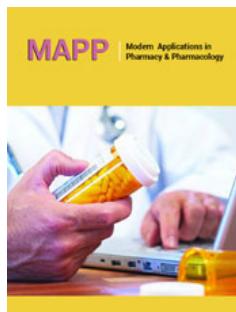


Radioiodine-Valuable Addition to Therapy of Glioblastoma Multiforme

Agata Czarnywojtek^{1,2*}, Magdalena Borowska¹ and Krzysztof Pietrończyk³

ISSN: 2637-7756



***Corresponding author:** Agata Czarnywojtek, Department of Pharmacology, Poznan University of Medical Sciences, Poland

Submission: May 16, 2023

Published: May 22, 2023

Volume 3 - Issue 3

How to cite this article: Agata Czarnywojtek*, Magdalena Borowska and Krzysztof Pietrończyk. Radioiodine-Valuable Addition to Therapy of Glioblastoma Multiforme. Mod Appl Pharm Pharmacol. 3(3). MAPP.000561. 2023.

DOI: [10.31031/MAPP.2023.03.000561](https://doi.org/10.31031/MAPP.2023.03.000561)

Copyright@ Agata Czarnywojtek, This article is distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits unrestricted use and redistribution provided that the original author and source are credited.

Opinion

I would like to present a new hypothetical method of treating Glioblastoma Multiforme (GM), which has hitherto been used as a standard in neurosurgery, chemotherapy and radiotherapy. Is it possible to treat GM with Radioiodine Thyroid (RIT) alone without using the sodium iodide symporter (NIS) gene? After all, the NIS has been detected not only in the thyroid but also in various cancers [1-8].

The administration of RIT is completely harmless and hypothyroidism may, depending on the dose, be the only complication. Indeed, it has recently been shown that, in the case of thyroid cancer, for example, the maximum dose of RIT is 37,000MBq (1,000mCi) [9,10]. Is it worth using the ablative dose of 740MBq (20mCi) of RIT to treat GM in outpatient conditions, with the possibility of repeating it? What advantages can this have? After all, GM patients live a very short time. Yet the NIS gene expression has been observed in GM, albeit only in animals. Thus, it may be better to start applying RIT now. As early as 1955, Amyes et al. [11] localised brain tumours using radioactive iodine and phosphorus. In this procedure, a needle probe was used for the first time, which proved to be very useful in quickly locating and defining the affected area. Radioactive isotopes of various elements are increasingly used in nuclear medicine. Radioisotopes of various elements are increasingly used in nuclear particles. This is where beta rays can be effective, in addition to imaging. Currently, an experimental NIS gene is used, but I have very little time and maybe RIT should be used to treat GM as soon as possible, but in a dose ranging from 740MBq (2mCi) to as much as 5,550MBq (150mCi), for example. However, it has been proven that thyroid tumours accumulate up to 37,000MBq (1,000mCi) of RIT [12,13]. This further proves that the use of RIT does not have adverse effects and may only lead to hypothyroidism. It is also worth remembering that the activity of radioiodine used in the treatment of a hyperactive multinodular goitre is 150-200 μ Ci/g of thyroid tissue, calculated based on the following formula: (thyroid weight (g)x150-200 μ Ci \times 1/T24 iodine intake after 24 hours). RIT can be used in higher doses ranging from 370MBq (10mCi) to 740MBq (20mCi) in outpatient conditions, for example, in Grave's disease and hyperfunctioning nodular goitre [14,15].

It is not always possible to remove a general grade IV GM. Therefore, in accordance with the current state of knowledge, standard therapy is applied including neurosurgery [16], classical radiotherapy [17,18], modulated electrohyperthermia (mEHT) [19], chemotherapy (e.g., temozolomide) [20] and humanised monoclonal antibody (e.g., pembrolizumab) [21-23]. Perhaps it is worth trying RIT? Attention has also been paid to targeted therapy that uses tyrosine kinase inhibitors (imatinib, sunitinib and sorafenib) [24-28], as well as the latest drugs, such as crizotinib, entrectinib or larotrectinib [29,30]. NanoTherm® therapy is also used in GM patients who have exhausted conventional treatment methods [31]. Recently,

Individualised Multimodal Immunotherapy (IMI) has been developed based on cancer vaccines [32-42] and oncolytic viruses [14,43,44]. It may be worth applying non-virological therapy in the form of RIT, even without genetic aspects, as was the case before. Over 60 years ago, Amyes et al. [11] determined the location of brain tumours (in rats) using radioactive iodine and phosphorus. It may be worth revolutionising the current therapy and using RIT to treat GM. Very importantly, this therapy can be completely free, and even if there is a charge, it does not have to be very high. Hypothyroidism is the only side effect. Patients, however, may gain a new life having been freed from GM.

