ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at: www.ijmacr.com

Volume – 5, Issue – 2, March - April - 2022, Page No. : 52 – 56

A descriptive clinical pharmacological analytical research study in evidence-based medicine on the pharmacotherapeutic rationale of oncoimmunotherapeutic vaccines

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How to citation this article: Dr. Moumita Hazra, "A descriptive clinical pharmacological analytical research study in evidence-based medicine on the pharmacotherapeutic rationale of oncoimmunotherapeutic vaccines", IJMACR- March - April - 2022, Vol – 5, Issue - 2, P. No. 52 – 56.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

The molecular identification of human cancer antigens has initiated the innovative development of antigen-specific immunotherapy based on different approaches. Oncotherapeutic vaccines are used either as a substitute therapy in the treatment of chemo resistant or chemo refractory, and radioresistant or radio refractory malignancies; or are used as a combinati on oncotherapy, along with chemotherapy, radiotherapy, pharmaco-oncoimmunotherapeutic targeted therapy, and surgical therapy. The mono therapeutic potential of pharmaco-immunotherapeutic anti-cancer vaccines is still in the investigative stages. This study was a descriptive clinical pharmacological analytical research study in evidence-based medicine on the pharmacotherapeutic rationale of oncoimmunotherapeutic vaccines.

Keywords: Pharmaco-on coimmuno therapeutic Vaccines, Molecular Pharmacology, Clinical Research, Descriptive Analytical Research, Evidence-Based Medicine, Clinical Pharmacology.

Introduction

The molecular identification of human cancer antigens has initiated the innovative development of antigen-specific immunotherapy based on different approaches. Oncotherapeutic vaccines are used either as a substitute therapy in the treatment of chemo resistant or chemo refractory, and radioresistant or radio refractory malignancies; or are used as a combination oncotherapy, along with chemotherapy, radio therapy, pharma coimmuno therapeutic targeted therapy, and surgical therapy. The mono therapeutic potential of pharmaco-oncoimmunotherapeutic anti-cancer vaccines is still in the investigative stages.[1-2]

Objective

This study was a descriptive clinical pharmacological analytical research study in evidence-based medicine on the pharmacotherapeutic rationale of on coimmuno therapeutic vaccines.

Methods

Ethical Approval: At first, the Institutional Ethics Committee clearance and approval was taken. The study was conducted in accordance with the ethical principles of Declaration of Helsinki and Good Clinical Practices contained within the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH-E6 and ICH-E17), and in compliance with the global regulatory requirements. Informed consent was obtained from the patient participants. This study involved no risk to any patient.

Study Design

The study design was a molecular pharmacological and clinical pharmacological multi-variate, multi-Centre, retrospective, qualitative, descriptive, analytical research study.

Study Population

The study population was global patients, suffering from various stages of malignancies or borderline malignancies. The study population database was a global heterogenous multi-disciplinary experimentations and study literature on pharmaco-onco-immuno-therapeutic vaccines.

Study Period

The study period was 1.5 years, from January, 1999 to February, 1999; January, 2002 to June, 2002; June, 2015; April, 2016 to June, 2016; May, 2017; and June, 2021, to March, 2022.

Place of Study

This research study and the compilation of the study literature was conducted in the Departments of Pharma cology, Clinical Pharmacology, Molecular Pharma cology, Rational Pharma cotherapeutics, Pharma coepidemiology, Pharma covigilance, Pharma cogenomics, Evidence-Based Medicine, Clinical Pathology, Pathology, Molecular Diagnostics, Clinical Oncology, Clinical Medicine, Clinical Research, and Molecular Medicine, Dr. B. R. Ambedkar Medical College and Hospitals, J. J. M. Medical College and Hospitals, Karnataka, India; Presidency College, West Bengal, India; Dr. Moumita Hazra's Polyclinic And Diagnostic Centre, Dr. Moumita Hazra's Academic Centre, Dr. Moumita Hazra's Educational Centre, Hazra Nursing Home, Hazra Polyclinic And Diagnostic Centre, Dr. Moumita Hazra's World Enterprises, West Bengal, India, World; Gouri Devi Institute of Medical Sciences and Hospital, West Bengal, India; Mamata Medical College and Hospitals, Telangana, India; Rama Medical College Hospital and Research Centre, Rama University, Uttar Pradesh, India; Hi-Tech College of Nursing, Odisha, India; and Mahuya Diagnostic Centre and Doctors' Chamber, West Bengal, India.

