Original Article

Immunotherapy during COVID-19 Pandemic: An Experience at a Tertiary Care Center in India

Abstract

Introduction: COVID-19 pandemic has been a curse for cancer patients. The lack of understanding and unawareness in handling cancer patients during this pandemic has worsened their conditions. To analyze the real-world scenario, we studied 13 patients who were given immunotherapy during this COVID pandemic era and tried to analyze their outcome or any serious adverse effect that they suffered. This was a pilot study which would pave the way for further bigger studies in future. The aim of the study was to collect the details of patient receiving immunotherapy during COVID-19 pandemic. The data collected included the diagnosis, certain investigations, and the effects of the immunotherapy drugs and its side effects. **Results:** During this COVID pandemic period starting from March 20 to June 20, we have been regularly giving immunotherapy drugs such as nivolumab, pembrolizumab, and atezolizumab to our patients. We had given six patients nivolumab, six patients pembrolizumab, and one patient atezolizumab. Of the 13 patients who continued to receive immunotherapy in COVID pandemic era, 4 patients were receiving immunotherapy for lung cancer, 3 for head-and-neck malignancy, 2 for relapse lymphoma, and 1 each for hepatocellular carcinoma, renal cell cancer, malignant melanoma, and soft-tissue cancer. One of the patients receiving atezolizumab had actually progressed after receiving pembrolizumab. There was no Grade 3 or 4 toxicity to these drugs and most of our patients continued to be in stable disease/partial remission. One patient had died just after receiving one cycle of nivolumab. **Conclusion:** COVID-19 infection has posed an unforeseen predicament both for the patients and the treating oncologist. In absence of any previous data, it is very difficult to manage cancer patients where the treatment itself is thought to harm the patients. This is a humble effort to bring to the notice of the world that immunotherapy can be continued during COVID pandemic, provided we take all due precautions.

Keywords: *Immunotherapy, nivolumab, pembrolizumab*

Abhishek Pathak, Alpana Gupta[1], Anvesh Rathore[2], Rahul Sud[3], Shiv Shankar Swamy[2], Tejas Pandaya[4], AP Dubey[5], Bhupesh Guleria[6]

Department of Medical Oncology, Command Hospital, Kolkata, [1]Transfusion Centre, Kolkata, [2]Department of Medical Oncology, Army Hospital (Research and Referral), Delhi, [3]Department of Medical Oncology, Command Hospital (Bangalore), [4]Department of Radiation Oncology, Command Hospital, Kolkata, [5]Shanti Mukund Hospital, New Delhi, [6]Command Hospital, Pune, Maharashtra, India

Introduction

The three pillars of cancer treatment include surgery, radiotherapy, and chemotherapy. However, in the past 20–25 years, we have developed the fourth important pillar in the form of immunotherapy which has brought a paradigm shift in oncological care. There are various immunotherapy drugs which are regularly used in oncological practice, such as nivolumab, pembrolizumab, and atezolizumab. These drugs target the axis between programmed death-1 (PD-1) and its ligand (PD-L1) which are present on our immune cells and tumor cells. These drugs inhibit the various check points which keep our immune cells in control. Once these check points are inhibited, the immune cells multiply rapidly and kill the tumor cells. The use of these drugs has rapidly changed the treatment and prognosis of many malignancies over the past decade. They can be used as monotherapy for high PD-L1-tumors or along with other chemotherapy drugs resulting in significant improvements in overall survival.[1]

This article has been written with sole motive of sharing our experience of using immunotherapy drugs in the present pandemic caused by coronavirus.

Coronaviruses are a family of enveloped, positive sense, single-strand RNA viruses which cause mild respiratory disease to severe acute respiratory syndrome. Hence, it was named coronavirus 2.[2]

It was in December 2019, in Wuhan (in Hubei Province of China) which recorded a cluster of a pneumonia cases caused by a novel coronavirus. And very soon, it resulted in epidemic in China followed

How to cite this article: Pathak A, Gupta A, Rathore A, Sud R, Swamy SS, Pandaya T, *et al.*, Immunotherapy during COVID-19 Pandemic: An Experience at a Tertiary Care Center in India. Clin Cancer Investig J 2021;10:22-8.

