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In this issue

Patient Recruiting Expert Offers Tips for Getting the Most Out of Your Budget

By William Myers

Recruiting patients for a clinical trial can be a long and expensive process, but smart trial sponsors and sites use a mix of traditional and new media in order to maximize their recruiting budget, a veteran patient recruiting consultant said.

Steven Pyffer, senior director of patient outreach at ThreeWire, a Minneapolis-based clinical trial patient recruiting company, offered some tips on getting the most from recruiting budgets during a May 30 WCG webinar: Cutting the Costs of Clinical Trial Recruitment.

Among his tips:

- Radio is scalable, Pyffer said, and can be "intrusive" – i.e., an ad forces itself on to a potential patient's attention because they're part of "a captive audience." Pyffer says that money spent on radio gets the best return when it is focused on targeted stations that are unique or nearly unique to that market — a smooth jazz station or a talk radio station because listeners are likely committed to the niche and are less likely to change channels. The most efficient use of ad buys on radio are promotional spots during the day — preferably morning or evening rush hours — and only during weekdays.
- Television ad buys should focus on local network stations, not cable, Pyffer

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Big Data and Technology Increasingly the Focus of Clinical Trial Service Providers

By Suz Redfearn

The media buzz last week on reported layoffs at IBM Watson Health ranged from calling it a "bloodbath" to something more surgical. Eventually, IBM Watson Health confirmed the layoffs at some of its acquired businesses, but wouldn't say how many, and said it was continuing to hire in other new areas.

The volatility was a bit of a surprise as IBM Watson Health has become a major player in the healthcare space over the past couple of years, focusing on combining its artificial intelligence capabilities with acquisitions and partnerships with healthcare Big Data services.

In March, Watson announced that a venture with the Mayo Clinic for matching patients to clinical trials helped increase enrollment by an average of 80 percent in studies of systemic therapies for breast cancer. Over 11 months of the project, the time needed to screen an individual patient for clinical trial matches also fell when compared to traditional manual methods, they said in a joint press release.

The business mergers of technology and Big Data firms in healthcare mirrors a trend in the clinical trials space, as many large CROs have dramatically transformed themselves to provide more services on both fronts.

This is especially pronounced among the top seven largest CROs, which all have more

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Industry Briefs

Trump Signs Right-to-Try Into Law

President Trump on Wednesday signed into law the Right-to-Try Act establishing a pathway for terminally ill patients to use non-FDA-approved drugs, calling the legislation "great for the people" and a "fundamental freedom," but it was a castoff remark he made about lower drug prices that had everyone talking. Referring to the legislation, Trump thanked HHS Secretary Alex Azar and FDA Commissioner Scott Gottlieb at the signing ceremony and also credited Gottlieb for his efforts to shorten the development and approval process. "You have a lot of things in the wings that frankly if you moved them up, a lot of people would have a great shot," he said, adding that "hundreds of thousands of lives" would be saved by the new legislation. The law allows terminally ill patients who have exhausted all other options to try experimental treatments that have not yet received FDA approval. Eligible treatments must have completed a Phase I trial, be in the process of active development, and be the subject of an NDA, BLA or IND. The new law has its critics among industry and patient advocacy groups with reservations about its potential impact on patient safety. The Association of Clinical Research Organizations came out strongly against the bill's passage, calling the legislation "deeply flawed."

ACRO argued the bill does not go far enough to protect patients and "compromises the clinical trial process [and] undermines the FDA's authority to assess safety and effectiveness." After several iterations, the version of the bill that finally passed is "devoid of all patient protections" and "does not set a standard for informed consent, has a much broader definition of eligibility and contains vastly weaker reporting requirements," according to the National Organization for Rare Disorders. "Thus, not only will this legislation be ineffective, as all Right to Try laws are, it will also present a danger to the many patients we represent." In a statement following the signing ceremony, Gottlieb said the FDA recognizes "the important balance between making sure patients have the assurances Congress intends, while enabling timely access to promising treatments in these devastating circumstances." He said the agency will "implement this new law consistent with these longstanding values."

