



## CASE REPORT

# Recurrent Desmoplastic Infantile Ganglioglioma Treated with Antineoplastons: Partial Response and Overall Survival of > 11.8 Years in a Ten-Month-Old Female

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## Abstract

**Introduction:** Desmoplastic infantile tumors (DIT) are rare neoplasms of the central nervous system that occur in infants and young children. According to the World Health Organization (WHO) grading system, DIT are classified into three subtypes: Desmoplastic infantile astrocytoma (DIA), desmoplastic infantile ganglioglioma (DIG), and desmoplastic/nodular medulloblastoma (DNMB). DIA and DIG are WHO grade 1 while DNMB is WHO grade 4. Recurrent WHO grade 1 DIT have a very poor prognosis and there is no standardized therapy.

**Objectives:** 1) To review the efficacy of current treatments for recurrent DIT, 2) To determine the antitumor activity of ANP (Antineoplaston therapy) in recurrent DIG; and 3) To evaluate the tolerance of ANP in patients with recurrent DIG. A 10-month-old child received treatment at the Burzynski Clinic (BC) according to BT-10, "Phase II Study of Antineoplastons A10 and AS2-1 in Children with Brain Tumors". In this single arm study, ANP was delivered every four hours via a subclavian catheter and a programmable infusion pump. Tumor response was assessed by sequential brain MRIs utilizing gadolinium enhancement.

**Findings:** After resection of her DIG, this child was evaluated and treated at the BC. Baseline MRI of the brain, performed May 10, 2012, showed a left frontal enhancing mass measuring 18.00 cm<sup>2</sup> in size. ANP began on May 14, 2012. On August 27, 2012, MRI of the brain showed an enhancing brain tumor measuring 7.92 cm<sup>2</sup> in size, a 56.0% decrease from baseline and indicating achievement of a partial response (PR). ANP was discontinued on February 10, 2014. Brain MRIs performed between August 5, 2013,

and July 17, 2019, all showed an enhancing brain tumor measuring 4.20 cm<sup>2</sup> in size, a 76.7% decrease from baseline, indicating a persistent PR. The patient subsequently received no anti-cancer therapy. The last brain MRI completed at the time of this report was performed elsewhere on July 6, 2023, and did not demonstrate enhancement, possibly indicating achievement of a complete response (CR). The date of last contact was February 15, 2024, at which time the patient's overall survival since the start of treatment (OS) was 11.8 years. Conclusions: A ten-month-old female child with a recurrent DIG was treated with ANP and was alive and well more than 11.8 years later despite achieving only a partial response while on ANP. This may be due to an ANP effect on the invasiveness of the recurrent DIG and underscores the importance of OS in the evaluation of ANP's therapeutic efficacy.

## Keywords

Antineoplastons, Brain tumor, Desmoplastic infantile tumor, Desmoplastic infantile ganglioglioma, Phase II study, Recurrent desmoplastic infantile ganglioglioma

## Abbreviations

ANP: Antineoplaston Therapy; Antineoplastons: Antineoplastons A10 and AS2-1; A10: Atengenal; AS2-1: Astugenal; BC: Burzynski Clinic; CR: Complete Response; CSF: Cerebrospinal Fluid; DIA: Desmoplastic Infantile Astrocytoma; DIG: Desmoplastic Infantile Ganglioglioma; DIT: Desmoplastic Infantile Tumor; DNMB: Desmoplastic/Nodular Medulloblastoma; FDA: Food and Drug Administration; GFAP: Glial Fibrillary Acidic Protein; GTR: Gross Total Resection; ICH: International Conference

**Citation:** Burzynski SR, Burzynski GS, Janicki T, Marquis A, Beenken S (2024) Recurrent Desmoplastic Infantile Ganglioglioma Treated with Antineoplastons: Partial Response and Overall Survival of > 11.8 Years in a Ten-Month-Old Female. Int J Brain Disord Treat 10:050. doi.org/10.23937/2469-5866/1410050

**Accepted:** July 19, 2024; **Published:** July 21, 2024

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on Harmonization; IND: Investigational New Drug; LPS: Lansky Performance Score; MRI: Magnetic Resonance Imaging; OR: Objective Response; OS: Overall Survival since the start of treatment; PD: Progressive Disease; PR: Partial Response; RT: Radiation Therapy; SD: Stable Disease; SAE: Serious Adverse Event; STR: Subtotal Resection; T2-FLAIR: T2-Fluid Attenuated Inversion Recovery; WHO: World Health Organization

## Introduction

Desmoplastic infantile tumors (DIT) are neoplasms of the central nervous system (CNS) occurring in infants and young children, which are characterized by a large cystic mass with solid components and have a peak incidence in the first year of life [1]. They are rare, representing less than 1% of all pediatric brain tumors [1]. Usually located in the parietal or frontal lobes of the brain, these tumors can originate in multiple areas including the temporal and occipital lobes, cerebellum, and brainstem [2]. According to the World Health Organization (WHO) grading system, DIT are classified into three subtypes: desmoplastic infantile astrocytoma (DIA), desmoplastic infantile ganglioglioma (DIG), and desmoplastic/nodular medulloblastoma (DNMB). DIA and DIG are WHO grade 1 while DNMB is WHO grade 4.