Submitted : 20-Aug-2020
Revised : 09-Oct-2020
Accepted : 29-Oct-2020
Published : 19-Feb-2021

Address for correspondence:
Dr. Anvesh Rathore, Department of Medical Oncology, Army Hospital (Research and Referral), Delhi, India.
E-mail: drsonikrathore@gmail.com

Access this article online

Website: www.ccij-online.org

DOI: 10.4103/ccij.ccij_125_20

Quick Response Code:

by global pandemic. In February 2020, the World Health Organization designated the disease COVID-19, which stands for coronavirus disease 2019.[1]

The most understood pathophysiology for the morbidity and mortality in COVID-19 patients is due to immune dysregulation leading to a condition called as "cytokine storm." COVID-19 causes uncontrolled immune response in the body in severly ill patients. This is caused primarily due to increase in number of pro-inflammatory cytokines such as IL6 and IL 10 and excessive chemokines such as CXCL10, CCL2, CCL3, and CCL4.[3] Since COVID-19 infection alters the immunological enviorment milleu, it is difficult to predict whether giving immunotherapy would increase the severity of infections or the rate of adverse effects?[4]

At present, there are no data of usage of immunotherapy in COVID setting. Hence, with this background, this article was written to share our experience in managing cancer patients with immunotherapy (nivolumab, pembrolizumab, and atezolizumab) during this COVID-19 pandemic.

Objectives

1. Enumerate the investigations and diagnosis of patient receiving immunotherapy
2. Enumerate the adverse effects of immunotherapy
3. Study the outcome after reassessment based on iRecist criteria.

Inclusion criteria

1. All patients receiving immunotherapy drugs at our day-care center during the past 2 months.

Exclusion criteria

1. All cancer patients who were not receiving immunotherapy drugs admitted in our ward.

Ethical clearance

Ethical clearance was obtained from the institutional review board after deliberating upon the advantages and disadvantages of continuing immunotherapy in our patients during the COVID epidemic.

Data collection

a. The following details of all patients who were receiving immunotherapy were recorded such as age, sex, diagnosis, stage, and number of cycles of immunotherapy drugs
b. Prior to giving immunotherapy, patients were screened using Arogya Setu app. This is a questionnaire-based app issued by the Government of India which categorizes individuals into whether they are safe or at high risk of COVID infection based on their symptoms, proximity to any COVID-19-positive patients, and travel history www.mygov.in › aarogya-Setu-app
c. Routine examination and investigations were conducted to assess for any adverse event (AE). Such as complete physical examination, deramatological examination, thyroid evaluation/serum cortisol, baseline electrocardiography, and contrast-enhanced computed tomography chest in case of any X-ray finding suggestive of pneumonitis in a symptomatic patient.
d. The response assessment was done on the basis of iRECIST criteria.

Statistical analyses

This is an observational study wherein details of the patients receiving immunotherapy will be analyzed for their efficacy and adverse effect.

Results

During this COVID-19 pandemic period starting from March 20 to June, we have been regularly giving immunotherapy drugs such as nivolumab, pembrolizumab, and atezolizumab to our cancer patients in second-line therapy. We had given six patients nivolumab, six patients pembrolizumab, and one patient atezolizumab [Chart 1].

Of the 13 patients who continued to receive immunotherapy in COVID-19 pandemic era, 4 patients were receiving immunotherapy for lung cancer, 3 for head-and-neck malignancy, 2 for relapse lymphoma, and 1 each for hepatocellular carcinoma (HCC), renal cell cancer (RCC), malignant melanoma, and other malignant soft-tissue tumors. One of our carcinoma lung patients receiving atezolizumab had actually progressed after receiving pembrolizumab.

