Time spent at home among older adults with acute myeloid leukemia receiving azacitidine- or venetoclax-based regimens

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Received: January 21, 2022.
Accepted: June 10, 2022.
Early view: July 21, 2022.

https://doi.org/10.3324/haematol.2022.280728

Abstract

Time at home is a critically important outcome to adults with acute myeloid leukemia (AML) when selecting treatment; however, no study to date has adequately described the amount of time older adults spend at home following initiation of chemotherapy. We queried records from a multi-institution health system to identify adults aged ≥60 years newly diagnosed with AML who were treated with azacitidine or venetoclax and evaluated the proportion of days at home (PDH) following diagnosis. Days were considered "at home" if patients were not admitted or seen in the emergency department or oncology/infusion clinic. Assessed covariates included demographics and disease risk. Associations between PDH and baseline characteristics were evaluated via linear regression, adjusted for log length of follow-up. From 2015-2020, 113 older adults were identified. Most received azacitidine plus venetoclax (51.3%) followed by azacitidine monotherapy (38.9%). The mean PDH for all patients was 0.58 (95% confidence interval: 0.54-0.63, median 0.63). PDH increased among survivors over time. PDH did not differ between therapy groups (adjusted mean, azacitidine plus venetoclax: 0.68; azacitidine monotherapy: 0.66; P=0.64) or between disease risk categories (P=0.34). Compared to patients receiving azacitidine monotherapy, patients receiving azacitidine plus venetoclax had longer clinic visits (median minutes: 127.9 *vs*. 112.9, P<0.001) and infusion visits (median minutes: 194.3 *vs*. 132.5, P<0.001). The burden of care for older adults with AML treated with "less intense" chemotherapy is high. The addition of venetoclax to azacitidine did not translate into increased time at home. Future prospective studies should evaluate patient-centered outcomes, including time at home, to inform shared decision-making and drug development.

Introduction

The prognosis for older adults diagnosed with acute myeloid leukemia (AML) is poor. Historically, less than 40% of older adults (aged ≥60 years) survived 1 year from the time of diagnosis.[1,2] Recently, however, treatment decision-making paradigms have shifted with the addition of venetoclax to azacitidine, a prior standard therapy. This combination has been associated with superior remission rates and overall survival compared to azacitidine alone.[3] Prior research has demonstrated that patients with AML prefer treatments that allow increased time at home.[4] In a national survey of patients with AML, most were willing to accept a reduction in remission rates in exchange for an increase in the amount of time spent at home, although preferences for treatment outcomes varied.[5] An accurate understanding of the amount of time patients can anticipate spending at home is therefore critical to inform patient-centered treatment decisions for older adults with AML.

Descriptions of patients' time at home and treatment burden in the setting of advanced solid tumors have recently been published.[6,7] However, no study has adequately described the amount of time older patients spend at home while receiving therapy for AML. To address this knowledge gap, we aimed to quantify the amount of time older patients with AML spend at home and the amount they spend engaged in AML-related care with initiation of first-line azacitidine- or venetoclax-containing regimens.

Methods

Setting and patients

We queried records from University of North Carolina (UNC) Health to identify adults aged ≥60 years diagnosed with AML from 2015-2020. Those receiving first-line azacitidine and/or venetoclax were included. Records from 12 other health systems were available via electronic health data exchanges. Individuals receiving oncology care not reflected in available records were excluded. The UNC institutional review board approved the protocol.

Demographic and clinical variables

Demographic variables included age, race, sex, marital status, employment, and area-level measures (rurality[8] and median household income[9]). Driving times/distances to clinical encounters from patients' addresses were calculated via the Google Maps Application Program Interface (Google, LLC, Mountain View, CA, USA).[10] Clinical variables included disease risk according to European LeukemiaNet (ELN) 2017 criteria[11] and dates of diagnosis, death/last follow-up, and all clinic/emergency department/inpatient encounters.

Outcomes

The primary outcome was proportion of days at home (PDH),[6,7,12] defined as the number of days subjects were not engaged in cancer-related care divided by total follow-up days. Individuals were deemed "engaged in care" if hospitalized (for any cause), seen in an emergency department (for any cause), or seen in an oncology/infusion clinic. Outpatient visits in non-oncology settings were not counted as engaged in cancer-related care. Counting began at diagnosis, with censoring at the end of 2020.

Time commitment was also quantified via visit durations, calculated from check-in/check-out timestamps. Only appointments at UNC Health were included, as timestamps were not available for other health systems.

Overall survival was calculated via the Kaplan-Meier method. Treatment response was assessed, with individuals achieving a best response of complete remission, complete remission with incomplete hematologic recovery, or a morphological leukemia-free state being considered to have achieved remission.[11]

Analysis

Descriptive statistics are provided as medians and interquartile ranges (IQR) or frequencies and percentages. Associations between patients' characteristics and treatment regimens were assessed via modified Poisson models and characterized using relative risks. Cox proportional hazards models were used to examine associations between overall survival and demographic, disease, and treatment variables. Remission was used as a time-varying covariate in a Cox proportional hazards model to assess association between remission and survival. Competing risks analysis was used to analyze the association between baseline characteristics and cumulative incidence of remission while adjusting for deaths. Paired *t*-tests were used to evaluate the impact of remission on pre- and post-remission time at home among those who entered remission. Median visit durations were stratified by treatment group with hypothesis testing via Wilcoxon rank-sum.

