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Association of Polypharmacy and Potentially Inappropriate Medications With Frailty Among Older Adults With Blood Cancers

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Abstract

Background: Polypharmacy and potentially inappropriate medications (PIMs) are common among older adults with blood cancers, but their association with frailty and how to manage them optimally remain unclear.

Patients and Methods: From 2015 to 2019, patients aged ≥75 years presenting for initial oncology consult underwent screening geriatric assessment. Patients were determined to be robust, prefrail, or frail via deficit accumulation and phenotypic approaches. We quantified each patient's total number of medications and PIMs using the Anticholinergic Risk Scale (ARS) and a scale we generated using the NCCN Medications of Concern called the *Geriatric Oncology Potentially Inappropriate Medications* (GO-PIM) scale. We assessed cross-sectional associations of PIMs with frailty in multivariable regression models adjusting for age, gender, and comorbidity.

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Results: Of 785 patients assessed, 603 (77%) were taking ≥5 medications and 421 (54%) were taking ≥8 medications; 201 (25%) were taking at least 1 PIM based on the ARS and 343 (44%) at least 1 PIM based on the GO-PIM scale. Among the 468 (60%) patients on active cancer treatment, taking ≥8 medications was associated with frailty (adjusted odds ratio [aOR], 2.82; 95% CI, 1.92–4.17). With each additional medication, the odds of being prefrail or frail increased 8% (aOR, 1.08; 95% CI, 1.04–1.12). With each 1-point increase on the ARS, the odds of being prefrail or frail increased 19% (aOR, 1.19; 95% CI, 1.03–1.39); with each additional PIM based on the GO-PIM scale, the odds increased 65% (aOR, 1.65; 95% CI, 1.34–2.04).

Conclusions: Polypharmacy and PIMs are prevalent among older patients with blood cancers; taking ≥8 medications is strongly associated with frailty. These data suggest careful medication reconciliation for this population may be helpful, and deprescribing when possible is high-yield, especially for PIMs on the GO-PIM scale.

Background

The majority of patients with hematologic malignancies are older adults, many of whom have multiple chronic conditions in addition to blood cancer.[1-3] As comorbidities accumulate with age, so do the number of medications and their risk of producing adverse effects.[4,5] Taking ≥5 medications, also known as *polypharmacy*, is associated with adverse effects in older adults.[6] Older adults with cancer have an even higher risk of adverse effects, because medications are often added to offset adverse effects and symptoms of cancer or chemotherapy.[7-10] Indeed, it has been demonstrated that most older adults with blood cancers take ≥5 medications,[9] and recent work in older adults with solid tumors showed that polypharmacy defined as ≥8 medications was highly discriminatory for impairment in physical function.[11]

Certain prescription drugs, called *potentially inappropriate medications* (PIMs), are associated with adverse effects in older patients.[12-14] These medications are potentially inappropriate because there are alternatives with safer adverse effect profiles. Examples include corticosteroids (oral), sedatives, antihistamines, opioids, and antipsychotics. In the general older population, polypharmacy and PIMs have been found to be a risk factor for the development and progression of frailty.[15-19] Older patients with cancer are also undoubtedly affected. Indeed, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Older Adult Oncology include a list of medications commonly used for supportive care that are of concern for older adults.[20,21] This list has the potential to be a cancer-specific PIMs scale, but the association of the listed medications with adverse outcomes in patients with cancer has yet to be demonstrated.

