REVIEW ARTICLE

Now Virus against Cancer: A Review

Amit Kumar[1], Santosh Kumar[2], Anurag Kumar[3], Kanika Kayastha[4], Trilochana Kumar[5], Ujjwal Chandra Jha[6]

1-Post Graduate Student. Dept: of Oral and maxillofacial Pathology, Rama Dental College Hospital And Research Centre, Kanpur U.P. 2-B.D.S, King George Medical College, Lucknow U.P. 3,4-B.D.S, Saraswati Dental College, Lucknow U.P. 5-B.D.S, Rama Dental College Hospital And Research Centre, Kanpur U.P. 6-post graduate student. Dept: of Conservative and Endodontics, Rama Dental College Hospital And Research Centre, Kanpur U.P.

Correspondence to:
Dr. Amit Kumar, Post Graduate Student. Dept: of Oral and maxillofacial Pathology, Rama Dental College Hospital And Research Centre, Kanpur, U.P.
Contact Us: www.ijohmr.com

ABSTRACT

Currently, the main emphasis in cancer therapy is made for the destruction of tumors, and all studies being focused on finding new ways of destroying cancer cells. This has introduced viruses as newly developed weapons to fight against cancer. Viruses infect specific cells in the body and kill them by exhausting their resources. Hence these Viruses can be reprogrammed to infect tumor cells and avoid normal cells thus killing cancer cell selectively. The dangerous part of viruses can be removed via genetic manipulations thus preventing side effects. Modified viruses can also improve the human immune system and help it to fight cancer. New research data demonstrates that viral therapy can be highly successful. It has been observed that an, genetically engineered herpes virus called Talimogene Laherparepvec (T-VEC) that provokes an immune response against cancer has become the first treatment of its kind to be approved for use in the paving the way for a long-awaited class of therapies. Many viruses preferentially infect cancer cells and thus ravage a tumor while leaving healthy cells untouched.

KEYWORDS: Oncolytic virus, Herpes simplex virus, T-VEC

INTRODUCTION

Cancer is a name applies to a group of diseases characterized by the proliferation of abnormal cells above their usual boundaries that can then invade adjacent parts of the body and/or spread to other organs. Other common terms used are malignant tumors and neoplasms. Cancer affects almost any part of the body and has many anatomic and molecular subtypes that each forcing specific management strategies.

Cancer is the second most main cause of death globally and accounted for 8.8 million deaths in 2015. Most common types of cancer in the male are lung, prostate, colorectal, stomach and liver cancer, while in female breast, colorectal, lung, cervix, and stomach cancer are the most common.[1]

To fight against cancer viruses as newly developed weapons. Viruses are considered as nature's nanoparticles- a vast untapped bio resource. Around 2400 viral species are known, with extraordinarily diverse morphologies and biochemical compositions.[2]

The virus has single- or double-stranded RNA or DNA genomes wrap into icosahedral or helical protein shells, sometimes encased in a lipid envelope. The diameters of viruses range from 20 to 500 nm, and their genomes from 3000 to 375 000 nucleotides. The viral genome is protected by particle, carries it from cell to cell in the infected host organism & transmits it from infected to uninfected hosts. Once it is delivered into a susceptible target cell, the viral genome highjack the cellular biosynthetic machinery to produce progeny viruses that spread to adjacent cells, leading to a specific pattern of tissue destruction leading to provoke innate and adaptive immune responses, which fight and protects the host from infection and future exposures to the same virus. The viral genome can be seen as a new class of tissue-destructive drug as a form pharmacological perspective, and the viral particle as a Nano-sized nucleic acid delivery vehicle.[3]

ONCOLYTIC VIROTHERAPY

A new therapeutic approach for cancer treatment which has recently been accepted is Oncolytic virus therapy. An oncolytic virus is defined as a genetically engineered or naturally occurring virus that can selectively replicate in and kill cancer cells without harming the normal tissues.[4] Oncolytic virus therapy intervenes tumor regression through two distinct mechanisms. First, many viruses acquired an innate tropism for cancer cells where they can multiply and kill established tumor cells. Secondly, the tumor cells which are been killed can serve as a target for cross-priming tumor-specific immune responses generating systemic anti-tumor immunity. This mechanism of generating systemic anti-tumor immunity is important since tumor cells that are not infected by the virus will be targeted & eliminated by the immune system.[5]

HISTORY

Viruses began to be engaged in cancer therapy around the end of the nineteenth century. Doctors around 1950s noticed that cancer patients who were vaccinated for a non-related viral infection, showed signs of improvement in cancer; this has been greatly credited to the production of tumour necrosis factors and interferon in response to

How to cite this article:
Kumar A, Kumar S, Kumar A, Kayastha K, Kumar T, Jha UC. Now Virus against Cancer: A Review. Int J Oral Health Med Res 2017;4(2):56-59.

viral infection, but oncolytic viruses are being genetically designed that selectively target and lyse only cancerous cells in the host body.

