR, Weaver RA, Janicki T, et al. Longterm survival of high-risk pediatric patients with primitive neuroectodermal tumors treated with Antineoplastons A10 and AS2-1. *Integ Cancer Ther.* 2005; 4(2):168-177.
  27. Burzynski SR. Targeted Therapy for Brain Tumors. In: Yang AV, ed. *Brain Cancer Therapy and Surgical Interventions.* New York Nova Science Publishers, Inc; 2006.
  28. Burzynski SR, Janicki, TJ, Weaver RA, Burzynski B. Targeted therapy with Antineoplastons A10 and AS2-1 of high grade, recurrent, and progressive brainstem glioma. *Integ Cancer Ther.* 2006;5(1):40- 47.
  29. Burzynski SR. Treatments for astrocytic tumors in children: Current and emerging strategies. *Ped Drugs.* 2006;8:167-168.
  30. Burzynski SR. Recent clinical trials in diffuse intrinsic brainstem glioma. *Cancer Ther.* 2007;5:379- 390.
  31. Burzynski S, Janicki T, Burzynski G, Marszalek A. Long-term survival (>13 years) in a child with recurrent diffuse pontine gliosarcoma: A case report. *J Ped Hematol Oncol.* 2014;36(7):e433-9.
  32. Burzynski SR, Janicki TJ, Burzynski GS, Marszalek A. 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.* 2014;5:565-577.
  33. Burzynski SR, Janicki TJ, Burzynski GS. 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.* 2014; 5:946-956.
  34. Burzynski SR, Burzynski GS, Janicki TJ. Recurrent glioblastoma multiforme—A strategy for long-term survival. *J Cancer Ther.* 2014;5:957-976.
  35. Burzynski SR, Janicki TJ, Burzynski, GS, Marszalek A, Brookman S. 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.* 2014;5:977-988.
  36. Burzynski SR, Janicki TJ, Burzynski GS, Brookman S. 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.* 2014; 5:1423-1437.
  37. Burzynski GS, Janicki TJ, Marszalek A. Long-term survival (>20 years) of a child with brainstem glioma treated with antineoplastons A10 and AS2-1: a case report. *Neuro-Oncol.* 2014; 11:16.
  38. Burzynski SR, Janicki TJ, Burzynski GS, Marszalek A. 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.* 2014;30:2051-2061.
  39. Burzynski SR, Burzynski G, Janicki J, Marszalek A. Complete response and Long-term survival (>20 years) of a child with tectal glioma: A case report. *Pediatr Neurosurg.* 2015; 50(2):99-103.
  40. Burzynski SR, Janicki TJ, Burzynski G. 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.* 2015;442:13-23.
  41. Burzynski SR, Janicki TJ, Burzynski GS, Marszalek A. 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.* 2015;4:28-38.
  42. Burzynski SR, Burzynski GS, Marszalek A, Janicki J, Martinez-Canca J. Long-term survival (over 20 years), complete response and normal childhood development in medulloblastoma treated with Antineoplastons A10 and AS2-1. *J Neurol Stroke.* 2015; 2(3):00054.
  43. Burzynski SR, Burzynski GS, Marszalek A, Janicki TJ, Martinez-Canca JF. Long-term survival over 21 years and pathologically confirmed complete response in pediatric anaplastic astrocytoma: A case report. *J Neurol Stroke.* 2015; 2(6):00072.
  44. Burzynski SR, Burzynski GS, Brookman S. A Case of Sustained Objective Response of Recurrent/Progressive Diffuse Intrinsic Pontine Glioma with Phenylbutyrate and Targeted Agents. *J Cancer Ther.* 2015;6:40-44.
  45. Burzynski SR, Janicki, T, Burzynski G, Marszalek A. 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.* 2015;6:334-344.
46. Burzynski SR, Janicki T, Burzynski G. 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.* 2015;6:1063-1074.
47. Burzynski SR, Janicki TJ, Burzynski GS. 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.* 2016;5(2):38-48.
48. Burzynski SR, Janicki TJ, Burzynski GS. A phase II study of antineoplastons A10 and AS2-1 in children with low-grade astrocytomas—Final report (Protocol BT-13). *J Cancer Ther.* 2016; 7(12):837-850.
49. Burzynski SR, Janicki TJ, Burzynski GS. Antineoplastons A10 and AS2-1 in the Treatment of children with optic pathway glioma: Final Report for protocol BT-23. *Cancer Clin Oncol.* 2017 6(1):25-35.
50. Burzynski SR, Janicki TJ, Burzynski GS, Marszalek A. A phase II study of Antineoplastons A10 and AS2-1 in children with brain tumors. Final Report (Protocol BT-10). *J Cancer Ther.* 2017;8:173-187.
51. Burzynski SR, Janicki T, Beenken, S. Treatment of Recurrent Glioblastoma Multiforme (rGBM) with Antineoplaston AS2-1 in Combination with Targeted Therapy. *Cancer Clin Oncol.* 2019; 8:1-15.
52. Burzynski, SR, Janicki, T, Burzynski, GS, Beenken, S. 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.* 2021;7:073-078.
53. Burzynski, SR, Burzynski, GS, Janicki, T, Beenken S. 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.* 2021;6:038-044.
54. Burzynski, SR, Janicki T, Burzynski GS, Beenken S. 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.* 2021;6.