Nivolumab

Out of the six patients who were getting nivolumab [Table 1], there was one female and the rest five were males. One patient died during therapy. He was 65-year-old individual, a case of metastatic malignant melanoma. The onset of the disease was in 2019 when he presented a nonhealing ulcer in foot. He received one cycle of nivolumab and died on April 24, 2020 due to progressive disease. Most of our patients are receiving nivolumab in second line or beyond.

Our first patient is 32-year-old female, a case of relapse Hodgkin's lymphoma. She has been treated with adriamycin, bleomycin, vinblastine, and dacarbazine followed by

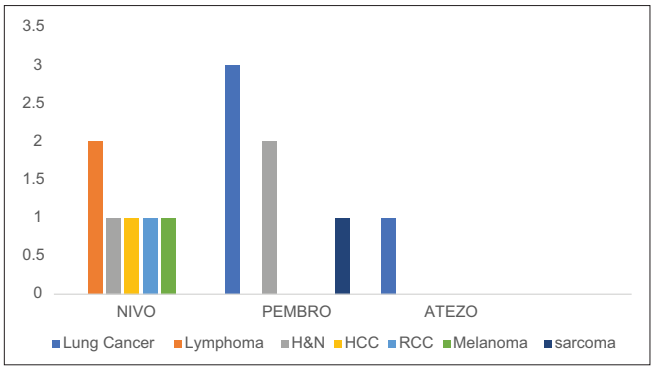

Chart 1: Distribution of immunotherapy

Table 1: Details of patients receiving nivolumab

Sex	Age	Diagnosis	Dose	PD1/PDL1	Chemotherapy	Response	AE
Female	32	HL	180 mg	Not known	1. POST 4# ABVD	PR	
					2. POST 8# ABVD - PD	PD	
					3. DHAP 3# - PDRT 30 GY/10# - 13/03/2017 TO 21/03/2017	PD SD	
					4. GEM+OX 2# - SD	PR	
					5. BeGVP 2# - PR	PR	
					6. BeEAM 2# - ASCT in PR (14/10/2017)	iCR	
					7. Nivolumab 6# AFTER COVID-19		
Male	56	RCC	180 mg	Unknown	Tablet pazopanib for last I year Injection Nivolumab 4# till mid may	PD Response awaited	Anemia Fatigue
Male	80	HCC	240 mg	Unknown	Sorafenib for 1 month Nivolumab 5#	Did not tolerate iSD	NO
Male	39	NHL	240 mg	Unknown	1. RCHOP - OCT 2017 (CIVIL)	CR	Neutropenia
					2. GDP/RGDP - JAN 2018 BMT DONE - FEB 2019	PD iCR	
					3. Nivolumab - 17/04/2020 TO TILL DATE		
Male	39	CA Nasopharynx	240 mg	Unknown	Pst CCRT + Adjuvant Nivolumab 4#	PD Awaiting response	
Male	61	Malignant melanoma	240 mg	>1%	Death May 12, 2020 after receiving a single dose ON 24/04/2020	Died	

PDL1: Programmed death ligand 1, PD1: Programmed death 1, AE: Adverse event, iSD: Immune stable disease, iCR: Immune complete response, PR: Partial response, HCC: Hepatocellular carcinoma, RCC: Renal cell cancer, CA: Cancer, CCRT: Concurrent Chemo Radiotherapy, NHL: Non Hodgkin's Lymphoma

gemcitabine with oxaliplatin, BeGV protocol and the autologous stem-ell transplantation (ASCT). She had progressed after all these treatments and is now on nivolumab and tolerated six cycles during COVID pandemic.