Functional decline, cognitive impairment, and frailty are prevalent in older adults with blood cancers, and polypharmacy and PIMs risk exacerbating these geriatric syndromes as well as toxicity and other adverse outcomes during cancer treatment.[4,22-27] On the other hand, there are sparse data regarding the best ways to identify PIMs for older adults with blood cancers, and whether polypharmacy and PIMs are associated with frailty in this population. Frailty is a state of reduced physiologic reserve that leaves one vulnerable to future stressors, and evidence in other populations of older adults suggest that polypharmacy is strongly linked

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to frailty,[15] identifying it as a potential modifiable risk factor. Investigating the association of polypharmacy and PIMs with frailty in older patients with blood cancers is critical as oncologists in busy clinics aim to address nonchemotherapy medication risks/benefits in the context of optimizing patient function.[28] Identifying measures of polypharmacy and PIMs that predict frailty would guide deprescribing, minimize frailty, and reduce risk of toxicity during treatment of hematologic cancers.[29]

In this context, we examined the prevalence of polypharmacy and PIMs in a large cohort of patients with blood cancers and examined different polypharmacy and PIMs definitions' cross-sectional associations with frailty and one of its underlying domains: cognitive impairment. We hypothesized that polypharmacy and PIMs would be prevalent and associated with increasing frailty, but that the presence of PIMs would be more strongly predictive. We based our hypothesis on the supposition that an increase in the total number of medications—and dichotomizing above or below a certain cutoff—does not confer as strong a risk of frailty as does an increase in the number of inappropriately prescribed medications, the latter of which also points to deprescribing interventions.

Patients and Methods

Study Design/Population

We undertook a cross-sectional analysis using data from the Older Adult Hematologic Malignancies (OHM) Program at Dana-Farber Cancer Institute (DFCI).[4,22,23,30-32] All transplant-ineligible patients aged ≥75 years who presented for initial consultation in the leukemia, lymphoma, and myeloma clinics at DFCI between February 2015 and November 2019 were eligible. Those who consented to participate in the study underwent an in-person screening geriatric assessment administered by a research assistant on the same day as their initial hematologic oncology consultation.[4] The screening geriatric assessment included patient-reported and objective measures, spanning domains of comorbidity, functional status, physical performance (eg, gait speed), and cognition. All measures collected in the geriatric assessment are included in supplemental eTable 1 (available with this article at JNCCN.org). Patients were classified as receiving active treatment based on the initial oncology consult note recommending initiation or continuation of cancer-focused therapy.

Polypharmacy and PIMs

All prescribed and over-the-counter medications that patients were taking at the time of their initial consultation were extracted from the electronic health record (EHR). Only previously prescribed medications listed in the medical reconciliation documentation in the oncologist's note were included; new prescriptions ordered by DFCI clinicians were not. Patients taking ≥5 medications were considered to have polypharmacy. We also included an alternative definition of polypharmacy in our analyses as ≥8 medications.[6,11]

Extracted medications were identified as potentially inappropriate using 2 different continuous scales (Table 1). The Anticholinergic Risk Scale (ARS)[13] is a tool developed and used in aging research to estimate the extent to which patients may be at risk for anticholinergic adverse effects from their medications, including cognitive dysfunction and

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delirium. The ARS ranks medications according to anticholinergic potential, from 0 (no or low risk) to 3 (high risk). Each patient's total risk is quantified by summing the ARS scores of all medications. We also developed a PIMs scale more specific to older adults with cancer using the list of medications commonly used for supportive care that are of concern in older patients that is provided in the NCCN Guidelines for Older Adult Oncology, Version 1.2020.[20,21] This list is regularly updated by oncologists and geriatricians to assist with the identification of medications often encountered in oncology practice that carry risks for older patients.[33] We translated the list into the Geriatric Oncology Potentially Inappropriate Medications (GO-PIM) scale to quantify PIMs for each patient, where patients receive 1 point for each PIM taken on the list. These scales are described in greater detail in supplemental eAppendix 1.

Frailty and Cognitive Impairment

From the screening geriatric assessment, frailty status was derived using both frailty phenotype[34] and deficit-accumulation[35] approaches. In brief, the frailty phenotype uses 5 criteria to determine frailty status: slow gait speed, weakness measured by grip strength, self-reported exhaustion, low physical activity, and weight loss. The average time to complete this assessment is 5 to 10 minutes. The deficit-accumulation method counts aging-related health deficits across multiple domains to define frailty as the proportion of deficits in an individual out of the total number of possible deficits measured. The average time to complete this assessment is 15 to 20 minutes. Patients were classified as robust, prefrail, or frail based on the more severe assessment between both scales (see supplemental eTable 1 for details, including cutoff values). Medications were not included in either frailty assessment. Treating oncologists were blinded to initial frailty classification in order to minimize potential influence on treatment recommendations.