Similarly, Hermida et al. [45] and Gursoy et al. [46] write that RIT has been used in patients with amiodarone-induced thyrotoxicosis (AIT) with very low uptake (RAIU) [47,48]. However, the authors used very high radioiodine activities {up to 2960MBq (80mCi 131I)}, which are not routinely used in the treatment of hyperthyroidism. None of the patients after RIT therapy had any adverse effects during AIT; only hypothyroidism occurred [47,48]. In the case of AIT, Antithyroid Drugs (ATDs), including thiouracil thionamide derivatives {PTU, propylthiouracil (Thyrosan [Sun-Farm])} and imidazole [MMI, thiamazole, Metizol (INC Polfa-Rzeszów)], were followed by angranulocytosis, hepatitis or vasculitis and lupus-like syndrome [49-51]. At that time, it was necessary to use RIT as the authors believed that the use of RIT in individual GM therapy might successfully complement other therapies [47,48,50]. This therapy can play a very important role in the case of GM relapse. Although there are no current human experiments, positive results have been obtained in Wistar rats [52] and mice [5] (for a combination of the NIS gene and RIT). The authors believe that administering RIT as soon as possible to GM patients who have had another relapse will provide a completely different perspective in non-genetically modified therap.

References

- Arczewska KD, Godlewska M, Krasuska W, Łyczkowska A, Kiedrowski M, et al. (2019) Expression of pendrin and NIS iodide transporters in human breast tumor and peri-tumoral tissue. *Arch Med Sci* 18(4): 1041-1050.
- Spitzweg C, Dietz AB, O Connor MK (2000) *In vivo* sodiumiodide symporter therapy of prostate cancer. *Endocr J* 47(Suppl 2000): 110.
- Elisei R, Vivaldi A, Ciampi R, Pinuccia F, Fulvio B, et al. (2006) Treatment with drugs able to reduce iodine efflux significantly increases the intracellular retention time in thyroid cancer cells stably transfected with sodium iodide symporter complementary deoxyribonucleic acid. *J Clin Endocrinol Metab* 91(6): 2389-2395.
- Huang M, Batra RK, Kogai T, Lin YQ, Jerome MH, et al. (2001) Ectopic expression of the thyroperoxidase gene augments radioiodide uptake and retention mediated by the sodium iodide symporter in non-small cell lung cancer. *Cancer Gene Ther* 8(8): 612-618.
- Dwyer RM, Bergert ER, O'Connor MK, Gendler SJ, Morris JC, et al. (2006) Sodium iodide symporter-mediated radioiodide imaging and therapy of ovarian tumor xenografts in mice. *Gene Ther* 13(1): 60-66.
- Mitrofanova E, Unfer R, Vahanian N, Wayne D, Erica R, et al. (2004) Rat sodium iodide symporter for radioiodide therapy of cancer. *Clin Cancer Res* 10(20): 6969-6976.
- Schipper ML, Weber A, Behe M, Rüdiger G, Werner J, et al. (2003) Radioiodine treatment after sodium iodide symporter gene transfer is a highly effective therapy in neuroendocrine tumor cells. *Cancer Res* 63(6): 1333-1338.
- Boland A, Ricard M, Opolon P (2000) Adenovirus-mediated transfer of the thyroid sodium/iodide symporter gene into tumors for a targeted radiotherapy. *Cancer Res* 60(1): 3484-3492.