Our patient (S No 4) is 39-year-old male known case of non-Hodgkin lymphoma (diffuse large B-cell lymphoma). The onset of his disease was in September 2017. Since 2017, he has been treated with R-CHOP and ISRT 45 Gy/25 # till April 2018. He had an early relapse within 4 months, thereafter he received salvage regime of gemcitabine and carboplatin followed by ASCT. Posttransplant, the patient had a disease-free interval for almost 1 year and again relapsed in March 2020. At present, he is on injection nivolumab. He has completed six cycles and is in partial remission.

Our patient with metastatic RCC (clear cell) who progressed after pazopanib for almost 1 year had a progressive disease was started on nivolumab. The dose given to him was at 3 mg/kg and not the recommended 240 mg every 2 weeks. This was done as the patients had anemia and sever fatigue. He had tolerated nivolumab. He could get four cycles of nivolumab till mid-May and then could not report due to lockdown.

A 80-year-old male was a case of multicentric HCC who did not tolerate sorafenib and was started on nivolumab. He had a stable disease after 5#. There was no adverse effect.

A 39-year-old male was a case of recurrent carcinoma of the nasopharynx. He was earlier treated with concurrent chemoradiation followed by two more lines of chemotherapy (cisplatin/cetuximab and TIP protocol). He had progressed after these treatments and now on nivolumab.

Pembrolizumab

There are six patients who were receiving immunotherapy in the form of pembrolizumab [Table 2]. Of the six people, three of them were receiving pembrolizumab for lung cancer. Two of them had PDL1 status of 5% and one had PDL1 status of 70%. Almost all of them responded to immunotherapy. Most of them responded symptomatically and their performance status has improved.

There was a young female of 44 years with metastatic soft tissue sarcoma. She received six cycles of mesna, doxorubicin, ifosfamide, dacarbazine protocol (MAID) regimen and progressed while on treatment. Since she had a PDL1 status >1%, she was started on pembrolizumab. She has completed only two cycles and is awaiting any response assessment.

Pembrolizumab was given to two cases of head-and-neck malignancy, one of recurrent carcinoma of the oral cavity and second one of recurrent case of carcinoma of the nasopharynx.

Atezolizumab

Only one patient received atezolizumab during this COVID pandemic era [Table 3]. He is a 41-year-old male, a case of adenocarcinoma of the lung. He was diagnosed in August 2018. He had a doubtful skeletal lesion at the onset.

Table 2: Details of patients receiving Pembrolizumab

Rel	Age	Diagnosis	PDL1	Line of chemotherapy	Response
Female	59	Carcinoma lung	5%	Pembrolizumab + carboplatin	PD
				3# Pembrolizumab	iSD
Female	44	STS with METS	1%	MAID 6#	PD
				2 # Pembrolizumab	Awaiting response
Male	21	Carcinoma oral cavity	Unknown	1. Docetaxel + CIS + 5FU + Cetuximb - 30/03/2019 TO 24/08/2019 WBPET - PD	PD
				2. Pembrolizumab 6# - 25/02/2020 TO 17/03/2020 AFTER COVID-19	iSD
Male	74	NSCLC	70%	1. PEMEXTED + CDDP - 21/06/2019 TO 27/08/2019 08/11/2019	PD
				2. Pembrolizumab 6#	iPR
Self	40	MET Carcinoma lung	5%	NACCRT	PD
				1. Paclitaxel + Carboplatin 2# - 06/09/2018 TO 12/10/2019	PD
				2. Paclitaxel + Carboplatin - 6#	PD
				3. Pembrolizumab + PEMXTED - 04/09/2018 TO 03/2020	PD
				4. Atezolizumab- 19/03/2020 TO TILL DATE	iPR
Self	39	Carcinoma nasopharynx	Not known	1. DOXCE+Carboplatin 3# 14/06/2013 TO 27/07/2013 WBPET FEB 2016 - MILD	PD
				2. ADJ CETUXI + CIS 5# - 26/08/16 TO 23/03/2016	PD
				3. CETUXI + CDDP+5FU 6# - 09/12/2016 TO 04/04/2017	PD
				4. Paclitaxel + Carboplatin 5# - 13/09/2017 TO 27/12/2017	PD
				5. TIP 6# - 02/09/2019 TO 18/12/2019	PD
				6. Pembrolizumab 8# - 1	iPR
				7. Nivolumab 4# - 01/05/20 TO TILL DATE	

