SERIOUS BACTERIAL INFECTIONS

ADDRESSING DIFFICULT TO TREAT INFECTIONS IN HOSPITALS

With hospital infections resulting in around 37,000 deaths every year in Europe alone[11], we are in desperate need of new tools to combat the growing problem of antibiotic resistance. As the fight against this silent pandemic grows more urgent, GARDP is helping to develop a new antibiotic that could treat serious bacterial infections.

In high-income countries, around 7% of hospitalized patients will contract a bacterial infection, with that proportion rising to 1 in 3 in intensive care units (ICUs)[12]. The elderly and immunocompromised are particularly vulnerable, with 1 in 10 cancer deaths being due to severe sepsis rather than the cancer itself[13].

Although the data show that a low percentage of COVID-19 patients develop serious bacterial infections—around 3–5%, according to the most recent studies[14]—this is a complex problem that depends largely on the quality of the infection prevention and control measures hospitals have in place. That quality tends to be lower in LMICs, where far more hospitalized patients—10% of all patients and one in two ICU patients[12]—will contract a bacterial infection than in high-income countries.

Moreover, despite the relatively low rates of serious hospital-acquired bacterial infections in COVID-19 patients, the same studies show that around 80% of all hospitalized COVID-19 patients receive prophylactic antibiotic treatments[15]. As a result of these unnecessary antibiotic prescriptions, the pandemic could end up contributing to a rise in drug-resistant infections.

A GROWING PROBLEM

Antimicrobial resistance is making serious hospital infections much more difficult to treat. Hospitals generally reserve the carbapenem class of antibiotics for those patients whose infections are caused by bacteria resistant to cephalosporins and other beta-lactam antibiotics. However, increasing use of carbapenems has resulted in emerging resistance in key members of the *Enterobacterales* family of bacteria and some strains of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. These bacteria can enter the body through

[11] *WHO. 'Report on the Burden of Endemic Health Care-Associated Infection Worldwide'. 2011.*
[12] *WHO Healthcare-associated infections factsheet. https://www.who.int/gpsc/country_work/gpsc_ccisc_fact_sheet_en.pdf.*
[13] *The PEW Charitable Trusts. https://www.pewtrusts.org/en/research-and-analysis/data-visualizations/2020/broken-antibiotics-market-puts-cancer-treatments-at-risk.*
[14] *Contagion. https://www.contagionlive.com/view/bacterial-coinfections-among-us-patients-with-coronavirus-disease-2019.*

wounds, surgery incisions, ventilators and catheters, which could lead to lung, urinary tract, abdominal and bloodstream infections. To combat the unique resistance mechanisms that are making carbapenems less effective at treating certain strains of these bacteria, we urgently need to develop new drugs.

In many South African hospitals, for instance, 95% of *A. baumannii* are now carbapenem-resistant[16]. And the problem is getting worse.

MOUNTING A RESPONSE

To address this challenge, the objective of **GARDP**'s Serious Bacterial Infections (SBI) programme is to identify, review and evaluate both recovered assets and new chemical entities in development that show activity against WHO's priority pathogens.

Last year, in the first of several anticipated partnerships for the SBI programme, **GARDP** signed an agreement with Venatorx Pharmaceuticals to accelerate the development of and access to cefepime-taniborbactam, a new compound that could show activity against infections caused by two of the three WHO priority pathogens: carbapenem-resistant *Enterobacterales* and *Pseudomonas*. Taniborbactam blocks the activity of enzymes produced by these two pathogens that makes them resistant to carbapenems so that its companion antibiotic, cefepime, can go to work. As a result, cefepime-taniborbactam has the potential to become a safe and effective treatment for adults and children with serious bacterial infections, including those caused by bacteria that are resistant to last-line antibiotics.

PUSHING SAFELY THROUGH THE PANDEMIC

Our collaboration with Venatorx includes an observational study that will examine the frequency, treatment methods and outcomes in patients with carbapenem-resistant bacterial infections. Since such infections are particularly prevalent in India and South Africa, the sites involved in the observational study will be located in these two countries and are likely to participate in a future interventional trial of cefepime-taniborbactam in serious carbapenem-resistant bacterial infections. An additional objective of the observational study is knowledge exchange in regards to clinical trials for regulatory purposes, with the potential for creating clinical trial networks in India and South Africa that other programmes can use for future antibiotic studies.

We are also supporting a phase 3 Venatorx-sponsored trial to test the efficacy and safety of cefepime-taniborbactam in patients with complicated urinary tract infections (cUTI). This pivotal trial will pave the way for the initial new drug registration and eventual approval of cefepime-taniborbactam by the FDA and EMA. In addition, we will conduct trials to enable cefepime-taniborbactam to be used in children and newborns (see 'Children's Antibiotics'). Once approved for clinical use, Venatorx has granted **GARDP** exclusive rights to license and distribute cefepime-taniborbactam throughout most LMICs.

Unfortunately, the COVID-19 pandemic has hampered our progress on these fronts. With researchers unable to visit sites due to travel restrictions and ICU

[15] *Langford B J, So M, Folgori L, Raybardhan S, Leung V, Soucy J R et al. 'Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis'. Clinical Microbiology and Infection. 2021;27(4).*
[16] *National Institute for Communicable Diseases of South Africa. https://www.nicd.ac.za*

workers focusing on caring for COVID-19 patients, both the start of the observational study and the cUTI clinical trial have suffered delays. Despite these issues, **GARDP** and Venatorx have completed some important preliminary steps for the observational study. We have agreed the protocol for the observational study, while all countries have now re-opened for enrolment in the cUTI trial and are actively recruiting patients. We aim to complete enrolment for the cUTI study in 2021 and begin recruiting for the observational study in early 2022.

*"Our partnership with **GARDP** is vital for advancing cefepime-taniborbactam through phase 3 clinical trials and affording access to patients, including children, who are more susceptible to hard-to-treat bacterial infections."*

CHRISTOPHER J. BURNS, Ph.D.
PRESIDENT AND CEO OF VENATORX PHARMACEUTICALS