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Clinical Profile and Results in Cancers Treated with Nivolumab: A Single Centre Study

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Abstract

Introduction: Immunotherapy is also called as biologic therapy or biotherapy. Immunotherapy is quickly becoming an important component in the multipronged approaches being developed to treat certain forms of cancer. The goal of immunotherapy is to strengthen the body's own natural ability to combat cancer by enhancing the effectiveness of the immune system. This study tries to compile response rates and side effect profile of Nivolumab. **Methods:** Patients with performance status of 3 or less than 3, who failed on 2 or more lines of therapy except melanoma and have received minimum 3 cycles of Nivolumab were taken in to this study. Study subjects followed for minimum of 3 cycles for assessment. Each patient received 240 mg of Nivolumab once in 15 days for 3 - 6 cycles. **Results:** The median age of 20 patients was 53 years (26 - 79 yrs). 18 patients were male and 2 patients were female. Progressive disease (PD) was observed in 12 patients with immunotherapy treatment and partial response (PR) was observed in 3 patients, and stable disease (SD) in 5 patients. **Conclusion:** This is one of the Indian study mainly reporting experiences with Nivolumab. Large sample size is required to conclude about the efficacy of the study. Nivolumab is more tolerated in Indian patients compared to other reported studies.

Keywords

Cancer, Immunotherapy, Nivolumab

1. Introduction

The global cancer burden is expected to nearly double to 21.4 million cases and 13.2 million deaths by 2030 [1]. Consistently cancer is treated by the different practice like surgery, radiation and chemotherapy. When in early 1900 Dr Wil-

liam Coley started using immunotherapy in cancer where it is well founded in Asthma and Arthritis. One hallmark of cancer is immune evasion, in which the immune system does not mount an effective antitumor response [2]. Immunotherapy is also called as biologic therapy or biotherapy. Immunotherapy is quickly becoming an important component in the multipronged approaches being developed to treat certain forms of cancer. The landscape of cancer therapy has been recently transformed by the emergence of immunotherapy involving the targeting of immune checkpoints. The goal of immunotherapy is to strengthen the body's own natural ability to combat cancer by enhancing the effectiveness of the immune system [3]. There are three known main categories of immunotherapy: immune response modifiers (cytokines), monoclonal antibodies and vaccines [4]. Nivolumab (ONO-4538/BMS-936558/MDX-1106) is a fully human IgG4 monoclonal antibody that targets programmed cell death-1 (PD-1), one of the T-cell surface membrane receptors. Nivolumab received the world's first regulatory approval in Japan in July 2014 for the treatment of unresectable malignant melanoma. Nivolumab is also undergoing development for the treatment of other indications based on checkmate trails [5]. Nivolumab is approved by Food and Drug Administration (FDA) for Melanoma Non-Small Cell Lung Cancer (NSCLC), Renal Cell Carcinoma (RCC), Hodgkin Lymphoma, Head and Neck Cancer, Urothelial Carcinoma, Colorectal Cancer, and Hepatocellular Carcinoma (HCC) and approved with combination in other indications [6]. The maximal tolerated dose (MTD) for nivolumab has not been identified, and a similar safety profile has been demonstrated across tumour types and dose levels (0.1 - 10 mg/kg). More recently FDA both 3 mg/kg nivolumab and 240 mg fixed dose are based on pharmacokinetic data [7]. This study explores response rates and side effect profile of Nivolumabin a single centre.

2. Methods

In this study, a total of 20 eligible patients who received Nivolumab in HCG Cancer Speciality Center from 2017 to March 2018 were prospectively analysed.