Recurrent WHO grade 1 DIT are very rare with only a small number of cases being reported (see Discussion). Recurrence can occur more than 10 years after initial diagnosis and treatment [3] and can be of a different WHO grade [4]. DIT can harbor mutations in the BRAF gene, which have been associated with tumor recurrence or progression [5,6] and/or be affected by an altered methylation status of the MGMT gene, possibly influencing response to chemotherapy [7].

The imaging technique utilized for diagnosing DIG is magnetic resonance imaging (MRI) [2]. Findings include 1) A cystic mass with a mural nodule; 2) Mass effect, such as compression of the ventricles, midline shift, and/or edema of the surrounding brain tissue; 3) Contrast enhancement, especially in the solid component; and 4) Calcifications, which appear as hypointense foci on both T1- and T2-weighted images [8-10]. The solid component of the tumor is isointense or slightly hyperintense on both T1- and T2-weighted images while the cystic component is hyperintense on T2-weighted images and hypointense on T1-weighted images [8-10].

The symptoms and signs of DIG are generally the result of increased intracranial pressure, which results in head enlargement, bulging anterior fontanelle, headache, vomiting, lethargy, and seizures. Other symptoms and signs develop depending on the location and size of the DIG, including visual disturbances, motor weakness, incoordination, and developmental delay [11].

The diagnosis of DIG is based on the MRI findings (see above) and the histopathological examination

of tumor tissue, which confirms the presence of both glial and neuronal cells, and a desmoplastic reaction. The tumor cells usually express both glial and neuronal markers, such as glial fibrillary acidic protein (GFAP) and synaptophysin, respectively [12].

The treatment of DIG is primarily surgical, and the goal is to achieve a gross total resection (GTR) of the tumor. Since DIG is usually a benign tumor with a low recurrence rate, GTR provides the best prognosis for the patient. However, DIGs may require additional surgical resection, adjuvant chemotherapy and/or radiation therapy (RT) therapy if the tumor is incompletely resected, recurs, and/or demonstrates malignant features [13].

We present here the use of ANP (IV Antineoplaston therapy), which consists of Antineoplaston A10 (Atengenal) and Antineoplaston AS2-1 (Astugenal), in the treatment of recurrent DIG in a ten-month-old child.

## Materials and Methods

A 10-month-old female child was in good health until April 2012, when she developed “staring spells” and was admitted to a children’s hospital. She underwent an MRI of the brain on April 9, 2012, which showed a left-sided frontal tumor. On April 13, 2012, the child underwent subtotal resection (STR) of the tumor. Examination of the microscopic sections of the surgical specimen revealed a DIG. Her physicians recommended further surgery followed by chemotherapy, but the child’s parents determined that their daughter be treated at the Burzynski Clinic (BC). She was evaluated there on May 7, 2012, having had only surgical treatment up to that time. In addition to the “staring spells”, the child’s mother described her daughter as having perioral cyanosis and shallow breathing. The physical examination was essentially normal except for a left frontotemporal surgical scar. The child’s Lansky Performance Status (LPS) was 100%. The patient immediately began ANP according to Protocol BT-10, “Phase II Study of Antineoplastons A10 and AS2-1 in Children with Brain Tumors”. In this single arm study, ANP was delivered every four hours via a subclavian catheter and a programmable infusion pump.

The objectives of BT-10 were to 1) “To determine the efficacy of Antineoplaston therapy in children with a brain tumor, as measured by an objective response to therapy (complete response, partial response, or stable disease)” and 2) “Evaluate the adverse effects of and tolerance to Antineoplastons A-10 and AS2-1 in these patients”. Eligibility criteria for BT-10 included 1) Histologically confirmed brain tumor for which no curative therapy existed; 2) Baseline MRI of the brain performed within two weeks of the start of treatment, 3) Tumor size  $\geq 5$  mm; 4) Age of 6 months to 17 years; 5) LPS of 60% to 100%; and 6) Life expectancy  $\geq 2$  months.

