The Pharmacist Activist

Volume 15, No. 17 • September 15, 2020

"I sought the Lord, and he answered me; he delivered me from all my fears." Psalm 34:4

Editorial

Coronavirus Conundrum: Part 3*

We have learned enough to remove mandates/restrictions. Let's open up and go back to work and school!

(*Note: Parts 1 and 2 are in the May 1 and May 15 issues of *The Pharmacist Activist*).

Perhaps the only thing we have learned with absolute certainty is that the SARS-CoV-2 virus (COVID-19) is deadly for many who are exposed. Almost all of us know a family member or friend who has been stricken with the infection and hospitalized. As the death toll for which COVID-19 is the cause or a contributing factor approaches 200,000 in the U.S., our country has been faced with an unprecedented health challenge. However, although fatal consequences for many are undisputed, there is ongoing debate regarding the actual number of deaths attributable to COVID-19 alone, in the context of many victims having other risk factors (e.g., age, smoking, diabetes, obesity).

There is agreement that the vast majority of those who have died are elderly who have one or often more underlying illnesses or other risk factors, and that children, adolescents, and young adults who are exposed to the virus are very unlikely to experience serious infection, and may not even experience symptoms. There are exceptions. There is general agreement regarding certain precautions, but much less agreement and, indeed, controversy regarding certain of the mandates and restrictions that have been imposed (e.g., closure of businesses, wearing masks, social distancing).

Much has been learned about the characteristics of the COVID-19 virus and its transmission, as well as the science that underlies the infection. However, at each step of the learning process, additional challenges are recognized with the realization that there is much more to be learned. As much as we may want evidence to support decisions, actions, and opinions, that evidence is not available now and will not be in the near future. As a result, almost all decisions, actions, and opinions regarding COVID-19 are debated or criticized, often with a political motivation.

In the meantime, businesses are closed or capacities are restricted, unemployment increases, schools are closed or only provide virtual but compromised learning, athletic events are canceled or can't have fans, individuals who are hospitalized or in long-term care facilities can't have visitors, and a much larger number of individuals are isolated, depressed, desperate, and suicidal. The economic impacts both now and for the future are impossible to estimate.

What level of risk is acceptable?

Every activity in which we participate has some risk, and even inactivity has physical and/or mental risks. Therefore, the question becomes, "What level of risk is acceptable?" We know that the "regular flu" (influenza virus) causes or contributes to thousands of deaths in the U.S. each year, with an estimate of at least 24,000 deaths in the 2019-20 flu season. In the context of COVID-19 concerns, deaths from the flu

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have hardly been mentioned in recent months although some suspect they have been included in the COVID-19 death counts.

A number of years ago the scarcity of supplies of gasoline resulted in a reduction of maximum speed limits (e.g., to 55 mph on interstate highways) to increase mileage and preserve gasoline. The reduction of speed limits was claimed by some (but debated by others) to reduce the number of accidents and fatalities. It could be argued that a reduction in the speed limit to 35 mph would substantially decrease the number of traffic fatalities, but very few would agree with that action. Indeed, when gasoline was again available in abundant supplies, speed limits were increased with little attention given to the relationship to vehicular deaths.

Smoking is a causative or contributing factor to the deaths of an estimated 480,000 Americans each year, far more than even the worst predictions of casualties from COVID-19. Yet many of those with strong opinions about COVID-19 are inactive and silent about the risks of smoking. Is the difference in deciding an acceptable level of risk based on the fact that COVID-19 kills people faster?

Some have suggested that COVID-19 mandates and restrictions should not be lifted until effective vaccines are available. Vaccines will provide an important forward step but, like influenza vaccines, will not be effective in many individuals although they are expected to significantly reduce the number of deaths. Consideration of the other questions regarding COVID-19 vaccines (e.g., need for booster shots?) are beyond the scope of this commentary.

We have learned enough to move forward

My age and medical issues place me among those at high risk if I am exposed to COVID-19. I observe the recommended precautions of limiting activities, avoiding crowds, wearing a mask, social distancing, etc. By the time you read this, my wife and I will have hosted in our home a "greet and meet reception" in support of a candidate for Congress (Dasha Pruett) in our district. Several individuals declined our invitation because of COVID concerns, but 25 people will be attending and we will observe appropriate precautions. We know the neighbors and other friends who are attending well, and are confident that they would not come if they were not feeling well, are very respectful and cautious with regard to the virus, and will be at minimal and acceptable risk.