- Pacini F, Fuhrer D, Elisei R, Handkiewicz-Junak D, Leboulleux S, et al. (2022) 2022 ETA consensus statement: What are the indications for post-surgical radioiodine therapy in differentiated thyroid cancer? *Eur Thyroid J* 11(1):e210046.
- Luster M, Pfestroff A, Hänscheid H, Verburg FA (2017) Radioiodine therapy. *Semin Nucl Med* 47(2): 126-134.
- Amyes EW, Deeb PH, Vogel PJ, Adams RM (1955) Determining the site of brain tumors-the use of radioactive iodine and phosphorus. *Calif Med* 82(3): 167-170.
- Yang J, Zheng R, Liang M, Yingying J, Lin L, et al. (2019) Association of the cumulative dose of radioactive iodine therapy with overall survival in patients with differentiated thyroid cancer and pulmonary metastases. *Front Oncol* 9: 558.
- Dorn R, Kopp J, Vogt H, Peter H, Robert GC, et al. (2003) Dosimetry-guided radioactive iodine treatment in patients with metastatic differentiated thyroid cancer: Largest safe dose using a risk-adapted approach. *J Nucl Med* 44(3): 451-456.
- Ross DS, Burch HB, Cooper DS, Greenlee MC, Peter L, et al. (2016) 2016 American thyroid association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid* 2016; 26(10): 1343-1421.
- Wartofsky L, Glinoer D, Solomon D, Nagataki S, Lagasse R, et al. (1991) Differences and similarities in the diagnosis and treatment of graves' disease in Europe, Japan and United States. *Thyroid* 1(2): 129-135.
- Kirkpatrick DB (1984) The first primary brain-tumor operation. *J Neurosurg* 61(5): 809-813.
- Parvez K, Parvez A, Zadeh G (2014) The diagnosis and treatment of pseudoprogression, radiation necrosis and brain tumor recurrence. *Int J Mol* 15(7):11832-11846.
- Ellingson BM, Chung C, Pope WB, Boxerman JL, Timothy JK, et al. (2017) Pseudoprogression, radionecrosis, inflammation or true tumor progression? challenges associated with glioblastoma response assessment in an evolving therapeutic landscape. *J Neurooncol* 2017; 134(3): 495-504.
- Fiorentini G, Szasz A (2006) Hyperthermia today: Electric energy, a new opportunity in cancer treatment. *J Cancer Res Ther* 2(2): 41-46.
- Alifieris C, Trafalis DT (2015) Glioblastoma multiforme: Pathogenesis and treatment. *Pharmacol Ther* 152: 63-82.
- Baxi S, Yang A, Gennarelli RL, Niloufer K, Ziwei W, et al. (2018) Immune-related adverse events for anti-PD-1 and anti-PD-L1 drugs: Systematic review and meta-analysis. *BMJ* 14: 360:k793.
- Reardon DA, Kim TM, Frenel JS, Armando S, Juanita L, et al. (2016) ATIM-35 Results of the phase 1B keynote-028 multi-cohort trial of pembrolizumab monotherapy in patients with recurrent PD-L1-positive Glioblastoma Multiforme (GBM). *Neuro Oncol* 18(6): 25-26.
- Aurisicchio L, Pallocca M, Ciliberto G, Gennaro C, Fabio P, et al. (2018) The perfect personalized cancer therapy: Cancer vaccines against neoantigens. *J Exp Clin Cancer Res* 37: 1-10.
- Palande V, Siegal T, Detroja R, Gorohovski A, Glass R, et al. (2022) Detection of gene mutations and gene-gene fusions in circulating cell-free DNA of glioblastoma patients: An avenue for clinically relevant diagnostic analysis. *Mol Oncol* 16(10): 2098-2114.
- Gleevec (Imatinib mesylate) tablet. Daily Med, National Library of Medicine, Maryland, USA.

