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Oncology Trials Outpacing Rest of the Field in Complexity and Duration, Study Shows

By Charlie Passut

Clinical trials in all therapeutic areas are increasing in complexity, but oncology trials are outstripping the rest of the field due to enrollment challenges, protocol deviations and a burgeoning amount of data that are adding months to their timelines.

The three phases of oncology trials each take 14 to 18 months longer, on average, than trials for other drugs, lasting almost 12 years compared to almost eight years for nononcology trials, according to a new report by the Tufts Center for the Study of Drug Development (CSDD).

The report says trials of oncology drugs are more difficult to execute because they typically involve more countries and investigative sites and require more patient visits per protocol. They also generate a much higher volume of data compared to trials for other drugs — for example, 3.1 million data points per protocol in phase 2 oncology compared to 1.9 million in nononcology.

The number of investigational drugs targeting cancer has nearly quadrupled since 2000, to 1,489 trials in 2021, up from 421 two decades earlier. Oncology drug developers are increasingly shifting toward precision medicine, embracing new molecular targets and improvements in genetic sequencing technologies, CSDD says.

But as sponsors of cancer treatments shift their focus to precision medicine, it becomes harder to find participants that fit

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As the Pandemic Eases, Sites Focus On Improving Study Startup Times

By Charlie Passut

Delays to study startup caused by the pandemic have eased with institutional sites now saying they've been able to reduce time needed for the process from six months on average to two or three months.

Independent sites are saying they can get study startup done in a couple of weeks or less. And the competitive drive to reduce study startup times has sites looking at every tool available to improve the process.

Before the pandemic, Holly Jones, Northeast Georgia Medical Center's (NGMC) director of research, said NGMC was averaging two to three months for study startups, but the pandemic caused trials to be put on hold, delaying startups to an average closer to six months. "We're back down to somewhat normal now, but sponsor communication is absolutely critical," she said.

"I encourage all of my staff to respond to emails within 12 to 24 hours, especially when it's a study startup activity," Jones said. "We have activated trials in around one month, but that depends on the scope of the trial and communications with the sponsor."

Jones said NGMC has outsourced the drafting and review of coverage analysis (CA) to a consulting firm. NGMC then creates an internal budget based on the CA and kicks off the clinical trial agreement (CTA) negotiations with a sponsor.

see **Study Startup Times** on page 9 »

COVID-19 Update

COVID-19 Drug Research Roundup

COVID-19 Therapies:

An inhaled interferon beta (IFN-beta) therapy from **Synairgen** significantly reduced the rate of hospitalization in patients with COVID-19, according to the recent phase 2 clinical trial of SG016. The investigational COVID-19 treatment, dubbed SNG001, is an IFN-beta formulation used for nebulization, which facilitates direct delivery of the therapy into the lungs. The recent SG016 study included 221 patients with COVID-19 who were either hospitalized or receiving care at home. Hospitalized patients who received SNG001 were significantly more likely to recover from severe lower respiratory illness caused by SARS-CoV-2 than those enrolled in the placebo group. Patients who received the investigational nebulized therapy also showed reduced breathlessness and no limitations on activities. A combined analysis using data from the hospital and the home cohorts showed that patients treated with SNG001 had a 3.41 greater likelihood of recovering compared with patients randomized to placebo.

Eiger BioPharmaceuticals' peginterferon lambda (Lambda) has been added to the phase 3 TOGETHER COVID-19 study, an ongoing, randomized trial assessing multiple treatments in outpatients with newly diagnosed COVID-19. Eiger's Lambda is a first-in-class, type 3 interferon designed to stimulate immune responses important for inducing protection against viral infections. In the newly added TOGETHER arm that includes a single subcutaneous dose of Lambda, researchers will compare the active intervention and placebo arms in terms of the rates of emergency room visits and/or hospitalizations. The Lambda arm, among the other treatment arms in this study, will aim to enroll up to 800 patients who are considered to be at high risk for complications associated with COVID-19. Currently, the TOGETHER platform study is recruiting patients at 11 sites in Brazil, but investigators may expand to sites in Canada.

The first patient has been enrolled in a phase 2 trial studying **Partner Therapeutics'** inhaled Leukine (sargramostim) therapy in nonhospitalized patients with COVID-19 at risk for disease progression. The randomized, double-blind, phase 2 SCOPE trial is investigating whether Leukine, an FDA-approved drug that increases white blood cell production, can lower the risk of disease progression and also reduce the rate of hospitalization in patients with COVID-19. The study plans to enroll up to 400 patients at sites across the U.S. as well as in Latin and South America. Primary endpoints include rates of emergency room visits and hospitalizations. In August 2020, Partner initiated a study to evaluate Leukine's efficacy in hospitalized patients with COVID-19 who required oxygen. The results from this study have yet to be released.