During the 1940s and 1950s, animal's clinical trial started. the 1950s and 1960s interest in the field has varied during this time, but by end in the 1980s it started moving high and researched taking pace, and a resurgence of interest in the past two decades, finally the first marketing approval of an oncolytic virus was granted by China's State Food and Drug Administration regulators for the genetically modified oncolytic adenovirus H101 in November 2005 for the cure of head and neck cancer.[6,7]

TALIMOGENE LAHERPAREPVEC

The most popular virus which has gained the most attention is an attenuated herpes simplex virus, type 1 (HSV-1) genetically engineered to express human granulocyte macrophage-colony stimulating factor (GM-CSF), termed Talimogene laherparepvec (T-VEC).[5] T-Vec was created and initially developed by BioVex, Inc. under the brand OncoVEXGM-CSF. Advancement was carried by Amgen, which acquired BioVex in 2011.[8] This virus has been precisely adapted for selective tumor cell replication and induction of host immunity.[5]

The virus has now been tested in a prospective, randomized phase III clinical trial in which a significant improvement in durable and objective response rates was seen in patients with advanced melanoma.[8] In October 2015 approval for T-vec was given by the U.S. Food and Drug Administration to treat melanoma.[9]

The herpes simplex virus, type 1 and type 2 (HSV-1 and HSV-2), both belong to the Herpesviridae family, Alphaherpesvirinae subfamily. Herpes simplex virus type 1 is a human pathogen but is rarely associated with genital area infection, Herpes simplex virus type 2 is an also common human pathogenic virus and is strongly associated with sexually transmitted diseases. Acute HSV-1 infection generally involves gingivostomatitis. Chronic HSV-1 infection is also been described and is characterized by a skin keratitis.[10]

By the assistance of hereditary building herpes simplex infection sort 1(HSV-1), is changed into Talimogene laherparepvec, a lytic, infectious, and human pathogen approx 200 nm in distance across with a substantial genome (152 kb) that was viewed as a helpful vector. To begin disease, HSV-1 gets connects to cell surface receptors previously a snappy combination of the viral envelope with the cell layer happens, allowing the vehicle of the viral DNA to the cell core. Beginning connection is interceded by the communication of viral glycoproteins with cell surface heparin sulfate. This is trailed by viral official with cell surface receptors, for example, nectin-1 and herpesvirus passage arbiter A, which are comprehensively communicated over a wide assortment of human cell types.[11]

Talimogene laherparepvec is a constricted type of HSV-1 that has been changed to reduce viral pathogenicity and also to initiate particular tumor lysis and increment antigen introduction. In particular, the two duplicates of the quality encoding ICP34.5 have been erased, which is required to decrease pathogenicity and give tumor-specific replication due to the oncogenic disturbance of the protein kinase R (PKR) pathway. Set up of ICP34.5, the quality encoding human administrative cytokine Granulocyte-Macrophage Colony Stimulating Factor state invigorating variable (GM-CSF) has been embedded. GM-CSF raises the safe reaction to tumors, draws in and instigates myeloid forerunner cells to multiply and separate, and enlists and animates dendritic cells. Talimogene laherparepvec is additionally changed by evacuation of the ICP47 quality, which keeps ICP47 from blocking antigen introduction, in this manner reestablishing immunogenicity. This expulsion additionally prompts hoisted articulation of the HSV US11 quality as a quick early quality, as opposed to late quality, which empowers US11 to piece PKR movement before PKR can end protein union, prompting expanded replication of ICP34.5-erased HSV-1 in tumor cells.[12] Successive organization of talimogene laherparepvec, particular intratumoral replication and ensuing oncolysis straightforwardly decimates disease cells and discharges offspring infections, tumor-related antigens, and threat-related sub-atomic components. The offspring infections at that point contaminate other nearby tumor cells, heightening the 'threat' flags and engendering the antitumor effect.[12,13]