Gadolinium-enhanced MRIs of the brain were used

in the diagnosis and follow-up of the patient's brain tumor. They were performed every 8 weeks for the first two years and then less frequently. T2-weighted, T2-fluid attenuated inversion recovery (T2-FLAIR), T1 weighted, and T1-weighted contrast-enhanced images were obtained. DIT exhibited patchy gadolinium-enhancement and sequential T1-weighted contrast-enhanced images were utilized to determine the effect of therapy [14].

As determined by MRI of the brain, the product of the two greatest perpendicular diameters of each measurable ( $\geq 5$  mm) and enhancing lesion was calculated. Tumor size was defined as the sum of these products [14,15]. 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% or greater reduction in total measurable and enhancing tumor size. CR and PR required a confirmatory brain MRI performed at least four weeks after the initial finding. Progressive disease (PD) indicated a 25% or greater increase in total measurable and enhancing tumor size, or new measurable and enhancing disease, while stable disease (SD) did not meet the criteria for PR or PD [14].

This Phase II trial was conducted in accordance with the U.S. Code of Federal Regulations, Title 21, Parts 11, 50, 56 and 312; the Declaration of Helsinki (1964) including all amendments and revisions; the Good Clinical Practices: Consolidated Guideline (E6), International Conference on Harmonization (ICH) and Guidance for Industry (FDA). By participating in this study protocol, the investigators agreed to provide access to all appropriate documents for monitoring, auditing, IRB review and review by any authorized regulatory agency. A summary of the study is presented in CT.gov, NCT00003458.

## Results

Baseline MRI of the brain performed May 10, 2012 (Figure 1) showed a left frontal enhancing mass measuring 18.00 cm<sup>2</sup> in size. As described above, this ten-month-old child was accrued to BT-10 and began treatment on May 14, 2012. The starting dose of A10 was 0.90 g/kg/d. It gradually increased to 21.45 g/kg/d and subsequently reduced to 15.26 g/kg/d. The starting dose of AS2-1 was 0.06 g/kg/d. It gradually increased to 0.46 g/kg/d and subsequently reduced to 0.33 g/kg/d.

On August 27, 2012 (Figure 1), MRI of the brain showed an enhancing brain tumor measuring 7.92 cm<sup>2</sup> in size, a 56.0% decrease from baseline and indicating achievement of a PR. ANP was discontinued on February 10, 2014. Brain MRIs performed between August 5, 2013, and July 17, 2019, all showed an enhancing brain tumor measuring 4.20 cm<sup>2</sup> in size, a 76.7% decrease from baseline, indicating a persistent PR. The patient subsequently received no anti-cancer therapy. The last

brain MRI completed at the time of this report was performed elsewhere on July 6, 2023 (Figure 1), and did not demonstrate enhancement, possibly indicating achievement of a CR. The date of last contact was February 15, 2024, at which time the patient's overall survival since the start of treatment (OS) was 11.8 years.

Adverse events were graded according to the Common Terminology Criteria for Adverse Events Version 3.0. The patient presented here experienced one serious adverse event (SAE) that was not thought to be related to ANP (somnolence). She fully recovered from this SAE.

Consent was obtained from the patient for publication of the brain MRI images (Figure 1).