Eli Lilly has initiated the development of an anti-SARS-CoV-2 antibody that will hopefully combat known COVID-19 variants. This decision falls on the heels of a recent FDA decision to revoke the single-use emergency authorization of the pharma's COVID-19 antibody therapy bamlanivimab after concerns it wasn't effective against emerging SARS-CoV-2 strains. Lilly's bamlanivimab, an antibody born from a collaboration with **AbCellera**, previously demonstrated a lack of robust efficacy against B.1.351, a highly infectious COVID-19 variant. In response, AbCellera evaluated the blood of a convalescent patient who had recovered from COVID-19 and discovered another antibody candidate, LY-CoV1404, which binds to a component of the receptor-binding domain. AbCellera, Lilly and other research partners examined the efficacy of LY-CoV1404 against the original COVID-19 strain as well as variants B.1.1.7, B.1.351, P.1, B.1.526, B.1.427 and B.1.429. The antibody fully neutralized the tested variants and featured a potency against the original variant between 9 ng/mL to 22.1 ng/mL. Based on these preclinical data, Lilly has entered LY-CoV1404 into the BLAZE-4 trial to see if the antibody retains its neutralization potency in patients with mild-to-moderate COVID-19. The therapy will be given alone or with other monoclonal antibodies.

Biotech company **Adagio Therapeutics** has treated its first patient in a phase 2/3 COVID-19 trial of ADG20, a monoclonal antibody. The new pivotal trial, referred to as EVADE, was initiated based on positive preliminary data from an ongoing phase 1 trial of healthy volunteers. The EVADE trial is a global study that will be conducted at more than 100 sites. Investigators will examine whether a single, intramuscular injection of the therapy is effective for preventing COVID-19 both before as well as after exposure to the novel coronavirus. The early-phase study showed that a single intramuscular dose of ADG20 was well-tolerated at up to 600 mg per dose. The pharmacokinetic data suggested the therapy could offer up to 12 months of protection against a SARS-CoV-2 infection. Also, the initial serum virus neutralizing activity of ADG20 against COVID-19 was similar to that seen in patients who received an mRNA COVID-19 vaccine.

COVID-19 Vaccines:

Pfizer and BioNTech announced Friday that they have submitted the required six months of clinical data on their jointly developed COVID-19 vaccine to the FDA, beginning the process of rolling review of their biologics license application (BLA). If the BLA is approved, the mRNA vaccine would be the first

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COVID-19 Update

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to win full FDA approval. The vaccine received Emergency Use Authorization (EUA) for use in patients age 16 and older in December. The companies will submit the remainder of the data required for the BLA — manufacturing and facility information — in the coming weeks. **Pfizer and BioNTech** also have requested expansion of the current EUA to allow the vaccine to be administered in adolescents age 12 to 15. Once the companies have collected six months of safety and efficacy data on this age group, they plan to submit a supplement to the BLA.

Novavax has launched a pediatric expansion of the phase 3 PREVENT-19 trial studying the company's recombinant protein vaccine, NVX-CoV2373, against COVID-19. The additional treatment arm will include up to 3,000 patients between the ages of 12 and 17 who will be treated with the vaccine across 75 U.S. sites. The objective of this expansion study is to examine the efficacy, safety and immunogenicity of NVX-CoV2373 in these adolescent patients. Two-thirds of participants will be randomized to two doses of the vaccine, while one-third will receive two doses of placebo. Both the vaccine and the placebo doses will be administered 21 days apart. At six months following the initial vaccinations, a blinded crossover will take place to ensure each adolescent receives the active vaccine candidate. Investigators will monitor patients for up to two years after the final dose to examine long-term safety outcomes.

Serum Institute of India's (SII) COVID-19 vaccine, Covovax, will likely enter late-stage clinical trials by the middle of May. This is based on a recommendation from the Data Safety Monitoring Board, which recently reviewed initial safety data of 200 patients who received the vaccine in a phase 2 clinical trial. The phase 3 trial has also been given the green light from the Drugs Controller General of India. Currently, the SII and the Indian Council of Medical Research are conducting a phase 2/3 randomized study evaluating the safety and immunogenicity of Covovax in adults in India. A total of 19 sites across India are participating in the study. In addition to Covovax, the SII also produced the Covishield vaccine with partners **AstraZeneca** and Oxford University. **Novovax**, another SII partner, entered into a license agreement with SII last year to develop and commercialize Novovax's NVX-CoV2373 vaccine for India as well as for other low- and middle-income countries.

New data from a phase 1 trial suggests **Vaxart's** COVID-19 vaccine candidate VXA-CoV2-1 features broad cross coronavirus activity. In the 9-person, open-label study, researchers found that VXA-CoV2-1 generated higher CD8+ T-cell responses than those observed with the currently authorized COVID-19 vaccines from **Moderna** and **Pfizer/BioNTech**. According to the findings, the authorized mRNA vaccines induced fewer T-cell responses when pitted against Vaxart's vaccine candidate. Vaxart also believes the T-cell responses against the S and N proteins of the virus offers hints that VXA-CoV2-1 may be effective against new SARS-CoV-2 variants. The investigators also found that immunoglobulin A antibodies were triggered in the mucosa. This finding suggests the mucosal responses could have cross-reactive activity against various other coronaviruses not related to COVID-19, including SARS-CoV-1, MERS and the common cold viruses 229E, NL63, HKU1 and OC43.

