

# Reasons for Regimen Modifications of Antineoplastic Agents in an Outpatient Oncology Clinic in Puerto Rico

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**Objective:** Evidence-based modifications to antineoplastic therapy regimens are common. The reasons for those changes are varied and include dose rounding, adjustments based on organ function or changes in weight of the patient, and adverse reactions. Given this complexity, proper documentation, and use of computerized provider order entry (CPOE) systems are essential in promoting optimal decision making and patient outcomes. The objective of this study is to explore common reasons for therapeutic regimen modification and their documentation.

**Methods:** This was a descriptive, retrospective study. Patients who received services at the infusion clinics of a specialized oncology hospital during May 2023, and whose regimen was modified between the months of August 2022 and May 2023 were included. Changes were recorded with their explanations, as detailed by physicians. Physical records from the Department of Pharmacy were also verified.

**Results:** The most documented reason for changes in therapeutic regimens of patients, by both physicians and pharmacy, was dose rounding (31.61% and 45.48%, respectively). Adverse effects recorded by physicians included neurotoxicity and gastrointestinal toxicity (5.16% and 3.55%, respectively). In the evaluated documentation, 14.19% of changes showed discrepancies in both records and 2.6% were not justified in either.

**Conclusion:** Dose rounding was the most common reason for antineoplastic regimen modifications documented by physicians and pharmacists. Record reviews showed opportunities to improve consistency and clarity of data. Strengthening standardized documentation and interprofessional collaboration may optimize clinical decision-making.

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*Key words: Regimen modifications, Antineoplastics, Dose rounding*

In the setting of oncology, modifications to antineoplastic therapy regimens are common. Reasons for these changes are varied, but a main factor in the decision is patient safety. For example, doses could be changed in the presence of serious or discomfiting side effects, (such as chemotherapy induced nausea and vomiting), organ dysfunction, weight fluctuations, decreasing performance status or after considering the risks and benefits of therapy. The latter is especially important in patients receiving palliative care where dose reductions can be considerable. Another reason for dosage modifications is rounding as a method of waste and cost reduction. These changes tend to be slight, with usual recommendations being no more than a 10% difference from the intended dose (1). All these modifications should be done taking into consideration evidence-based recommendations and institutional protocols.

Given the implications of these regimen modifications, various organizations such as the American Society of Health-System Pharmacists (ASHP) and the International Society of Oncology Pharmacy Practitioners (ISOPP) have published statements emphasizing the responsibility of the oncology pharmacist of verifying medical orders of antineoplastic agents, with the intent of guaranteeing their appropriateness (2, 3). Interprofessional collaboration between physicians and pharmacists is widely recognized as a critical component of oncology care. Pharmacists are instrumental in reviewing antineoplastic therapy orders, suggesting dose adjustments, and ensuring compliance with

institutional protocols. Combining the expertise of both professionals helps promote patient safety and supports evidence-based decisions, especially when therapy regimens need to be modified. To be able to perform this task effectively proper documentation of the causes for a change in therapeutic regimen is key. Without complete information, the healthcare team may make decisions without important context, which can result in suboptimal patient outcomes.

Appropriate and complete documentation is also key in building a safe computerized provider order entry (CPOE) system, and in promoting its optimal use (4). A study conducted in a Swedish oncology clinic showed that many medical records and orders lack important information, especially regarding rationales for regimen modifications. Furthermore, that study also found that inappropriate documentation was often accompanied by a lack

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of consideration of factors that should guide the decisions made regarding a patient's treatment (e.g., drug-drug interactions) (5).

The objective of this study was to assess whether a specialized oncology hospital's documentation practices provided the necessary information to determine the reasons behind antineoplastic regimen modifications. Therapeutic regimen modifications are primarily physician-driven; however, pharmacists can counsel on evidence-based changes, and, in some instances, modifications can be made automatically per hospital protocol. Thus, both the electronic health record system of the institution and handwritten records kept at the Department of Pharmacy were used as sources of information for the months of August 2022, through May 2023. Information was considered sufficient if either source documented the clinical or operational reason for a change in the dose or regimen.

## Methods

This was a descriptive and retrospective study performed at a specialized oncology hospital. It included patients who received treatment with antineoplastic agents at the outpatient oncology infusion clinic of the institution during May of 2023. Additionally, patients needed to have registered changes done to their treatment regimens during the months of August 2022 and May 2023. Such changes could include any alteration in dose, scheduling, or regimen composition. Patients who only received oral antineoplastic drugs not processed through the Pharmacy Department of the hospital were excluded. This study was approved by the hospital's Institutional Review Board (IRB).

