Oral chemotherapy adverse events based on Oral Chemotherapy Education (OCE) sheets

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Oral Chemotherapy Education

Introduction

- In 2015 there was $27.8 billion spent on targeted oncologics in the US and 39% of this cost was due to oral oncolytics. In 2010, oral oncolytics accounted for 26% of the total cost for targeted oncologics and 19% in 2005. This increase shows that more and more new therapies are developed to be administered orally.[1]
- Despite increased convivence compared to parenteral therapy, oral oncolytics often come with many adverse effects that may affect patients' adherence, therefore, when choosing between medications it is important to choose agents with the least adverse effects to improve adherence.
- The National Community Oncology Dispensing Association (NCODA) in collaboration with the Association of Community Cancer Centers (ACCC), Oncology Nursing Society (ONS) and Hematology/Oncology Pharmacy Association (HOPA) provides caregivers and patients with Oral Chemotherapy Education (OCE) sheets which includes information about oral chemotherapy and their side effects. [2]

Objectives

- The primary objective of this study was to analyze the adverse event risk scores for currently available oral oncolytics.
- The secondary objective was to define the most common adverse effects of oral chemotherapy agents available.

Methods

An independent reviewer gathered data on a total of 103 medications for which an OCE sheet was provided by NCODA. Each medication was given one point for each adverse effect that has a known incidence of at least one third or more based on the prescribing information. Adverse events happening at lower incidence rates were not included in this analysis. After collecting adverse event data for all the medications we saw that the highest number of adverse events were 17, therefore, we divided this number in 3 to create risk score groups. Medications with 5 or less points were defined as lowest risk of adverse events, those having 6 to 11 points were considered moderate risk of adverse events and those with 12-17 points were considered high risk for adverse events. For our secondary objective, we compiled the list of all the adverse events listed for the reviewed medications and analyzed which adverse event occurred most frequently among the medications reviewed.

Results

Based on our analysis the 48% of oral chemotherapy agents have a moderate risk for adverse events and 14% are at high risk. As displayed in table 1, high risk is defined as having 12 or more side effects, moderate risk is having 6-11 side effects and low risk if having 5 or less side effects all with at least a 30% incidence. Therefore, we can see that oral chemotherapy is associated the most with having low and moderate risk for adverse effects. The medications that were included in this analysis are included in Table 2 with their respective risk scores. The most common adverse event among these agents was a decrease of white blood cell, hemoglobin and increase risk for infection, the next highest occurring adverse event was diarrhea, nausea or vomiting and fatigue and the third highest adverse event was changes in liver function, electrolytes and laboratory values. These adverse events happened frequently in more than 50% of the oral chemotherapy agents we analyzed. Other adverse events that happened in at least 10 medications are displayed in table 3.

Table 1. Risk scoring definitions and results

Risk Score	Definition	Number, percent of oral oncolytics
Low Risk	≤ 5 side effects with a ≥ 30% incidence	40 (38.8%)
Moderate Risk	6-11 side effects with a ≥ 30% incidence	49 (47.6%)
High Risk	≥12 side effects with a ≥ 30% incidence	14 (13.6%)

Table 2. Oral oncolytics by risk score results

Low Risk					
Eltrombopag	Exemestane	Letrozole	Abiraterone	Thioguanine	Idelalisib
Enzalutamide	Nilutamide	Lomustine	Apalutamide	Topotecan	Lorlatinib
Fostamatinib	Flutamide	Mitotane	Ixazomib	Acalabrutinib	Osimertinib
Methotrexate	Chlorambucil	Neratinib	Melphalan	Bexarotene	Tazemetostat
Voxelotor	Estramustine	Ruxolitinib	Mercaptopurine	Enasidenib	Venetoclax
Anastrazole	Gefitinib	Tamoxifen	Procarbazine	Encorafenib	Zanubrutinib
Bicalutamide	Hydroxyurea	Larotrectinib		Etoposide	

Moderate Risk					
Alectinib	Trifluridine/Tipiracil	Bosutinib	Panobinostat	Afatinib	Pazopanib
Cyclophosphamide	Vismodegib	Cobimetinib	Pexidartinib	Ceritinib	Sonidegib
Dasatinib	Vorinostat	Dacomitinib	Pomalidomide	Dabrafenib	Alpelisib
Duvelisib	Binimetinib	Glasdegib	Talazoparib	Gilteritinib	Axitinib
Ivosidenib	Brigatinib	Nilotinib	Temozolomide	Ibrutinib	Capecitabine
Lapatinib	Fedratinib	Niraparib	Tucatinib	Olaparib	Crizotinib
Trametinib	Vandetanib	Palbociclib	Erlotinib	Thalidomide	Erdafitinib
Vemurafenib	Ripretinib		Lenalidomide	Abemaciclib	Selpercatinib
Ribociclib	Selinexor				

High Risk					
Ponatinib	Imatinib	Rucaparib	Pemigatinib	Lenvatinib	Everolimus
Tretinoin	Midostaurin	Sorafenib	Cabozantinib	Sunitinib	Selumetinib
Entrectinib	Regorafenib				

Table 3. Most common adverse events in oral oncolytics

Adverse event	Number
Decreased white blood cells and increased risk for infection	63
Decreased hemoglobin	63
Diarrhea	58
Nausea or vomiting	58
Fatigue	58
Changes in liver function	54
Changes in electrolytes and other laboratory values	54
Decreased platelet count and increased risk of bleeding	46
Changes in kidney function	24
Decreased appetite or weight loss	24
Rash or itchy skin	22
Muscle or joint pain or weakness or muscle spasms.	22
Fluid retention or swelling	18
Abdominal pain	17
Mouth irritation or sores	16
Headache	15
Constipation	14
Hair loss (alopecia).	13

Adverse events that occurred in 10% or less of medications analyzed are not included in this table.

Discussion

Due to different terminology, some adverse effects were coupled into one. These included the following: "back pain" was included part of the "muscle or joint pain or weakness or muscle swelling" side effect for lenalidomide and "decreased sex drive and/or impotence" was included in the "decreased sex drive" for flutamide. Other side effects were not added to our analysis although they had 30% incidence since they only occurred in one of the oral chemotherapies, these are the following: heartburn for sunitinib, flu like symptoms and mouth dryness for tretinoin, and skin tags for vemurafenib. Additionally, it is important to mention that these adverse events do not include contraindications or other serious adverse events that have an incidence rate of less than 30% since we wanted to focus on the most common side effects among oral chemotherapy. Also, this data is solely based on the OCE sheets provided by NCODA therefore other adverse events that may be associated with the medications may not be included in this analysis.

Conclusion

Based on our results, we can see that 39%, 48% and 14% of oral chemotherapy agents have at least 5, 6-11 and more than 12 side effects with an incidence of 30% or more associated with them, respectively. We also observed that the most common adverse event associated with oral chemotherapy agents is a decreased white blood cell count and increased risk for infection and decreased hemoglobin, these occur at an incidence of 30% or more in 63 oral oncolytics (61% of medications studied). The next most common are nausea or vomiting, diarrhea and fatigue, these occurred in 58 oral oncolytics (58% of medications studied). Overall the results of this study can help providers better educate patients on the possible adverse events seen with their medication. Additionally, this study also helps to shine light on the most common adverse events seen in oral chemotherapy. This can potentially help guide therapy based on the risk of adverse events and alternative therapies available. Further study can be done on parenteral chemotherapy agents in order to compare different formulation of therapies and their respective adverse events for the treatment of various cancer types.

References

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