PDH was evaluated in terms of total PDH over the entire study period and on a monthly (30 days) basis. For monthly analyses, only patients surviving the entirety of a particular month were included in that month's total. PDH was described via summary statistics for the overall cohort and stratified by categorical variables. Associations between PDH and baseline characteristics were evaluated via linear regression models. Regression models were adjusted for the log of duration of follow-up, and adjusted means are presented. Adjusted mean PDH values presented in this analysis were evaluated at the average follow-up time of 8.6 months. A multivariable linear regression model with distance from UNC Medical Center, age, ELN risk, and adjustment for duration of follow-up was performed to further characterize these associations.

Results

Demographics

We identified 372 individuals aged ≥60 years with a new diagnosis of AML treated within the UNC Health system from 2015 to 2020. Of these, 137 received azacitidine and/or venetoclax as first-line therapy. Twenty-four individuals were excluded because of incomplete records, yielding a final cohort of 113 patients.

The median age of these 113 individuals was 73 years (range, 61-95 years), with the majority (51.3%) of patients being between 70 and 79 years old (Table 1). The majority of the cohort was white (80.4%), and 56.6% were male. Most were retired or otherwise not currently employed (89.6%). Most were living with a spouse or long-term partner (66.4%) and had health insurance (89.4%). The median distance from home address to the UNC Medical Center was 42.3 miles (IQR, 27-93 miles).

Disease and treatment

ELN risk category was favorable for 8.1%, intermediate for 30.6%, and adverse for 61.3% of the cohort (Table 1). Patients received azacitidine plus venetoclax combination therapy (51.3%), azacitidine monotherapy (38.9%), and other venetoclax-containing regimens (9.7%) as first-line treatment. Baseline demographic covariates and ELN risk were similar across therapy groups (*P* for all associations >0.05) except that there were more individuals aged 80-

89 years in the azacitidine plus venetoclax group compared to the azacitidine monotherapy group (27.6% *vs.* 9.1%, respectively; *P*=0.036). Treatment was initiated in an inpatient setting for 10.9% of individuals in the azacitidine plus venetoclax group and for 0% of the azacitidine monotherapy group.

Table 1. Demographic and disease characteristics of older adults with acute myeloid leukemia receiving azacitidine and/or venetoclax.

Variable	All patients (N=113)	AZA monotherapy (N=44)	AZA+VEN (N=58)	*P**
Demographics				
Age group, N (%)				
60-69 years	26 (23.0)	12 (27.3)	11 (19.0)	(reference)
70-79 years	58 (51.3)	24 (54.5)	30 (51.7)	0.55
80-89 years	**24 (21.2)**	**4 (9.1)**	**16 (27.6)**	**0.036**
≥90 years	5 (4.4)	4 (9.1)	1 (1.7)	0.34
Race, N (%)				
White	90 (80.4)	34 (79.1)	47 (81.0)	(reference)
Black or African-American	19 (17.0)	8 (18.6)	10 (17.2)	0.85
Other	3 (2.7)	1 (2.3)	1 (1.7)	0.83
Sex, N (%)				
Female	49 (43.4)	20 (45.5)	25 (43.1)	0.81
Male	64 (56.6)	24 (54.5)	33 (56.9)	(reference)
Employment status, N (%)				
Not employed or retired	86 (89.6)	33 (91.7)	46 (88.5)	(reference)
Employed or self-employed	10 (10.4)	3 (8.3)	6 (11.5)	0.59
Marital status, N (%)				
Not partnered	37 (33.6)	16 (38.1)	21 (30.9)	0.38
Partnered	73 (66.4)	26 (61.9)	47 (69.1)	(reference)
Insurance status, N (%)				
Uninsured	12 (10.6)	6 (13.6)	5 (8.6)	0.47
Insured	101 (89.4)	38 (86.4)	53 (91.4)	(reference)
Rurality, N (%)				
Rural	5 (4.5)	1 (2.3)	4 (6.9)	0.17
Urbanized area	9 (8.1)	5 (11.6)	4 (6.9)	0.36
Urbanized cluster	97 (87.4)	37 (86.0)	50 (86.2)	(reference)
Household income quartile, N (%)				
First (lowest income)	28 (25.5)	10 (23.3)	16 (28.1)	(reference)
Second	28 (25.5)	14 (32.6)	10 (17.5)	0.17
Third	29 (26.4)	8 (18.6)	16 (28.1)	0.71
Fourth (highest income)	25 (22.7)	11 (25.6)	15 (26.3)	0.78
Disease and treatment				
First-line treatment, N (%)				
Azacitidine	44 (38.9)	44 (100)	---	---
Azacitidine + venetoclax	58 (51.3)	---	58 (100)	---
Venetoclax + other medication	11 (9.7)	---	---	---
ELN 2017 risk, N (%)				
Favorable	9 (8.1)	3 (7.1)	6 (10.3)	0.50
Intermediate	34 (30.6)	13 (31.0)	19 (32.8)	0.75
Adverse	68 (61.3)	26 (61.9)	33 (56.9)	(reference)

AML: acute myeloid leukemia; AZA: azacitidine; VEN: venetoclax; ELN: European LeukemiaNet. Missing data not available in records: race (n=1 subject), employment status (n=17), marital status (n=3), rurality (n=2), household income (n=3), ELN risk (n=2). *Comparison between categorical variables assessed via the χ^2 test. Statistically significant result shown in bold.

