ASSESSING ALTERNATIVE DOSING STRATEGIES FOR GRANULOCYTE-COLONY STIMULATING FACTOR (G-CSF) USE WITH mFOLFOX6 THERAPY FOR ADJUVANT TREATMENT OF COLORECTAL CANCER

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BACKGROUND

• Colorectal cancer is the third most commonly diagnosed cancer worldwide, and is the second most common cause of cancer death for males and the third most common cause of cancer death for females in Canada1

• Patients with solid tumors receiving myelosuppressive chemotherapy are at risk of experiencing hematologic toxicity including febrile neutropenia (FN)

• Since the risk of developing FN is less than 20% in patients receiving mFOLFOX6 therapy for adjuvant treatment of colorectal cancer, the recommendation is not to use granulocyte-colony stimulating factor (G-CSF) for primary prophylaxis2

• However, there are still other risk factors for treatment delay besides FN, which include neutropenia and thrombocytopenia

• G-CSF is used to reduce the occurrence, duration and severity of neutropenia as well as limit the risk of developing FN, which can result in infection, hospitalization and more significant delays in treatment

• Clinical studies in breast cancer setting suggest an average of 11 injections per chemotherapy cycle are required to achieve recovery of the absolute neutrophil count (ANC) to within the normal range3, while the filgrastim (Neupogen®) product monograph suggests up to 14 consecutive days of G-CSF use is well tolerated

• There has been research in breast cancer patients that has shown that alternative dosing strategies with G-CSF (fewer doses) outside of traditional clinical recommendations can be effective in managing neutropenia4

• A study by Choi et al found the mean number of injections of G-CSF per cycle to be 5, when used as primary prophylaxis in colorectal patients receiving FOLFOX5

• The goal of our study was to optimize treatment efficacy while minimizing drug cost for patients, and to identify a successful dosing protocol that can minimize the time pharmacists spend on monitoring patients

DESIGN

• 31 colon and 25 rectal cancer (non-metastatic) patients who had adjuvant treatment between 2005 and 2013 were monitored throughout their mFOLFOX6 chemotherapy

• Mean age of all patients (31 females: 25 males) was 55 years [21-79]

• 15 patients completed 8 cycles of mFOLFOX6 and 29 patients completed 12 cycles of mFOLFOX6. Three (3) and nine (9) patients received 6-7 cycles and 9-11 cycles respectively

• All patients received at least three (3) cycles of G-CSF; mean start time was cycle 4

• 29 patients (52%) started their first G-CSF cycle with five (5) doses and 22 patients (39%) started their first G-CSF cycle with four (4) doses. The remaining 5 patients started with either 3 or 6 doses

• 49 patients (88%) started G-CSF on day 4 of treatment; seven (7) on day 5

• A clinical pharmacist reviewed interim blood counts and modified the G-CSF dosing strategy based on absolute neutrophil count, and recorded any chemotherapy delays

RESULTS

41 patients (73%) experienced no delays in treatment after initiation of G-CSF

15 patients (27%) experienced a delay in treatment: neutropenia (8) and thrombocytopenia (7)

14 patients (25%) experienced bone pain from G-CSF use, which is within the range of 10-30% seen in scientific papers

Almost all patients (93%) experienced some form of neuropathy from mFOLFOX6 treatment

20 patients (36%) received the full dosage of their mFOLFOX6 therapy, while the remaining 36 patients (64%) had a dose decrease in either their 5-FU and/or oxaliplatin

DISCUSSION

Although 15 patients experienced a delay in treatment, there were only two patients (4%) that developed neutropenia because of receiving insufficient G-CSF. These two patients received four doses of G-CSF before the delay. The other six patients that became neutropenic were caused by patient non-compliance (1), pharmacist error (2), hospitalization (1), bone pain (1), or delay caused by allergic reaction (1)

Thrombocytopenia made up half of the treatment delays (mean delay: 14 days). From this study, the rate of platelet decline before initiation of G-CSF and afterwards is roughly the same so we can not say that G-CSF impairs platelet counts beyond what myelosuppressive therapy does (data not shown). These delays were most likely caused by oxaliplatin

Overall this study provided a insight into alternative dosing strategies of G-CSF in the colorectal cancer setting by showing that five doses is sufficient to get a patient to completion of their planned course of therapy with minimal delays

G-CSF use in the colorectal setting should be administered as shown in Table 1. with the need to replicate this study in a randomized trial to determine efficacy of the alternate day 5 dose strategy

REFERENCES