PDL1: Programmed death ligand 1, iSD: Immune stable disease, iPR: Immune Partial response, CA: Cancer

Table 3: Detail of patient receiving Atezolizumab

Sex	Age	Diagnosis	PD1/PDL1	Chemotherapy	Cycles	Response
Male	41	Metastatic lung cancer	5%	1. CCRT		PD
				2. Paclitaxel + Carboplatin	6	PD
				3. Pemetrexed + Pembro	8	PD
				4. Atezolizumab + Bevacizumab + gemcitabine	6	iPR

PDL1: Programmed death ligand 1, PD1: Programmed death 1, iPR: Immune Partial response, CCRT: Concurrent Chemo Radiotherapy

However, he was treated with curative intent with definitive CCRT followed by six cycles of adjuvant paclitaxel and carboplatin. He also received radiotherapy to the skeletal site and bisphosphonate. After a (Treatment Free Interval) TFI of almost 1 year, he had a progressive disease. His EGFR/ALK/Ros 1 had no actionable mutation. PDL1 was 5%. He was started on pemetrexed and pembrolizumab. He received 8# till February 2020 when the disease again progressed. Although there were no data to suggest use of other immunotherapies following progression on one, he was started on atezolizumab, bevacizumab, and gemcitabine combination. Response assessment after six cycles showed it to have a partial remission. At present, the patient is comfortable; he had Garde 2 neutropenia. No other adverse effect was noted.

Discussion

Management of cancer patients has been a great challenge for medical oncologists across the world during the COVID pandemic. The fear of making person immunosuppressed after giving chemotherapy had put oncologists all over the world on back foot. The issues were further aggravated by lesser number of patients reporting to hospitals for the fear of getting infected. It has taken us some time to understand and prepare ourselves to give chemotherapy in the present scenario.

There are no data to support or guide us in present; a situation has never earlier happened. Things get further confusing when we wanted to continue or initiate immunotherapy in the present setting. It was seen that there was immune dysregulation in serious patients infected with COVID-19. This damaging immune response was termed as cytokine storm.[5] Biopsies from COVID

infected patients revealed infiltration of macrophages and monocytes, interferon gamma, and tumor necrosis factor. These pro-inflammatory cells lead to pulmonary edema and irreversible lung damage.[6]

The basis of all immunotherapy is to accentuate the production of immune cells which can destroy tumor cells. The main mechanism by which they do is to inhibit the checkpoints which were in place to control the over production of these immune cells. Hence the use immunotherapy in patients with COVID-19 infection, was thought to have its own challenges. Another very important concern was the most common adverse effect associated with immunotherapy, i.e., pneumonitis. In case any patient on immunotherapy developed respiratory abnormality, it would be difficult to ascertain whether it was because of drug toxicity or COVID infection. Another important caveat is the use of steroids in the present setting.

PD1 (CD 279) is a part of immunoglobulin present on the surface of activated T-cell.[7] The immunotherapy drugs which were given to our patients were nivolumab, pembrolizumab, and atezolizumab. These drugs are termed as checkpoint inhibitors. They act at PD1/PDL1 receptors. Pembrolizumab and nivolumab are inhibiting PD1 and atezolizumab PD-L1 blockers.