Response to treatment and survival

Among the full cohort, 34.5% of patients achieved remission (complete remission, complete remission with incomplete hematologic recovery, or a morphological leukemia-free state). The 6-month competing risk-adjusted event rate of remission was 0.31. Higher remission rates were observed among those receiving azacitidine plus venetoclax (6-month competing risk-adjusted event rate 0.50, unadjusted 58.9%) than among those receiving azacitidine alone (6-month competing risk-adjusted event rate 0.10, unadjusted 9.5%) (hazard ratio [HR]=7.50, 95% confidence interval [95% CI]: 2.76-20.40, *P*<0.001) (*Online Supplementary Table S1*). Increased distance from the UNC Medical Center was associated with lower remission rates in these competing risk-adjusted analyses (HR=0.93 for every 10 additional miles away, 95% CI: 0.87-0.997, *P*=0.042). No other factors, including demographic variables and ELN risk category, were associated with having achieved remission (*P* for all associations >0.05).

The median overall survival for the full cohort was 7.7 months (95% CI: 3.8-10.9) and was similar across therapy groups (*Online Supplementary Table S2*). There were also no significant associations observed between overall survival and ELN risk, race, sex, or other demographic variables (*P* for all associations >0.05). When evaluated as a time-varying covariate, having achieved remission was associated with superior survival, with a hazard ratio for death of 0.56 (*P*=0.043), indicating achieving remission was associated with longer survival.

Proportion of days at home

Over the full follow-up period, the mean PDH was 0.58 (95% CI: 0.54-0.63) with a median of 0.63. PDH was positively associated with length of follow-up, with a statistically significant association between PDH and log length of follow-up time (regression coefficient 0.15, 95% CI: 0.12-0.17, *P*<0.0001). After adjusting for log follow-up time, the adjusted mean PDH was 0.67 (95% CI: 0.63-0.71). PDH was similar among those with adverse-risk (adjusted mean 0.65), intermediate-risk (0.69, *P*=0.34), and favorable-risk AML (0.64, *P*=0.81). PDH did not differ significantly among therapy groups: azacitidine plus venetoclax (adjusted mean 0.68), azacitidine alone (0.66, *P*=0.64 when compared to azacitidine plus venetoclax), and other venetoclax-containing regimens (0.65, *P*=0.65). There was also no significant difference in the proportion of days spent as inpatients or in outpatient clinics between patients in the azacitidine and azacitidine plus venetoclax groups (*Online Supplementary Table S3*).

Patients who had longer driving distances to UNC spent more time engaged in oncologic care, and thus less time at home (regression coefficient for PDH -0.0008 per mile, 95% CI: -0.0013 to -0.0002, *P*=0.011). Patients who lived farther than 50 miles from UNC spent approximately 7% more days (amounting to 2.1 more days per month) engaged in oncology care than those who lived closer (adjusted mean PDH 0.63 *vs*. 0.70 for those <50 miles, *P*=0.04). Patients who lived farther from UNC spent more days in hospital (26% of all follow-up days spent as inpatients for those living ≥50 miles *vs.* 20% for those living <50 miles from UNC). After adjusting for age, ELN risk, and median household income, the association between increased distance from the medical center and decreased PDH remained but was no longer statistically significant (*P*=0.08). There was no association seen between distance from UNC and chemotherapy regimen received. Other than driving distance, no individual covariate (including patient's age) had a significant association with PDH when adjusted for length of follow-up (all *P*>0.05).

When evaluated on a month-by-month basis, the PDH rose over time among survivors (Table 2). For example, among patients who survived the full month, the mean PDH was 0.51 (95% CI: 0.47-54, n=105) in month 1 following diagnosis, 0.64 (95% CI: 0.58-0.70, n=75) in month 3, and 0.77 (95% CI: 0.72-0.82, n=57) in month 6. This pattern is demonstrated in Figures 1 and 2, which summarize person-days at home *versus* person-days engaged in care for 12 months following diagnosis, including contributions of person-days from those who did not survive the full month. Early in follow-up, most care days consisted of inpatient hospitalization (28% of all person-days in the first month), with a decline in hospitalization burden over the ensuing 12 months among survivors (4% of all person-days in month 12). The proportion of days seen in a clinic remained relatively constant over the year following diagnosis (in a range of 16-21% of all person-days). Patterns in monthly PDH were similar between those receiving azacitidine monotherapy and those receiving azacitidine plus venetoclax (Figure 3, Table 2). There was no significant difference in types of visits between those receiving azacitidine monotherapy and those receiving azacitidine plus venetoclax. The rate of early hospitalizations (days hospitalized during the first 30 days following diagnosis) was also similar between recipients of azacitidine monotherapy and azacitidine plus venetoclax, despite the higher percentage of patients within the azacitidine plus venetoclax group initiating therapy while admitted. Among the 38 patients who entered remission, more days were spent at home following remission than prior to remission. For this group, 53% (95% CI: 46-60%) of days prior to remission were spent at home compared to 72% (95% CI: 66-78%, *P*<0.0001) of days after remission.

