



## Quackery

### Antineoplastons: when is enough enough?

Antineoplastons are an experimental cancer therapy that is not approved by the US Food and Drug Administration (FDA) for any indication. To date, there have been no randomised, controlled trials showing efficacy of antineoplastons. However, side-effects of this therapy can include serious neurological toxicity. So, how can such therapy continue to be in use after more than four decades, and be administered to thousands of patients, without any proven safety or activity data?

Antineoplastons were first proposed as a potential cancer treatment in 1976 by Dr Stanislaw Burzynski, a Polish-educated physician, MD, and PhD in Biochemistry from the Medical Academy of Lublin (Lublin, Poland). He moved to the USA in 1970 and joined the laboratory of Dr Georges Ungar in the Department of Anaesthesia at the Baylor College of Medicine (Houston, TX, USA).<sup>1</sup> While at the Baylor College of Medicine, Dr Burzynski isolated compounds from human blood and later urine (aminoacids and peptides), which he called antineoplastons and suggested had antitumour activity. Antineoplastons are a combination of sodium phenylacetate acid and phenylacetylglutamine that can be administered either orally or intravenously.<sup>2</sup> Dr Burzynski described this concoction as a non-toxic natural form of cancer protection, and began production of different synthetic versions in his laboratory.<sup>3</sup> In the late 1970s, he left Baylor and opened his own clinic, the Burzynski Clinic (Houston, TX, USA), where he and a small team of physicians have now treated thousands of patients with cancer using this unproven therapy, charging thousands of dollars.<sup>4</sup> In fact, the Cancer Research UK website suggests that a year's course of treatment at the Burzynski Clinic costs between US\$30 000 and \$60 000.<sup>5</sup> Recently, the Burzynski Clinic has started requiring patients to provide a deposit before treatment starts, and their website informs patients that they do not accept insurance to pay for any portion of the treatment.<sup>6</sup> In fact, patients often fundraise to meet the cost of treatment, as they have to pay for this alternative therapy out of their own pockets.<sup>7</sup> How is this possible considering this treatment is not FDA-approved?

A comprehensive review of antineoplastons is provided by the National Cancer Institute's Physician Data Query (PDQ) database, a resource that contains up-to-date, comprehensive, evidence-based cancer information summaries.<sup>2</sup> As of today, no phase 3 randomised, controlled trials of antineoplastons in patients with cancer have been reported in the literature. A PubMed search identified slightly more than 100 articles on antineoplastons as of April 1, 2018 (using "antineoplaston" as the search term), with most consisting of case reports published in low

impact journals, phase 1 clinical trials, and a few phase 2 clinical trials, with about a third of these being authored by Dr Burzynski and his associates.<sup>4</sup> Although these non-controlled studies have often reported disease remission in patients with cancer, independent investigators have been unsuccessful in reproducing these results and have criticised the quality of the published data, citing an absence of robust evidence scientific rigor in these studies.<sup>8-11</sup>

Between 1991 and 1995, the National Cancer Institute (NCI) initiated a multicentre phase 2 trial of antineoplastons, which I was involved with, at three cancer centres in the USA (Memorial Sloan-Kettering Cancer Center, New York, NY; the Mayo Clinic, Rochester, MN; and the National Institutes of Health Clinical Center, Bethesda, MD). In 1995, after over \$1 million having been spent, the trial was terminated prematurely because of both parties—the NCI and Dr Burzynski—accusing one another of attempting to undermine the project.<sup>12,13</sup> The objective of our Phase 2 study in patients with anaplastic astrocytoma or glioblastoma multiforme who had recurred after radiation, was to assess the pharmacokinetics, side-effect profile, and activity of antineoplastons A10 (NSC 648539) and AS2-1 (NSC 620261). Patients received escalating doses of A10 and AS2-1 via multiple intermittent intravenous injections. Neurocortical toxicity (eg, somnolence, confusion, and exacerbation of an underlying seizure disorder) was noted in more than half of the patients. The small sample size—nine patients were treated, of whom six (67%) had evaluable data and none showed tumor regression—precluded definitive

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For a full reference list see Online for appendix

The **Burzynski Clinic website** is available at <http://www.burzynskiclinic.com/>

For the **Cancer Research UK entry on antineoplastons** see <http://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment/complementary-alternative-therapies/individual-therapies/antineoplaston-therapy>

For the **NCI's PDQ entry on antineoplastons** (updated 09/08/2016) see <https://www.cancer.gov/about-cancer/treatment/cam/hp/antineoplastons-pdq>

For more on the **concept of disproven therapy** see *CA Cancer J Clin* 2004; **54**: 110-18.