During the ceremony, Trump also made a side remark that unnamed major drugmakers would announce "voluntary massive drops in prices" in "two weeks" adding that "for the first time ever in this country, there will be a major drop in the cost of prescription drugs." At the White House daily press briefing Wednesday, Press Secretary Sarah Sanders said the White House could not provide further details, "but we do expect some specific policy pieces to come out on that soon." Industry groups appeared puzzled as to what the president was referencing, although the Association for Accessible Medicines responded to the remark in a tweet, saying it looks forward to continue working to reduce prices and out-of-pocket costs. PhRMA declined to comment and BIO did not respond to a comment request.

Age, Kidney Health May Be Keeping Women from Heart Failure Trials, Researcher Finds

Age and relatively poor kidney health may be keeping women from enrolling in heart failure clinical trials, a Swedish researcher says. Just 21 percent of patients enrolled in the recent PARADIGM-HF were women and researchers at Umeå University are blaming the trials' target doses of angiotensin-converting-enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB), which the researchers say "disproportionately excluded women." "In the community-based heart failure population, just 26 percent of women with heart failure and a reduced ejection fraction could reach the target dose compared to 43 percent of the men," lead researcher Helena Norberg wrote for her colleagues in a study published in the journal of the European Society of Cardiology on Monday. That, in turn, may be due to the facts that women in the subject population tended to be significantly older (81 years old for women versus 75 years old for men) and have worse kidney function than the men, Norberg said. "Future trials in heart failure should use achievement of maximum tolerated doses, rather than fixed target doses, as entry criteria to ensure that women are more represented," Norberg wrote.

Researchers Struggle to Make Informed Consent Forms Understandable to Patients, Study Finds

Researchers are still struggling to come up with informed consent paperwork that is accessible to their patients, a team of Mexican researchers has found. The team examined informed consent forms for industry-sponsored multinational clinical trials for arthritis over a 17-year period and then tested patients' perceptions about the process they were enrolling in. Researchers concluded that all of the informed consent forms were anywhere from "somewhat difficult to read" or "average" in difficulty. The mean "readability" score for all the forms was 57, "without significant changes from 1999 to 2016," lead author Hector de la Mora-Molina wrote for the team. There still remains a gap between patients' claimed understanding of informed consent and their knowledge of basic ideas. "The disparity between the readability" of informed consent forms and patients' health literacy "continues even after decades of attempts of regulatory agencies and numerous published suggestions," the researchers concluded. The study was published in Seminars in Arthritis & Rheumatism.

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said. Like radio, it's intrusive, and the best value ad buys are again during business hours. What's key to a television ad buy is a website with a simple, memorable URL. In markets where only a single site is running a trial, television is less valuable "because that person might be calling from four hours away," Pyffer said.

- Newspapers aren't as scalable as broadcast media and they're less intrusive, but they're "definitely part of the mix" when considering a recruiting budget, Pyffer said. The best buys tend to be in commuter papers of the kind handed out at mass transit stations, he said.
- Websites can be valuable, but the landing page and URL should be something that's easy to recall and be markedly different from a branding name. A trial testing a new glaucoma medicine, for instance, might use the URL myeyecare.com, for instance, Pyffer said.
- Facebook can be effective (although Twitter does not seem to be) but some sponsors are leery of public comments on the site, Pyffer said.
- In any media, it can be important to mention compensation available to patients, Pyffer said. Sponsors can be a little leery of that, too, Pyffer said, but it has proven again and again to be a valuable recruiting tool. The exception is when the compensation on offer is too low; when sponsors are offering a range of compensation depending on patients' circumstances, recruiters should use phrases such as "up to" the maximum amount in discussing compensation. In February, the FDA attempted to bring some clarity to the issue with updated guidance to institutional review boards and clinical investigators clearly allowing reimbursements to patients in clinical trials for lodging and travel.

"Websites can be valuable, but the landing page and URL should be something that's easy to recall and be markedly different from a branding name."

—Steven Pyffer, senior director of patient outreach, ThreeWire

Pyffer also had some tips for things to avoid. In considering whether to hire a recruiter, sponsors should steer clear of those who focus on clinical trial "awareness" rather than patients, he said.