Cognition was measured using the delayed recall section of the Montreal Cognitive Assessment (MoCA)[36] and the Clock-in-the-Box test (CIB),[37] a measure of executive functioning. We used the 5-word delayed recall list from the MoCA to screen for impairment in short-term memory.[4] We defined remembering ≤2 words as probable cognitive impairment, based on prior work.[4,37] The CIB test is a validated modification of the Clock Drawing Test.[4] The CIB testing takes approximately 2 minutes and correlates well with performance on the more comprehensive Mini-Mental State Examination and measures of independent function in community-dwelling older persons.[4] Consistent with previous studies,[37] we defined a score ≤4 as probable cognitive impairment.

Covariates

Age at enrollment and gender were extracted from the EHR. The Charlson comorbidity index (CCI) score was also calculated for each patient, based on information extracted from the oncology consultation note.

Statistical Analysis

Population characteristics were summarized using proportions. Chi-square analyses were performed in the total population to assess for associations between having ≥1 medication in each class of PIMs in the GO-PIM scale and frailty status (robust vs prefrail or frail) for

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the full cohort. Analyses assessing the association of polypharmacy and PIMs with frailty and cognitive impairment were performed in the subset of patients recommended to initiate or continue active treatment, given the higher risk in these patients for adverse effects and drug–drug interactions.

Ordinal regression was used to estimate the association of each polypharmacy measure (continuous, ≥5 medications, and ≥8 medications) and PIM measure (continuous ARS and GO-PIM scales) with increasing frailty severity (robust, prefrail, and frail). Logistic regression was used to estimate the association of each polypharmacy/PIM measure with cognitive impairment. Univariable analyses were followed by multivariable analyses, adjusting for age (as continuous variable), gender, and comorbidity (CCI score, as a continuous variable)—variables known to be predictive of outcomes in patients with cancer that could act as confounders in our analyses.[38,39] The proportional odds assumptions were evaluated by comparing the intercepts and logits of each covariate and comparing to logits from multiple binary logistic models across the different outcome levels. Results in Brant-Wald tests showed no significant differences to suggest that the proportional odds assumption was violated. This article adheres to reporting guidelines set forth in the STROBE statement.[40]

Results

Study Population Characteristics

A total of 785 of 913 (86%) eligible patients agreed to enroll in the OHM Program at the time of this analysis (Figure 1). Table 2 displays baseline characteristics of the study population. Overall, 334 (43%) patients were aged ≥80 years and 499 (64%) were male. There was similar representation from each disease type (leukemia, n=240 [31%]; lymphoma, n=272 [35%]; multiple myeloma, n=273 [35%]). A total of 468 (60%) patients were recommended by their oncologists to initiate or continue active cancer treatment. Seventeen (2%) patients had a CCI score of 0 to 1, 246 (31%) had a score of 2–3, and 416 (53%) had a CCI score of ≥4; data regarding CCI score was missing for 106 (13.5%) patients.

Prevalence of Polypharmacy and PIMs

A total of 603 (77%) patients had polypharmacy defined as ≥5 medications, whereas 421 (54%) had polypharmacy defined as ≥8 medications (Table 2). Regarding PIMs, 68 (9%) patients had an ARS score of 1, 75 (10%) had a score of 2, 36 (5%) had a score of 3, and 22 (3%) had a score of ≥4. A total of 201 (25%) patients were taking at least 1 PIM based on the ARS, and 343 (44%) were taking at least 1 PIM based on the GO-PIM scale. Corticosteroids (109 [13.9%] patients prescribed ≥1 oral steroid) and benzodiazepines (95 [12.1%] patients prescribed ≥1 benzodiazepine) were the most common PIMs.

