The Pharmacist Activist

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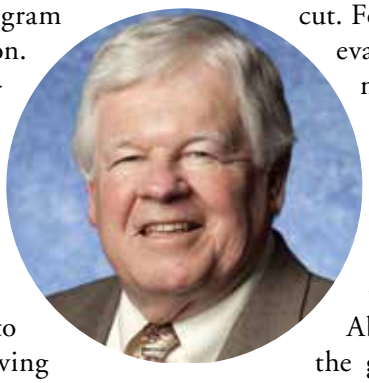
Editorial

Time Out!*

My primary symptoms were fatigue and shortness of breath upon exertion that continued to worsen. A visit to my family physician in mid-April revealed abnormalities in my electrocardiogram (EKG) and a low hemoglobin concentration. I was referred to my cardiologist who ordered an echocardiogram and a stress test (that was very brief because of my acute shortness of breath). The results suggested probable blockage of blood vessels, a need for cardiac catheterization, and an expectation that I would need to have one or more stents inserted. My cardiologist responded to the results of the catheterization by observing that he was "thrilled but surprised." He was thrilled because the procedure did not identify any problem associated with my heart or blood vessels, but surprised because he expected otherwise. This was great news but not an explanation for my worsening symptoms, and an appointment with a hematologist was scheduled.



Several days later I experienced a minor cut while shaving with bleeding that would typically stop within seconds. However, the bleeding did not stop and continued for 10 minutes, 15 minutes…, and still did not stop. My wife Sue indicated that we should go to the Emergency Department of our local hospital but I did not feel that was necessary, primarily because I thought we would be viewed as over-reacting for going to the Emergency Department for a shaving cut. Fortunately, Sue's better judgment prevailed. My evaluation revealed a further reduction in the hemoglobin concentration and other hematologic abnormalities. I was admitted to the hospital and the hematologist ordered additional blood studies and a bone marrow biopsy. A diagnosis was determined – acute myeloid leukemia (AML). The hematologist informed me that the best hospital to be treated for AML was the Abramson Cancer Center (established through the generous philanthropy of healthcare management leader and pharmacist Leonard Abramson) at the Hospital of the University of Pennsylvania (HUP), and insisted that I be admitted the next day.

HUP

Following admission to HUP, the diagnosis of AML was quickly confirmed. A treatment "team" with extensive expertise and experience met with me and thoroughly explained the treatment plan they were recommending. I was very impressed with the approach they took in discussing the treatment they proposed. They wanted Sue and me to thoroughly understand

it and to agree with it and approve it. We quickly agreed with the recommendations and I made the following observations:

1. I have a strong faith in God. To not agree with the proposed or another treatment plan would mean that my faith was not strong enough to believe that God could use this strategy to enable His will to be accomplished.

2. Although I have some knowledge about AML and the drugs used in treating it, I was fortunate to be under the care of a team of health professionals that had such extensive expertise that I had no questions about their recommendations and judgments, nor would I seek another opinion. I would note that the recommendations of the treatment team were in the context of the numerous uncertainties pertaining to the disease, patient risk factors, and the medications that make it impossible to predict treatment outcomes for an individual patient.

Induction chemotherapy was initiated that afternoon and, coupled with monitoring and the management of complications, I was hospitalized for more than 4 weeks. The ramifications of the disease and treatment resulted in much of my hospitalization being characterized by extreme fatigue and, at times, disorientation and confusion. Everything else, even reading and responding to emails, was put on hold.

Notwithstanding the inevitable challenges, I can't say enough about the excellent expertise and quality of the treatment and services provided by the health professionals, and the caring manner in which they provided them. These qualities were also exhibited by the support staff and I was impressed by how many of them had worked at HUP for many years.

Of special interest and importance to me was the fact that pharmacists, most of whom were my former students, were members of the treatment teams and had an important role in the recommendations and decisions regarding drug therapy. In my discussions with the physicians and nurses, it was a pleasure to hear how much they respected and valued the participation of the pharmacists as members of the team.

My hospitalization was anything but uneventful. In addition to the anticipated challenges presented by the disease and chemotherapy, I experienced unexpected events including a severe allergic reaction, an acute gout attack, impaired kidney function, and a twisted colon.

Discharge and readmissions

Following more than four weeks in the hospital, I was discharged to my home. However, three days later I experienced a fever and was readmitted to the hospital for treatment of an infection. Following a week of intravenous antibiotic therapy, I was discharged again. Three days later I again experienced a fever and was readmitted to the hospital. The infections were thought to be originating at the PICC line (peripherally inserted central catheter). A 7-day course of vancomycin via intravenous infusion was initiated and the PICC line was removed. Within four days the infection had cleared but it was considered important to complete the 7-day course of antibiotic therapy. However, there was another option that would avoid staying in the hospital for a longer period to receive vancomycin infusions. Linezolid (Zyvox) has a similar antibacterial spectrum as vancomycin and is effective following oral administration. Switching to linezolid should provide no change in the effectiveness of the antibiotic treatment and would permit earlier discharge from the hospital by as much as three days.

But there was another factor. My insurance coverage for medications requires prior authorization for the use of linezolid because of its cost (approximately $1,000 for the 6 tablets I would need). Prior authorization was requested and approved, but not for more than 24 hours after the request was initiated. Yet one more example of a broken prescription drug insurance system that would deny or delay the use of a drug that would avoid the much greater expense of several additional days of hospitalization.