26. Sun L, Liang C, Shirazian S, Zhou Y, Todd M, et al. (2003) Discovery of 5-[5-fluoro-2-oxo-1,2-dihydroindol-(3Z)-ylidenemethyl]-2,4- dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide, a novel tyrosine kinase inhibitor targeting vascular endothelial and platelet-derived growth factor receptor tyrosine kinase. *J Med Chem* 46(7): 1116-1119.
27. Strumberg D (2005) Preclinical and clinical development of the oral multikinase inhibitor sorafenib in cancer treatment. *Drugs Today* 41(12): 773-784.
28. Murphy DA, Makonnen S, Lassoued W, Michael DF, Christopher C, et al. (2006) Inhibition of tumor endothelial ERK activation, angiogenesis, and tumor growth by sorafenib (BAY43-9006). *Am J Pathol* 169(5): 1875-1885.
29. König D, Hench J, Frank S, Laura D, Ivana BH, et al. (2022) Larotrectinib response in NTRK3 fusion-driven diffuse high-grade glioma. *Pharmacology* 107(7-8): 433-438.
30. Subbiah V, Velcheti V, Tuch BB, Ebata K, Busaidy NL, et al. (2018) Selective RET kinase inhibition for patients with RET-altered cancers. *Ann Oncol* 29(8): 1869-1876.
31. <https://www.magforce.com/news/?article=375>
32. Schirrmacher V (2020) Cancer vaccines and oncolytic viruses exert profoundly lower side effects in cancer patients than other systemic therapies: A comparative analysis. *Biomedicines* 8(3): 61.
33. Schirrmacher V, Lorenzen D, Van Gool SW, Stuecker W (2017) A new strategy of cancer immunotherapy combining hyperthermia/oncolytic virus pretreatment with specific autologous anti-tumor vaccination-A review. *Austin Oncol Case Rep*. 2(1): 1006.
34. Lowenfeld L, Mick R, Datta J, Shuwen Xu, Elizabeth F, et al. (2017) Dendritic cell vaccination enhances immune responses and induces regression of HER2 pos DCIS independent of route: Results of randomized selection design trial. *Clin Cancer Res* 23(12): 2961-2971.
35. Obara W, Kanehira M, Katagiri T, Renpei K, Yoichiro K, et al. (2018) Present status and future perspective of peptide-based vaccine therapy for urological cancer. *Cancer Sci* 109(3): 550-559.
36. Chamani R, Ranji P, Hadji M, Azin N, Ebrahim E, et al. (2018) Application of E75 peptide vaccine in breast cancer patients: A systematic review and Meta-analysis. *Eur J Pharmacol* 831: 87-93.
37. Hilf N, Kuttruff-Coqui S, Frenzel K, Valesca B, Stefan S, et al. (2019) Actively personalized vaccination trial for newly diagnosed glioblastoma. *Nature* 565(7738): 240-245.
38. Schirrmacher V, van Gool S, Stuecker W (2019) Breaking therapy resistance: An update on oncolytic Newcastle disease virus for improvements of cancer therapy. *Biomedicines* 7(3): 66.
39. Artusio E, Hathaway B, Stanson J, Whiteside TL (2006) Transfection of human monocyte-derived dendritic cells with native tumor DNA induces antigen-specific T-cell responses *in vitro*. *Cancer Biol Ther* 5: 1624-1631.
40. Anguille S, Van de Velde AL, Smits EL, Van Tendeloo VF, Juliusson G, et al. (2017) Dendritic cell vaccination as postremission treatment to prevent or delay relapse in acute myeloid leukemia. *Blood* 130(15): 1713-1721.
41. Wang B, He J, Liu C, Chang L (2006) An effective cancer vaccine modality: Lentiviral modification of dendritic cells expressing multiple cancer-specific antigens. *Vaccine* 24(17): 477-3489.
42. Van Gool SW, Makalowski J, Feyen O, Prix L, Schirrmacher V, et al. (2018) The induction of Immunogenic Cell Death (ICD) during maintenance chemotherapy and subsequent multimodal immunotherapy for Glioblastoma (GBM). *Austin Oncol Case Rep* 3(1): 1010.
43. Gubin MM, Artyomov MN, Mardis ER, Schreiber RD (2015) Tumor neoantigens: Building a framework for personalized cancer immunotherapy. *J Clin Investig* 125(9): 3413-3421.
44. Schirrmacher V (2015) Oncolytic Newcastle disease virus as a prospective anti-cancer therapy. A biological agent with potential to break therapy resistance. *Expert Opin Biol Ther* 15(12): 1757-1771.
45. Hermida JS, Tcheng E, Jarry G, Moullart V, Arlot S, et al. (2004) Radioiodine ablation of the thyroid to prevent recurrence of amiodarone-induced thyrotoxicosis in patients with resistant tachyarrhythmias. *Europace* 6(2): 169-174.
46. Gursoy A, Tutuncu NB, Gencoglu A, Anil C, Demirer AN, et al. (2008) Radioactive iodine in the treatment of type-2 amiodarone-induced thyrotoxicosis. *J Natl Med Assoc* 100(6): 716-719.
47. Czarnywojtek A, Stangierska IW, Woliński K, Płazińska M, Kobylecka M, et al. (2014) Radioiodine therapy in patients with type II amiodarone induced thyrotoxicosis. *Pol Arch Med Wewn* 124(12): 695-703.
48. Czarnywojtek A, Stachowiak MZ, Woliński K, Płazińska MT, Miechowicz I, et al. (2014) Results of preventive radioiodine therapy in euthyroid patients with history of hyperthyroidism prior to administration of amiodarone with permanent atrial fibrillation-a preliminary study. *Endokrynol Pol* 65(4): 269-274.
49. Joseph F, Younis N, Jones DB (2003) Treatment of carbimazole-induced agranulocytosis and sepsis with granulocyte colony stimulating factor. *Int J Clin Pract* 57(2): 145-146.
50. Wiersinga WM (1997) Amiodarone and the thyroid. In: Weetman AP, Grossman A, (Eds.), *Pharmacotherapeutics of the Thyroid Gland*, Springer Verlag, Berlin, Germany, pp. 225-287.
51. Otsuka F, Noh JY, Chino T, Shimizu T, Mukasa K, et al. (2012) Hepatotoxicity and cutaneous reactions after antithyroid drug administration. *Clin Endocrinol (OXF)* 77(2): 310-315.
52. Faivre J, Clerc J, Gerolami R, Herve J, Longuet M, et al. (2004) Long-term radioiodine retention and regression of liver cancer after sodium iodide symporter gene transfer in wistar rats. *Cancer Res* 64(21): 8045-8051.