NEWS IN BRIEF

Coordinating the COVID-19 pipeline

As the COVID-19 drug pipeline explodes, a fragmented approach to coronavirus drug development risks compromising the potential evidence base.

Researchers have already opened over 180 clinical trials of potential COVID-19 treatments for recruitment, and nearly 150 could start soon. An analysis of some of these trials by The Centre for Evidence-Based Medicine shows that interventional products span everything from repurposed antivirals and anti-inflammatory agents to cell therapies and traditional Chinese medicines. And a systematic review of the currently ongoing trials, published on *medRχiv*, cautions that the poor methodological quality, small sample sizes and long execution time of currently registered trials could compromise the collection of high-quality clinical evidence.

Zhi Hong, CEO of Brii Biosciences and former head of infectious disease research at GlaxoSmithKline, is amongst those who has raised concerns. The fragmentation of the field could make it hard to enrol patients into trials of the most promising agents, he cautioned in a commentary in *Biocentury*.

Credit: Peter Zelei Images/Moment/Getty

In an attempt to coordinate the COVID-19 clinical trial landscape, the WHO has now launched the Solidarity Master Protocol. By establishing consistent end points, control arms and inclusion–exclusion criteria, this umbrella trial — in hospitalized patients with COVID-19 infection — could increase the value of the emerging trial data set.

The first four arms of the Solidarity trial will test: Gilead's RNA polymerase inhibitor remdesivir, first developed for the treatment of Ebola; chloroquine or hydroxychloroquine, anti-malarial drugs that were only included in the trial after public interest in these agents picked up; ritonavir plus lopinavir, a combination of anti-retroviral drugs that did not improve COVID outcomes in preliminary trial results published in the *NEJM*; and ritonavir plus lopinavir in combination with IFNβ, an immunomodulatory agent that may boost the efficacy of the anti-retroviral agents.

Solidarity investigators can add other arms to the adaptive trial as necessary.

The WHO is also working on a master protocol for vaccine development. Moderna has already dosed a first patient with its mRNA vaccine, and other candidates are gearing up to enter trials.

Asher Mullard

COVID-19 brings drug development to a halt

With governments ramping up and enforcing social distancing measures to slow the onslaught of COVID-19, clinical trial work in other areas has come grinding to a halt.

Large and small companies alike have started shuttering clinical trial operations. For instance, Eli Lilly, which runs a roughly US$6 billion a year R&D operation, announced early on that it will "delay most new study starts and pause enrolment in most ongoing studies".

The halt is affecting all therapeutic areas, with the exception of potential COVID-19 drugs. Cancer clinical trials — which account for over one-third of the drug development pipeline — have been cut to "almost zero" at Yale University, lung cancer researcher Roy Herbst recently told *Nature*. Investigators have halted these trials in part because of social distancing measures and decreased staffing throughout hospitals and research organizations, but also over concerns that many cancer patients are particularly vulnerable to infection. The shut down could take a heavy toll on long-running and large clinical trials, where missing drug dosing and data collection will complicate the analysis of results. Alzheimer prevention trials, for example, could be hard hit.

Preclinical work in both academia and industry has also taken a hit, although exceptions are currently in place in some regions to facilitate ongoing lab work.

Asher Mullard

UK outlines its antibiotic pull incentive plan

The UK government has outlined a plan to pay up to £100 million per new antibiotic under a first-of-its-kind "subscription-based payment model". This paves the way for a global pull incentive of up to US$4 billion for new antibiotics, if other governments follow suit.

Faced with a dwindling antibiotic pipeline and increasing risk of antibiotic resistance, infectious disease experts have long argued that market entry rewards are needed to encourage work on much-needed new antibiotics. The UK's NHS and NICE have now disclosed a plan to pay drug developers £10 million per year for a decade for each of 2 new antibiotics against WHO priority pathogens, under an antibiotic pull incentive programme. The pilot programme is set to start selecting products to assess later this year, and contracts are set to be finalized by April 2022.

John Rex, CMO at F2G, and Kevin Outterson, Executive Director at CARB-X, noted in an analysis of this plan that if other countries chip in equivalent amounts, scaled to GDP, the total value of this antibiotic pull incentive would be around $4 billion. "Overall, we see this as an outstanding step forward," they write. "England cannot (and should not) do this alone. Every member of the G20 needs to step up as well! If they do not do this, the total reward will be inadequate to sustain a vibrant pipeline and R&D community."

Asher Mullard

FDA relaxes cardiovascular trial requirements for diabetes drugs

In 2008, the FDA shook the diabetes drug development community with its call for long-term and expensive cardiovascular outcomes trials to rule out cardiovascular risk for new diabetes drugs. Twelve years on, the agency is dropping this requirement.

Under a newly released draft guidance, the agency is now instead establishing minimum requirements for the safety databases for new type 2 diabetes drugs. Phase III trials must include at least 4,000 patient-years of exposure to a new drug, they write. At least 500 patients must have established chronic kidney disease, at least 600 patients must have established cardiovascular disease and at least 600 patients must be older than 65 years of age.

This regulatory revision reflects the deliberations of a meeting of the FDA's Endocrinologic and Metabolic Drugs Advisory Committee in 2018.

The number of newly initiated industry-sponsored clinical trials of type 2 diabetes drugs is down markedly — by about 50% — since the 2008 mandate of cardiovascular outcomes trials, researchers from Sanofi reported last year in *Therapeutic Innovation & Regulatory Science*. Sanofi subsequently exited diabetes research. It remains to be seen whether the new guidelines will reinvigorate research in this space.

Asher Mullard