It was in March 2011 that immune checkpoint inhibitor ipilimumab was approved in melanoma. In September 2014, the US FDA approved pembrolizumab for use I metastatic melanoma. Since then, these immunotherapy drugs have been used for lung cancer non-small cell lung cancer (NSCLC), bladder cancer, RCC, head-and-neck cancer, hepatocellular cancer, gastric cancer, Hodgkin's lymphoma, and triple negative breast cancer, and of late, there has been an approval of these drugs most of the cases as second line. Though there was a prerequisite of getting a PDL1 status testing done prior to initiation of immunotherapy in NSCLC while, in most of the other diseases its use in second line setting is not mandatory.[8]

Among genitourinary malignancies, tumor PDL1 expression is mandatory in platinum ineligible metastatic urothelial cancer (mUC) prior to initiation as single-agent treatment. However, no such requirement is for platinum refractory mUC or metastatic RCC.[9]

In our study, there were six patients who are getting nivolumab. They were cases of head-and-neck malignancy, relapse lymphoma, RCC, HCC, and malignant melanoma. Of the six, there is one female and the rest five are males. Most of our patients are receiving nivolumab in second line or beyond setting.

There were six patients receiving pembrolizumab. Three of six were for lung cancer and remaining were of sarcoma and head-and-neck cancer.

The only patient receiving atezolizumab was of lung cancer.

All these patients were started on these drugs prior to COVID pandemic. They all had tolerated these drugs well. Most of them were admitted patients, and hence, it was decided to continue with their treatment.

Since most of the patients were patients admitted in the ward and had shown no symptom of COVID infection, they were not tested for COVID infection. The dose intensity and frequency of these immunotherapies were maintained. This was possible in our setting as most of our patients were admitted in the hospital for the entire duration.

These drugs have their unique side effects termed as immune-related AEs (irAEs).[10] The most common and important irAEs are pneumonitis dermatologic, diarrhea/colitis, hepatotoxicity, and endocrinopathies. The major issue in using immunotherapy during COVID pandemic is the overlap of respiratory complaints and imaging picture between the drug toxicity and COVID infection. Various studies have shown that the classical COVID-19 pneumonia has imaging features like ground-glass opacities (GGO) (87%), vascular enlargements in the lesion (72%), and mixed consolidation and GGO (65%). Almost 50% of the patients had features of traction bronchiectasis. Lesions are peripheral in distribution and in almost 80% bilateral and lower lung involvement.[11]

Similarly, the pulmonary toxicities of immunotherapy drugs are divided into four grades depending on the severity of the symptoms as per the NCCN guidelines.

They are as follows:

1. Grade 1 – Asymptomatic/pneumonitis confined to <25% of lung parenchyma or a single lobe
2. Grade 2 – Symptomatic with fever, cough, chest pain, and shortness of breath (moderate pneumonitis)
3. Grade 3 – Severe pneumonitis involves all lobes of the lung or >50% of lung parenchyma
4. Grade 4 – Life-threatening pneumonitis involving difficulty in carrying out activity of daily living.

Fortunately, none of our patients developed any respiratory complaints; hence, we did not require to do COVID testing or HRCT.

The main modalities of treatment of these toxicities are withholding of the drug and use of steroids. Among our patients, none of them had any dermatological, endocrine, hepatic, rheumatological, or gastrointestinal side effects. Two patients had fatigue (Grade 1) which did not require any dose modification. There were three patients who had moderate neutropenia. The possible explanation for this neutropenia could be that these patients were heavily treated with multiple lines of chemotherapy. Since they responded to granulocyte stimulating factors, no further evaluation was done.

The response assessment was done on the basis of iRECIST criteria.[12] The iRECIST criteria are originally

based on RECIST 1.1. The responses as per this criterion are classified as immune complete response, immune partial response (iPR), immune stable disease iSD, immune unconfirmed progressive disease, or immune-confirmed progressive disease (iCPD).

Among the patients receiving nivolumab, two of six were in CR, one of six had stable disease, two of six had not yet been reassessed, and one died due to progressive disease. Of the six patients receiving pembrolizumab, three of isx had stable disease, two of six had partial remission, and one has not yet been reassessed. The only patient receiving atezolizumab had an iPR.