## Discussion

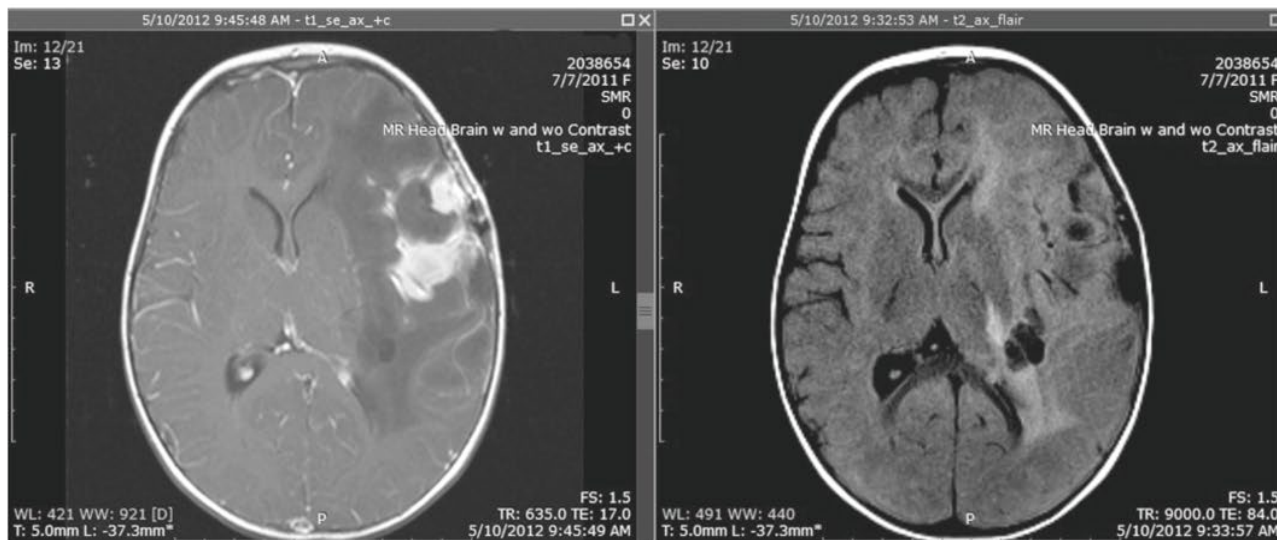
A second surgical procedure, chemotherapy, and RT have been utilized in the treatment of recurrent DIT. The use of chemotherapy and RT in recurrent DIT and their effect on OS requires further study as the existing data is sparse. However, important information on the treatment and prognosis of recurrent DIT in general can be illustrated by a single institution's experience - see below.

Imperato and colleagues, in a retrospective review, studied the treatment and outcome of 12 consecutive and fully documented DIT patients treated at the Santobono-Pausilipon Children's Hospital in Naples, Italy between 2008 and 2019. The median age was 3.5 years (range, 2-14 years). No child less than one year of age was treated [16].

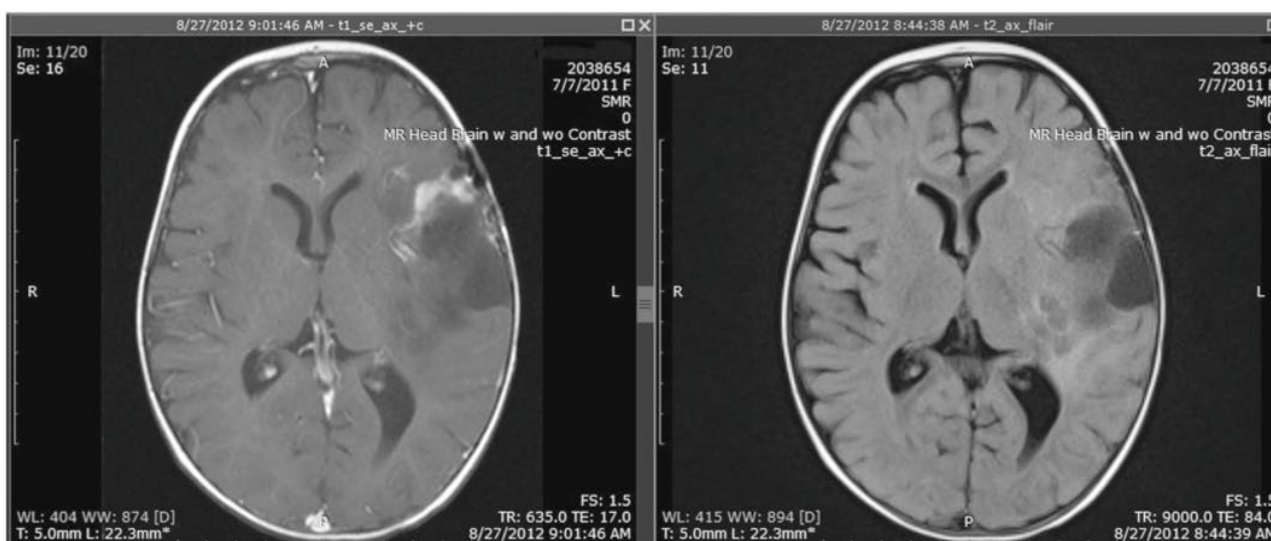
A microsurgical technique was performed in all surgical procedures. IV sodium fluorescein was used to optimize intraoperative recognition of infiltrating DIT during the last three years of the study. Eight patients underwent gross total resection (GTR) or STR (66.7%), three patients had less than an STR (25.0%), and one patient underwent biopsy only (8.3%) [16].

