[MUSIC PLAYING]

ANNA LOK: Well, yet another regimen. This is a modified Merck regimen. So this is modified from Zepatier. Grazoprevir is the same drug as in Zepatier. This is a protease inhibitor. But ruzasvir is a second generation NS5A inhibitor. and [INAUDIBLE] polymerase inhibitor. And here, you look at some patients were from genotype one, two, and three, a trial of 16 weeks. Across the board, again, very impressive SVR rate, except for genotype two patients if you give them a very short duration of therapy.

But again here, there seems to be an impact where the patients have baseline resistance associated very particularly to NS5A. And if they do, for both genotype two and genotype three patients with certain variants, the SVR rate goes down.

What about side effects? Unfortunately, with this regimen, we don't have a placebo group that we can compare. All we can say is that, when you take these three drugs with ribavirin and obviously with ribavirin because of the anemia, you're going to have more side effects. But we can't really tell what is due to the drugs and what is just what we experience in life.

But it seems like, in absence of ribavirin, it's, generally speaking, a reasonably well tolerated drug. So where do we stand now? We have multiple regimens, either two or three DAAs. And we consistently can achieve at least 95% SVR in DAA-naive patients, including genotype three cirrhosis patients.

12 week treatment for most patients, but eight week treatment would be sufficient for some patients. And we have from more than one regimen for patients who have impaired kidney function. But what about the patients who have failed DAA? Well, HCV is an RNA virus, And RNA viruses have a very high error rate during replication. So even in patients who've never been treated with DAA if you do testing, you find resistance associated substitutions in some of the patients.

And with some regimens, baseline resistance variation will decrease your SVR rate with some really potent, very good regimens. It doesn't seem to make a big difference. When patients are treated and they fail, often times-- most of the time-- you will find drug resistance variants Even if they were not present, you now select for resistance variants. That's why the patients have fail to achieve SVR.

Well, how important is it if they have failed regimen impact on future treatment? If this is resistance variance to protease inhibitors, they don't last very long. Within a few months, they tend to disappear. If this is resistance variance to NS5A inhibitors, they tend to persist for a long time-- oftentimes, years. So that could impact response rate to future treatment.

Resistance variance to polymerase inhibitors is uncommon. And it tends to compromise the virus replication, so they're extremely rare. But one thing is we have multiple regimens. Do do your research to know what you're doing. Pick the right regimen for the patients. Check with drug-drug interactions. And make sure patients are complying with the treatment. Although the treatment is very successful, you hate to select for drug resistance variance. Because in some instances, it does make future treatment a little bit more difficult.

So do we have drugs that work for patients who have failed DAA? So this is one regimen. And this is the sofosbuvir/velpatasvir plus voxilaprevir. So this is basically an occluser, or occluser plus a protease inhibitor. And in this case-- although these patients have been exposed to DAA, they have not received NS5A inhibitors. So these are mostly sofosbuvir failure or protease inhibitor failure.

And what you can see is that the three drugs work better than the two drugs. With two drugs, if they have cirrhosis, the SVR rate is not as good. But there are other regimens. And again, this is for patients who have not been exposed to and NS5A. This is the GP regimen from FDA, where they use some trials of 16 weeks of treatment. And here is for genotype 3 patients plus or minus cirrhosis. And you see very high rate of SVR, regardless of whether the patient's have cirrhosis or not.

Well, what if the patients already have NS5A? These would be your Harvoni failures, or your Viekira failures. They have been exposed to NS5A. Now, if you use the new Gilead regimen-- well, the soon to be new-- sofosbuvir/velpatasvir plus voxilaprevir for 12 weeks-- again, pretty good. There were some relapses, most in genotype 1A and 3. But overall, more than 90% SVR rate across the different genotypes.

There are other regimens. Again, this is the Merck three drug regimen. So this is the polymerase inhibitor, the protease inhibitor, and the second generation NS5A inhibitor. And again, fairly high rate of SVR. But here, they use a longer duration of therapy-- 16 weeks with ribavirin, or 24 weeks with ribavirin. And I think they're going to try to see if 12 weeks would do just as well.

And we recently heard data on the GP regimen that also does just as well for patients with NS5A failures. However, for patients with failure to combination of protease and NS5A inhibitors, the SVR rate does drop. And it looks like they may need three drug regimen.

So we do have rescue therapy for DAA failure. More than 90% SVR is feasible with 2, 3 DAAs in patients who failed DAA combo, that did not include NS5A inhibitor. So if the previous regimen did not include NS5A, it's easier to retreat. If it included NS5A, chances are, you're going to really need three drugs. And a minimum duration I think is going to be 12 weeks. For some regimens, maybe ribavirin would make a difference. And we know shorter testing for base time resistance is really necessary at this time. We just need to look at some of the post data little bit more carefully.

So what's the HCV treatment landscape in 2017 with multiple interferon III DAA combination. Many of them are also ribavirin-- actually, most of them are ribavirin 3-- high efficacy SVR rates consistently 95% or higher. In most patient populations, including the traditionally difficult ones-- blacks, child stage cirrhosis, interferon experience, HIV co-infection, end stage kidney disease, post liver transplant, even genotype 3 cirrhosis. It's simple oral, ranges from one to three pills a day if ribavirin is not needed, with multiple regimens to have pan-genotype activity.

We don't think about it, but in many parts of the world, I was told that they can get the generic version of DAA combination therapy for like $500 for 12 weeks. But the genotype testing is going to cost $300. So having pan-genotype regimen is going to be important in those parts of the world.

And I've shown you the responses in clinical trials of replicating clinical practice. And we have motive one rescue regimen for DAA failures expected to be proofed sometime in 2017. And these other three new regimens that I expect will be coming down the pipeline.

The first two should be approved sometime in 2017. This may take a lot longer, might be 2018. And so what we now can see is that we can cure hepatitis C. And what does cure really mean? Well, cure also can decrease transmission, because we don't have a hepatitis C vaccine. And you all hear about the opioid epidemic that we're facing. And a lot of young people are spreading hepatitis C like crazy. So if we treat these people, we can make them less likely to transmit the infection, because they're no longer carrying the virus. But for the patients themselves, there's also improvement in clinical outcome.

And it's not just improvement in liver outcome-- decreasing cirrhosis, liver failure, liver cancer, and need for transplantation-- but also, hepatitis C can cause extra hepatic problems, increasing the risk of diabetes, increasing the risk of kidney problems. And already, the data show that if you cure the patients of hepatitis C, you improve all cause mortality. You improve the quality of life, decrease diabetes, kidney and cardiovascular outcomes. And you make the brain work better. And therefore, there is the IDSA guidelines recommend that we should consider treatment for every single patient. And we should fight insurance to get patients on treatment. Thank you.