Preclinical models have indicated talimogene laherparepvec-prompted tumor lysis and enlarged antitumor safe reactions in various distinctive disease cell lines and creature models. Information demonstrating that HSV-1 antigen and DNA are specifically communicated in tumors infused with talimogene laherparepvec which indicated prove that the direct antitumor impacts of talimogene laherparepvec happen mainly at the infusion site. Likewise, the expanded region involved by CD8+ T cells inside both infused and uninjected tumors demonstrated the improvement of an aberrant fundamental antitumor invulnerable reaction following talimogene laherparepvec infusion. In murine models, both infused and uninjected tumors were decreased or cleared and mice additionally created protection from the consequent test with a similar tumor cells. Drawn out survival following treatment with talimogene laherparepvec was additionally seen in a mouse tumor model. [13]

The first-in-human trials were directed in pre-treated patients with the bosom, head and neck, gastrointestinal diseases, and melanoma, to decide the security profile and organic action of talimogene laherparepvec and to recognize an appropriate measurement plan for future examinations. Clinical trials have demonstrated the security and viability of talimogene laherparepvec in patients. Talimogene laherparepvec was very much

endured with no most extreme endured measurements achieved (which empowered a multi-dosing timetable to be characterized) and organic movement (infection replication, GM-CSF articulation, neighborhood responses, and HSV-1 antigen-related tumor rot) was observed.[14]

Stage I, Phase II and Phase III clinical trial were led and results were overwhelming. It began in 2006, a Phase I clinical trial was directed for T-VEC and security profile, ideal dosage and plan, and biologic impacts of treatment was resolved. This examination included 30 patients with headstrong bosom growth (n = 14), head and neck disease (n = 5), colorectal malignancy (n = 2), and melanoma (n = 9) who had tumors in cutaneous, subcutaneous, or nodal locales that were receptive to coordinate infusion. The natural movement was watched clinically which appeared, viral replication and putrefaction at the infusion site, GM-CSF articulation, cytokine and antinuclear counteracting agent levels. No entire or halfway reactions happened by standard clinical reaction criteria, disregarding infused sores and close-by injuries show leveling by clinical examination. Histological examination of biopsies indicated aggravation and corruption in 14 out of 19 biopsies where a tumor was identified. Conversely, non-tumor cells inside the tumor microenvironment demonstrated no confirmation of corruption, therefore supporting the tumor specificity of viral disease. Too, ranges of rot unequivocally recolored for HSV proteins, while non-tumor tissue infrequently recolored emphatically for the virus. [15]

In light of the biologic action that was found in the Phase I think about, a Phase II trial was led in 50 patients with organizing III and IV melanoma that was not surgically operable. [16]

A randomized stage III examination known as the OPTiM trial turned into the primary investigation of an oncolytic infection to show a measurable critical clinical advantage for the treatment of melanoma.[17]

The most widely recognized unfavorable occasions with talimogene were exhaustion (50.3% of patients), chills (48.6%), pyrexia (42.8%), queasiness (35.6%), influenza-like sickness (30.5%), infusion site torment (27.7%) and regurgitating (21.2%). The vast majority of these were gentle to moderate.[18]

Disabled mending can happen at infusion locales, especially in those with basic dangers, for example, past radiation treatment or sores at inadequately vascularised ranges. Treatment-related cellulitis at the infusion site was accounted for in 3.1% of patients. Talimogene can cause insusceptible interceded impacts, for example, glomerulonephritis, vasculitis, and pneumonitis. Intensifying psoriasis and vitiligo have likewise been seen in patients amid treatment.

This medication contains live infection, so it is contraindicated in extremely immune-compromised patients and those taking long haul, high-dosage steroids. It can possibly cause spread herpetic contamination in immunocompromised patients.

As patients treated with talimogene have been found to shed live infection so to evade transmission, close contacts including relatives, sexual accomplices, and medicinal services experts ought to keep away from coordinate contact with infused sores and body liquids from the patient. Specifically, persistent contact with newborn children, pregnant ladies, and individuals who are immunocompromised is not prescribed. Patients ought to stop and cautioned that touching and scratching infusion locales can spread the infection to different parts of the body.[18, 19]

Debilitated recuperating can happen at infusion destinations, especially in those with hidden dangers, for example, past radiation treatment or sores at ineffectively vascularised ranges. Treatment-related cellulitis at the infusion site was accounted for in 3.1% of patients. Talimogene can cause invulnerable interceded impacts, for example, glomerulonephritis, vasculitis, and pneumonitis. Intensifying psoriasis and vitiligo have likewise been seen in patients amid treatment. [19]

CONCLUSION

Oncolytic infections are at last developing as possibly valuable anticancer medications. Information as of now rising up out of continuous clinical trials are to a great degree empowering, demonstrating that tumor relapses can happen even after foundational infection conveyance. In addition, critical difficulties remain. In impossible to miss, the clinical effectiveness of oncolytic infections must be supported in the event that they are to end up noticeably a genuinely viable tumor treatment. T-VEC is first oncolytic infection, affirmed by FDA is another class of medications that intervene hostile to tumor action by specifically killing tumor cells and optionally inciting fundamental tumor-particular invulnerability. T-VEC is currently affirmed for the treatment of melanoma in the wake of exhibiting a clinical advantage in a clinical trial and is related with a mediocre security profile, comprising of gentle normal side effects and neighborhood infusion site responses.