"That's a red flag," said Pyffer. "Awareness: That means literally nothing to me. The only measure that really counts is enrolled patients. That's the only thing."

Any recruiter, he argued, should be able to offer sponsors or sites raw numbers of patients successfully enrolled in trials. They should also be able to offer something like real-time tracking of patients enrolling in a given trial.

Others are a bit more sanguine about the importance of awareness. For example, programs such as PopUp Star, a global competition designed to help grow clinical trials at the grassroots level focus more on awareness. In this program, during a 10-day period in early April, teams competed in Boston, MA; Charleston, SC; Winston-Salem, NC; and Sydney, Australia, to engage more than 1,500 individuals.

Pyffer's not buying it. He said groups that are selling sponsors or sites on awareness are selling "hocus-pocus."

"The only thing I want to know about is how many patients were enrolled for whatever protocol," he says.

Once referrals start coming in, though, it's essential that they're being directed to a professional, well-run site, Pyffer said. The best measure is how quickly sites make contact after a referral — first contact should be made within hours, not days, he said.

"If you're not able to respond to a referral within a day or so, there's really no reason to invest the money," he said. "So much time is elapsing and the percentage of the person moving on is a lot less."

"You have to see if they're truly engaged," Pyffer said of sites. "The one advantage we have is that everything is tracked through mypatient.com, so we can see how they're doing with processing of referrals."

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Big Data and Technology (continued from page 1)

than $1 billion in annual revenue. Data from the Tufts Center for the Study of Drug Development (CSDD) shows that a whopping 72 percent of the transactions (mergers, acquisitions, strategic partnerships) in the upper end of the CRO space since 2015 were "nontraditional" —buying or merging with entities that are not other CROs, or being acquired by organizations outside the space.

The driver? Competition.

It's fierce, said Doug Peddicord, executive director of the Association of Clinical Research Organizations (ACRO), so CROs are now aggressively "stacking vertically" to provide as many services as possible in an effort to stand out.

And, said Neal McCarthy, managing director of investment banking firm Fairmount Partners and close watcher of the CRO space, many of these unusual acquisitions have been designed to take better advantage of Big Data.

"Among the potential benefits is squeezing value out of the data that is already being collected," said McCarthy.

Peddicord agrees. "All those mountains of data, which previously were just mountains of data, now can be used."

Here are key examples of odd bedfellows now in the space:

- The lab company LabCorp bought the CRO Covance in 2015. At first, this one was a head scratcher, said Ken Getz, founder and board chair of the Center for Information and Study on Clinical Research Participation (CISCRP) as well as associate professor and director of sponsored programs at Tufts CSDD. "It baffled the market, but eventually it was realized that it's a pretty shrewd move because it gives Covance access to a lot of de-identified patient data and the use of the blood monitoring services of LabCorp."

It also works well for LabCorp, which can now reduce its reliance on government and large insurance companies, and add a group of giant customers who will pay top dollar for speed and great service — in an industry that's seeing prices increase, said McCarthy.

- Quintiles, the biggest CRO in the space, "merged with" but essentially was bought by market and sales research services company IMS Holdings in 2016, essentially pairing a commercialization company with a huge CRO. The new entity became IQVIA.

Peddicord said this was "one of the more unusual combos" at first blush, but it soon became clear that the focus was on capturing real-world evidence to drive innovations and fill out the vertical stack.

- The CRO PPD bought two very large site groups, CRA/Radiant (in 2015) and Synexus (in 2016). And CRO ICON bought the robust site group PMG Research in 2015.

A few CROs tried a similar strategy about 15 years ago, buying up site groups, but back then the efforts crashed and burned, said Peddicord. Now, though, technology has evolved to make a move like this actually make sense.

"Technology now has the potential to allow sites to be a part of the CRO business based not on people services, but on data services," said Peddicord.

The evolution of the CRO space is permanent. That is reflected in changes at ACRO, which recently altered their bylaws to allow in not just companies that conduct clinical research on behalf of sponsors, but companies and organizations that "support the conduct of clinical research."