I received the linezolid, was discharged from the hospital on a timely basis, and have been infection-free at home while experiencing significant improvement in my strength and mobility.

Treatment results

Following the completion of the initial chemotherapy, an appropriate interval of time is permitted to elapse and a bone marrow biopsy is then conducted to assess the effects of the treatment. The biopsy results provided the best news I could have hoped for – no evidence of leukemia cells! Approximately 3 weeks later, another bone marrow biopsy was performed and provided the same encouraging results. I am very thankful to report that I am now in remission! Because leukemia cells often recur, additional chemotherapy treatments (consolidation

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New Drug Review

Edoxaban tosylate monohydrate
(Savaysa – Daiichi-Sankyo)

Anticoagulant

New Drug Comparison Rating (NDCR) = 2
(significant disadvantages)
in a scale of 1 to 5 with 5 being the highest rating

Indications:
To reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation; for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) following 5-10 days of initial therapy with a parenteral anticoagulant.

Comparable drugs:
Apixaban (Eliquis), rivaroxaban (Xarelto), dabigatran (Pradaxa).

Advantages:
- Is administered once a day (compared with apixaban and dabigatran that are administered twice a day);
- Less likely to interact with other medications.

Disadvantages:
- May be less effective (is noninferior to warfarin shereas comparable drugs are more effective for certain indications);
- Should not be used in patients with a creatinine clearance greater than 95 mL/minute;
- Labeled indications are more limited (compared with apixaban and rivaroxaban that are also indicated for the prophylaxis of DVT in patients undergoing knee or hip replacement surgery);
- Treatment of DVT and PE should be preceded by parenteral anticoagulant therapy (compared with apixaban and rivaroxaban for which the recommendations do not include prior parenteral anticoagulation).

Most important risks/adverse events:
Contraindicated in patients with active pathological bleeding; risk of bleeding (risk factors include the concomitant use of other medications that may be associated with bleeding events (e.g., aspirin, antiplatelet agents, chronic use of nonsteroidal anti-inflammatory agents); risk of epidural or spinal hematomas in patients receiving neuraxial anesthesia or undergoing spinal puncture (boxed warning); discontinuation of treatment may increase the risk of thrombotic events (coverage with another anticoagulant should be strongly considered); concurrent use with rifampin should be avoided; renal function should be evaluated prior to initiating treatment (should not be used in patients with a creatinine clearance greater than 95 mL/minute).

Most common adverse events:
Clinically relevant non-major bleeding (9%), rash (4%), abnormal liver function tests (5%).

Usual dosage:
Patients with nonvalvular atrial fibrillation – 60 mg once a day; dosage should be reduced to 30 mg once a day in patients with a creatinine clearance of 15 to 50 mL/minute; in patients with DVT or PE, 60 mg once a day following 5 to 10 days of therapy with a parenteral anticoagulant; dosage should be reduced to 30 mg once a day in patients with a creatinine clearance of 15 to 50 mL/minute, in patients who weigh less than or equal to 60 kg, or patients who are taking certain concomitant P-glycoprotein inhibitors; if treatment must be discontinued for a reason other than pathological bleeding, coverage with another anticoagulant should be considered.

Product:
Tablets – 15 mg, 30 mg, 60 mg.

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therapy) are recommended to reduce the risk of recurrence, and I am tentatively scheduled to have two of these treatments.

The support system

Sue was at the hospital for most of every day and our children and their families visited frequently. They were a wonderful source of love and encouragement. Close friends brought Sue to the hospital many mornings and picked her up in the evenings to spare her from dealing with the traffic, parking, etc. as part of the 45-minute trip. Many prayers were offered on my behalf. I also received very kind and gracious messages from many friends, colleagues, and current and former students via cards, emails, and on the Caring Bridge website where my son provides updates regarding my status (www.caringbridge.org/visit/danhussar). These greetings have been a great source of encouragement and I appreciate them very much. I am not in a position to personally acknowledge the numerous communications I received. However, many of those who sent them receive *The Pharmacist Activist* and I hope that they will accept these comments as evidence of my deep appreciation.

Looking forward

The results of my initial chemotherapy are very encouraging but I am realistic in recognizing that the disease can return and have a very different outcome. Even more importantly, I have experienced an even greater appreciation for the value of my faith, and for the prayers, love, support, and encouragement provided by my family, friends, and many others whom I have had the privilege of coming to know.

This experience has been a "time out" during which I have had much more time to think about my priorities. I feel that God has more for me to do which will include showing greater support and encouragement for others with needs in the manner that they have been provided for me.

"The Lord is my strength and my shield;
my heart trusts in him and I am helped."
Psalms 28:7

Daniel A. Hussar

*The Pharmacist Activist *was not published in April, May, and June during this "time out." Publication resumes with this July issue.*

New Drug Review - *continued*

Comments:

Like apixaban and rivaroxaban, edoxaban is a factor Xa inhibitor, whereas dabigatran is a direct thrombin inhibitor and warfarin is a vitamin K antagonist. Warfarin is the only one of these anticoagulants for which a specific antidote (vitamin K) is currently available. In the clinical studies, edoxaban was determined to be noninferior to warfarin in reducing the risk of stroke and systemic embolism, and noninferior to warfarin with respect to recurrent venous thromboembolic events. The incidence of major bleeding (e.g., intracranial hemorrhage) was less with edoxaban compared with warfarin. Like the other new oral anticoagulants, edoxaban has not been studied in patients with mechanical heart valves or moderate to severe mitral stenosis, and it is not recommended in these patients.

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