Association of Polypharmacy and PIMs With Frailty

A total of 131 (17%) patients were frail and 457 (58%) were prefrail. Table 3 displays the prevalence of different classes of PIMs classified by the GO-PIM scale, according to frailty status. Compared with robust patients, prefrail and frail patients were more likely

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to be on benzodiazepines (13.6% vs 7.6%; P=.031), selective serotonin reuptake inhibitors (SSRIs; 12.9% vs 6.1%; P=.009), and opioids (12.1% vs 2.0%; P<.001). Corticosteroids (oral) were also prevalent in prefrail and frail patients relative to robust patients (15.3% vs 9.6%; P=.056).

In older patients recommended to continue or initiate active cancer treatment (n=468), univariable analyses revealed that all polypharmacy and PIM measures were associated with frailty (supplemental eTable 2). After adjustment for age, gender, and comorbidity (CCI score), all associations were maintained aside from the association between polypharmacy defined as ≥5 medications.

When modeled as continuous variables, both the ARS and GO-PIM scales had stronger associations with frailty than the polypharmacy scales (reflecting total number of medications regardless of medication class or risk), with the GO-PIM scale carrying the strongest association (Table 4). Overall, with each additional medication on a patient's medication list, the odds of being prefrail or frail increased by 8% (adjusted odds ratio [aOR], 1.08; 95% CI, 1.04–1.12). With each 1-point increase on the ARS, the odds increased by 19% (aOR, 1.19; 95% CI, 1.03–1.39). With each additional PIM based on the GO-PIM scale, the odds increased by 65% (aOR, 1.65; 95% CI, 1.34–2.04).

Cognitive Impairment

A total of 111 (14%) patients had probable impairment in delayed recall (MoCA), and 146 (19%) had probable impairment in executive functioning (CIB test). In univariable analyses (supplemental eTable 2), only polypharmacy defined as ≥8 medications was significantly associated with executive dysfunction (OR, 1.72; 95% CI, 1.08–2.77). This association weakened after adjustment for age, gender, and comorbidity (CCI; aOR, 1.61; 95% CI, 0.99–2.63).

Discussion

In this large cohort of older adults with blood cancers, polypharmacy and PIMS were prevalent. Corticosteroids (oral), benzodiazepines, and SSRIs were the most commonly prescribed PIMs, and prefrail and frail patients were more likely to be taking these, along with opioids. Polypharmacy (≥8 medications) and PIMs were strongly associated with frailty, independent of age, gender, and comorbidity. We were able to operationalize the NCCN list of medications of concern into a measurable scale (GO-PIM) to identify and quantify PIMs. Increasing number of PIMs per the GO-PIM scale carried a stronger association with frailty compared with total number of medications or increasing PIMs as classified by the ARS.

Polypharmacy and PIMs can be defined in different ways, and our analysis suggests that optimal definitions may differ for different cancer populations. This becomes apparent when comparing our findings to prior studies in older adults with solid and liquid tumors.[41-49] In our cohort, polypharmacy defined as ≥8 medications was associated with frailty, reinforcing the finding by Mohamed et al[11] that ≥8 medications best detected functional impairment in older adults with advanced solid tumors. Outlaw et al[41] found that for older patients

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with gastrointestinal malignancies (n=397), polypharmacy defined as ≥9 medications was associated with frailty and lower mental health–related quality of life. Maggiore et al[50] found that among 500 older patients with solid tumors, polypharmacy defined by 4 to 9 medications and ≥10 medications was not associated with higher risk of chemotherapy-related toxicity and hospitalizations.