Time spent in a clinic

For visits occurring within the UNC Health system, the median duration of oncology provider visits was 123.3 minutes (IQR, 80.1-185.2 minutes) (Table 3). The median duration of an infusion encounter was 169.3 minutes (IQR,

Table 2. Proportion of person-days spent at home by month from diagnosis among older adults with acute myeloid leukemia, stratified by first-line therapy.

Month	Full cohort (N=113)		AZA monotherapy (N=44)		AZA+VEN (N=58)		Other VEN-containing regimen (N=11)	
	N	Mean PDH (95% CI)	N	Mean PDH (95% CI)	N	Mean PDH (95% CI)	N	Mean PDH (95% CI)
1	105	0.51 (0.47-0.55)	38	0.54 (0.48-0.61)	56	0.47 (0.41-0.53)	11	0.62 (0.47-0.76)
2	89	0.57 (0.52-0.62)	32	0.60 (0.52-0.68)	47	0.57 (0.51-0.63)	10	0.47 (0.28-0.65)
3	75	0.64 (0.58-0.70)	28	0.63 (0.54-0.72)	39	0.67 (0.58-0.75)	8	0.56 (0.30-0.83)
4	66	0.70 (0.65-0.76)	26	0.71 (0.62-0.79)	34	0.69 (0.60-0.78)	6	0.79 (0.56-1.02)
5	59	0.76 (0.71-0.81)	23	0.77 (0.71-0.84)	32	0.73 (0.65-0.81)	4	0.86 (0.59-1.12)
6	57	0.77 (0.72-0.82)	23	0.76 (0.70-0.82)	31	0.78 (0.70-0.86)	3	0.73 (0.45-1.02)
7	54	0.76 (0.71-0.82)	21	0.80 (0.73-0.87)	30	0.75 (0.66-0.84)	3	0.66 (0.00-1.32)
8	48	0.75 (0.68-0.82)	17	0.70 (0.61-0.79)	28	0.78 (0.68-0.88)	3	0.73 (0.30-1.17)
9	41	0.76 (0.69-0.82)	16	0.78 (0.71-0.86)	23	0.76 (0.66-0.86)	2	0.55 (0.34-0.76)
10	38	0.78 (0.70-0.85)	16	0.81 (0.72-0.90)	21	0.77 (0.65-0.89)	1	0.53 (---)
11	35	0.76 (0.68-0.84)	16	0.77 (0.66-0.89)	18	0.75 (0.62-0.87)	1	0.63 (---)
12	32	0.77 (0.69-0.85)	16	0.76 (0.65-0.88)	15	0.78 (0.64-0.93)	1	0.70 (---)

AZA: azacitidine, VEN: venetoclax, PDH: proportion of days at home, 95% CI: 95% confidence interval. Number of subjects (N) reflects number of individuals in each group surviving at the end of the respective month. PDH for each month was calculated as the proportion of person-days not engaged in oncologic care among these survivors.

93.8-307.7) and the median duration of a laboratory encounter was 43.3 minutes (IQR, 25.7-83.3). Receipt of azacitidine plus venetoclax was associated with longer clinic visits (median 127.9 *vs*. 112.9 minutes, *P*<0.001) and infusion visits (median 194.3 *vs*. 132.5 minutes, *P*<0.001) compared to receipt of azacitidine monotherapy. Patients spent a median of 66 minutes (IQR, 30-110 minutes) in the two-way drive time to/from clinic for each day with an appointment. The median drive time was shorter among those receiving azacitidine plus venetoclax monotherapy than among those receiving azacitidine monotherapy (median 50 *vs*. 66 minutes, *P*<0.0001).

Discussion

The recent development of multiple novel effective chemotherapeutic agents has expanded treatment options for older adults with AML. Increasingly, patients are empowered to participate in a shared decision-making process that considers their values and preferences with respect to the anticipated outcomes of treatments. Time spent at home represents a critical but under-reported outcome of cancer therapies.[7,13,14] We have previously shown that patients with AML are willing to sacrifice remission rates to achieve time at home.[5] Currently, clinical trials in AML do not routinely capture, nor report, the time at home experienced by patients following chemotherapy. Reliably capturing this outcome in routine care and clinical trials will enable rational, data-driven shared decision-making regarding chemotherapy.