Overall, 98 patients were identified, and their records were reviewed to ascertain the changes made to their therapy and the reasons for those modifications. Each patient was deidentified by assigning them a number which was used to contain their information summarized in a spreadsheet created in Microsoft Excel. This tool included their initial regimen, the modifications done, and the reasons found for those changes, as documented in the physician, as well as by the Pharmacy Department. The sheet also included demographic information, including age, sex, and type and stage of cancer. After collecting the information, data was summarized using descriptive parameters such as percentages or frequencies, generated by the Excel software. Information was kept in a single computer, located at the Pharmacy Department of the hospital, under password protection.

## Results

A total of 98 patient records were analyzed in this study. Table 1 shows a summary of the demographic data of the enrolled patients. Enrollees were mostly female, with an average age of 61 years. The most common malignancy among patients was breast cancer (16.33%). The most common stage for solid tumors among patients was stage IV. Regimens were widely varied, with FOLFOX-6 being the most common.

When examining documentation, there were many recorded reasons for therapeutic modifications of antineoplastic drug regimens. Rounding was one the most cited motivators for changes in dose, with 31.61% of cases documented by physicians. Similarly,

**Table 1.** Summary of demographic data

| Sex                             | Count of sex          | Average of age |
|---------------------------------|-----------------------|----------------|
| F                               | 71                    | 61.22          |
| M                               | 27                    | 60.21          |
| Total                           | 98                    | 60.49          |
| Cancer type                     | Count of cancer type  | %              |
| Breast                          | 16                    | 16.33%         |
| Colon                           | 14                    | 14.29%         |
| Endometrial                     | 11                    | 11.22%         |
| Ovarian                         | 10                    | 10.20%         |
| Rectal                          | 9                     | 9.18%          |
| Pancreas                        | 4                     | 4.08%          |
| Prostate                        | 3                     | 3.06%          |
| Stomach                         | 3                     | 3.06%          |
| Others*                         | 28                    | 28.57%         |
| Cancer stage^                   | Count of cancer stage | %              |
| I                               | 10                    | 11.24%         |
| II                              | 6                     | 6.74%          |
| III                             | 24                    | 26.97%         |
| IV                              | 39                    | 43.82%         |
| Unspecified                     | 10                    | 11.24%         |
| Regimen                         | Count regimen         | %              |
| FOLFOX-6 q14d                   | 14                    | 11.76%         |
| PACLIitaxel + CARBOplatin q21d  | 9                     | 7.56%          |
| FOLFOX-6 + Bev q14d             | 5                     | 4.20%          |
| FOLFIRI + Bev q14d              | 5                     | 4.20%          |
| CISplatin + XRT weekly          | 4                     | 3.36%          |
| R-CHOP q21d                     | 3                     | 2.52%          |
| Sacituzumab govitecan q21d      | 3                     | 2.52%          |
| FOLFIRI q14d                    | 3                     | 2.52%          |
| PACLI + CARBO + Bev -> Bev q21d | 3                     | 2.52%          |
| Others#                         | 70                    | 58.82%         |

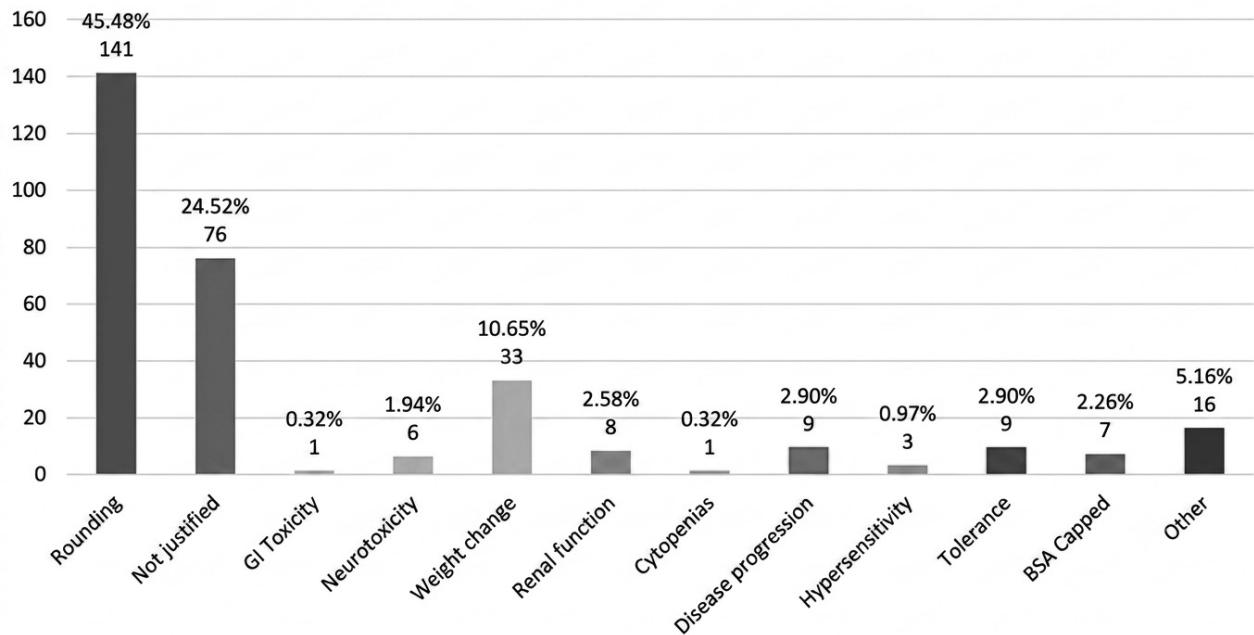
\*Cancers that constituted 2% or less of the obtained sample were grouped under others.