Piedmont Health's Piedmont Atlanta Hospital, in partnership with **Moderna**, has become the first to launch a trial to evaluate Moderna's COVID-19 vaccine in liver and kidney transplant recipients. The COVE Transplant clinical trial began last month and has enrolled eight transplant recipients and two control participants. The target enrollment is set at 220 transplant recipients and 20 healthy volunteers. The findings from this study could hold important clinical implications, given patients who receive transplants are at high risk of severe COVID-19-related outcomes. A recent study has also found that organ transplant patients and other immunocompromised individuals do not generate sufficient antibody levels against SARS-CoV-2 after an injection with a COVID-19 vaccine. Only 17 percent out of 436 participants in that Johns Hopkins study had detectable antibodies following the first COVID-19 injection.

HDT Bio and its Indian partner **Gennova Biopharmaceuticals** have launched a phase 1/2 trial to evaluate the safety and immunogenicity of a COVID-19 vaccine candidate in healthy participants. The vaccine, developed by the two companies in July 2019, uses a lipid inorganic nanoparticle formulation that delivers immune-stimulating ribonucleic acid fragments to specific targeted cells. HDT Bio and Gennova suggest that even a reduced dose of the vaccine can stimulate the immune system, which could improve safety and ultimately reduce costs associated with production. HDT Bio recently stated that additional clinical trials of the vaccine are planned to start in the U.S. and Brazil sometime this year.

The **Institute for Biological Research** in Israel is considering hitting the restart button on an ongoing trial studying the BriLife COVID-19 vaccine. This consideration was proposed after findings from a phase 1/2 trial show that a single but high dose of the two-dose vaccine was just as effective as both vaccine doses. Relaunching the study could help researchers know for sure that one dose will be as effective and as safe as two doses in a larger study population.

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COVID-19 Update

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But the move would likely delay getting the vaccine to the public, if it ultimately receives approval. Data from currently running clinical trials of the BriLife vaccine have not yet been publicly disclosed. Likewise, little is known regarding the vaccine's efficacy and safety as it relates to authorized vaccines from **Moderna** and **Pfizer**. Israel's Institute for Biological Research also recently announced it will move its vaccine clinical trials from Israel to Argentina, since many Israelis have already received a COVID-19 vaccine.

Moderna believes a COVID-19 vaccine booster shot can increase the body's immune response to several COVID-19 variants, according to new human trial data. Study volunteers were given a third dose of the company's authorized mRNA-1273 vaccine or mRNA-1273.351, a booster vaccine specifically targeting the B.1.351 variant. In the patients who received the third mRNA-1273 shot or the mRNA-1273.351 booster, there was an increase in neutralizing antibodies after vaccination to levels either similar or higher to those observed against the original COVID-19 strain. At 15 days following the booster shot, the investigators found the variant-specific vaccine was more effective than the currently authorized COVID-19 vaccine at increasing levels of antibodies against the B.1.351 strain. Overall, safety and tolerability of the shots were comparable to the safety and tolerability findings from the previous phase 2 and 3 trials of the original vaccine. Currently, Moderna is testing a combination vaccine termed mRNA-1273.211 in a treatment arm of a phase 2 study.

Health Canada has expanded authorization for **Pfizer's** and **BioNTech's** COVID-19 vaccine BNT162b2 for use in children between the ages of 12 and 15. Canada decided to expand its authorization based on phase 3 pediatric trial data that showed the vaccine generated robust antibody responses in adolescents. The study included 2,260 patients between 12 and 15 years of age. There were no cases of COVID-19 among participants who received the vaccine, while 18 participants in the placebo arm developed the disease during the study. Side effects were considered consistent with those reported in study participants between the ages of 16 and 25. The FDA is considering a similar pediatric authorization for the vaccine in the U.S., and regulators in the European Union are currently reviewing an expanded use filing for the vaccine.

Industry Briefs

FDA Plans to Complete Hundreds of Delayed BIMO Inspections by Year's End

The FDA said last week that it plans to gradually resume on-site clinical trial inspections beginning in July with the intent to be back to normal operations by September.

The agency hopes to complete more than 280 domestic clinical investigator and trial site inspections under its Bioresearch Monitoring (BIMO) program before the end of the fiscal year, as it looks to recover from the pandemic-forced slowdown in 2020.

The agency temporarily postponed routine inspections in March 2020, saying it would conduct only inspections it considered mission-critical.

The FDA's report on inspections shows that the pace of BIMO inspections picked up between October 2020 and March 2021, reaching 236 completed mission-critical inspections, up from 172 mission-critical inspections in the previous six-month period.

The FDA also conducted 29 BIMO priority inspections — certain routine surveillance and for-cause inspections that were not deemed mission-critical by the agency — in the past 12 months; 15 were between March 2020 and September 2020 and 14 between October 2020 and March 2021.

Going forward, the FDA will use a three-tiered system of inspection priority, with Tier 1 covering inspections deemed mission-critical, Tier 2 for higher-priority and Tier 3 for lower-priority inspections. For BIMO, agency crisis or emergency response for-cause work is considered a Tier 1 priority, as are inspections needed for approval for a high-priority product. Tier 2 will apply to BIMO's prioritized domestic inspections and Tier 3 to routine surveillance inspections.