REFERENCES

1. http://www.who.int/cancer/en/
2. Condit RC. Principles of virology. In: Knipe DM, Howley PM, editors. Fields Virology. Lippincott Williams and Wilkins; 2001. pp. 19–51.
3. Parato KA, Senger D, Forsyth PA, Bell JC. Recent progress in the battle between oncolytic viruses and tumours. Nat Rev Cancer. 2005 Dec;5(12):965-76.
4. Larson C, Oronsky B, Scicinski J, Fanger G. R, Stirn M, Oronsky A, et al. Going viral: a review of replication-selective oncolytic adenoviruses. Oncotarget. 2015;6(24):19976-19989.
5. Rehman H, Silk AW, Kane MP, Kaufman HL. Into the clinic: Talimogene laherparepvec (T-VEC), a first-in-class intratumoral oncolytic viral therapy. J Immunother Cancer.

2016 Sep 20;4:53.
6. Kelly, E; Russell, SJ. "History of oncolytic viruses: genesis to genetic engineering". Molecular Therapy. 15 (4): 651–9.
7. Mahua Dey, Brenda Auffinger, Maciej S Lesniak, Atique U Ahmed. Antiglioma oncolytic virotherapy: unattainable goal or a success story in the making? Future Virol. 2013 Jul; 8(7): 675–93.
8. http://www.nytimes.com/2011/01/25/business/25amgen.html?_r=0
9. http://www.reuters.com/article/us-amgen-fda-idUSKCN0SL2YH20151027
10. Adams RD, Braunwald E, Petersdorf RG, Wilson JD (eds).Lerner AM. Infections with herpes simplex virus. In:. Harrison's Principles of Internal Medicine. McGraw-Hill, Inc.: New York, 1980; pp 847–52.
11. Shen Y, Nemunaitis J. Herpes simplex virus 1 (HSV-1) for cancer treatment. Cancer Gene Ther .2006 ;13:975–92
12. Liu BL, Robinson M, Han ZQ et al ICP34.5 deleted herpes simplex virus with enhanced oncolytic, immune stimulating, and anti-tumour properties. Gene Ther .2003; 10:292–303
13. Kohlhapp FJ, Kaufman HL Molecular pathways: mechanism of action for talimogene laherparepvec, a new oncolytic virus immunotherapy. Clin Cancer Res. 2016; 22:1048–1054.
14. Hu JC, Coffin RS, Davis CJ et al A phase I study of OncoVEXGM-CSF, a second-generation oncolytic herpes simplex virus expressing granulocyte macrophage colony-stimulating factor. Clin Cancer Res.2006; 12:6737–6747
15. Hu JC, Coffin RS, Davis CJ, Graham NJ, Groves N, Guest PJ, et al. A phase I study of OncoVEXGM-CSF, a second-generation oncolytic herpes simplex virus expressing granulocyte macrophage colony-stimulating factor. Clin Cancer Res. 2006;12(22):6737–47.
16. Senzer NN, Kaufman HL, Amatruda T, Nemunaitis M, Reid T, Daniels G, et al. Phase II clinical trial of a granulocyte-macrophage colony-stimulating factor-encoding, second-generation oncolytic herpesvirus in patients with unresectable metastatic melanoma. J Clin Oncol. 2009;27(34):5763–71.
17. Andtbacka RHI, Kaufman HL, Collichio F, Amatruda T, Senzer N, Chesney J, et al. Talimogene laherparepvec improves durable response rate in patients with advanced melanoma. J Clin Oncol. 2015;33(25):2780–8.
18. Andtbacka RH, Kaufman HL, Collichio F, Amatruda T, Senzer N, Chesney J, et al. Talimogene laherparepvec improves durable response rate in patients with advanced melanoma. J Clin Oncol 2015;33:2780-8.
19. Talimogene laherparepvec for melanoma. Australian Prescriber. 2017;40(1):38-39.

Source of Support: Nil
Conflict of Interest: Nil