^Cancer stage is reported for solid tumor cancers only. Hematologic malignancies included accounted for 11.22% of cases (11 patients).

#Therapeutic regimens that accounted for less than 2% of the data were grouped under others.

rounding was the most common reason for changes documented by pharmacy (45.48%). Various types of side effects and toxicities of medications were mentioned on both records. These included neurotoxicity, gastrointestinal toxicity and cytopenia. Details on specific side effects and toxicities observed are provided in Figure 1 and Figure 2. Additionally, some instances of modifications (31.94%) were not adequately justified in the documentation from physicians. This compares to a 24.52% found in the pharmacy records. Finally, 1.94% of modifications documented as rounding were not done according to institutional policies for such modifications. That is, some entries did not adhere to the institutional requirement of changes being within a 10% of the calculated dose to ensure safety and efficacy.

Figure 1. Reasons for regimen modifications, as documented by Pharmacy Department.

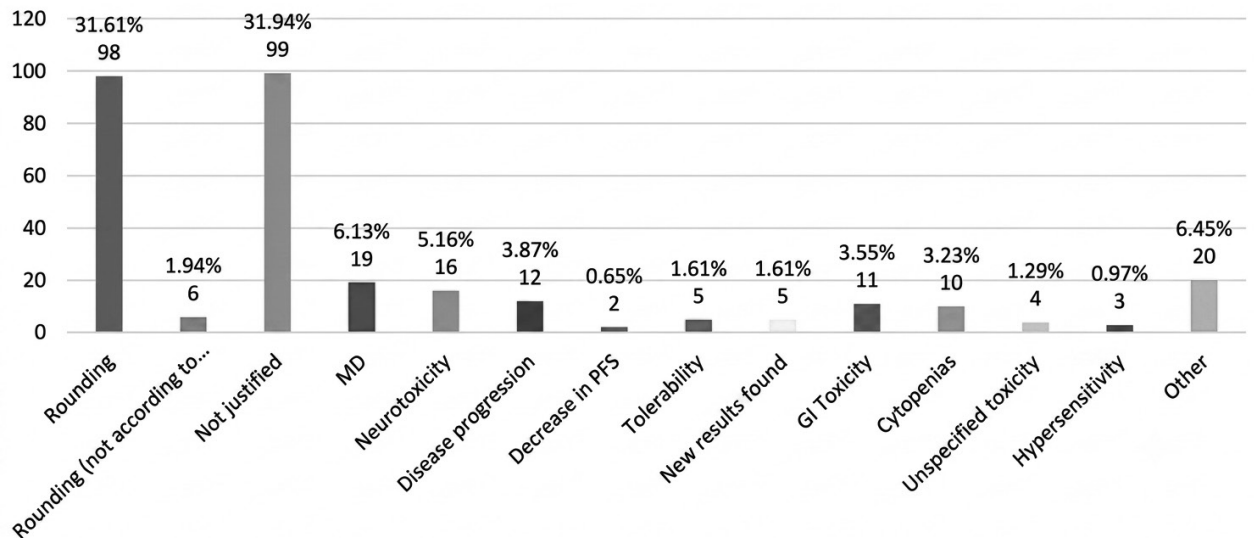


Discussion

The most common reason for modifying therapeutic regimens was dosage rounding, which has been proven to be effective as a means of cost management and waste reduction. Studies have shown that changes of 10% or less in doses are adequate, as they are unlikely to cause a clinically significant reduction in effectiveness

of therapy and could help institutions better allocate resources and optimize daily workflows (1). However, some cases were found where rounding was not performed in accordance with the protocol (1.94%). As per hospital policy, dose rounding should be recommended if a change within 10% of difference between the intended dose and the dose that would be given could result in less of the medication's units being used. Some of these cases may

Figure 2. Reasons for regimen modifications, as documented by prescribing physicians.



represent errors in documentation where rounding was mistakenly entered as the reason in the electronic health record of the patient.