Read the report here: https://bit.ly/3b8OfCN.

Study: COVID-19 Vaccine Trial Consent Forms Were Too Long, Complex

Informed consent forms used for COVID-19 vaccine clinical trials were unnecessarily long, difficult to read and required recipients to have at least a ninth-grade reading level — compared to a norm of sixth-grade — to fully comprehend, according to a new study.

Researchers from the Perelman School of Medicine's Department of Medical Ethics and Policy at the University of Pennsylvania analyzed informed consent documents that AstraZeneca, Johnson & Johnson, Moderna and Pfizer issued during their phase 3 COVID-19 vaccine trials.

The researchers found the informed consent forms averaged nearly 22 pages in length with 8,333 words. It would take an average reader, at a reading rate of 240 words per minute (wpm), nearly 35 minutes

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Industry Briefs

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to finish reading a form, not accounting for any rereading. Adults with a slower reading ability (175 wpm) would require more than 47 minutes to read a form without stopping.

All of the forms studied exceeded a ninth-grade reading level, which is higher than the recommended sixth-grade reading level for such forms.

Read the published study here: https://bit.ly/3h8IYin.

Industry Urged to Publish Unredacted Clinical Trial Data

Sponsors of drug trials should publish clinical trial reports without redacting confidential information, the International Coalition of Medicines Regulatory Authorities (ICMRA) and the World Health Organization (WHO) said in a statement last week.

The organizations said pharma companies should provide voluntary unrestricted access to clinical trial results data "within short timelines and without waiting for legal changes."

ICMRA and the WHO also pressed the industry to provide wider access to clinical data for all new medicines and vaccines, regardless if they were given full approval, conditional approval, emergency-use approval or were rejected.

Read the joint statement here: https://bit.ly/3tnQqsl.

Survey Shows U.S. Trials Embracing Direct-to-Patient Shipment of Supplies

Sponsors say direct-to-patient (DTP) distribution of clinical supplies, including investigational drugs, is an important service to offer and nearly two-thirds say it's essential to successful execution of a clinical trial, according to a new survey, especially as trials become more virtual.

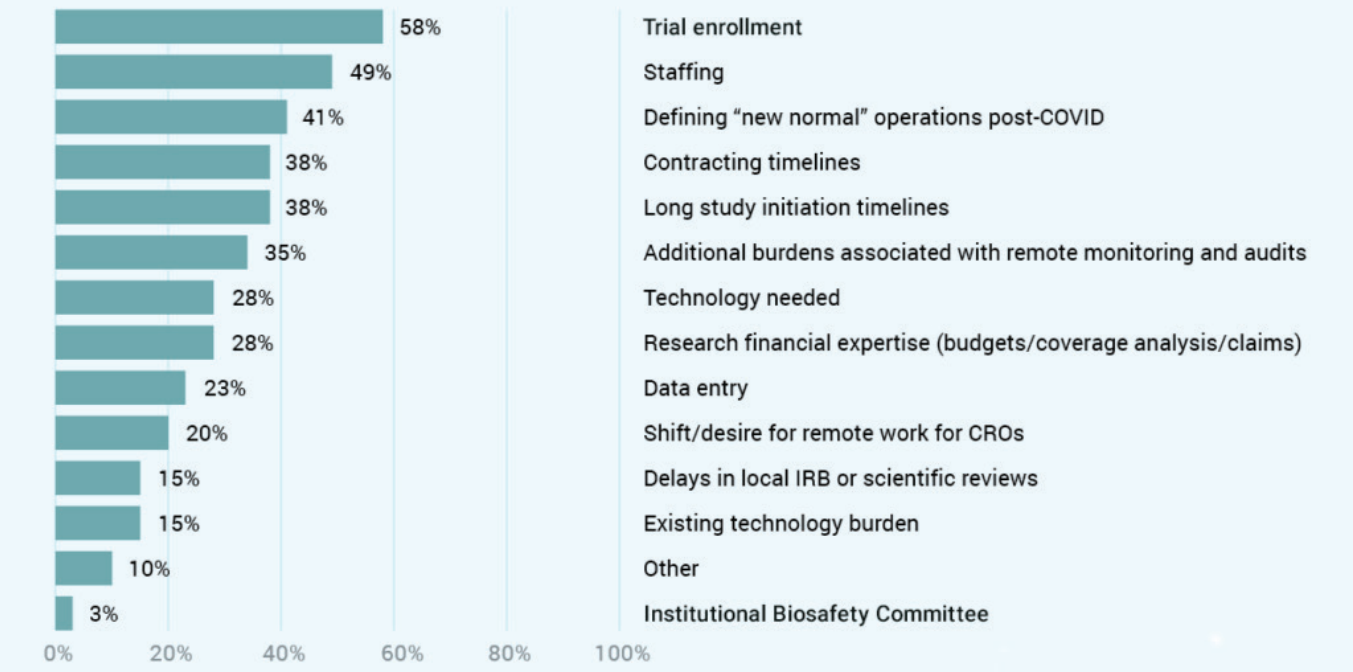
When asked how likely they are to run remote, or home-based, clinical trials that would include remote monitoring of patients through point-of-care devices and testing within the next two to three years, 27 percent of sponsors said between 1 percent and 15 percent of their future studies will be remote, while 25 percent answered that between 15 percent and 30 percent of their studies will be remote. Another 18 percent of respondents said more than 30 percent of their future studies will be remote within that time frame, while 23 percent said they had no plans to run remote studies and 8 percent said they already were.

