Coronavirus and Tetraphase

By David Shlaes — March 20, 2020

Dr. David Shlaes' primary expertise is in bacterial infections and antibiotics. So it's not surprising that our ACSH advisor is wondering about secondary bacterial infections from coronavirus infections. Will there be antibiotics to combat the infections this time? How about next time?

Obvious from the title, today's blog is going to ramble a bit. I don't apologize.

Everyone is very excited about the start [1] of coronavirus vaccine trials. Take a cold shower. These vaccines are mRNA based. Once you know a gene sequence, mRNA is fairly easy to construct. This approach to vaccine discovery is technologically “cool,” and scientifically attractive. It has, however, never breached the species barrier in humans. Side effects have been prominent in some trials. And then there is the problem of vaccine enhancement of disease that has been shown for a naturally occurring coronavirus infection of cats. (This has been a problem in the development of a vaccine for Respiratory Syncytial Virus in humans for decades). I would consider these approaches to be scientifically exciting, but more likely to fail than to succeed.

A recent paper [2] from China explored risk factors for mortality among patients admitted to the hospital with covid-19. Of 813 patients, 191 were included in the study (many of the rest were still hospitalized and hence had no outcome to measure). Of 191, 32 required mechanical ventilation and 31 (97%) died. Ten of the 32 developed ventilator-associated bacterial pneumonia. No details on these secondary bacterial infections were provided, but bacterial resistance is rampant in
China. One can only hope that, at least, they had effective antibiotics for these incredibly unfortunate patients.

In other news, Tetraphase was sold to AcelRx for $14 million – less than cash on hand in an all-stock deal. For those of you who don’t know (I didn’t), AcelRx is a company focused on sublingual formulations of drugs for pain control. Why they would be interested in a limited antibiotic like eravacycline I don’t know. This is essentially a bankruptcy without the bankruptcy filing.

I consulted for Tetraphase for a number of years starting as eravacycline was entering its phase I trials. I even helped design their failed phase 3 trials in complicated UTI. But the basis of that trial, and of my belief in the potential for eravacycline, was its oral bioavailability. I said from the beginning of my interactions with the company that I felt that without an oral drug, they did not have a path to commercial success. I retired just before the cUTI trial began but followed the data closely. The trial was an adaptive design with an interim evaluation to choose between two oral doses used to follow-up intravenous therapy. The interim data suggested that both oral doses were equally effective, and the higher dose was chosen for the continuation of the phase 3 trial. As is so often the case, the interim results were misleading, and the data failed to show non-inferiority to the levofloxacin IV/oral comparator. Most of the failures in the eravacycline arm were those who received early oral therapy. To me, that signaled a failure for the drug as a whole. Tetraphase decided to continue by carrying out a second phase 3 trial in intraabdominal infection hoping that eravacycline’s advantage of low side effects compared to Pfizer’s tigecycline would provide sufficient market for them in this single indication. That proved to be more hope that real. Eravacycline achieved $8 million in sales as of November last year.

I’m sure I will get anonymous on my site again saying that Tetraphase got what it deserved. Maybe so. I certainly never thought that the single indication of intraabdominal infection for an IV only drug would work commercially and I’m not sure that the analysts did either. But this is yet another nail in the coffin of investor confidence in antibiotic R&D. And, there is more of this to come. So far, the efforts in Sweden, the UK and here in the US to take baby steps to support the antibiotic market have been (and I believe will continue to be) inadequate to bolster investor confidence. We need a bolder approach from a country or region willing to lead.

And this takes me back to the coronavirus pandemic. How important will secondary bacterial infections be in the ultimate mortality rate? Will we have effective antibiotics to combat these secondary bacterial infections. What about the next pandemic?