conclusions about treatment activity.<sup>12</sup> The status of clinical trials using antineoplastons as investigational drugs for various cancers remains unknown, and to date, a few studies are listed on the ClinicalTrials.gov website as not yet recruiting.<sup>14</sup>

Although Dr Burzynski claimed success in use of antineoplastons for the treatment of various cancers, and some of the clinic's patients provided anecdotal testimonies of benefit,<sup>15</sup> there is no peer-reviewed, scientific evidence of the clinical activity of these compounds. Furthermore, the consensus among the oncology community is that antineoplaston therapy is unproven. Although antineoplaston therapy is promoted as a non-toxic alternative to chemotherapy, it is in fact a form of chemotherapy with substantial known side effects, including severe neurotoxicity.<sup>2,16</sup> Moreover, independent scientists have been unable to reproduce the positive results reported in Dr Burzynski's studies.<sup>2</sup> Cancer Research UK states that available scientific evidence does not support claims that antineoplaston therapy is effective in treating or preventing cancer;<sup>5</sup> and antineoplaston treatment has been labeled as a disproven therapy (no therapeutic value), as opposed to an unproven therapy (of unknown therapeutic value) in a review of therapies offered outside conventional cancer treatment centres and based on theories outside the biomedical spectrum.<sup>17</sup> In 1998, three oncologists were enlisted by the *The Cancer Letter* to independently review Dr Burzynski's clinical trial research on antineoplastons. They concluded that the studies were flawed, poorly designed, and unlikely to produce interpretable results, and questioned the validity of Dr Burzynski's research methods.<sup>18</sup>

Dr Burzynski has been the subject of various FDA inspections and warning letters for selling an investigational agent and promotional advertising of an unapproved cancer therapy (ie, selling such unapproved products with unsubstantiated therapeutic claims constitutes a violation of the Federal Food, Drug and Cosmetic Act). Over the past decade, the FDA has issued several warning letters to the Burzynski Research Institute, with regard to protocol violations and non-adherence to the applicable statutory requirements and FDA regulations governing the protection of human subjects, as well as to the Institute's institutional review board, also known as an independent ethics committee, for violations to good manufacturing practices at the clinical supply manufacturing facility (Burzynski Manufacturing Facility).<sup>19-21</sup> The Burzynski Clinic has also made use of so-called compassionate use exemptions. According to an investigative report published

in August, 2016, the clinic has also benefited from political lobbying of Dr Burzynski's supporters. From 2011 to 2016, 37 members of Congress wrote to the FDA about Dr Burzynski to grant constituents these compassionate use exemptions.<sup>22</sup> Dr Burzynski has also tried to circumvent federal rules by citing Texas' right-to-try drugs law.

In recent years, the Texas Medical Board has filed complaints against Dr Burzynski, including allegations of misleading patients into paying exorbitant charges and accepting care from providers without substantial education or training related to cancer treatment, as well as misrepresentation to patients of unlicensed people as licensed medical doctors.<sup>23,24</sup> In February, 2017, the Texas Medical Board (Austin, TX, USA) recommended revoking Dr Burzynski's medical license and fining him \$360 000; however, a month later the board sanctioned Dr Burzynski with probation and fined him only \$40 000.<sup>25</sup> Dr Burzynski has also been embroiled in other lawsuits involving insurance fraud and medical negligence; some of these cases were dismissed, but the outcomes of others remain unknown.<sup>26</sup> Nonetheless, the Burzynski Clinic has also been aggressive in threatening legal action against those that criticise antineoplastons or the clinic's activities.<sup>27</sup>

For over four decades, antineoplaston therapy has been—and is still—available in the USA through Dr Burzynski and his associates. Although they have tried, the FDA and state medical board have been unable to shut down this practice. "These organizations are supposed to protect the public from practitioners like Burzynski, but all too often they fail at their charges, in this case spectacularly", said Dr David Gorski (Wayne State University, Detroit, MI, USA).<sup>1</sup> As of today, the Burzynski Clinic continues to offer antineoplaston therapy, as advertised on its website and the website of the Burzynski Research Institute.<sup>28,29</sup> The Memorial Sloan-Kettering Cancer Center states that "there is no evidence to support the anticancer effects of antineoplastons in humans."<sup>30</sup> The facts are clear; there is no scientific basis to support antineoplaston theory, treatment side-effects can include severe neurological toxicity, antineoplastons are not approved by any drug regulatory authorities worldwide for prevention or treatment of any disease, and there is no clear evidence of benefit. This quackery has continued for 40 years and caused serious harm to desperate patients. Enough is enough!

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The views expressed here are those of the author and do not necessarily reflect the views of the National Cancer Institute, the National Institutes of Health, the Department of Health and Human Services, or the United States government.