Catalent and FiercePharma surveyed 234 individuals involved in clinical supply and operations at sponsor companies. Their survey shows sponsors are also more appreciative of the way DTP distribution, often in the form of patient kits, can optimize clinical site operations and improve supply-chain efficiency. Thirty-four percent of sponsors said better inventory management and the ability to pool supplies centrally was the biggest benefit of using a central pharmacy located within the same site as their clinical distribution hub or depot, rather than using a clinical site pharmacist or an off-site central pharmacy to dispense DTP kits. Another 24 percent of respondents said shorter supply chains and fewer handoffs were the most important benefit, while 21 percent said the potential for reducing the number of clinical sites and pharmacists were the biggest perceived gain.

Read the survey here: https://sforce.co/3h8739c.

Data Point

What are the top issues impacting your site today?



Source: WCG Knowledge Base™

Up and Coming

This feature highlights changes in clinical trial organizations' personnel.

Aeterna Zentaris

Michael Teifel, former research and development leader at Cleara Biotech, has been named senior vice president of nonclinical development and chief scientific officer at Aeterna Zentaris.

Azitra

Synthetic biology company Azitra has hired **Francisco Salva** to serve as its new CEO. Salva previously served as CEO of Complexa.

Carmine Therapeutics

Carmine Therapeutics has appointed **Don Haut** to CEO. Previously, Haut served as chief business officer at AskBio.

CatalYm

CatalYm has hired **Phil L'Huillier** to helm the company as its new CEO. L'Huillier previously served as head of the European innovation hub and business development at MSD, formerly known as Merck and Co. in North America.

Codagenix

Johanna Kaufmann, former scientific director of immuno-oncology at GlaxoSmith-Kline, has been named the new executive vice president of oncology at Codagenix.

Engitix Therapeutics

Mike Burbridge has been named the new vice president of oncology and immuno-oncology at Engitix Therapeutics. Burbridge is the former program director of external innovation at Servier Centre for Therapeutic Innovation in Oncology.

Genespire

Julianne Smith has been named chief development officer at gene therapy company Genespire. Smith is the former vice president of translational sciences at Cellectis. Genespire has also appointed **Smaragda Angelidou** to head of chemistry, manufacturing and controls. Angelidou most recently served as senior director of tech transfer and product delivery projects at Autolus.

Himalaya Therapeutics

Himalaya Therapeutics has appointed **Howe Li** to chief medical officer. Previously, Li served as CEO of Tigermed-IntelliPV and currently serves as CEO of DeltaMed.

Invectys

Clinical-stage amino therapy company Invectys has appointed **Praveen Tyle** to president and CEO. Previously, Tyle served as executive vice president for research and development at Lexicon Pharmaceuticals.

Isosceles Pharmaceuticals

William Humphries, former president of Ortho Dermatologics, has been named the new CEO of Isosceles Pharmaceuticals.

Jaguar Gene Therapy

Jaguar Gene Therapy has appointed **Joseph McIntosh** to chief medical officer. McIntosh previously served as chief medical officer at Aruvant Sciences.

KalVista Pharmaceuticals

Paul Audhya has been named chief medical officer at KalVista Pharmaceuticals. Audhya is the former senior vice president of global medical affairs at Arena Pharmaceuticals.

Karyopharm Therapeutics

Richard Paulson has taken over Karyopharm Therapeutics as its newest CEO. Paulson was formerly the executive vice president of Ipsen Pharmaceuticals and CEO of Ipsen North America.

Kyowa Kirin North America

Ernesto Aycardi, former chief medical officer at Xenon Pharmaceuticals, has been named chief development officer at Kyowa Kirin North America (KKNA). KKNA also recently named **Eslie Dennis** the company's new chief medical officer. Dennis previously served as vice president and head of global medical affairs at Roche Tissue Diagnostics.

MOMA Therapeutics

MOMA Therapeutics has hired **Peter Hammerman** to take on the chief scientific officer role. Hammerman previously served as global head of oncology translational research at Novartis Institutes for BioMedical Research.

Myeloid Therapeutics

Myeloid Therapeutics has named **Bruce McCreedy** the company's new chief scientific officer. McCreedy formerly served as senior vice president of cell therapy and immuno-oncology research at Precision Biosciences.

Synthekine

Naiyer Rizvi has been appointed chief medical officer at Synthekine. Previously, Rizvi was Price Family professor of medicine, director of thoracic oncology and co-director of cancer immunotherapy at Columbia University Medical Center.