COVID-19 statistics continue to be alarming, but are often misinterpreted and excessively intimidating. I do not minimize the extent of the consequences of exposure (death!). However, many do not recognize that COVID "cases" are often individuals who have tested positive for COVID but who have not experienced even mild symptoms. "Cases" also include those whose tests are false positives, the frequency of which, as well as lab errors, can't be reliably estimated.

We have learned with clothing and the dosages of medications that "One size doesn't fit all." Similarly, there is not one strategy or mandate regarding COVID-19 that is appropriate and applicable for all individuals, businesses, schools, athletics, and communities. We have learned enough about the dangers of COVID-19 to remove mandates and restrictions, and to open up and return to work, school, and most other activities while observing appropriate precautions!

Most individuals will be highly responsible and observe precautions, as will owners of restaurants and other businesses that have been closed or had restricted capacity because they will not risk problems that could result in another closure. Children and young adults are at the least risk of active COVID-19 infection, and most schools and colleges are well positioned to open up and provide in-person instruction and socialization in a safe and effective manner. For students, faculty, and employees who are at higher risk, provisions can be made to fulfill their responsibilities virtually or through other means.

Colleges of pharmacy and other health professional schools must provide leadership and models for restoring in-person educational experiences. They are preparing graduates who will be on the front-lines with personal risk in providing services and treatment for patients with health needs. Faculty and administrators who are at lesser risk should not impose restrictions that will limit the quality and scope of instruction and experience for their students who are preparing to accept a higher level of risk!

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Election Prediction

The specificity and scope of opinion polls has become very extensive, longer-lasting, and presumably more sophisticated and accurate. Almost every demographic and factor for which individuals might have opinions are examined in detail. Over a period of many months, the polling results may vary widely, and specific margins of error are identified. Some new poll(s) is/are released daily and are extensively analyzed and interpreted by the media. It has become a very big business.

I have a prediction that can save you a lot of time in following polls during September and October. By November 1, two days before the election, the polling companies will state that the Presidential election is "too close to call."

Daniel A. Hussar

New Drug Review

Risankizumab-rzaa
(Skyrizi – AbbVie)

Agent for Psoriasis

New Drug Comparison Rating (NDCR) = 4
(significant advantages)
in a scale of 1 to 5 with 5 being the highest rating

Indication:
Administered subcutaneously for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or for phototherapy.

Comparable drugs:
Guselkumab (Tremfya), tildrakizumab (Ilumya).

Advantages:
- May be more effective (based on noncomparative studies);
- Is administered less frequently (every 12 weeks for maintenance treatment compared with guselkumab that is administered every 8 weeks);
- May be self-admiºnistered (compared with tildrakizumab that is administered by a healthcare provider).

Disadvantages:
- Each dose requires two injections (compared with a single injection of the comparable drugs).

Most important risks/adverse events:
Infections (treatment should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated; if a serious infection occurs during treatment or an infection is not responding to standard therapy, discontinuation of risankizumab should be considered); tuberculosis (patients should be evaluated for tuberculosis prior to initiating treatment); live vaccines should not be administered during the period of treatment.

Most common adverse events:
Upper respiratory tract infection (13%), headache (4%), fatigue (3%), injection site reactions (2%), tinea infections (1%).

Usual dosage:
Administered subcutaneously – 150 mg (two injections) at Weeks 0 and 4, and then every 12 weeks.

Product:
Single-dose prefilled syringes – 75 mg (should be stored in a refrigerator).

Comments:
Certain interleukins (primarily IL-23 and IL-17A) have been identified as having a role in the occurrence and worsening of psoriasis, and risankizumab is the seventh monoclonal antibody that inhibits specific ILs that have been approved for the treatment of patients with psoriasis. The p19 and p40 subunits of IL-23 are present in higher concentrations in psoriatic lesions. Ustekinumab (Stelara) inhibits the p40 subunit that is shared by IL-23 and IL-12, and was the first IL inhibitor to be marketed (2009) for the treatment of patients with moderate-to-severe plaque psoriasis. Guselkumab, tildrakizumab, and risankizumab, marketed in 2017, 2018, and 2019, respectively, bind to the p19 subunit of IL-23, thereby inhibiting its binding to the IL-23 receptor and also preventing subsequent release of pro-inflammatory cytokines such as IL-17A. Secukinumab (Cosentyx), ixekizumab (Taltz), and brodalumab (Siliq) are inhibitors of IL-17A, and were marketed in 2015, 2016, and 2017, respectively.