Here, we demonstrate the feasibility of quantifying the time at home older patients achieve following first-line therapy and report, for the first time, a comparison between current treatments. Older AML patients receiving azacitidine, azacitidine plus venetoclax, or other venetoclax-containing regimens spent an average of 42% of their days engaged in oncology care. This time commitment was observed for AML patients despite patients receiving "less intensive" chemotherapy compared to intensive induction chemotherapy that often necessitates a lengthy period as an inpatient. Even among survivors 1 year from diagnosis, 24% of days were devoted to their cancer treatment, reflecting the need for ongoing close monitoring and potential transfusion support among those with AML. These data are similar to those from a smaller group of patients receiving hypomethylating agents in an Australian study published prior to the approval of venetoclax.[12]

The time commitment faced by patients with AML is striking when compared to that by patients with advanced solid cancers. Rocque and colleagues reported that women with newly diagnosed metastatic breast cancer spent 7 to 10% of days in the 3 months following diagnosis engaged in oncology care.[6] Among adults with newly di-

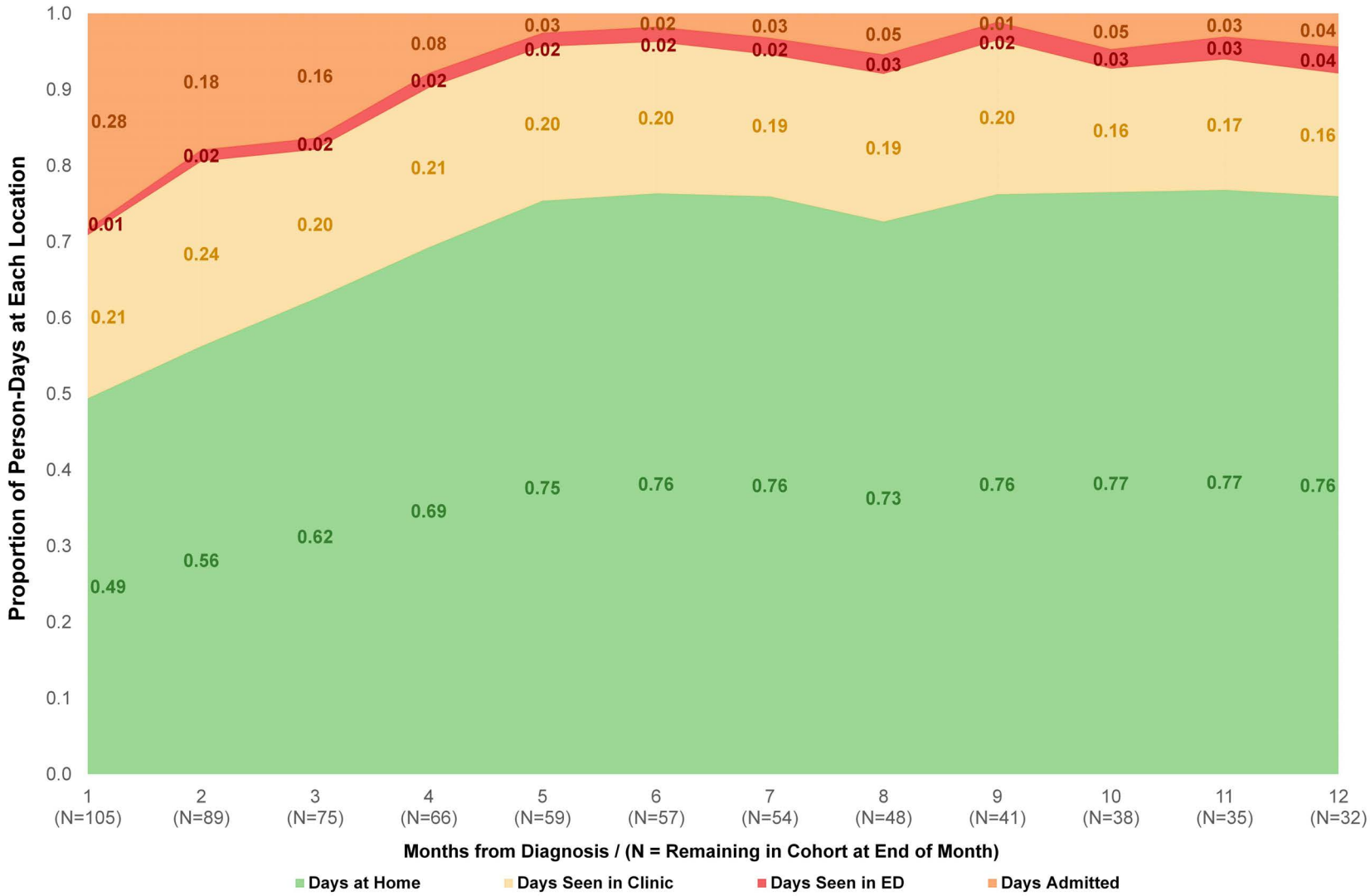

Figure 1. Proportion of person-days spent at home and engaged in cancer care among older adults with acute myeloid leukemia treated with azacitidine and/or venetoclax. The figure displays the person-days either at home (not engaged in care) or seen in each venue (clinic, emergency department, or hospital) among survivors. The proportion of days spent at home rose in the year following diagnosis, with a decline in the proportion of care-days consisting of inpatient hospitalization over the same period. Values of the proportion of days at home in this figure differ slightly from monthly proportion values (PDH) in Table 2, as the PDH values in Table 2 were calculated only among survivors for a full month, whereas this figure reflects person-day contributions from individuals who did not survive the entirety of the respective month. ED: emergency department.