Prior studies examining polypharmacy and PIMs in older patients with hematologic malignancies found mixed results, but the sample sizes were smaller, ranging from 80 patients with multiple myeloma (polypharmacy defined as ≥5 drugs in 64%) to 399 with acute leukemia (polypharmacy defined as ≥5 medications associated with worse overall survival in patients aged <60 years but not in those aged ≥60 years).[44-48] Most also did not control for comorbidity,[9] which raises the potential for confounding by indication: the risk ascribed to high number or inappropriate medications could be driven by underlying comorbidities for which the medications were prescribed.[51] Finally, our cohort of patients is older (age ≥75 years) than most previously studied cohorts, which may explain some differences in results.

Chen et al[9] recently conducted a systematic review and meta-analysis of studies in older adults with cancer and found that polypharmacy (39 studies) and PIMs (13 studies) were both associated with all-cause mortality; polypharmacy was significantly associated with hospitalization, treatment-related toxicity, and postoperative complications. Polypharmacy was defined using cutoffs ranging from ≥3 to ≥10 medications, and PIMs were defined using the American Geriatrics Society's Beers 2015 criteria,[46] Screening Tool of Older People's Prescriptions (STOPP),[52 *] and others.[9,53] Heterogeneity (I^2) was moderate to considerable and varying definitions of polypharmacy in different populations (ages and cancer types) likely contributed to heterogeneity.[54]

Given our results, we advocate against simply classifying patients as "having polypharmacy" or "not having polypharmacy." We suggest that blood cancer clinicians aiming to deprescribe make use of PIM scales to identify high-risk medications. When modeled continuously, we found that measures of PIMs (ARS and GO-PIM scale) had stronger associations with frailty than measures of polypharmacy (total number of medications). We also found that an increasing number of PIMs classified by the GO-PIM scale carried a stronger association with frailty compared with an increasing number of PIMs classified by the ARS or the total number of medications.

A novel aspect of our analysis is the conversion of the NCCN list of medications commonly used for supportive care that are of concern in older adults with cancer[20] into a measurable scale. The GO-PIM scale's performance compared with the 2 polypharmacy measures and the ARS reflects its cancer-specific focus, wherein high-risk medications were included based on evidence in geriatric oncology. For example, oral corticosteroids are often used for supportive care and are a mainstay of multiple myeloma regimens but carry risks of muscle weakness, hyperglycemia, and delirium.[55,56] Opioids are necessary for patients with cancer-related pain, but nonopioid analgesics such as acetaminophen can be tried first along with nonpharmacologic interventions such as physical therapy. The high prevalence of benzodiazepines in our population is of particular concern, given their association with

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impaired coordination, falls, and cognitive impairment that nearly always calls for safer alternatives.[14,57,58] The NCCN Guidelines provide alternatives for treating the conditions for which each PIM was originally prescribed, such as cognitive behavioral therapy for insomnia or safer medications for anxiety.[20] A PIMs measure that identifies cancer-specific PIMs strongly linked to frailty, provides deprescribing interventions, and can be refined regularly based on updated NCCN Guidelines[33] makes the GO-PIM scale an attractive tool to aid oncology teams in personalized medication management for older adults with blood cancers.

Our analysis has limitations. Our study sample is large but cross-sectional, so we cannot determine directionality of association and prospective trajectory. Our patients also came from a single tertiary center, which likely underestimates the true prevalence of frailty among older community-dwelling adults with cancer. Although 2 investigators (T.T. Hshieh, C. DuMontier) reviewed all the medication lists and adjudicated any discrepancies, we were unable to confirm all supplemental and over-the-counter medications patients may have been taking. Moreover, we measured cognitive impairment using brief screening tests; associations between polypharmacy/PIMs and more rigorous assessments of cognitive impairment may have yielded different results. Finally, we have not measured the association of polypharmacy and PIMs with other important outcomes for older adults with cancer, such as quality of life, care utilization, and overall survival.