Another commonly cited reason for dose modifications was the incidence of side effects, such as cytopenia, neurotoxicity, and gastrointestinal toxicity. The presence of these side effects, in some level, was to be expected due to the nature of the therapies involved. For example, a study conducted by Denduluri and Patt, et. al. (6) found that myelotoxicities (which are possible with some cancer treatments) often lead to a reduction in dose or delay to be needed, to mitigate the consequences of this adverse effect. Another, more recent study found that breast cancer patients often experienced toxicities that motivated reductions in dose of their treatments (7).

When comparing the electronic health records for enrolled patients and the physical records kept at the Department of Pharmacy, discrepancies were found in 14.19% of the cases, where the reasons documented differed between sources. Moreover, 2.6% of the modifications were not justified with a reason for the change in either record. These discrepancies highlight the importance of structured interprofessional collaboration between physicians and pharmacists, integrating the expertise of both professionals in reviewing therapy orders and documenting regimen modifications. Kim et al. showed that real-time documentation reduced undocumented discrepancies at discharge from 65.8% to 33.9% and improved physician-pharmacist communication, supporting patient safety and collaboration. They also reported that these incomplete records have been associated with medication errors, adverse drug events, and inadequate patient education (8). A factor that may explain the inconsistencies found in our study may have been a lack of experience in using the electronic health record system, since it was a recent addition to the hospital's workflow. Thus, while electronic health systems and CPOE have been shown to promote higher quality services (4), as with any recent change an acclimation period may show better use by involved staff. However, further analysis is required to determine any factors contributing to these observations.

This study had some limitations. Firstly, being a retrospective study, important context of the situations found during data collection may be lacking. Additionally, omission bias is a possibility. *Observer bias in data extraction* could have occurred as all data were obtained by a single investigator and this could have led to inadvertent omissions or misinterpretations of regimen modifications. The study was also conducted at a single center and the sample of patients enrolled in the study may not be representative of the population that receives care at the specialized oncology clinic where the study took place limiting the generalizability of the findings. However, the data and conclusions obtained from this project can prove beneficial, so that the institution can better prioritize the potential issues identified and so that new interventions may be developed to improve professional practices.

## Conclusion

This study found that dose rounding was the most frequent reason for antineoplastic regimen modifications documented by physicians and pharmacists. Review of both electronic and pharmacy records revealed inconsistencies and gaps in

documentation, highlighting the need for standardized practices. The information found in this study will help promote optimal documentation practices at the institution, to better comply with practice standards and develop better interprofessional interactions in the provision of health services. Implementing targeted training and reinforcing CPOE use may further improve documentation quality and patient safety.

## Resumen

**Objetivo:** Las modificaciones basadas en evidencia de los regímenes antineoplásicos son comunes. Sus razones incluyen redondeo de dosis, ajustes por función de los órganos, cambios en peso y reacciones adversas. La documentación adecuada y el uso de sistemas computarizados de órdenes médicas (CPOE, por sus siglas en inglés) son esenciales para la toma de decisiones óptimas y mejores resultados clínicos. El objetivo de este estudio es explorar razones frecuentes de modificación de regímenes y su documentación. **Métodos:** Este fue un estudio descriptivo y retrospectivo. Se incluyeron pacientes que recibieron servicios en las clínicas de infusión de un hospital especializado en oncología durante mayo de 2023, y cuyo régimen fue modificado entre los meses de agosto de 2022 y mayo de 2023. Los cambios fueron registrados junto con sus explicaciones, tal como los detallaron los médicos. Además, se verificaron los registros físicos del Departamento de Farmacia para obtener información adicional. **Resultados:** La razón más documentada para los cambios analizados fue el redondeo de dosis (31.61% y 45.48%, respectivamente). Los efectos adversos registrados por los médicos incluyeron neurotoxicidad y toxicidad gastrointestinal (5.16% y 3.55%, respectivamente). El 14.19% de los cambios evaluados presentaron discrepancias en los registros y el 2.6% no fueron justificados. **Conclusión:** El redondeo de dosis fue la causa principal de modificaciones en los regímenes antineoplásicos, según lo documentado por médicos y farmacéuticos. La revisión de los expedientes mostró oportunidades para mejorar la consistencia y la claridad de los datos. Fortalecer la documentación estandarizada y la colaboración interprofesional puede optimizar la toma de decisiones clínicas.

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