Telix Pharmaceuticals

Telix Pharmaceuticals has hired **Richard Valeix** to take on the role of president of Europe, Middle East and Africa (EMEA). Valeix previously served as general manager for France, Switzerland, Belgium, Netherlands and Luxembourg as well as global head of marketing and sales for Novartis' Advanced Accelerator Applications.

Theseus Pharmaceuticals

Tim Clackson has been named CEO of Theseus Pharmaceuticals. Clackson is the former president and chief technology officer at Xilio Therapeutics.

Verge Genomics

Verge Genomics has hired **Robert Scannevin** to take on the role of chief scientific officer. Scannevin previously served as head of research at Yumanity Therapeutics.

Features

Oncology Trials

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increasingly selective criteria. That hurdle, combined with the high number of sites and countries involved in the trials, "underscores the challenges associated with finding, competing for and enrolling patients [in oncology]," CSDD said.

"The design, executional complexity and customization [of oncology trials] is driven in large part by the genetic targeting of, and competition for, patients," CSDD senior research analyst Zachary Smith, a coauthor of the study, told *CenterWatch Weekly*. "This has impacted cycle times and enrollment performance substantially, particularly in two key areas: the larger number of countries and investigative sites, and the total number of data points."

Success at finding eligible trial participants was far more challenging for oncology trials, especially in phase 2, where only 14 percent of participants screened were enrolled and eventually completed the trial compared to 54 percent in nononcology trials.

To overcome enrollment challenges, phase 2 and phase 3 oncology protocol designs typically have larger numbers of protocol deviations and substantial amendments, CSDD found. For example, phase 2 oncology studies between 2014 and 2019 averaged 121.8 protocol deviations compared to 75.8 for other studies. The number of unplanned and unbudgeted substantial amendments made to phase 2 and phase 3 oncology studies were 50 percent to 70 percent higher than for other drugs.

The number of drugs in clinical trials worldwide grew 4.1 percent annually between 2000 and 2020, but CSDD found the number of oncology drug trials grew at a faster rate, 6.5 percent, compared to nononcology drugs, which grew 3.6 percent annually. Consequently, oncology drugs accounted for a 23.1 percent share of all drugs in clinical development in 2020, up from 14.8 percent in 2000.

Although oncology drug trials take longer, sites address the problem by doing many activities in parallel. The mean number of days in phase 1, phase 2 and phase 3 trials between 2014 and 2019 were 1,018, 1,482 and 1,769 days, respectively, for oncology drugs. That compares to 573, 991 and 1,214 days, respectively, for nononcology drugs. But CSDD researchers found that an entire oncology drug development program — from filing an investigational new drug application, through all three trial phases to application for FDA approval — is on average only five months longer than other drug development programs. The overall timeline is trimmed down, according to CSDD, by conducting many phase 2 and 3 activities, especially internal reviews, in parallel.

CSDD also found that oncology protocols undergo many more internal reviews prior to finalization, particularly in phase 3, compared to protocols for other drugs. Between 2014 and 2019, phase 2 oncology protocols went through an average of 4.8 internal reviews compared to 3.9 reviews for other protocols. Phase 3 oncology protocols had an average of 9.7 reviews compared to 5.9 reviews for other protocols. At the same time, the number of endpoints, eligibility criteria and distinct procedures for oncology drugs were either comparable or lower than that for other drugs.

Total endpoints in phase 2 and phase 3 oncology protocols during the five-year period studied averaged 18.5 and 14.6, respectively, compared to 21.6 and 21.0 in nononcology. The total number of eligibility criteria averaged 29.3 and 30.2 in oncology protocols, respectively, vs. 32.3 and 30.1 in other protocols. And the number of distinct procedures averaged 34.4 and 34.1 in oncology protocols compared to 31.8 and 35.1 in nononcology protocols.

Meanwhile, the average number of pages in the protocol when the study is completed was considerably higher for oncology drugs (121.3 in phase 2, 130.3 in phase 3) compared to other drugs (110.2 in phase 2, 111.2 in phase 3), reflecting cancer trials'"scientific and executional complexity," CSDD said.

Despite the complexity, phase 3 oncology trials started faster between 2014 and 2019 — 140.2 days on average compared to 171.5 days for other drugs — because "sponsors and their collaborators have become more proficient at executing protocols," according to CSDD. However, the time between a trial's completion and the completion of a study report about it was much longer in phase 3 oncology trials (213.5 days) compared to nononcology (154.1 days), due to a growing share of trials involving "more sophisticated crossover, adaptive and master protocol designs," CSDD said.

CSDD researchers did find that regulatory reviews for oncology drugs were 2.5 months shorter, on average, than for nononcology drugs "as the former frequently benefit from expedited review pathways and are more than twice as likely to receive priority review status."

Smith said several of the study's findings surprised CSDD researchers. "All of them relate to the extent to which companies must go to find and enroll patients for cancer clinical trials today," he said. "What I found surprising was how consistently the increasing complexity of oncology trials was outpacing the increasing complexity of nononcology trials."