How are CROs' customers reacting? Do sponsors favor these greatly expanded CROs?

It's too soon to tell. Said Getz, sponsors are still in the process of trying to understand these new animals in the marketplace, and uptake could be slow as the biopharma industry is typically very conservative and squeamish about adopting anything new.

Peddicord said the jury is still out, for now, on how sponsors will react. But he added that he eventually expects to see these massive vertically and horizontally expanded CROs — with their very robust data offerings — become very popular among sponsors in this age of value-based drug pricing.

"Ultimately, drugs' cost will be based on the value they create in the healthcare system, and in order to get to value pricing, you have to do value contracting between payers and pharmaceutical companies," he said. "In order to get to that, you have to do value-based development as well. I think there's where the data revolution really is a necessary condition because it's the mountains of real world evidence and outcomes data that will drive the value conversation between providers both of services and manufacturers of drugs, and the payers."

Drug & Device Pipeline News

Company	Drug/Device	Medical Condition	Status	Sponsor Contact
NeoImmune Tech, Inc.	HyLeukin-7	brain cancer	Phase I trial initiated enrolling up to 75 subjects	neoimmunetech.com
Atox Bio	Reltecimod	Abdominal sepsis and Stage 2/3 Acute Kidney Injury (AKI)	Phase II trial initiated enrolling 120 subjects at approximately 50 level 1 trauma centers in the U.S.	atoxbio.com
Atox Bio	Reltecimod	Necrotizing Soft Tissue Infections (NSTI)	Phase III trial initiated enrolling 290 subjects at approximately 70 level 1 trauma sites in the U.S.	atoxbio.com
Synedgen	Catasyn Advanced Technology Wound Hydrogel	wound care	510(k) clearance granted by the FDA	synedgen.com
Novartis	Promacta (eltrombopag)	Severe aplastic anemia (SAA)	sNDA approval granted by the FDA	novartis.com
Nektar Therapeutics	NKTR-181	chronic lower back pain	NDA approval granted by the FDA	nektar.com
Sage Therapeutics	brexanolone (SAGE-547)	postpartum depression (PPD)	NDA approval granted by the FDA	sagerx.com
MicroVention, Inc.	Low profile Visualized Intraluminal Support (LVIS) and LVIS Jr. neuro stent devices	wide-necked saccular intracranial aneurysms	PMA granted by the FDA	microvention.com
Dova Pharmaceuticals	Doptelet (avatrombopag)	thrombocytopenia in adults with chronic liver disease scheduled to undergo a procedure	Approval granted by the FDA	dova.com
TherapeuticsMD	Imvexxy (TX-004HR)	moderate-to-severe dyspareunia (vaginal pain associated with sexual activity), symptom of vulvar and vaginal atrophy (VVA)	Approval granted by the FDA	therapeuticsmd.com
BioMarin Pharmaceutical	Palynziq (pegvaliase-pqpz)	Henylketonuria (PKU)	Approval granted by the FDA	biomarin.com
Zeto, Inc.	zEEG	dry electrode electroencephalography (EEG) headset	Approval granted by the FDA	zeto-inc.com
Astellas Pharma Inc.	gilteritinib	Relapsed or refractory Acute Myeloid Leukemia (AML) with a FLT3 mutation	Priority Review granted by the FDA	aastellas.us
Pfizer	Xalkori (crizotinib)	Metastatic non-small cell lung cancer (NSCLC) with MET exon 14 alterations with disease progression on or after platinum-based chemotherapy	Breakthrough Therapy Designation granted by the FDA	pfizer.com
Pfizer	tafamidis	Transthyretin cardiomyopathy	Breakthrough Therapy Designation granted by the FDA	pfizer.com
Yamo Pharmaceuticals, LLC	L1-79	autism spectrum disorder (ASD)	Fast Track Designation granted by the FDA	yamopharma.com
Genea Biocells	GBC0905	Facioscapulohumeral muscular dystrophy (FSHD)	Orphan Drug Designation granted by the FDA	geneabiocells.com