agnosed metastatic pancreatic cancer, who face a similarly poor prognosis as that of older adults with AML, Bange and colleagues described a cohort median of 10% of days devoted to cancer care following diagnosis.[7] Older patients with AML spend over four times as many days engaged in oncology care as these patients. Time at home for patients with other hematologic malignancies has not been routinely reported outside of the context of end-of-life or hospice care.[15]

In a phase III trial of adults deemed ineligible for intensive chemotherapy, the addition of venetoclax to azacitidine increased remission rates and improved median overall survival from 9.6 to 14.7 months.[16] In the current study, patients receiving azacitidine plus venetoclax had superior remission rates; however, this did not translate into a greater proportion of time at home for this group in aggregate. Patients receiving venetoclax also had longer clinic visits and longer visits for infusion, potentially related to a greater need for transfusion support. These data suggest that the clear benefit seen from the addition of venetoclax in clinical trials may not result in a substantial improvement in time spent at home for patients.

This finding was surprising as we anticipated that remission would translate into prolonged survival, fewer clinic visits, fewer visits to the infusion center, and fewer admissions. We therefore performed a *post hoc* analysis looking at time at home before and after remission. Among the minority of individuals who entered remission, more days were spent at home after remission than prior to achieving remission. However, in aggregate, remission status did not correlate with the overall PDH throughout follow-up. Assessment of this relationship is complicated, as multiple factors may contribute to increasing time at home further from diagnosis, including achieving remission, better management of an individual's symptoms further into treatment, and early deaths of the sickest individuals who may account for the greatest time engaged in care. Survival in our azacitidine plus venetoclax cohort was also shorter than that described in some other real-world-data analyses[17,18] which likely resulted in decreased time at home achieved by these patients. However, similar survival results have been described in other retrospective