Conclusions

We found that polypharmacy defined as taking ≥8 medications and increasing PIMs on the ARS and GO-PIM scales are associated with frailty in older adults with blood cancers. PIMs on the GO-PIM scale were the most strongly associated with frailty. Evidence is emerging in populations of older adults with solid tumors that interventions aimed at ameliorating polypharmacy and PIMs may lead to reduced falls and treatment-related adverse effects.[10,59-62] These findings warrant further exploration in older adults with blood cancers using tools like the GO-PIM scale for targeted deprescribing. For example, embedding the GO-PIM scale in EHRs to automate the detection of PIMs could make targeted “point-of-care” deprescribing feasible in the clinic, which in turn may be associated with a reduction in adverse outcomes.[51] Moreover, leveraging existing databases to identify interactions between PIMs and cancer therapies[63] could improve safety in older adults with blood cancers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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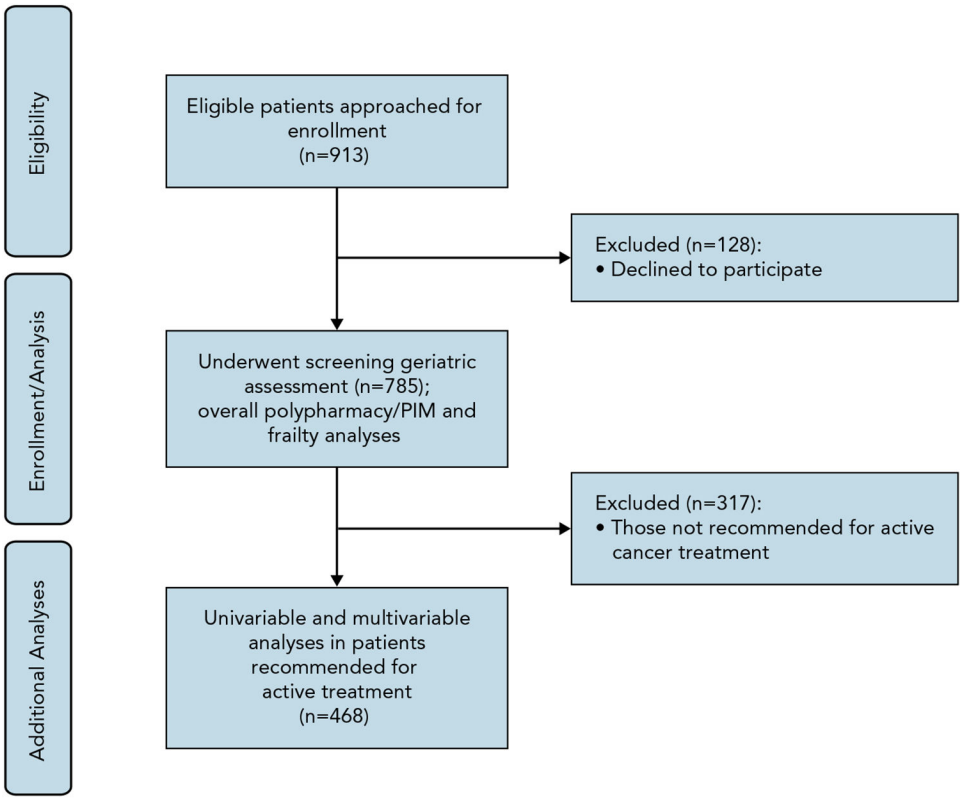

Figure 1.
Study selection flow diagram. Abbreviation: PIM, potentially inappropriate medication.

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Table 1.