Inclusion Criteria: Patients with performance status of 3 or less than 3, failed on 2 or more lines of therapy except melanoma and have received minimum 3 cycles of Nivolumab were taken in to this study. Patients who had financial toxicity were excluded from this study. Study subjects observed minimum of 3 cycles for assessment with PETCT and based on response followed till progression or death. Microsatellite instability (MSI) and Programme Death Ligand (PD-L1) expression was not tested in these entire patients. Standard Response Evaluation Criteria in Solid Tumors (V.1.1) [8] criteria for response assessment and CTCAE 4.0 version for toxicity assessment is used for analysis. Base line clinical examination, TSH, serum amylase, RBS, LFT, and CBC were done and monitored before each cycle of treatment. CT/PET-CT/MRI is used for response assessment before and after treatment. Each patient received 240 mg of Nivolumab once in 15 days for 3 - 6 cycles. All the patients were followed until progression or death

due to any cause.

Primary objective of this study was to assess the response rate of Nivolumab and evaluation of toxicity was secondary objectives.

3. Results

There were total 20 patients were included for the analysis and all patients were able to complete minimum 3 - 4 cycles of Immunotherapy.

The median age of 20 patients was 53 years (26 - 79 yrs). 18 patients were male and 2 patients were female. Immunotherapy is given as 1st line in 6 patients and ≥2 lines in 14 patients. With regards to safety, all of our patients are well tolerated with immunotherapy except for grade 1/grade 2 anaemia/thrombocytopenia in 6 patients. Progressive disease (PD) was observed in 12 patients with immunotherapy treatment and partial response (PR) were observed in 3 patients, stable disease (SD) in 5 patients (Table 1).

4. Discussion

Immunotherapy is an advanced treatment for metastatic cancer, where it mainly involves with the body's natural immune response to cancer and secondly it helps the immune system to find and kill cancer cells. In this era it has shown lot of promise to increase overall response and survival of the patients. This study explores immunotherapy response in advanced and metastatic cancer patients in

Table 1. Baseline demographic and clinical characteristics of patients received Nivolumab.

Patient Characteristics	Whole group
AGE	53 (26 - 79 yrs)
SEX	
Male	18 (90%)
Female	2 (10%)
ECOG (PS)	
0 - 1	14 (70%)
>2	6 (30%)
Metastatic Sites	
1	7 (35%)
≥2	13 (65%)
Line of Immunotherapy	
1st line	6 (30%)
≥2 line	14 (70%)
ADRs with Immunotherapy	
No toxicity	14
Toxicity	6 (Anaemia)
AVG Duration of Immunotherapy	(3 - 6 cycles)
Response rate (3 - 6 cycles)	
PR	3
SD	5
PD	12

single centre. All six patients with metastatic melanoma received first line treatment with immunotherapy and 2 patient had SD (20%) and 4 had PD, whereas checkmate trail 037 trail used this drug in 2nd line and had 32% of response rate [7]. In the 4 HCC patients, 2 patients progressed and 2 patients achieved stable disease, while in checkmate 40 trail, it has shown 15% overall response [8]. Out of 4 patients with NSCLC only 1 patient had PR, other 3 patients were progressed. Whereas checkmate 057 trails, there was 19% responses rate [9]. Out of 3 carcinoma bladder patients, 1 patient obtained PR, other patients were achieved SD [1] and PD [1], and there was 19.6% response in checkmate 275 trails [10]. In head & neck patients out of 3 only 1 patient got partial response and 1 patient acquire stable disease, in checkmate 141 trail it was detected 13.3% [11]. As response rate varies from 15% to 30% in various cancers as per the immunotherapy trails, patients in this study also had similar response rates except in HCC. Small sample size in individual cancer is limiting factor in this study.

Most of our patient had only grade 1 - 2 fatigue (60%), where as it was around 12% - 24% in various single studies [12]. There was no grade III-IV adverse events observed in the study and no patient were discontinued on treatment due to side effects. In various FDA approved trails for Nivolumab grade III toxicity was 12% - 69% and grade IV was 7% - 20% [13] [14].

This is one of the Indian study mainly reporting experiences with Nivolumab. Large sample size is required to conclude about the efficacy of the study. Nivolumab is more tolerated in Indian patients compare to other reported studies.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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