

# Racial Differences in Accepting Pegfilgrastim Onpro Kit (On-Body Injector) Use Among Cancer Patients

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Volume 1 Issue 6- 2019

Received Date: 12 Feb 2019

Accepted Date: 22 Feb 2019

Published Date: 25 Feb 2019

## 2. Keywords

Chemotherapy; Pegfilgrastim; Neutropenia; Leukopenia.; Fever; Side effects

## 1. Abstract

**1.1. Background:** Neulasta Onpro kit eliminates need for additional clinic visit after chemotherapy. Given the racially diverse population in our institution, we investigated acceptance of Onpro kit among patients on chemotherapy.

**1.2. Research Design and Methods:** Single-institution, retrospective review conducted in patients with GI tumors who received Onpro kit within 1 hour of completion of systemic chemotherapy from Jan 2014 through Jan 2018. Clinic/nursing notes and pharmacy records were reviewed to identify patients who refused Onpro kit and to discern reasons for refusal, including racial reason.

**1.3. Results:** Total 238 orders for kit were voided amongst 68 patients (Caucasian 41; African American 7; Spanish 3; Asian 17). Overall, 15/68 patients refused kit (22%) of these 87% were Asian. The reasons for refusal included dislike of bulky attachment to skin, request to place kit on stomach instead of arm, trepidation over unwitnessed administration of drug, fear of reaction, disposal at home, fear of pain, lack of confirmation of proper dose administration, and need for MRI.

**1.4. Conclusions:** While Onpro kit is an attractive alternative, 22% of patients with voided orders, mainly of Asian race, declined its application. We believe the current study represents the first look at important racial differences in accepting Onpro kit. Consideration of patients' cultural heritage, race, ethnicity and education may facilitate communication between physicians and patients to achieve optimal cancer care.

## 3. Introduction

Neutropenia is a serious adverse complication of myelosuppressive chemotherapy that predisposes patients to life-threatening infection, hospitalization and delays in treatment. This is associated with significant mortality as well as increased health-care associated costs [1]. Chemotherapy induced neutropenia has been mitigated by advent of granulocyte stimulating factors. The first of this class of drug to be widely used was filgrastim, a recombinant version of endogenous growth factor that stimulates the proliferation and differentiation of neutrophils. Due to its small size, filgrastim is rapidly cleared by the kidneys and requires daily dosing. Pegfilgrastim, a filgrastim molecule linked to a large polyethylene glycol molecule, is a popular alternative as the large PEGylated moiety slows renal clearance and requires dosing only

once during a chemotherapy cycle [2]. Per the dosing administration instructions, pegfilgrastim should not be given 14 days before or 24 hours after administration of cytotoxic chemotherapy. This is largely based on a theoretical risk of paradoxically increasing hematologic toxicity as G-CSF is thought to increase the population of chemotherapy-susceptible granulocyte precursors [3]. This dosing regimen is cumbersome; often requiring patients to make additional office visits. In light of this, the dosing of pegfilgrastim has been made moot through the introduction of the OnPro® Delivery Kit [4]. This is a device that can be adhered to the skin on the day of chemotherapy administration and auto-injects the recipient on the following day, thus eliminating the need for a return office visit. While this is an attractive alternative, some patients may hesitate or decline its use either due to

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a bulky attachment to their skin or having fear of reaction during an un-witnessed administration of pegfilgrastim without the physical supervision of trained medical personnel.

It is a fact that racial and ethnic differences exist in the incidence, disease course and outcomes of many cancer and non-cancer conditions. These differences are not only limited to insurance status, income, age, quality of health services but also ethnic or religious beliefs or religious limitations, such as Jehovah's witness refusing human products [5]. In this era of shared doctor-patient decision-making, it is crucial to identify and improve patient-level factors, especially preferences for treatment in order to improve quality of health care [6]. Differences in treatment choices between African-Americans and whites in medical conditions such as coronary artery disease, cervical cancer and end-stage osteoarthritis have been demonstrated in the recent medical literature [7-9]. Moreover, the reluctance or refusal to accept proven therapies by minority patients can lead to health disparities [5]. Once these important factors pertinent to racial differences are identified, we can undertake interventions to address and resolve such differences in patient decision-making. However, no study has examined racial/ethnic differences in acceptance of the Onpro kit among cancer patients.

The primary objective of this study is to determine whether there are differences between different ethnic cancer patient populations with respect to their willingness to receive the Onpro kit and to identify what demographic or psychosocial factors, specifically race and lack of familiarity with treatment associated with treatment preferences [10].

#### 4. Patients and Methods

A single center, retrospective study was performed of patients with gastrointestinal (GI) malignancies who received pegfilgrastim Onpro kit as an adjunct to cytotoxic chemotherapy. Patients were treated at the Tufts Medical Center Cancer Center from January 2014 through January 2018 and received pegfilgrastim within 1 hour of completion of chemotherapy. The decision to administer pegfilgrastim was based on standard guidelines (ASCO or NCCN guidelines). Patients had an average of 4 risk factors for febrile neutropenia: advanced disease, age > 65, gender and chemotherapy regimen [11,12]. Moreover, many patients had previously received other chemotherapy with a limited bone marrow reserve.