PIM Scales, Scoring, and Individual Medications in Each Scale

PIM Scale	Medications		
ARS[13,a]	**3 points**	**3 points (cont.)**	**2 points (cont.)**
	Amitriptyline hydrochloride	Thioridazine hydrochloride	Pseudoephedrine hydrochloride
	Atropine products	Thiothixene	Triprolidine hydrochloride
	Benztropine mesylate	Tizanidine hydrochloride	Tolterodine tartrate
	Carisoprodol	Trifluoperazine hydrochloride	
	Chlorpheniramine maleate		**1 point**
	Chlorpromazine hydrochloride	**2 points**	Carbidopa-levodopa
	Cyproheptadine hydrochloride	Amantadine hydrochloride	Entacapone
	Dicyclomine hydrochloride	Baclofen	Haloperidol
	Diphenhydramine hydrochloride	Cetirizine hydrochloride	Methocarbamol
	Fluphenazine hydrochloride	Cimetidine	Metoclopramide hydrochloride Mirtazapine
	Hydroxyzine hydrochloride and Hydroxyzine pamoate Hyoscyamine products	Clozapine	Paroxetine hydrochloride
		Cyclobenzaprine hydrochloride	Pramipexole dihydrochloride
	Imipramine hydrochloride	Desipramine hydrochloride	Quetiapine fumarate
	Meclizine hydrochloride	Loperamide hydrochloride	Ranitidine hydrochloride
	Oxybutynin chloride	Loratadine	Risperidone
	Perphenazine	Nortriptyline hydrochloride	Selegiline hydrochloride
	Promethazine hydrochloride	Olanzapine	Trazodone hydrochloride
		Prochlorperazine maleate	Ziprasidone hydrochloride

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PIM Scale	Medications		
GO-PIM scale[b]	**Corticosteroids (oral)**	**First-generation antihistamines (cont.)**	**Antipsychotics (cont.)**
	Hydrocortisone	Cyproheptadine	Perphenazine
	Methylprednisolone	Dexbrompheniramine	Pimozide
	Prednisone	Dexchlorpheniramine	Promazine
	Prednisolone	Doxylamine	Thioridazine
	Dexamethasone	Triprolidine	Thiothixene
			Trifluoperazine
	Benzodiazepines	**Antiemetic, prokinetic**	Triflupromazine
	Alprazolam	Metoclopramide	Aripiprazole
	Estazolam		Asenapine
	Lorazepam	**Phenothiazine antiemetic**	Clozapine
	Oxazepam	Prochlorperazine	Iloperidone
	Temazepam		Lurasidone
	Triazolam	**Histamine-2 receptor blockers**	Olanzapine
	Clorazepate	Famotidine	Paliperidone
	Chlordiazepoxide	Ranitidine	Quetiapine
	Clonazepam	Cimetidine	Risperidone
	Diazepam		Ziprasidone
	Flurazepam	**Selective serotonin reuptake inhibitor antidepressants**	
	Quazepam	Fluoxetine	**Antiepileptic drugs**
		Paroxetine	Phenobarbital
	Nonbenzodiazepine sedative	Sertraline	Phenytoin
	Zolpidem	Fluvoxamine	Carbamazepine
	Eszopiclone	Citalopram	
	Zaleplon	Escitalopram	**Opioids**
			Morphine
	First-generation antihistamines	**Antipsychotics**	Tramadol
	Diphenhydramine	Chlorpromazine	Hydrocodone
	Hydroxyzine	Fluphenazine	Oxycodone
	Promethazine	Haloperidol	Hydromorphone
	Brompheniramine	Loxapine	Fentanyl
	Carbinoxamine	Molindone	Methadone
	Clemastine		

Abbreviations: ARS, Anticholinergic Risk Scale; GO-PIM, Geriatric Oncology Potentially Inappropriate Medications; PIM, potentially inappropriate medication.

[a] To calculate the ARS score for a patient, identify medications the patient is taking and add the total points for each medication. Medications not on this list have a score of 0.

[b] This scale was generated using the NCCN list of Medications Commonly Used for Supportive Care That Are of Concern in Older Patients.[20] The total number of medications identified by this scale was quantified for each patient.

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Table 2.