Role of programmed death 1/programmed death ligand-1 testing prior to the use of immunotherapy

Immunotherapy drugs targeting PD1 and PDL1 with monoclonal antibodies have changed the way cancer has been treated worldwide. PD1 are receptors present on activated T- and B–cell, whereas PDL1 are receptors present on tumor cells.[13] In almost all of tumors where these checkpoint inhibitors are used, their response has been more in the tumors which express greater PDL1 expressions. Hence, overall, there are four PD-L1 IHC assays registered with the FDA, using four different PD-L1 antibodies (22C3, 28–8, SP263, and SP142), on two different IHC platforms (Dako and Ventana), each with their own scoring systems. The companion diagnostic tests have been defined for each drug and type of cancer where they are used. In melanoma, the use of nivolumab was dependent on the PD-L1 expression measured by the PD-L1 IHC 28-8 pharmDx assay.[14] The companion diagnostic test approved by the FDA for atezolizumab in urothelial malignancy is VENTANA PD-L1 (SP142) Assay.[15] Understanding of these platforms gives us an idea which platform was used in the clinical trial which led to approval of the drug in a particular setting. The details of the diseases and the role of testing for PDL 1 status are presented in Table 4. Apart from PDL1 status, other biomarkers such as molecular smoking signature, higher neoantigen burden, and DNA repair pathway mutations.[16]

Among the patients in our study, there was only one patient of the six patients receiving nivolumab who had PDL1 status >1%. Other patients received the drug in second/third-line setting or after ASCT. There were six patients who continued to receive pembrolizumab during this period. Three of six of the patients expressed PDL1 expression with one of them having an expression greater than >70%.The only patient receiving atezolizumab had expression <70%.

Table 4: Details of malignancy and role of programmed death ligand 1 testing

Malignancy	Drugs	Target	Indication	Requirement of PDl1 testing
Melanoma	1. Pembrolizumab	PD1	Unresectable/metastatic	No
	2. Nivolumab	PD1		
	3. Nivo + Ipi	PD1 + CTLA4		
Non-small cell lung cancer	1. Nivolumab	PD1	Metastatic disease/PD	No
	2. Atezolizumab	PDL1	first-line monotherapy	No
	3. Pembrolizumab	Pd1	Second-line monotherapy	Yes
				Yes
RCC	Nivolumab	PD1	Advanced disease second line	No
Gastric cancer	Pembrolizumab	PD1	Recurrent/metastatic disease after two lines of appropriate therapy	Yes
HCC	Nivolumab	PD1	Second line postsorafenib	No
Bladder cancer	Nivolumab	PD1	Second line locally advanced/metastatic disease (postplatinum-based therapy)	No
	Atezolizumab	PDL1		
	Durvalumab	PDL1		
	Avelumab	PDL1		
	Pembrolizumab	PD1		
Head and Neck Cancer	Pembrolizumab	PD1	Recurrent/metastatic with progressive disease	No
	Nivolumab	PD1		
MSI H/dMMR deficient solid tumors	Pembrolizumab	PD1	Second line on progression after adequate treatment	No
Classical Hodgkin's lymphoma	Nivolumab	PD1	post ASCT/fourth line	No
	Pembrolizumab	PDL1	Post 3 lines	No
MSI H/dMMR deficient colorectal tumor	Nivolumab	PD1	Metastatic colorectal cancer post5FU/Platinum/irinotecan	No

PDL1: Programmed death ligand 1, PD1: Programmed death 1, HCC: Hepatocellular carcinoma, RCC: Renal cell cancer

Limitations of the study

This study was conducted in an army hospital. Most of the patients were admitted in the wards and continued to remain in the hospital due to lockdown. They had limited or no exposure to COVID infection. Hence, the chances of these patients to develop any serious infection during these times were negligible.

This was a limitation of the study as patients in the real world cannot remain admitted for 3 months in any hospital, and hence, their chances of exposure to infection would generally be high.