Clinic and nursing notes and pharmacy records were obtained through review of individual electronic medical records. Data was reviewed to identify patients who refused Onpro kit and to discern reasons for refusal. As per our institutional guidelines that govern handling of chemotherapy agents and growth factors, the reasons of refusal were always required to be confirmed by

a staff physician whenever patient declined a growth factor or a chemotherapy agent in addition to counseling. Such data was collected and entered into the EMR for any future audit or insurance purposes. Discussions surrounding refusal of Onpro kit administration were also mandated to be reported in the EMR; e.g. injection already prepared but later refused by the patient.

### 5. Results

#### 5.1. Demographic Features

A total of 238 orders for the Onpro kit were voided amongst 68 patients during this tenure. The median age of patients was 60 years [range 32-87] with 46% of patients ≥ 65 years old. Races included Caucasian 41; African American 7; Spanish 3 and Asian 17. The most common malignancies included colorectal (40%), pancreatic (20%), gastric (20%) and others (10%). Patients received a variety of different chemotherapies. The most common regimens included mFOLFOX6, FOLFIRINOX, FOLFIRI, and gemcitabine with nab-paclitaxel or cisplatin (12%).

#### 5.2. Refusal of Onpro Kit

Overall, 15/68 patients refused the Onpro kit (22%). Among them, 13/15 were Asian (87%) and 2 were Caucasian (13%). The reasons for refusal included dislike of bulky attachment to their skin (n = 5), request to place kit on their stomach and not on their arm (n = 2), having trepidation over unwitnessed administration of drug (n = 1), fear of reaction (n = 2), disposal at home (n = 2), fear of pain (n = 1), lack of confirmation of proper dose administration (n = 1), and need to refuse as the patient was scheduled for a Magnetic Resonance Imaging (MRI) on that day (1) as summarized in (Table 1).

**Table 1:** Causes of Refusal to Onpro kit in Patients with Different Races

Patient	Race	Explanation for refusal
1	Asian	Dislike of bulky attachment to their skin
2	Asian	Dislike of bulky attachment to their skin
3	Asian	Dislike of bulky attachment to their skin
4	Asian	Dislike of bulky attachment to their skin
5	Asian	Dislike of bulky attachment to their skin
6	Asian	Request to place kit on their stomach and not on their arm
7	Asian	Request to place kit on their stomach and not on their arm
8	Asian	Having trepidation over un-witnessed administration of drug
9	Asian	Fear of reaction
10	Asian	Not comfortable with disposal at home
11	Asian	Not comfortable with disposal at home
12	Asian	Lack of confirmation of proper dose administration
13	Asian	Fear of Pain
14	Caucasian	Having trepidation over un-witnessed administration of drug
15	Caucasian	Need to refuse as the patient was scheduled for a magnetic resonance imaging (MRI) on that day

### 5.3. Toxicities

There were no episodes of grade 3 or 4 neutropenia or febrile neutropenia among all these patients and related adverse events were mainly bone pain as expected.

## 6. Discussion

In 2017, we presented the first study in GI malignancies to report the current study represents the first study to look at important ethnic differences in accepting the Onpro kit. This study detected ethnic differences and supports the importance of cultural factors in determining therapies chosen, underlying the need to facilitate communication between physicians and patients and to provide educational material to the patients to achieve optimal cancer care.

There has been a constant effort to overcome the challenge of delaying administering pegfilgrastim on the same day of chemotherapy but many studies show conflicting results [13-16]. Per the dosing administration instructions, pegfilgrastim should not be given 14 days before or 24 hours after administration of cytotoxic chemotherapy. This is largely based on a theoretical risk of paradoxically increasing hematologic toxicity as GCSF is thought to increase the population of chemotherapy-susceptible granulocyte precursors [3]. This dosing regimen is cumbersome; often requiring patients to make additional office visits. This was a main impetus to develop anew formulation, such as the OnPro® Delivery Kit [4]. This is a device that can be adhered to the skin on the day of chemotherapy administration and auto-injects the recipient on the following day, thus eliminating the need for a return office visit. While this is an attractive alternative, our study showed that over 20% of the patient who would qualify for this device decline its application for many reasons including the fear of unknown, not liking a bulky attachment to their skin or having trepidation over an un-witnessed administration of pegfilgrastim both for fear of reaction and/or lack of confirmation of proper dose administration.

In the current era of medicine, shared doctor-patient decision-making plays a crucial role in improving the patient-level factors, such as preferences for treatment, and subsequently can improve health care quality. As described earlier in the paper, ethnic as well as racial disparities towards acceptance of therapy is an under-explored field in both malignant and non-malignant diseases. Our study again supports the fact that in addition to other factors, reluctance to accept proven treatments by minorities can contribute to health disparities. Once identified, we must undertake interventions to address racial/ethnic differences in patient decision-making.

Our study has limitations. Most notably, the small sample size and being a single institution retrospective analysis, it may limit the extrapolation of results to a more diverse patient population.

However, it addresses an important clinical issue that warrants urgent attention to dissolve the racial disparity in acceptance of a FDA-approved treatment. Consideration of patients' cultural heritage may facilitate communication between physicians and patients to achieve optimal cancer care. It would be interesting to look at experience or market share of manufacturer in Asian countries. Moreover, translated patient brochures and videos could be very helpful.

## 7. Conclusions

We believe the current study represents the first study to look at important racial differences in accepting Neulasta Onpro® kit. This study detected racial differences and supports importance of cultural factors in determining therapies chosen, underlying the need to facilitate communication between physicians and patients and to provide educational material to the patients to achieve optimal cancer care.

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