DIT and DIG patients were not segregated in the reporting of follow-up. At the time of this report, seven patients had no evidence of disease (58.3%). They had a median follow-up of 96 months (range: 19-132 months). Two patients were alive with stable disease (16.7%) and with follow-up of 7 and 12 months. Two patients were alive with progressive disease (16.7%) with follow-up of 21 and 84 months. One patient died within 24 hours of surgery due to hemorrhage (8.3%). Imperato and colleagues concluded that GTR is the optimal treatment for DIT, that an established adjuvant chemotherapy regime is lacking, and that the role of RT in the treatment of DIT is unknown [16].

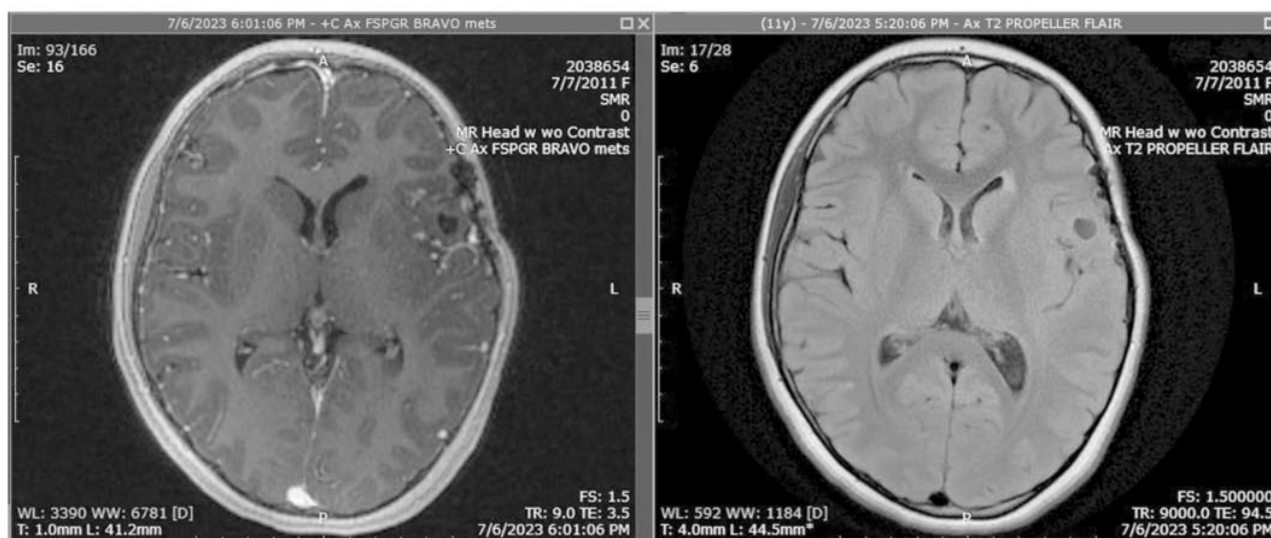
We present here the use of ANP in the treatment of a large recurrent DIG in a ten-month-old child following resection of the tumor performed elsewhere. In the absence of any standardized therapy, the use of



05 - 10 - 2012



08-27-2012



07 - 06 - 2023

**Figure 1:** Brain MRIs (axial): **May 10, 2012:** Baseline MRI of the brain showed a left frontal enhancing mass measuring 18.00 cm<sup>2</sup> in size; **August 27, 2012:** MRI of the brain showed an enhancing brain tumor measuring 7.92 cm<sup>2</sup> in size, a 56.0% decrease from baseline, indicating a PR; **July 6, 2023:** The last brain MRI completed at the time of this report was performed elsewhere and did not demonstrate enhancement, possibly indicating achievement of a CR.

CR: Complete Response; MRI: Magnetic Resonance Imaging; PR: Partial Response

ANP avoided the negative sequelae of repeat surgery, chemotherapy and/or RT. At last follow-up, the child was alive and well, showed no evidence of further tumor progression, and had an OS of > 11.8 years despite achieving only a PR on ANP. The prolonged OS may be due to an ANP effect on the invasiveness of the recurrent DIG and underscores the importance of OS in the evaluation of ANP's therapeutic efficacy.

We previously reported the case of a patient with glioblastoma (GBM) who obtained a PR with ANP and then underwent resection of the persistent GBM. At the time of surgery there was no evidence of involvement of the underlying brain parenchyma, also suggesting an ANP effect on the tumor's invasive potential. At last follow-up, this patient was experiencing good health, showed no evidence of tumor recurrence, and had an OS > 27 years [17]. This case also highlights the importance of OS in the evaluation of ANP's therapeutic efficacy.

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 Antineoplastons were isolated from blood and later from urine [18]. Subsequent studies of the isolated Antineoplastons demonstrated that Antineoplaston A10 and Antineoplaston AS2-1 were the most active ANPs. The chemical name of Antineoplaston A10 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 phenylacetylisoglutamate (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 [19].