The CSDD report was based on analyses of clinical trial data from sponsors, as well as data on 261 new drugs and biologics approved by the FDA's Center for Drug Evaluation and Research between 2014 and 2019. Protocol design and performance data from 223 protocols were provided by 20 major pharmaceutical and biotechnology companies.

Features

Study Startup Times

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NGMC also speeds up the process by submitting IRB applications in parallel to its contract and budget negotiations, Jones said.

Jill Johnston, president of study planning and site optimization for WCG, says the parallel submission process is an effective strategy, but it isn't always possible at larger institutions.

"They sometimes have SOPs or processes that prohibit that," she said. "They might need to negotiate the contract first before they'd ever consider sending it to the IRB or vice versa. However, this adds so much time to the overall process."

"We found that one aspect of streamlining the clinical trial study startup process was to move the legal reviews in-house," Jones said. "We have to work on a weekly basis, sometimes twice a week, with our legal team to ensure that they're reviewing our contracts in a timely manner. That has made an enormous difference in the time to study startup."

NGMC, a site network of four hospitals, attributes its success to a protocol feasibility checklist that helps them evaluate different areas of impact the trial could have on their sites.

Kira Harris, senior CRC for the Ohio Sleep Medicine Institute, agreed that a careful protocol review before accepting a trial is crucial, saying "every protocol has its own quirks and the best way to avoid deviations is to plan ahead, teasing out all these little details ahead of time and really thinking through how you're going to execute a visit and how you're going to remember all of the details."

Harris said sites need to determine if their staff can execute the protocol, who needs training, who should do what and who needs access. "It's good to think through what staff you realistically need without going overboard and then making sure those staff are available when you need them."

As contract and budget negotiations with sponsors get under way, Jones said either the research nurse manager or the principal investigator will then present the feasibility assessment to an interdisciplinary research operations committee (ROC) for their approval. The ROC includes representatives from the research team, IT and physicians, as well as clinical service line leaders and finance and compliance experts from the hospital system.

Jones said the ROC doesn't reject studies often — only about 5 percent of the time. "Those that are not approved by the ROC have glaring deficiencies in equipment or software that's required to conduct a study that the operational service line leaders cannot provide. We try to mitigate any of those denials prior to them hitting that committee through the department level discussions." Studies are also declined if there is insufficient staff to handle the workload, she said.

NGMC's approach did attract pushback from some groups, Jones conceded. "We have a central laboratory in our health system," she said. "In the beginning, they said they were very busy and they just did not have the bandwidth to attend meetings. That ended up being a conversation between the director of the lab and myself to say, 'I know you're very busy, you're not always able to attend these meetings. How can we communicate with you to make sure that you are not blindsided by the operations of the clinical trial?' It sometimes comes down to working with other groups and speaking their language on when you roll out any sort of new process. For some busy clinical areas, their first priority is not a clinical trial — their first priority may be a clinical service they're providing, and they have to meet certain metrics based on that."

Harris suggested that CRCs ask a site's clinical research associate for a visit-tracker spreadsheet to determine how many times a patient will ultimately visit a site and whether such visits would have any scheduling conflicts. CRCs should also conduct a mock visit to a site, walking through the entire protocol — including the informed consent and questionnaire processes.

Darlene Deecher, vice president for clinical development at AiViva BioPharma, said conducting a mock visit was great advice for sites. "I think sponsors should, when they're training with their CROs, literally suggest a mock visit, especially when the protocol is complicated. That would be helpful, rather than getting your first patient in and then finding out something wasn't done according to the protocol."

Drug & Device Pipeline News

Company	Drug/Device	Medical Condition	Status	Sponsor Contact
COVID-19 Trials and Actions				
HDT Bio Gennova Biopharmaceuticals	RNA-based COVID-19 vaccine	COVID-19	first patient dosed in phase 1/2 trial in India	hdt.bio
Adagio Therapeutics	ADG20 vaccine	COVID-19	phase 2/3 trial initiated	adagiotx.com
Novavax	NVX-CoV2373 vaccine	COVID-10 in patients age 12 to 17	pediatric expansion of phase 3 clinical trial initiated	novavax.com
Other Trials and Actions				
Genascence	GNSC-001	osteoarthritis	dosing of all patients in phase 1 trial complete	genascence.com
Neoleukin Therapeutics	NL-201	advanced solid tumors	phase 1 trial initiated	neoleukin.com
NervGen Pharma	NVG-291	nerve damage	first patient dosed in phase 1 trial	nervgen.com
Vivace Therapeutics	VT3989	refractory metastatic solid tumors	first patient dosed in phase 1 trial in the U.S. and Australia	vivacetherapeutics.com
Repare Therapeutics	RP-6306	PKMYT1 inhibitor-sensitive cancers	first patient dosed in phase 1 trial	reparerx.com
Landos Biopharma	NX-13	ulcerative colitis	first patient dosed in phase 1b trial	landosbiopharma.com
Vaxart	oral tablet norovirus vaccine	norovirus	first patient enrolled in phase 1b boosting regimen trial	vaxart.com
Cerecor	CERC-007	adult-onset Still's disease	first patient dosed in phase 1b trial	cerecor.com
Treadwell Therapeutics	CFI-400945	PLK4 inhibitor in patients with leukemia	first patient dosed in phase 1b/2 trial	treadwelltx.com
Merus	MCLA-129	advanced lung cancer and other solid tumors	first patient treated in phase 1/2 clinical trial	merus.nl
Peptomyc	OMO-103 lead compound	advanced solid tumors	first patient dosed in phase 1/2 trial	peptomyc.com
Carmot Therapeutics	CT-868	treatment of overweight and obese patients with Type 2 diabetes	IND for a phase 2 trial granted by the FDA	carmot-therapeutics.us
City of Hope	mushroom powder tablets	prostate-specific antigen levels	recruiting begun in phase 2 trial	cityofhope.org
Tessa Therapeutics	autologous CD30 CAR-T in relapsed/refractory cHL	relapsed or refractory Hodgkins lymphoma	enrollment of 12-patient cohort complete in phase 2 trial	tessatherapeutics.com
Galmed Pharmaceuticals	Aramchol	nonalcoholic steatohepatitis and fibrosis	IND for phase 3 trial granted by China's National Medical Products Administration	galmedpharma.com
Catalyst Biosciences	MarzAA	hemophilia A or B with inhibitors	first patient dosed in phase 3 trial	catalystbiosciences.com

