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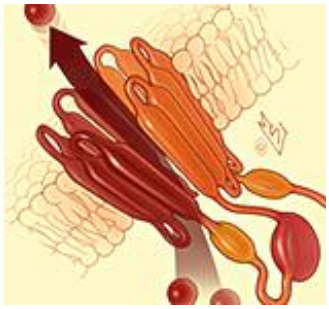

INTERVIEW WITH DR. SCOTT BELL: TRANSCRIPT

DR. PATRICK FLUME: I'm Dr. Patrick Flume, guest author of this *e*Cystic Fibrosis Review special edition. I'm am professor of medicine and pediatrics at the Medical University of South Carolina. I'm speaking with Dr. Scott Bell, professor and director of the Cystic Fibrosis Center at Prince Charles Hospital and group leader at the QIMR Berghofer Medical Research Institute in Queensland, Australia. Dr. Bell, thank you for joining us today.

DR. SCOTT BELL: Thanks very much, Patrick.

DR. PATRICK FLUME: I want to talk about your patients who have chronic Pseudomonas infections — what is your current practice using inhaled antibiotics in those patients?

DR. SCOTT BELL: To set the scene, we have a fairly limited choice of inhaled antibiotics. We have tobramycin in two preparations, tobramycin solution and tobramycin dry powder, and we also have Colistin solution for nebulization. So we are more limited than some parts of the world.

Some of the things our team would consider with a patient are their level of engagement with therapies, how adherent they are, what is their tolerance to the different nebulized antibiotic or inhaled antibiotic preparations, and what sort of nebulizer technology the patient has.

My general practice for patients with chronic *P. aeruginosa* is to advise month on/month off therapy with tobramycin and the tobramycin preparation really depends on patient preference and tolerability, but more and more patients are taking the dry powder for convenience rather than the nebulized solution.

DR. PATRICK FLUME: Do you ever use continuous inhaled antibiotics?

DR. SCOTT BELL: Yes, we do. I guess over the past two decades we've seen an increase in the number of patients with advanced disease who now live much longer than was the case two and three decades ago. These patients have severe lung disease and chronic infection and are the group of patients who are most likely to be frequently needing IV antibiotics for exacerbations. It's that group of patients we particularly focus on using continuous antibiotics.

Our practice is generally to rotate between the two available preparations, tobramycin and Colistin, assuming the patient is engaged with the therapy and also tolerant of those two drugs.

DR. PATRICK FLUME: Do you rotate on a 28 day schedule?

DR. SCOTT BELL: That is what we attempt to get, but there are some real world challenges in having patients do this continuously. That group of patients also tend to exacerbate quite frequently, despite the rotational antibiotics. So then the rotational antibiotics are interspersed with parenteral therapy to treat exacerbations.

DR. PATRICK FLUME: I know you've seen the data that I've presented at the North American CF Meeting on the Continuous Alternating Therapy trial, the CAT trial. What are your general impressions of the results from the CAT trial?

DR. SCOTT BELL: First, I think it demonstrates really clearly the challenges in undertaking these sorts of studies for two reasons. First, the standard of care with alternate month antibiotics has, I think,

inevitably led to clinicians doing exactly as I described before. Many clinicians already advise their patients with advanced disease who have frequent exacerbations to have continuous antibiotics. I think this is a big challenge that you and your investigators had, Patrick, in engaging patients, because whilst a lot of patients out there fitted the study criteria, many of them are already being treated with continuous alternating therapy.

I think also in the setting of a huge growth in clinical trials, specifically for CFTR modulation, the competition for patients for clinical trials has grown enormously, and that may also have contributed to some of the challenges you had.

Nevertheless, despite the study being underpowered, the data show some interesting trends data suggesting lower rates of exacerbations and hospitalization for respiratory indications and perhaps a slight improvement in lung function.

So there are some interesting trends to suggest that for this cohort of patients, continuous alternating therapy may have a role for our patients.

DR. PATRICK FLUME: Do you think that these study results will have any impact on your future use of inhaled antibiotics?

DR. SCOTT BELL: I guess the first point to make is that we don't have access to nebulized aztreonam at this point, so the specific combination can't be prescribed in our health care system at present. We are limited to the choices between tobramycin and Colistin, and I guess it reinforces the approach that many have taken, and that's alternating between two agents rather than using a single agent continuously. For many years it has been the standard practice in Europe to use long-term Colistin therapy. So what it tells me is perhaps alternating is better than continuous.

DR. PATRICK FLUME: Thank you, Scott, for being part of this *e*Cystic Fibrosis Review Special Edition Program.

DR. SCOTT BELL: Thanks very much, Patrick.