Study Procedure

This study, a clinical and molecular pharmacological multi-variate, qualitative, descriptive, analytical research study of the retrieved literature, derived through a thorough literature analysis from various available literature databases, was performed, to record, review, thoroughly analyse and delineate the molecular pharmacological basis of oncoimmunotherapeutic vaccines from a wide-ranged study literature containing molecular pharmacological researches, reviews, case presentations and varied databases about the pharmaco-oncoimmunotherapeutic rationale of the clinical use of vaccines in the treatment of cancer patients. After that, a multivariate evidence-based medical research study of comparative qualitative analysis of the global heterogenous multidisciplinary experimentations and study literature on pharmaco-oncoimmunotherapeutic

vaccines, affecting global malignant and borderline malignant patients, was conducted. This study was performed, by recording and the subsequent qualitative analyses of oncoimmunotherapeutic vaccines, retrieved from the study literature database, along with selective elucidations and elaborations of the deduced study results, to derive an explicit and comprehensive interpretation of the intricate molecular pharmacological mechanisms of oncoimmunotherapeutic vaccines, based on this evidence-based medicine research.

Results and Discussion

This thorough qualitative analytical research study of the retrieved literature recorded from different types of medical experimentations and medical databases about oncoimmunotherapeutic vaccines, elaborated the following molecular pharmacological findings:

Since time immemorial, vaccines have been used to adapt the immune system to recognize pathogens, and prevent and treat diseases, such as cancer. Vaccination for the prevention of infectious diseases represents a great success of Medicine. One example showing great promise with regard to cancer is the prevention of human papillomavirus-positive cervical cancer by vaccinating with a recombinant viral capsid protein. The generation of efficacious therapeutic vaccines faces, however, many hurdles, among which the selection of the appropriate target antigens and the quality of pre-existing T cell memory appear critical. Target tumor antigens include unique mutated antigens and shared nonmutated self-antigens. The choice between these types of antigens for vaccination could be a choice between inducing immunity (mutated antigens) or breaking tolerance and inducing autoimmunity (self-antigens). The more efficient type of antigen is still, and would always remain, investigational. Therapeutic cancer vaccines are attractive systemic immunotherapies that activate and expand antigen specific CD8 type and CD4 type T cells to enhance anti-tumour immunity.

In one approach with adoptive T cell therapy, autologous antigen-specific T cells are expanded *ex vivo* and reinfused to patients. Adoptive T cell therapy appears to be an effective treatment for patients suffering from Epstein Barr Virus-associated lymphomas as well as solid tumors. The alternative strategy is to expand tumor-associated antigen-specific T cells *in vivo* through vaccination, a procedure of potentially wider use. The adoptive transfer of cancer antigen-specific effector T cells in patients can result in tumor rejection, thereby demonstrating the immune system potential for cancer therapy. In a study, it was hypothesized that the direct induction of efficient tumor-specific effector and memory T cells through vaccination may be one of the ideal treatment modality. Therapeutic vaccines have two objectives: priming the antigen-specific T cells and reprogramming memory T cells (i.e., a transformation from one type of immunity to another, for example, regulatory to cytotoxic).

Some successful phase III clinical trials showing benefit to the patients revived cancer vaccines. Dendritic cells (DCs) are essential in generation of immune responses, and as such represent targets and vectors for vaccination. Different DC subsets elicit different T cells. Similarly, different activation methods result in DCs able to elicit distinct T cells. Different DC subsets elicit different T cells. Similarly, different activation methods result in DCs able to elicit distinct T cells. A careful manipulation of activated DCs will lead to the development of the next generation of highly efficient cancer vaccines. Mutated antigens have potential advantages, such as the following: 1) their T cell repertoire should not be deleted