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Drug & Device Pipeline News

(continued from page 10)

Company	Drug/Device	Medical Condition	Status	Sponsor Contact
Isofol Medical	Arfolitixorin	first-line metastatic colorectal cancer	recruiting complete in global phase 3 trial	isofolmedical.com
ObSeva	Yslty	moderate-to-severe endometriosis-associated pain	enrollment complete in phase 3 trial	obseva.com
Praxis Precision Medicines	PRAX-562	SCN2A development and epileptic encephalopathy	Orphan Drug designation granted by the FDA	praxismedicines.com
Cerapedics	P-15L	bone graft in cases of degenerative disc disease	Breakthrough Device designation awarded by the FDA	cerapedics.com
AstraZeneca	Farxiga (dapagliflozin) oral tablets	kidney function decline, kidney failure, cardiovascular death and hospitalization for heart failure in adults with chronic kidney disease who are at risk of disease progression	approved by the FDA	astrazeneca.com
Chiesi Global Rare Diseases	Ferriprox (deferiprone)	transfusional iron overload caused by sickle cell disease or other anemias in adults and children ages three years and older	approved by the FDA	chiesiglobalrarediseases.com
Merck	Keytruda in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy	locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma	approved by the FDA	merck.com

Research Center Spotlight

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Boston Clinical Trials

Boston, MA
617.477.4868
bct@bostontrials.com

Boston Clinical Trials is an independent multispecialty, women-owned/operated clinical research center.

Great Lakes Medical Research

Westfield, NY
716.326.4890
sbutton@glmr.info

Great Lakes Medical Research is a division of Westfield Family Physicians and conducts phase 2 to 4 clinical trials in an outpatient clinical setting, focusing on patient care and education.

Clinical Physiology Associates

Fort Myers, FL
239.936.4421
studycenter@clinphys.com

Clinical Physiology Associates, a multispecialty research group, has been conducting clinical trials for the pharmaceutical and medical device industries for 35+ years.

Northwell Health

Manhasset, NY
516.253.7753
neurosurgeryresearch@northwell.edu

Affiliated with North Shore University Hospital's Department of Neurosurgery, Northwell operates federal and industry-sponsored trials and is capable of participating in inpatient trials as well as outpatient at our local physician practices.

Doctors Research Network

South Miami, FL
305.662.1444
drn@miamifoot.com

Doctor's Research Network is a dedicated research center focusing mainly on lower extremity conditions. Our investigators have more than 25 years of experience in conducting clinical trials.

Quest Research Institute

Farmington Hills, MI
248.957.8940
dolly@questri.com

Quest Research Institute is based on a foundation of more than 20 years of clinical research experience and the successful completion of more than 350 phase 1 through 4 clinical protocols.

FXM Clinical Research Miami

Miami, FL
305.220.5222
info@fxmresearch.com

FXM Research is a privately owned and operated clinical research site that conducts phase 1, 2, 3 and 4 trials specializing in dermatology. Based in Miami, FXM also has branches in Fort Lauderdale and Miramar, Fla., Belize and St. Lucia.

Rainier Clinical Research Center

Renton, WA
425.251.1720
rcrc@rainier-research.com

Rainier Clinical Research Center is a privately owned, independent research clinic conducting phase 1 through phase 4 clinical trials of both drugs and devices.

wcg CenterWatch
www.centerwatch.com

300 N. Washington St., Suite 200 • Falls Church, VA 22046-3431
Phone: 866.219.3440 or 617.948.5100
Customer Service: customerservice@centerwatch.com

Editorial Director: Beth Belton, 703.538.7641, bbelton@wcgclinical.com
Reporter: Charlie Passut, 703.538.7664, cpassut@wcgclinical.com
Sales: Russ Titsch, 813.767.6463, russ.titsch@centerwatch.com