DOI: 10.4103/0971-5916.219024

Quick Response Code:

Immuno-Oncology, O. Michielin, G. Coukos, editors (Karger, Basel, Switzerland) 2015. 140 pages. Price: US$ 233.00/CHF 198.00/EUR 185.00

ISBN 978-3-318-05589-4

This book is the 42nd volume of the ongoing series entitled 'Progress in Tumor Research'. The book consisting of 140 pages is bound in hard cover with an appropriate illustration of tumour specific T cell cross talk with the tumour cell on the front cover. The preface introduces the chapters written by key opinion leaders in the respective fields with a view to translational research. The latest developments in the subject have been organized together between the covers of this compilation.

The first chapter, 'Immunotherapies in Early and Advanced Renal Cell Cancer' deals mainly with the effects of two monoclonal antibodies against CTLA4 and PD1 on renal cell cancer (RCC). The authors have described the different clinical trials with the above molecules either singly or in combination. Also, trials with combinations with tyrosine kinase inhibitors like sunitinib, pazopanib and vaccine trials with vaccinia vaccines and other adjuvant vaccine trials have been related with their efficacy studies, survival benefits and the adverse effects of these trials. The chapter would have been more communicative with the subjective description of the mechanism of action of various monoclonal antibodies used. It could have bridged the transitional gap between the clinicians and the scientists.

The chapter, 'Immunotherapy of Brain Tumors' is compiled lucidly and gives a brief introduction about the facets of glioma immunology and immunotherapy. The various approaches of glioma immunotherapy with trial reports have been dealt with, such as TSA (tumor-specific antigen), TAA (tumor associated antigen), dendritic cells, whole tumour cells, and tumor derived undefined antigens, along with past and ongoing vaccine trials on T cell therapies, anti- TGF β (transforming growth factor β) with antisense nucleotides and kinase inhibitors, anti-Treg and IDO, CTLA4 and PD1 inhibitors. The different ongoing immunotherapy trials in brain tumours have been tabulated. Glioma immunotherapy is a fast developing research area, so, probably all the recent findings were beyond the scope of the chapter with defined page limits. However, the readers would have benefitted with the outcome and side effects of the trials.

The chapter, 'Immunotherapy of Melanoma' elaborates meta-analyses of interleukin (IL) 2, interferon (IFN) γ, tumour necrosis factor (TNF) α either singly or in combination with chemotherapy trials. The immunotherapy drugs used for clinical trials are ipilimumab, pembrolizumab, nivolumab, and talimogene laherparepvec (T-VEC). The first three drugs are checkpoint inhibitors that "take the brakes off" the immune system and enable it to fight cancer; the last is an oncolytic virus therapy. Conventional therapies, such as radiation, cytotoxic drugs and targeted agents which help in antigen release and immune activation are also documented. A figure depicts the co-stimulatory and co-inhibitory receptor ligand interactions. An associated Table documents selected combination therapies with promising clinical data in metastatic melanoma. The chapter gives an overall scenario about melanoma immunotherapy, but addition of some basics could have made the chapter more comprehensible.

Chapter 4, 'Immunotherapy of Breast Cancer' elegantly describes the immunological implications of the immunotherapeutic trials. The chapter starts introducing the concept of 'immune editing'. The prognostic evaluation of Tumour Infiltrating Lymphocytes (TILs) in breast cancers have been described extensively making the text interesting. The authors also propose to develop an 'immunoscore' as an 'essential prognostic and potentially predictive tool in pathology reports' for traditional classification of breast cancers. Contrary to the existing dogma of immune suppression with chemotherapeutic drugs, the authors have listed the mechanisms of immune potentiation by different chemotherapeutic agents. Interaction of targeted therapies of breast cancer and the immune system and also vaccine-based therapies have been detailed. The associated Table in the chapter on 'immune signatures and the developments' is explicit.