Trial Results

Realm Therapeutics Completes Enrollment in Study for Atopic Dermatitis

Realm Therapeutics announced that the Company has completed enrollment in its Phase II study of PR022, Realm's first-in-class topical IL-4 / IL-13 inhibitor, for the treatment of Atopic Dermatitis. The trial is being conducted in the U.S. The Phase II study is a randomized, double-blind, vehicle-controlled, multicenter, parallel-group study assessing the safety and efficacy of multiple doses of PR022 in 122 adult patients with mild-to-moderate Atopic Dermatitis. Multiple endpoints are being explored, including Eczema Area and Severity Index (EASI), an investigator-assessed tool used to measure the extent (area) and severity of atopic eczema; Investigator Global Assessment (IGA), an investigator-assessed instrument measuring severity of Atopic Dermatitis on a 5 grade scale; as well as additional assessments of pruritus and quality of life. In pre-clinical models of Atopic Dermatitis, PR022 has shown immunomodulatory effects, without the same immunosuppressive side effects often associated with steroids, which are the current standard of care.

Genentech Reports Positive Results for IMpower130 Study

Genentech announced that the Phase III IMpower130 study met its co-primary endpoints of overall survival (OS) and progression-free survival (PFS). The co-primary endpoints were PFS as determined by the investigator using RECIST v1.1 in all randomized people without an EGFR or ALK mutation (intention-to-treat wild-type; ITT-WT) and OS in the ITT-WT population. The combination of TECENTRIQ (atezolizumab) plus chemotherapy (carboplatin and ABRAXANE [albumin-bound paclitaxel; nab-paclitaxel]) helped people live significantly longer compared to chemotherapy alone in the initial treatment of advanced non-squamous non-small cell lung cancer (NSCLC). IMpower130 is a Phase III, multicenter, open-label, randomized study evaluating the efficacy and safety of TECENTRIQ in combination with carboplatin and nab-paclitaxel versus chemotherapy (carboplatin and nab-paclitaxel) alone for chemotherapy-naïve patients with Stage IV non-squamous NSCLC. The study enrolled 724 people who were randomized equally (1:1) to receive TECENTRIQ plus carboplatin and nab-paclitaxel (Arm A), or Carboplatin and nab-paclitaxel (Arm B, control arm). During the treatment-induction phase, people in Arm A received TECENTRIQ and carboplatin on day 1 of each 21-day cycle, and nab-paclitaxel on days 1, 8 and 15 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit, whichever occurred first. People received TECENTRIQ during the maintenance treatment phase until loss of clinical benefit was observed. During the treatment-induction phase, people in Arm B received carboplatin on day 1 and nab-paclitaxel on days 1, 8 and 15 of each 21-day cycle for 4 or 6 cycles or until disease progression, whichever occurred first. People who were consented prior to a protocol revision were given the option to crossover to receive TECENTRIQ as monotherapy until disease progression.

Atox Bio Announces Enrollment of First Patient in Study for Acute Kidney Injury

Atox Bio announced that the first patient has been enrolled in the Phase II REAKT (Reltecimod E fficacy for Acute Kidney Injury T rial) study. The Phase II randomized, placebo-controlled study, will enroll 120 patients with abdominal sepsis and Stage 2/3 Acute Kidney Injury (AKI) (as described by KDIGO criteria) at approximately 50 level 1 trauma centers in the U.S. Patients will receive Reltecimod or placebo, administered as a single dose within 6 hours of the diagnosis of AKI, in addition to standard of care treatment. Reltecimod (AB103) is a rationally designed peptide that binds to the CD28 co-stimulatory receptor and restores the host's appropriate immune response to severe infections. By modulating, but not inhibiting, the body's acute inflammatory response, Reltecimod is designed to help control the cytokine storm that could otherwise quickly lead to morbidity and mortality. The primary endpoint is complete recovery from Stage 2/3 AKI, defined as alive, free of dialysis and return of serum creatinine to <150 percent of reference baseline. The primary end point is a clinical composite that evaluates both the local and systemic components of this disease. Important secondary endpoints include survival, resolution of organ dysfunction and other health economic outcomes such as days on the ventilator, days in the ICU, duration of hospital stay and need for hospital readmission.