ANP's mechanism of action differs from that of cytotoxic chemotherapy or RT. 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 400 mutated genes in the malignant genome and functions as a "molecular switch" which "turns on" tumor-suppressor genes and "turns off" oncogenes [20-21]. Hence, the antineoplastic action of ANP involves restoration of cell cycle control, induction of programmed cell death, and interference with cancer cell metabolism and nuclear transport.

## Conclusion

A ten-month-old female child with recurrent DIG was treated with ANP and at last follow-up was alive and well with an OS of > 11.8 years despite achieving only a PR on ANP therapy. The prolonged OS may be due to an ANP effect on the invasiveness of the recurrent DIG and underscores the importance of OS in the evaluation of ANP's therapeutic efficacy. ANP has proved to be an attractive option for patients with persistent, recurrent, disseminated, and/or metastatic brain tumors as it produces ORs and prolonged survival while avoiding the negative sequelae of chemotherapy, RT, and/or second surgery. Multiple Phase II clinical studies of ANP in a variety of low-and high-grade brain tumors under the Burzynski Research Institute's IND # 43,742 have now been completed and numerous articles have been published [22-69]. Based on our findings, we propose a multi-institutional Phase II clinical study of ANP in progressive DIT.

## Acknowledgements

The authors express their appreciation to Ramiro Rivera, Mohamed Khan, and Adam Golunski for their involvement.

## References

- Hargrave D, Chuang N, Bouffet E (2006) Desmoplastic infantile tumors. *Childs Nerv Syst* 22: 692-698.
- Sharma MC, Ralte AM, Gaikwad SB, Mahapatra AK, Mehta VS, et al. (2004) Recurrent desmoplastic infantile astrocytoma: A report of two cases. *J Neurooncol* 66: 167-172.
- Yilmaz C, Selek U, Palaoglu S, Soylemezoglu F (2009) Long-term recurrence of desmoplastic infantile ganglioglioma: A case report and review of the literature. *Clin Neuropathol* 28: 373-377.
- Stroink AR, Hoffman HJ, Hendrick EB, Humphreys RP (1986) Recurrent desmoplastic cerebral astrocytoma of infancy. Case report. *J Neurosurg* 65: 383-386.
- Chakrabarty A, Ganapathy S, Chagla L, Chacko AG, Rajshekhar V (2006) Recurrent desmoplastic infantile ganglioglioma with malignant transformation. *J Clin Neurosci* 13: 870-873.
- Schindler G, Capper D, Meyer J, Janzarik W, Omran H, et al. (2011) Analysis of BRAF V600E mutation in 1,320 nervous system tumors reveals high mutation frequencies in pleomorphic xanthoastrocytoma, ganglioglioma and extra-cerebellar pilocytic astrocytoma. *Acta Neuropathol* 121: 397-405.
- Chen Y, Takita J, Hiwatari M, et al. (2015) Reduced expression of DNA repair genes and chemosensitivity in 1p19q codeleted lower-grade gliomas. *J Neurooncol* 121: 289-297.
- Ginat DT, Meyers SP (2012) Intracranial lesions with high signal intensity on T1-weighted MR images: Differential diagnosis. *Radiographics* 32: 499-516.
- Koral K, Gargan L, Bowers DC, et al. (2017) Imaging characteristics of pediatric diffuse midline gliomas with histone H3 K27M mutation. *AJNR Am J Neuroradiol* 38: 295-300.