Conclusion

COVID-19 infection has posed an unforeseen predicament both for the patients and the treating oncologist. In absence of any previous data, it is very difficult to use immunotherapy drugs in present setting. Any overstimulation of immunity was thought to increase the severity of COVID-19 infection. This article was written to share our experience with the use of immunotherapy drugs during COVID-19 pandemic. The response we had achieved by the use of immunotherapy for our patients during COVID times has been very encouraging. This is a humble effort to bring to the notice of the world that immunotherapy can be continued during COVID pandemic provided we take all due precautions.

Financial support and Sponsorship

Nil.

Conflicts of interest

Nil.

References

1. Spranger S, Spaapen RM, Zha Y, Williams J, Meng Y, Ha TT, *et al*. Up-regulation of PD-L1, IDO, and T (regs) in the melanoma tumor microenvironment is driven by CD8(+) T cells. Sci Transl Med 2013;5:200ra116.
2. Pathak A, Ranjan S, Rathore A, Kapoor R, Gupta A. Chemotherapy in COVID-19 pandemic: To give or not to give? Int J Adv Med 2020;7:1035-9.
3. Xiong Y, Liu Y, Cao L, Wang D, Guo M, Jiang A, *et al*. Transcriptomic characteristics of bronchoalveolar lavage fluid and peripheral blood mononuclear cellsin COVID – 19 patients. Emerg Microbes Infect 2020;9:761-70.
4. Conti P, Ronconi G, Caraffa A, Gallenga CE, Ross R, Frydas I, *et al*. Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): Anti-inflammatory strategies. J Biol Regul Homeost Agents 2020;34:327-31.
5. Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, *et al*. Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China. Ann Oncol 2020;31:894-901.
6. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, *et al*. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: A descriptive study. Lancet Infect Dis 2020;20:425-34.
7. Naidoo J, Page DB, Li BT, Connell LC, Schindler K, Lacouture ME, *et al*. Toxicities of the anti PD1 and anti PDL1 immune check point antibodies. Ann Oncol 2015;26:2375.
8. Brahmer J, Reckamp KL, Bass P, Crino L, Eberhardt WE, Poddubskaya E, *et al*. Nivolumab versus docetaxel in advanced squamous cell NSCLC. N Engl J Med 2015:373:123-35.
9. Ancevski Hunter K, Socinski MA, Villaruz LC. PD-L1 testing in guiding patient selection for PD-1/PD-L1 inhibitor therapy in lung cancer. Mol Diagn Ther 2018;22:1-10.
10. Hahn AW, Sirohi D, Agarwal N. The role of PD-L1 testing in advanced genitourinary malignancies. Eur Urol Focus 2020;6:11-3.
11. Puzanov I, Diab A, Abdallah K, Bingham CO 3rd, Brogdon C, Dadu R, *et al*. Managing toxicities associated with immune checkpoint inhibitors: Consensus recommendations from the Society for Immunotherapy of Cancer (SITC) Toxicity Management Working Group. J Immunother Cancer 2017;5:95.
12. Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: A multicenter study. AJR Am J Roentgenol 2020;214:1-6.
13. Seymour L, Bogaerts J, Perrone A, Ford R, Schwartz LH, Mandrekar S, *et al*. iRECIST: Guidelines for response criteria for use in trials testing immunotherapeutics. Lancet Oncol 2017;18:e143-52.
14. Patel SP, Kurzrock R. PD-L1 expression as a predictive biomarker in cancer immunotherapy. Mol Cancer Ther 2015;14:847-56.
15. Larkin J, Chiarion-Sileni V, Gonzalez R, Grob JJ, Cowey CL, Lao CD, *et al*. Combined nivolumab and ipilimumab or monotherapy in untreated melanoma. N Engl J Med 2015;373:23-34.
16. VENTANA PD-L1 (SP142) Assay FDA Summary of Safety and Effectiveness Data; 2016.