Novo Nordisk Announces Results of PIONEER 2 Trial

Novo Nordisk announced the headline results from PIONEER 2, the second Phase IIIa trial with oral semaglutide for treatment of adults with type 2 diabetes. Oral semaglutide is a new GLP-1 analogue taken once daily as a tablet. PIONEER 2 was a 52-week, randomized, open-label, active-controlled, parallel-group, multicentre, multinational trial with two arms comparing the efficacy and safety of oral semaglutide with empagliflozin in people with type 2 diabetes mellitus, inadequately controlled on metformin. 816 people were enrolled in PIONEER 2 and randomized 1:1 to receive either 14 mg oral semaglutide or 25 mg empagliflozin once daily. The confirmatory endpoints were change in HbA1c and body weight from baseline to week 26. Key secondary endpoints included change in HbA1c and body weight from baseline to week 52. The most common adverse event for oral semaglutide was mild to moderate nausea, which diminished over time. The proportion of subjects who discontinued treatment due to adverse events was 11 percent for people treated with 14 mg oral semaglutide compared to 4 percent for people treated with 25 mg empagliflozin.

JobWatch

The Source for Clinical Research Jobs and Career Resources

Twice monthly, *CWWeekly* provides featured listings of clinical research job openings, upcoming industry conferences and educational programs from **JobWatch**, CenterWatch's online recruitment website for both clinical research employers and professionals.

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Jobs via Kelly Services

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Minneapolis, MN

Clinical Operations Program Leader
Cambridge, MA

Expert Clinical Manager III
East Hanover, NJ

Clinical Research Coordinator (CRC)
Phoenix, AZ

Clinical Affairs Manager
Redwood City, CA

Scientific Reviewer — NIH
Bethesda, MD

Clinical Research Associate
Emeryville, CA

Medical Administrative Assistant
Birmingham, MI

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More Jobs

Regulatory Data Specialist
National Institute of Allergy and Infectious Diseases
Bethesda, MD

Manager of Clinical Research Operations — Hem-Onc Clinical Trials
Penn State Health - Milton S. Hershey Medical Center
Hershey, PA

Consultant-Trial Capabilities
Eli Lilly and Company
Indianapolis, IN

Clinical Research Specialist
Planned Parenthood of Southern New England
New Haven, CT

Clinical Research Coordinator
Company Confidential
New York, NY

[VIEW ALL JOB LISTINGS]

Academic Programs

Boston College
Clinical Research Certificate Program
Chestnut Hill Campus, Newton, MA

Drexel University College of Medicine
Master's/Certificate Programs in Clinical Research Organization and Management
Online

University of North Carolina at Wilmington
MS Clinical Research and Product Development
Online

[VIEW ACADEMIC PROGRAM DETAILS]

Upcoming Event Highlights

Conferences

JUNE 13-14, 2018
Ensuring The Quality Connection with Your CMO
Philadelphia, PA

AUGUST 8-10, 2018
FDAnews - ICH E6 GCP Interactive Workshop
Waltham, MA

[VIEW ALL CONFERENCES]

Training Programs

JULY 1-31, 2018
Program Phlebotomy Training — Two Day Training
Various locations

[VIEW ALL TRAINING PROGRAMS]

Webinars

JUNE 14, 2018
Setting and Measuring Quality Objectives for Medical Devices
Dan O'Leary will walk you through the process and give you compliance tools to make warning letters a thing of the past. Special Bonus Material: Participants receive a checklist to help ensure the system is prepared for your next FDA Inspection, Notified Body audit, or MDSAP audit.

JUNE 21, 2018
The Real Impact of Common Rule in 2018: *Understanding Nuances, Facilitating Compliance & Implementing Best Practices*
Fully understand the key changes to the Common Rule and how they dramatically impact IRBs and virtually every entity engaged in clinical research. Changes to Informed Consent and Broad Consent, the Implementation of Limited IRB Review and much more.

[VIEW ALL WEBINARS]