Baseline Cohort Characteristics

Characteristic	Total Cohort n (%)
Total, N	785
Age	
75–79 y	451 (57.4)
80–84 y	233 (29.7)
85–89 y	83 (10.6)
≥90 y	18 (2.3)
Male gender, self-reported	499 (63.6)
Disease type	
Leukemia	240 (30.6)
Lymphoma	272 (34.6)
Myeloma	273 (34.8)
On active cancer treatment[a]	468 (59.6)
Polypharmacy (≥5 medications)	603 (76.8)
Polypharmacy (≥8 medications)	421 (53.6)
Frailty status	
Frail	131 (16.7)
Prefrail	457 (58.2)
Robust	197 (25.1)
CCI score	
0–1	17 (2.2)
2–3	246 (31.3)
≥4	416 (53.0)
Missing	106 (13.5)
MoCA delayed recall, positive for probable impairment	
Yes (0–2)	111 (14.1)
No (3–5)	652 (83.1)
Missing	22 (2.8)
CIB, positive for probable impairment	
Yes (0–4)	146 (18.6)
No (≥5)	610 (77.7)
Missing	29 (3.7)

Abbreviations: CCI, Charlson comorbidity index; CIB, Clock-in-the-Box; MoCA, Montreal Cognitive Assessment.

[a]Patients were classified as those recommended by their oncologist for active cancer-directed treatment versus those who were not, based on the initial oncology consult note recommending initiation or continuation of cancer treatment of the patient's blood cancer.

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Table 3.

Prevalence of Different Classes of PIMs[a] by Frailty Status

PIM Class[b]	Robust n (%)	Prefrail & Frail n (%)	*P* Value[c]
Total, n	197	588	
Benzodiazepines	15 (7.6)	80 (13.6)	.031
Antipsychotics	3 (1.5)	2 (0.3)	.104
First-generation antihistamines	5 (2.5)	14 (2.4)	1.000
Antiepileptics	0 (0.0)	2 (0.3)	1.000
Histamine-2 receptor blockers	9 (4.6)	38 (6.5)	.389
Selective serotonin reuptake inhibitors	12 (6.1)	76 (12.9)	.009
Opioids	4 (2.0)	71 (12.1)	<.001
Corticosteroids (oral)	19 (9.6)	90 (15.3)	.056
Nonbenzodiazepine sedatives	5 (2.5)	21 (3.6)	.646
Antiemetic prokinetic	2 (1.0)	2 (0.3)	.263
Phenothiazine antiemetic	6 (3.0)	23 (3.9)	.668

Abbreviations: GO-PIM, Geriatric Oncology Potentially Inappropriate Medications; PIM, potentially inappropriate medication.

[a]According to the GO-PIM scale.

[b]Patients with ≥1 medication.

[c]Chi-square tests were used to assess for association between ≥1 medication in each PIM class and frailty status (robust vs prefrail or frail).

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Table 4.

Multivariable Models of Association Between Polypharmacy and PIMs With Frailty and Cognitive Impairment

Variable[a]	Frailty[b] aOR (95% CI)	MoCA[b] aOR (95% CI)	Clock-in-the-Box[b] aOR (95% CI)
Polypharmacy			
<5 medications	Ref	Ref	Ref
≥5 medications	1.42 (0.91–2.22)	1.45 (0.74–3.08)	1.16 (0.66–2.10)
Polypharmacy			
<8 medications	Ref	Ref	Ref
≥8 medications	2.82 (1.92–4.17)	1.12 (0.64–1.95)	1.61 (0.99–2.63)
Polypharmacy			
Continuous	1.08 (1.04–1.12)	1.02 (0.97–1.07)	1.00 (0.96–1.05)
ARS score			
Continuous	1.19 (1.03–1.39)	0.95 (0.73–1.19)	0.89 (0.71–1.08)
GO-PIM scale			
Continuous	1.65 (1.34–2.04)	1.21 (0.89–1.61)	0.95 (0.72–1.22)

Abbreviations: aOR, adjusted odds ratio; ARS, Anticholinergic Risk Scale; MoCA, Montreal Cognitive Assessment; GO-PIM, Geriatric Oncology Potentially Inappropriate Medications; PIM, potentially inappropriate medication.

[a]All models controlled for age, gender, and Charlson comorbidity index scores.

[b]Frailty fit with ordinal logistic regression. MoCA and Clock-in-the-Box fit with logistic regression.