The chapter, 'Current Developments in Actively Personalized Cancer Vaccination' on a different arena on the development of neoantigenic epitopes in cancer patients, who have inter-individual heterogeneity

having immunogenic non-synonumous mutations and their correlation with TILs. The authors propose innovative mapping of each patient's individual tumour metanome signature for individualized therapeutic approach especially in the prediction of HLA Class II restricted peptides. Instead of DNA vaccines, RNA vaccines were found to be more promising, having an edge over the peptide vaccines. These personalized vaccines though have now entered clinical translation, but the main block in their application would be the cost effectiveness, especially in a developing country, where such fruitful treatment applications will have to await, due to economical reasons.

The chapter on 'Immune Checkpoint Inhibitors' describes immune check point inhibitors to "have set a paradigm shift in the treatment of metastatic cancers". The sequential process of development of anti-CTLA4 treatment in malignant melanoma along with the adverse effects has been elaborated. The results of nivolumab, pembrodizumab, MDX 1105 and MPDL3280A have also been discussed. Multicohort studies with successful combination trials of ipilimumab and nivolumab are also reported. A coloured illustration of the patterns of migration of tumour specific T cells adorns the chapter.

The chapter on "Radiotherapy and Immunotherapy: Improving Cancer Treatment through Surgery" sets a total turn around concept to the existing idea of immune suppression by radiotherapy (RT). It describes the stimulating effect of irradiation on the immune system and the use of RT as an "*in situ* vaccine". The shortfall of RT has been attributed to radio-resistance of Tregs. Abscopal effects and also improvement in combination therapies of RT with ipilimumab and anti-PDL1 in clinical trials has been elaborated in detail. The chapter is thought provoking about the potentials of RT with precise optimal radiation dosage, timings of both treatments and patient selection.

In the next chapter, 'Combination Therapies', the authors have articulated phased application of combination therapies of ipilimumab and nivolumab with chemotherapies showing improved immune related progression free survival (irPFS) when compared to monotherapies in NSCLC and SCLC (small cell lung cancer). Further combination therapies in preclinical and clinical trials have been mentioned and targeted therapies have been discussed. The authors aptly caution about the appropriate timing, dosage, sequence of administration of targeting agents and immune modulators and selection of appropriate target and agent for success of combination therapies. The strength of the chapter is a detailed four page Table of ongoing clinical trials with checkpoint inhibitors in lung cancer.

The chapter, 'Promise of Immunotherapy in Lung Cancer' describes intricately the immune evasion, the lung cancer types and a brief epidemiological description of lung cancers. The chapter relates the treatment successes shown by bevacizumab, cetuximab and ipilimumab and nivolumab and the failures of adoptive cell therapy along with strategies prolonging overall survival. The five associated Tables regarding clinical trials with therapeutic vaccines, monoclonal antibodies, current adoptive T cell transfer, immune checkpoint inhibitors and combination immune checkpoint treatments and a coloured schematic diagram of putative immunotherapeutic protocol capable of targeting a broad spectrum of cancer cells are assets of the chapter with a lucid flow of writing.

The last chapter, 'T Cell Engineering' describes vividly the development of chimeric T cell receptors (CAR) expression by T cells (re-directed T cells) by gene transfer. Difficulties of the different modalities tried both in animal models and therapeutic applications in clinical trials have been discussed. The authors admit that the commercial products of the re-directed T cells 'are very cost-, labour-, time-intensive, resulting in the slow spread of this cellular therapy among medical schools'. Since, engineered T cells would become a totally personalised cellular therapeutics as claimed by the authors; its wide application would be restricted as an immunotherapeutic protocol in oncological settings. The Tables on '*in vivo* and *in vitro* studies with redirected T cells' and 'Clinical trials with T cell' are informative.

Overall, this book forms an enjoyable and engaging reading material for the readers, who want to keep abreast with the recent developments in immunotherapeutic applications in various cancers. It would be an invaluable collection on the subject in different libraries.

Swapna Chaudhuri
Department of Laboratory Medicine
Calcutta School of Tropical Medicine
C. R. Avenue, Kolkata 700 073, India
swapna.chaudhuri@gmail.com