The effectiveness of risankizumab was evaluated in four clinical trials in which the co-primary endpoints were a reduction in the Psoriasis Area and Severity Index (PASI) score of at least 90% (PASI 90) from baseline to Week 16 and an improvement in the Physician Global Assessment (PGA) score to 0 (clear) or 1 (almost clear). In two of the studies, risankizumab, ustekinumab, and placebo were evaluated; PASI 90 responses for the three agents were 75%, 42%, and 5%, respectively, in the first study, and 75%, 48%, and 2% in the second study. PASI 100 responses were reported in 36%, 12%, and 0%, and 51%, 24%, and 2% of patients in the two studies, respectively. PGA scores of clear and almost clear were also significantly improved in patients treated with risankizumab. At Week 52, PASI 90 responses (82%; 81%) and PASI 100 responses (56%; 60%) with risankizumab in both studies were significantly higher than with ustekinumab. Results of another study in which risankizumab and adalimumab (Humira) were evaluated show significantly better response rates with risankizumab.

Daniel A. Hussar

Hydroxychloroquine Hysteria! - Part 2

I received numerous responses to my commentary regarding hydroxychloroquine (HCQ) in the August 15 issue of *The Pharmacist Activist*, most of which were supportive. Some of the responses challenged/criticized my opinion that HCQ is of value in the treatment of COVID-19 infection, and several alleged that my opinion was politically influenced (an allegation that I refute). I was able to continue the communication with several critics whom, as far as I can determine, do not know more about HCQ than I do. I asked these individuals what they would recommend for treatment if they or a member of their family would be diagnosed with symptomatic COVID-19 infection. They identified supportive care, as well as dexamethasone, and/or remdesivir if the severity of infection required hospitalization. I fully agree regarding the value of these treatments. However, at the early stage of symptomatic infection at which I recommend initiation of HCQ treatment (in the absence of important risk factors), they had no alternatives to suggest even though they reject the use of HCQ.

In just the short period of time since I wrote my last commentary, there have been two lengthy commentaries that I would encourage readers to review. One is in *Scientific American* (August 18; Tanya Lewis) and is titled, "Nine Covid-19 Myths That Just Won't Go Away." I agree with this writer that most of the nine statements identified are, indeed, myths. However, to identify the statement, "Hydroxychloroquine is an effective treatment" as a myth is an allegation with which I strongly disagree. The writer begins her discussion of this "myth" with the following statement:

> "When a small, now widely criticized study in France suggested the malaria drug hydroxychloroquine might be effective at treating the disease, Trump and others seized on it and have continued to tout the medication despite growing evidence that it does not benefit COVID-19 patients."

Several observations in this statement can be challenged but I consider it particularly unfortunate that the writer's identification of this issue as a myth is in such a political context, as are the discussions of several other "myths."

A pharmacist friend called my attention to a commentary in *Tablet* (August 14; Norman Doidge) titled, "Hydroxychloroquine: A Morality Tale." This article also has political overtones, but it provides the most comprehensive analysis and commentary regarding the critical and supportive studies and statements regarding HCQ of any I have seen, including the study in France that is disparaged by the *Scientific American* writer.

I have voiced previously my personal decision that, if I tested positive for COVID-19 and began to experience symptoms, I would immediately consult with my physician and plan to start taking HCQ. I view this as a course of action that *may* be of benefit, with the alternative being doing nothing other than to try to relieve symptoms, at least until the time that the infection may worsen and require hospitalization. It is also my understanding that the timing of taking HCQ at an early point in the infectious process is important, in contrast to waiting until serious complications may develop, at which point HCQ is likely to be of limited or no benefit. Yes, I acknowledge that the use of HCQ has risks, but with factors I presently experience that place me at higher risk of serious complications from COVID-19 infection, I consider the potential benefit of using HCQ to far outweigh any additional risk it introduces, and that doing nothing other than providing relief of symptoms early in the infection has an even greater risk.

Some will strongly disagree with the decision I would make for myself and recommend for family members and friends who experience symptomatic COVID-19 infection. Each individual, in consultation with her/his physician, must make a personal decision as to what course of action to take, and I will not challenge or criticize decisions that differ from my own. However, I also recognize that I have had more opportunity than most others to review and learn from the extensive experience, information, perspectives, and very divergent opinions with respect to the use of HCQ in patients with COVID-19 infection. In the context of a challenge with potentially deadly consequences, my question then becomes, to what extent do I have a responsibility to share my perspectives and opinions with others who might be interested or could benefit? Or should I be silent? My answer to those questions is that I have a responsibility to do so and I should be faulted if I don't. Some will reject or ignore my observations but, if even just one reader of *The Pharmacist Activist* can benefit, this commentary will have served its purpose.

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