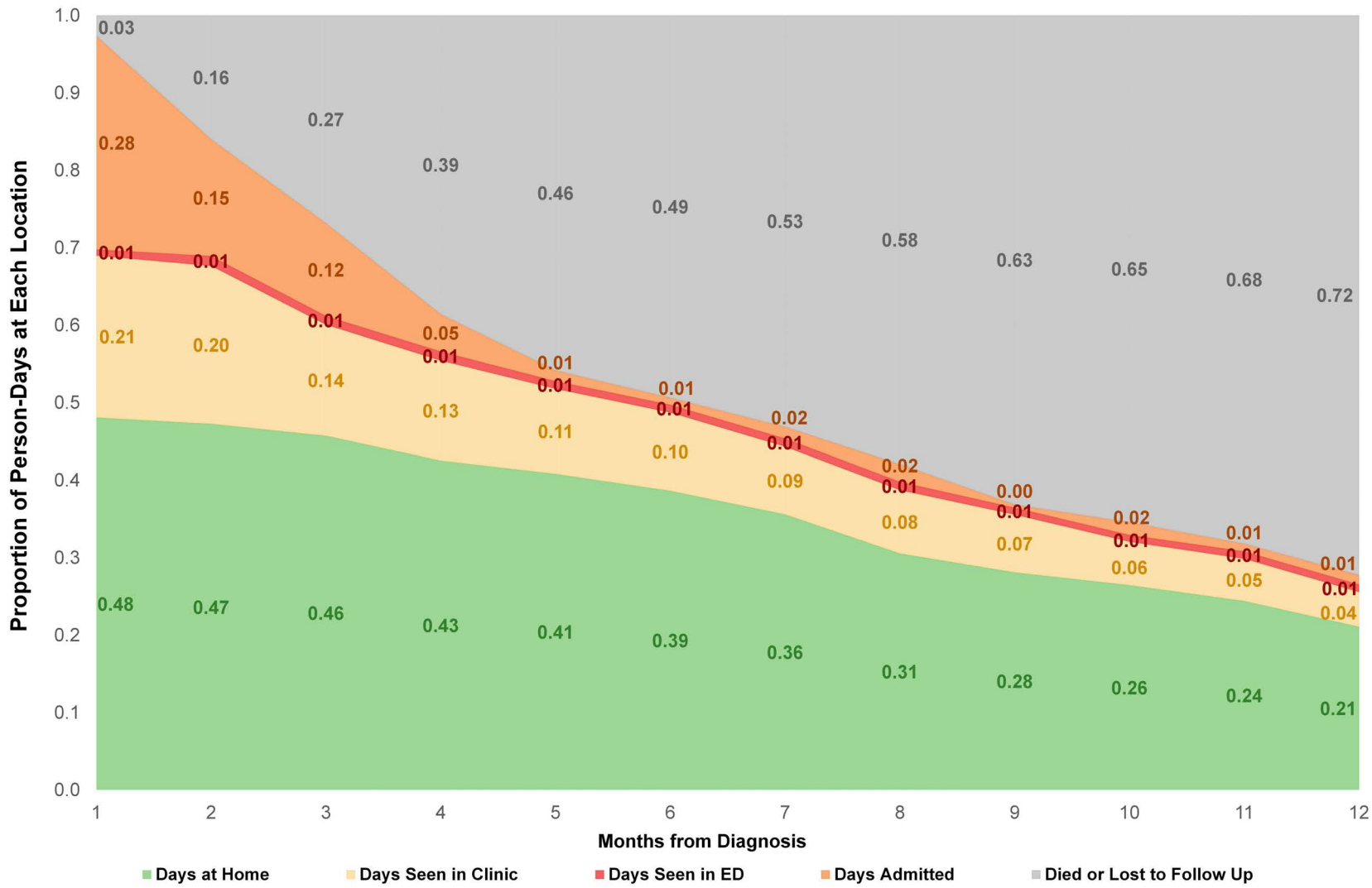

Figure 2. Proportion of person-days spent at home and engaged in cancer care among older adults with acute myeloid leukemia including decedents and those lost to follow-up. This figure displays the same data as in Figure 1, with the addition of individuals who died or were lost to follow-up. Values of the proportion of days at home in this figure differ slightly from monthly proportion values (PDH) in Table 2, as the PDH values in Table 2 were calculated only among survivors for a full month, whereas this figure reflects person-day contributions from individuals who did not survive the entirety of the respective month. ED: emergency department.

cohorts.[19] Furthermore, although we examined multiple variables when comparing therapies, confounding by other factors may be present. In particular, we did not quantify comorbidity or frailty other than by age alone. Adjusting for these factors may have altered our findings, especially for patients between the age of 80 and 89 years, who were over-represented in the azacitidine plus venetoclax cohort. Additionally, developing expertise in optimizing delivery of a complicated treatment regimen such as azacitidine plus venetoclax requires time and experience. As oncologists and cancer centers become more familiar with delivering venetoclax-based regimens, time at home may improve.

No significant differences were noted in the PDH following AML diagnosis based on age, race, sex, or disease risk according to ELN criteria in our cohort. We did observe a significantly lower PDH among those living farther from our primary referral hospital and comprehensive cancer center. This difference is partially attributable to more inpatient days experienced by patients living farther from the cancer center, a care-delivery pattern that has been described in the setting of other malignancies.[10] The association between increased distance from the medical center and decreased PDH was no longer significant when adjusted for age, ELN risk, and median household income, possibly related to a degree of collinearity between driving distance and patients' age.

This study has several additional limitations. Although records were captured from several health systems, this study includes only data from patients who were seen at least once at a single academic referral center. Consequently, the results may not be generalizable to adults treated entirely in community settings in which the burden of care may be different. Furthermore, the need for complete follow-up records to evaluate PDH may have biased our sample toward individuals with shorter survival and less time at home, as older adults with more stable disease may have experienced greater co-management with a local oncologist outside of the captured records. Similarly, we could not readily quantify days spent in inpatient rehabilitation facilities or nursing facilities, as these stays were not fully reflected in the medical records. A claims-based approach may allow this component of care burden to be assessed more fully. No data have been published

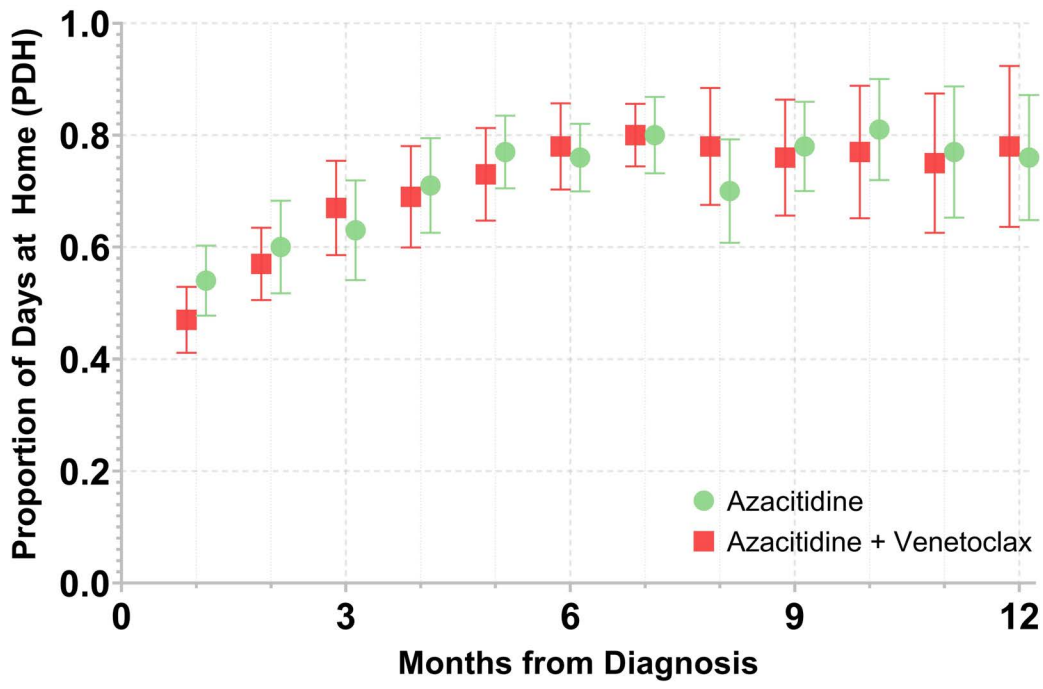

Figure 3. Proportion of person-days spent at home among older adults with acute myeloid leukemia treated with azacitidine with or without venetoclax in the year following diagnosis. Among survivors in each group, the proportion of days spent at home (and not engaged in oncologic care) rose over time, with generally similar proportions observed in each treatment group at each time point. Adjacent values for the two treatment groups are contemporaneous and have been offset for legibility. Error bars reflect 95% confidence intervals.

on the relative value patients with AML place on the specific health states in this study (e.g., clinic visits, infusion visits, hospitalization). We were, therefore, unable to adjust the reported time at home for perceived quality of this time to patients. Studies identifying the relative value of these health states would be informative to allow for quality-adjustment of the reported findings.