and they should be recognized as non-self by the immune system, as is the case with viral antigens; and 2) their potential resistance to negative selection in case the mutated protein is essential for cell survival. These antigens often require priming. For the sake of broadly applicable vaccines, often the targeted cancer antigens are nonmutated self-antigens for which 1) the repertoire of high avidity clones might be depleted through negative selection, and 2) the existing memory T cells might be polarized. These often include regulatory T cells (Tregs), either thymus-derived naturally occurring Tregs CD4 and CD25 high or periphery-induced Tr1 cells, which mainly produce IL-10, and Th3 cells, which mainly produce TGF-β. Another important component of existing repertoire are Th2 cells. Thus, the existing memory repertoire requires reprogramming from nonprotective immunity toward protective IFN-g–secreting Th1 cells. The analysis of immunological and clinical responses yields three patient groups: 1) one group showing neither clinical nor immunological responses, 2) one group showing some immunological response, but no clinical responses; and 3) one group composed of a few patients showing both immunological and clinical responses. These later patients are essential for performing in-depth mechanistic studies to explain the immune responses that lead to control tumor growth and eliminate established tumors. At least four components of the immune response appear critical for that response to be of therapeutic potential, as follows: 1) the quality of the elicited CTLs; 2) the quality of induced CD4 type Th cells; 3) the elimination and/or non-activation of Tregs; and 4) the breakdown of the immunosuppressive tumour microenvironment.

The different modalities of oncoimmunotherapy always increase the efficacy of comprehensive oncotherapy, while reducing the occurrence of frequent adverse effects caused by these Oncotherapeutic regimens, otherwise. The basic cancer vaccines used include cell based vaccines including whole cell vaccines, genetically modified tumour cell vaccine and dendritic cell vaccine, anti-idiotype antibody based vaccine, protein or peptide based vaccines, heat shock protein-based vaccine, viral, bacterial or yeast vectors based vaccines, mRNA or DNA nucleic acid based vaccines, vaccines based on tumour associated antigens like overexpressed proteins, differentiation antigens, cancer-testis antigens and oncofoetal antigens, and tumour specific antigens including oncogenic viral antigens, antigen presenting cells or molecular neoantigens based vaccines with specific CD8 type T cells and, CD4 type T cells, and nanoparticles vectors based vaccines. Current bioengineering techniques make use of hydrogels, modified polymers, emulsions, liposomes, virosomes, nano discs, cell membranes, self-assembled proteins, virus-like particles, and nucleic acids to deliver and develop biomaterial-based vaccines, used also for personalised oncotherapy. The development of anticancer immunotherapy includes the appropriate monotherapy or combination therapy with cellular vaccines, tumor-associated antigens (TAAs), neoantigens and chimeric antigen receptor T cells (CAR-T).

Combining cancer vaccines with multiple checkpoint blockade antibodies, novel multifunctional molecules, adoptive cell therapy and immune system agonists has been used as anti-cancer combination therapies. While these combinations build on the foundation of successful immune checkpoint blockade antibodies, it is

increasingly apparent that successful immunotherapy will also require a cancer vaccine backbone to engage the immune system, thereby ensuring that additional immune-oncology agents will engage a tumour-specific immune response.[1, 2]

Conclusion

This study was a descriptive clinical pharmacological analytical research study in evidence-based medicine on the pharmacotherapeutic rationale of on coimmuno therapeutic vaccines. This research study would remain a landmark to emphasise on the significance of the anti-cancer vaccines as effective systemic immunotherapies, that suitably and systematically enhance the life-long anti-neoplastic prophylactic immunity and maintain a very long-lived anti-malignant therapeutic patient-health.

Acknowledgements

My sincere acknowledgements to Departments of Pharma cology, Clinical Pharma cology, Molecular Pharma cology, Rational Pharma cotherapeutics, Pharmacoepidemiology, Pharma covigilance, Pharma Cogen omics, Evidence-Based Medicine, Clinical Pathology, Pathology, Molecular Diagnostics, Clinical Oncology, Clinical Medicine, Respiratory Medicine, Clinical Research, Zoology, and Molecular Medicine, Dr. B. R. Ambedkar Medical College and Hospitals, J. J. M. Medical College and Hospitals, Karnataka, India; Presidency College, West Bengal, India; Dr. Moumita Hazra's Polyclinic And Diagnostic Centre, Dr. Moumita Hazra's Academic Centre, Dr. Moumita Hazra's Educational Centre, Hazra Nursing Home, Hazra Polyclinic And Diagnostic Centre, Dr. Moumita Hazra's World Enterprises, West Bengal, India, World; Gouri Devi Institute of Medical Sciences and Hospital, West Bengal, India; Mamata Medical College and Hospitals, Telangana, India; Rama Medical College Hospital and Research Centre, Rama University, Uttar Pradesh, India; Hi-Tech College of Nursing, Odisha, India; Mahuya Diagnostic Centre and Doctors' Chamber, West Bengal, India; for the successful completion of this research project.

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