10. Perry A, Brat DJ (2018) Practical surgical neuropathology: A diagnostic approach. (2<sup>nd</sup> edn), Elsevier, Philadelphia, PA.
11. Chen Y, Wang L, Wang X (2018) Desmoplastic infantile ganglioglioma: A case report and literature review. *Medicine* 97: e13784.
12. Wu J, Armstrong TS, Gilbert MR (2011) Desmoplastic infantile ganglioglioma: A rare but distinct entity. *Arch Pathol Lab Med* 135: 1359-1362.
13. Chen JR, Wang H, Rosenblum MK (2019) Desmoplastic infantile ganglioglioma/astrocytoma. In: Perry A, Ellison DW, CNS tumors. Springer International Publishing, 21-29.
14. Wen PK, Macdonald DR, Reardon DA, Cloughesy TF, Sorensen AG, et al. (2010) Updated response criteria for high-grade gliomas: Response assessment in neuro-oncology (RANO) working group. *J Clin Oncol* 28: 1963-1972.
15. Chinot OL, Macdonald DR, Abrey LE, Zahlman G, Kerloeguen Y, et al. (2013) Response assessment criteria for glioblastoma: Practical adaptation and implementation in clinical trials of antiangiogenic therapy. *Curr Neuro Neurosci Rep* 13: 347.
16. Imperato A, Spennato P, Mazio F, Arcas E, Ozgural O, et al. (2021) Desmoplastic infantile astrocytoma and ganglioglioma: A series of 12 patients treated at a single institution. *Childs Nerv Syst* 37: 2187-2195.
17. Burzynski SR, Burzynski G, Janicki T, Beenken S (2022) Newly diagnosed glioblastoma: Partial response and > 27 years overall survival in a 37-year-old male treated with antineoplastons. *Recent Adv Clin Trials* 1: 1-7.
18. Burzynski SR (1976) Antineoplastons: Biochemical defense against cancer. *Physiol Chem Phys* 8: 275-279.
19. Burzynski SR (1986) Synthetic antineoplastons and analogs: Drugs of the future 11: 679-688.
20. Wen PK, Macdonald DR, Reardon DA, Cloughesy TF, Sorensen AG, et al. (2010) Updated response criteria for high-grade gliomas: Response assessment in neuro-oncology working group. *J Clin Oncol* 28: 1963-1972.
21. Chinot OL, Macdonald DR, Abrey LE, Zahlman G, Kerloeguen Y, et al. (2013) Response assessment criteria for glioblastoma: Practical adaptation and implementation in clinical trials of antiangiogenic therapy. *Curr Neuro Neurosci Rep* 13: 347.
22. Burzynski SR, Patil SS (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.
23. Burzynski SR, Janicki T, Burzynski G (2015) Comprehensive genomic profiling of recurrent classic glioblastoma in a patient surviving eleven years following antineoplaston therapy. *Cancer Clin Oncol* 4: 41-52.
24. Burzynski SR, Conde AB, Peters A, Saling B, Ellithorpe R (1999) A retrospective study of antineoplastons a10 and as2-1 in primary brain tumors. *Clin Drug Invest* 18: 1-10.
25. Burzynski SR, Weaver RA, Lewy RI, Janicki TJ, Jurida GF, et al. (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: 315-326.
26. Burzynski SR, Lewy RI, Weaver R, Janicki T, Jurida G (2004) Long-term survival and complete response of a patient with recurrent diffuse intrinsic brain stem glioblastoma multiforme. *Integ Cancer Ther* 3: 257-261.
27. Burzynski SR, Weaver R, Bestak M, Janicki T, Szymkowski B, et al. (2004) Treatment of primitive neuroectodermal tumors (PNET) with antineoplastons A10 and AS2-1 (ANP): Preliminary results of phase II studies. *Neuro Oncol* 6: 428.
28. Burzynski SR, Weaver R, Bestak M, Janicki T, Jurida G, et al. (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.
29. Burzynski SR, Weaver RA, Janicki T, Szymkowski B, Jurida G, et al. (2005) Long-term survival of high-risk pediatric patients with primitive neuroectodermal tumors treated with antineoplastons A10 and AS2-1. *Integ Cancer Ther* 4: 168-177.
30. Burzynski SR (2006) Targeted therapy for brain tumors. In: Yang AV, Brain cancer therapy and surgical interventions. Nova Science Publishers, Inc, New York.
31. 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. *Integr Cancer Ther* 5: 40-47.
32. Burzynski SR (2006) Treatments for astrocytic tumors in children: Current and emerging strategies. *Ped Drugs* 8: 167-168.
33. Burzynski SR (2007) Recent clinical trials in diffuse intrinsic brainstem glioma. *Cancer Ther* 5: 379-390.
34. Burzynski SR, Burzynski GS, Janicki TJ (2004) Recurrent glioblastoma multiforme: A strategy for long-term survival. *J Cancer Ther* 5: 957-976.
35. 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.
36. 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.
37. 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.
38. 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.
39. Burzynski GS, Janicki TJ, Marszalek A, Burzynski S (2014) Long-term survival (> 20 years) of a child with brainstem glioma treated with antineoplastons A10 and AS2-1: A case report. *Neuro Oncol* 11: 16.
40. 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.
41. 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: e433-e439.