This study represents an important step in understanding the experience of older adults with AML. A patient's time is a finite resource that is increasingly consumed by complex cancer care. When compared to those with other advanced cancers, older adults with AML face a markedly increased burden on their time due to oncology care. The recent therapeutic paradigm shift in AML is an opportunity to leverage these remarkable advancements into meaningful improvements in patients' lives. Future prospective studies should evaluate time at home as an endpoint as part of a broader strategy to incorporate patient-centered outcomes into drug development and shared decision-making strategies. Additionally, interventions directed at increasing time at home, such as utilization of virtual visits/telehealth or clustering of care, are critically needed to maximize patients' time at home. Early studies of increased utilization of telehealth in the context of the COVID-19 pandemic suggest patients often find this care-delivery approach satisfactory.[14] More intensive outpatient care models that support patients' time at home have also been described,[20] including all-outpatient "intensive" in-

Table 3. Time spent on oncology clinic appointments among older adults with acute myeloid leukemia treated with azacitidine and/or venetoclax.

	Full cohort (N=113)			AZA monotherapy (N=44)			AZA+VEN (N=58)			
	Median duration, minutes (IQR)	Visits (total number)	Visits per patient (mean)	Median duration, minutes (IQR)	Visits (total number)	Visits per patient (mean)	Median duration, minutes (IQR)	Visits (total number)	Visits per patient (mean)	*P*‡
Oncology provider*	123.3 (80.1-185.2)	2,110	18.7	112.9 (73.2-165.2)	714	16.2	127.9 (85.7-192.2)	1,006	17.3	<0.0001
Infusion	169.3 (93.8-307.7)	5,539	49.0	132.5 (77.1-237.1)	2,083	47.3	194.3 (104.8-343.1)	2,606	44.9	<0.0001
Laboratory	43.3 (25.7-83.3)	1,878	16.6	58.9 (29-113.8)	573	13.0	39.3 (24.6-71.8)	1,216	21.0	<0.0001
Driving† (two-way)	66 (30-110)	5,639	50.3	66 (24-110)	2,392	55.6	50 (36-152)	2,717	46.8	<0.0001

AZA: azacitidine; VEN: venetoclax. Median duration based on data from the University of North Carolina (UNC) Health system only. Numbers for total visits include data from UNC and other health systems (for provider visits and infusion visits) or UNC Health system only (for laboratory visits). *Oncology provider visits include encounters with physicians, nurse practitioners, physician assistants, or clinical pharmacist practitioners. †Drive times are calculated to the nearest minute with typical traffic and reflect time to/from the location of the clinical encounter, starting from the patients' home addresses. One patient from the azacitdine group was excluded from the drive-time calculations because of a documented home address outside of North Carolina/bordering states. ‡*P* values reflect comparisons of duration of visits or drive time between therapy groups via the Wilcoxon rank-sum test.

duction strategies for AML.[21] Whenever possible, such approaches to increase patients' time at home should be implemented as overall survival remains tragically short for older patients with AML.

Disclosures

None of the authors has a relevant conflict of interest. CEJ reports research funding (Conquer Cancer) outside the submitted work. ALB reports research funding (Carevive, Jazz Pharmaceuticals) and honoraria (Servier Pharmaceuticals) outside the submitted work. LAC reports research funding (Alexion Pharmaceuticals, Machaon Diagnostics) outside the submitted work. MCF reports research funding (Bellicum Pharmaceuticals, Macrogenics, Rafael Pharmaceuticals) and consulting (Macrogenics, Daiichi Sankyo, Agios) outside the submitted work. DRR reports research funding (Conquer Cancer, Palliative Care Research Cooperative Group) outside the submitted work.

Contributions

CEJ and DRR conceptualized the study and identified the study cohort; CEJ and KEB extracted data from charts; CEJ, HMH, AMD, and DRR designed the data analysis; HMH and AMD performed the data analysis; CEJ, KEB, ALB, LAC, MCF, and DRR contributed to interpretation of the results; CEJ drafted the manuscript. All authors reviewed the final manuscript.

Funding

The project described was supported by the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH) through Grant Award Number UL1TR002489 and by a National Research Service Award Post-Doctoral Traineeship from the Agency for Healthcare Research and Quality sponsored by The Cecil G. Sheps Center for Health Services Research at The University of North Carolina at Chapel Hill through Grant Award Number T32-HS000032. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Data-sharing statement

Data can be requested via e-mail to the corresponding author.

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