Low-intensity induction in acute myeloid leukemia. Always in the patients' best interest?

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The amount of time patients with acute leukemia spend in a healthcare setting is an aspect that is frequently ignored. There are several ways to measure patients' healthcare engagement. These range from simply calculating the percentage of days patients interact with healthcare, to calculating the percentage of hours spent in a healthcare setting to even adding commuting time. When evaluating low-intensity therapies for acute myeloid leukemia (AML), emphasis is usually placed on inpatient *versus* outpatient management of patients. In this issue of *Haematologica*, Jensen and colleagues address the issue of the amount of time patients with AML treated with low-intensity therapy spend in a healthcare setting.[1]

The investigators calculated the proportion of days spent at home (PDH) for patients with AML treated with azacitidine ± venetoclax across the University of North Carolina Health System using electronic health records. PDH was calculated as the number of days patients were not engaged in cancer care divided by the total number of days. Days engaged in cancer care included admission to a hospital for any reason, emergency department visits for any reason, and oncology/infusion clinic appointments. The study included 113 patients with 44 and 54 patients receiving azacitidine and azacitidine + venetoclax, respectively. The overall median PDH was 0.63 with an increase in PDH over time. The PDH was 51%, 64% and 77% for patients surviving at month 1, 3 and 6. To put this in perspective, the PDH is 97% for patients with stage I-III breast cancer[2] and 88% for patients with stage I lung cancer[3] (Figure 1). Jensen *et al.* found no difference between patients who did or did not receive venetoclax, between patients who did or did not achieve remission or between those who had good *versus* poor prognostic factors. However, these comparisons may not be accurate due to the small sample size and different characteristics of the patients. In addition they are less clinically relevant given that azacitidine + venetoclax is now the standard of

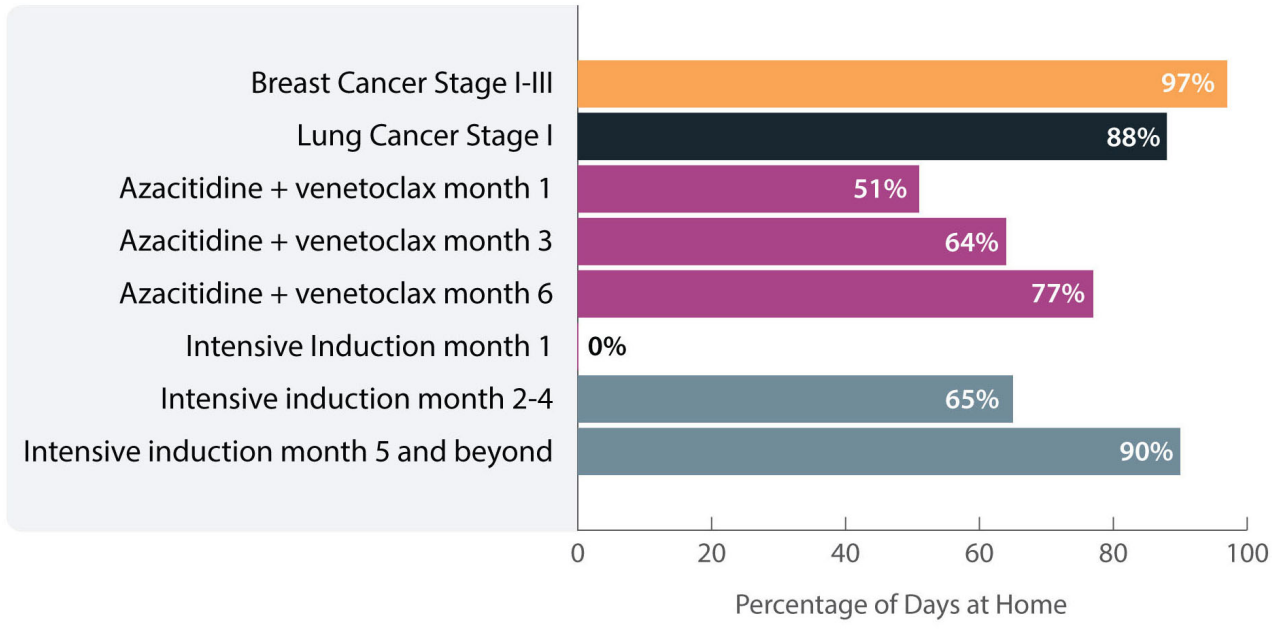

Figure 1. Percentage of days at home for patients with solid cancers or acute myeloid leukemia during various stages of low- or high-intensity treatment. The percentage for breast cancer patients is the median over 18 months. The percentage for lung cancer patients is the median in the first 60 days. The percentage for intensive induction is an estimate.

care for all patients with AML. In fact, the study provides reassurance that adding venetoclax to the treatment regimen does not decrease PDH.

Inpatient hospital stay increased with increasing distance to the hospital. This is not an unexpected finding as we are more likely to admit patients who live farther away and do not have adequate supportive care close to their homes.

The more important comparison which is not reported here is the difference between high-intensity (e.g., 7+3) and low-intensity (e.g., azacitidine + venetoclax) therapy. In most institutions,[4] all patients receiving intensive induction chemotherapy are admitted to the hospital for approximately 4 weeks. This is followed by three cycles of consolidation chemotherapy with supportive care (approximately 3-5 days of chemotherapy, with visits for laboratory checks and possible transfusions 3 times per week). If patients proceed to oral maintenance therapy after that the frequency of laboratory checks and office visits would range from 2-4/month. Based on this scenario, the estimated PDH for patients receiving intensive induction chemotherapy not proceeding to allogeneic hematopoietic stem cell transplantation is 0%, 65% and 90% for month 1, months 2-4 and month 5 thereafter, respectively (Figure 1).

So, azacitidine + venetoclax is clearly a step in the right direction to increase PDH, especially during induction. Following induction and for patients who are in remission we need to think of ways to decrease the amount of time patients spend in the healthcare setting. Patients with AML engage in cancer care for multiple reasons: inpatient hospital stays, outpatient treatment, outpatient clinic visits, and outpatient supportive care appointments

To reduce inpatient hospital stays, intensive induction chemotherapy can be administered in the outpatient setting. This approach is feasible in a select group of patients and in select institutions that can provide intensive outpatient monitoring and support. In such a setting, less than half of patients are eligible for outpatient intensive therapy. In addition, patients still spend a considerable number of days evaluated in a healthcare setting for laboratory checks and possible transfusions.[5]

For low-intensity therapy, home administration of chemotherapy, such as subcutaneous cytarabine or possibly subcutaneous azacitidine, would increase PDH. The development of oral substitutes would also increase PDH.

To reduce outpatient supportive care visits, home monitoring of laboratory parameters[6] and home transfusions are possible. Logistically these are difficult as they require significant resources including home nursing, early and systematic sample collection and close outpatient monitoring.[7] However, technology for remote visits, remote blood collection and vital sign monitoring[8] is an important under-implemented tool that has the potential to significantly increase PDH, reduce costs and improve patients' quality of life.

Disclosures

EA has acted as a consultant for Abbvie.

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