42. 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.
43. 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 Neurosurg* 50: 99-103.
44. 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.
45. 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.
46. Burzynski SR, Burzynski GS, Marszalek A, Janicki J, Martinez-Canca J (2015) Long-term survival (greater than 20 years), complete response, and normal childhood development in medulloblastoma treated with Antineoplastons A10 and AS2-1. *J Neurol Stroke* 2: 00054.
47. Burzynski SR, Burzynski GS, Marszalek A, Janicki TJ, Martinez-Canca JF (2005) Long-term survival over 21 years and pathologically confirmed complete response in pediatric anaplastic astrocytoma: A case report. *J Neurol Stroke* 2: 00072.
48. 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.
49. 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.
50. Burzynski S, 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: 38-48.
51. 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: 837-850.
52. 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.
53. Burzynski SR, Janicki T, Beenken S (2019) Treatment of recurrent glioblastoma multiforme (rGBM) with Antineoplastron AS2-1 in combination with targeted therapy. *Cancer Clin Oncol* 8: 1-15.
54. Burzynski SR, Janicki T, Burzynski GS, Beenken S (2021) Long-term survival (27.7 years) following IV Antineoplastron Therapy (ANP) in a 36-year-old-female with a progressive diffuse intrinsic pontine glioma (DIPG). *Int J Radiol Imaging Technol* 7: 073-078.
55. Burzynski SR, Burzynski GS, Janicki T, Beenken S (2021) Long-term survival (23 years) in a 26-year-old male after Antineoplastron therapy for a progressive, diffuse intrinsic pontine glioma: A case report. *Int J Brain Disorder Treat* 6: 038-044.
56. 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.
57. Burzynski SR, Janicki T, Burzynski GS, Beenken S (2021) Diffuse intrinsic pontine glioma in an 11-year-old female treated with antineoplastons: Complete response and > 25-year survival. *Pediatr Neonatal Med* 1: 1-5.
58. Burzynski SR, Janicki T, Burzynski GS, Beenken S (2022) A 25-year-old female with diffuse intrinsic pontine glioma surviving for more than nine years following treatment with antineoplastons. *Int J Clin Oncol Cancer Res* 7: 1-7.
59. 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: 99-105.
60. Burzynski SR, Burzynski G, Janicki T, Beenken S (2022) Newly diagnosed Multicentric Pilocytic Astrocytoma: Complete Response and > 22 Years Survival in a Six Year and Nine-month-old Female Treated with Antineoplastons. *Internat J Clin Oncol and Cancer Res* 7: 76-82.
61. Burzynski S, Burzynski G, Janicki T, Beenken S (2022) Recurrent and progressive ganglioglioma in an 11-year-old male treated with antineoplastons: Partial response with more than nine years and nine months survival and complete resolution of clinical symptoms/signs. *Biomed Res J* 37: 1-13.
62. Burzynski S, Burzynski G, Janicki T, Beenken S (2022) Outcomes in Four Children with Persistent, Recurrent, and Progressive Gangliogliomas Treated in Phase II Studies with Antineoplastons A10 and AS2-1. *Neurol Neurosci* 3: 1-9.
63. Burzynski S, Burzynski G, Janicki T, Beenken S (2022) Recurrent/persistent glioblastoma: Complete response and 24 years disease-free-survival in a 45-year-old female treated with antineoplastons. *Cancer Studies Therap* 7: 1-6.
64. Burzynski SR, Burzynski GS, Janicki TJ, Beenken SW (2023) Persistent pineoblastoma: Complete Response and > 26 Years Overall Survival in a Ten-month-old Female Treated with Antineoplastons. *Biomed Res Clin Prac* 7: 1-5.
65. Burzynski S, Burzynski G, Janicki T, Beenken S (2023) Newly diagnosed Anaplastic Astrocytoma: > 23 Year Survival in a 31-Year and 11-month-Old Female treated with Antineoplastons. *Neurol Neurosci* 4: 1-6.
66. Burzynski S, Burzynski G, Janicki T, Beenken S (2023) Inoperable optic pathway glioma: A seven-year-old male with > 35 years overall survival following treatment with antineoplastons. *Eur J Clin Med* 4: 9-14.
67. Burzynski S, Burzynski G, Janicki T, Beenken S (2023) Recurrent medulloblastoma: Complete response and > than 21 years and five months overall survival in a one-year and seven-month-old male treated with antineoplastons. *J Oncol Res Rev Rep* 4: 3-6.
68. Burzynski SR, Burzynski GS, Janicki T, Beenken S (2024) Recurrent pilocytic astrocytoma: Treatment with antineoplastons, complete response, and > 27 years overall survival. *Recent Adv Clin Trials* 4: 1-7.
69. Burzynski SR, Burzynski GS, Janicki T, Beenken S (2024) Recurrent/disseminated choroid plexus carcinoma: overall survival of > 23.6 years in a one-year and nine-month-old female treated with antineoplastons. *J Med Res Case Rep* 6.