Curr Pediatr Res2021; 25 (3): 401-409 *ISSN 0971-9032*
www.currentpediatrics.com

Developing clinical research culture in advancing medical research: An industry perspective.

Manish Narang[1*], Ramanpreet Walia[2], Upendra Kaul[3] and Krishnakutty Sudhir[4]

[1]Department of Medical Affairs, Abbott Vascular, PhD Scholar Amity Institute of Pharmaceutical Sciences, Amity University, Noida, India

[2]Department of Pharmaceutical Chemistry, Amity Institute of Pharmaceutical Sciences, Amity University, Noida, India

[3]Department of Cardiology, Batra Hospital and Research Centre, Delhi, India

[4]Department of Medical Affairs, Medical Affairs & Product Performance, Abbott Vascular, Santa Clara, USA

Abstract

The 20th century witnessed tremendous breakthroughs in medical research by virtue of a plethora of discoveries and advances in fundamental biology and disease management. The 21st century is taking medicine to unprecedented heights. Clinical research sponsored by a flourishing industry shaped our understanding of modern medicine. However, industry funded clinical research cannot answer all medical questions. In this review, we look at the growing impetus on investigator initiated studies, their impact on deeper understanding of real world needs, involvement of pharmaceutical, devices and imaging industry in supporting investigator or institution initiated research and instances of such successful endeavours that has changed the way medicine is practised. We also delve into the changing landscape of clinical research ecosystem in the light of recent advances in technologies like genomics, biologics, companion diagnostics and precision medicine system and the urgent need of creating and supporting a culture of research among individual clinicians, institutions, public and Government bodies in alleviating global disease burden. We recommend structural and functional models of association between the industry and investigator initiated research in order to overcome the traditional challenges of such research and pave the way for a fruitful and collaborative approach towards inclusive and comprehensive patient centric disease management.

Keywords: Clinical research, Investigator initiated research, Infrastructure, Research culture.

Accepted on March 9th, 2021

Introduction

In the last hundred years, basic research in general and clinical research in particular have advanced human knowledge about various diseases, their underlying mechanisms, pathophysiology, epidemiology, ways of prevention and cure. The journey has been fascinating. The history of controlled clinical research in modern era dates back to the 1747 Scurvy trial conducted by James Lind. However, the 1943 Patulin trial for common cold, conducted by The UK Medical Research Council (MRC) and the subsequent 1946 Streptomycin trial for Tuberculosis were landmarks in terms of meticulous design, patient enrolment, conduct and data analysis of controlled human studies [1,2]. Much has evolved since. In this review, we aim to delve on the ecosystem of various types of clinical research; the role of industry in Investigator Sponsored Studies (ISS); responsibilities of various stakeholders; funding, resource allocation, financial management & buy-in from institute and hospital management; forming effective partnerships for ISS and keys to conducting a successful research.

Research

The term 'research' may be broadly defined as the systematic investigation into and study of materials and sources in order to establish facts and reach new conclusions. According to the American sociologist Earl Robert Babbie, "Research is a systematic inquiry to describe, explain, predict, and control the observed phenomenon. Research involves inductive and deductive methods." Inductive research methods are used to analyze an observed event, while deductive methods are used to verify the observed event. Inductive approaches are associated with qualitative research and deductive methods are more commonly associated with quantitative research [3].

Clinical research

In the context of this article, we will focus almost entirely on clinical research. Clinical research is a component of medical and health research intended to produce knowledge valuable for understanding human disease, preventing and treating illness, and promoting health. Clinical Research is actually a continuum of studies involving interactions with patients, diagnostic clinical materials or data, or populations in any of the following categories: (i) Disease mechanisms (etiopathogenesis); (ii) Bi-directional integrative (translational)

research; (iii) Clinical knowledge, detection, diagnosis and natural history of disease; (iv) Therapeutic interventions including development and clinical trials of drugs, biologics, devices, and instruments; (v) Prevention (primary and secondary) and health promotion; (vi) Behavioural research; (vii) Health services research, including outcomes, and cost-effectiveness; (viii) Epidemiology; and (ix) Community-based and managed care-based trials [4].

- Good Clinical Practice (GCP): GCP is defined as a standard for the design, conduct, performance, and monitoring, auditing, recording, analysis and reporting of clinical trials or studies. It is an international standard guideline and forms the basis for human subject right, safety and welfare as well as quality, reliability and integrity of conduct and data collection in all clinical research. The guidance must be adhered to before, during and after a research study is undertaken [5].

Types of clinical research

Basic science: This encompasses all bench-top research. In today's multi-omics era, basic science is the pillar on which further translational research is built on. Most of these researches are Government funded (for example NIH) and executed through academia.

Industry initiated research: These are drug or device trials initiated and funded by the industry. An industry initiated clinical research is generally the last and often most expensive leg of the discovery journey, with the objective of obtaining a regulatory approval for marketing registration and market launch.

Investigator initiated studies (IIS): These are studies that are initiated and managed by a non-pharmaceutical company researcher/s who could be an individual investigator, an institution or a group of institutions, and a collaborative study group or a cooperative group [6].

Investigator initiated research: A vital cog in the wheel

The need: Often, industry initiated research is driven by scientific and commercial needs as perceived by the evolving dynamics and trends of the pharmaceutical and device market. While they are the main drivers of advancing patient care, they suffer from inherent drawbacks like restricted research settings, restricted patient population not representative of the real world, commercial interests not truly aligned with specific medical needs like rare diseases and so on. Clinical trials are not exhaustive in nature. They can't be designed to determine all the possible uses for a medication. Similarly, paediatric research is often neglected due to time and money already spent on adult trials, purely due to the burden of prevalence and hence commercial interests. Therefore, there is a definite gap to fulfil.

The namesakes: IIS are also known by several other names that include Investigator Initiated Research, Investigator Initiated Trials, Investigator Sponsored Trials, Non-commercial Trials, Academic Clinical Trials, Physician Led Studies and Investigator Driven Clinical Trials, Academic. The term investigator can also be substituted by the term "Academic" or "Physician" and the term "Clinical trial" can be replaced by "Study" [7].

The nomenclatures: In the context of IISs, specific nomenclatures are used by FDA. There is a distinction between an "investigator" and a "sponsor". An "investigator" is defined as the individual who conducts the clinical investigation, whereas a "sponsor" is the individual person or entity that takes responsibility for and initiates the clinical study. The "sponsor" in this case is not the "funder". A "sponsor-investigator" is an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The obligations of a "sponsor-investigator" include both those of a sponsor and those of an investigator. This means taking responsibility for all aspect of the study, including study design, regulatory approval, initiation, conduct, monitoring, reporting of safety data, analysis and publication of the results [8].

Issues addressed: Independent research outside the ambit of industry-initiated projects addresses the following critical aspects of clinical research:

- They are largely driven by questions that arise beyond the completion of Phase III studies that have not been studied during Phases I-III of drug development.
- They generate data on effectiveness and safety of a drug in the real-world setting and attempt to answer questions that clinicians face in their day-to-day practice.
- Some studies of a particular nature may not be of interest or commercially viable for the pharmaceutical industry, but critical to public health.
- They complement industry-initiated research and provide complete understanding of the disease and its management.

Advantages: i. A clinician-investigator may use an already licensed drug for a different therapeutic indication (off label) as deemed fit by his medical acumen and intellect. A classic example is the use of intravitreal injections of Bevacizumab for age-related macular degeneration [9].

ii. Comparison between two different treatment options available for a disease. For example, Bivalirudin versus Heparin with or without Tirofiban during primary percutaneous coronary intervention in acute myocardial infarction [10].

iii. Evaluation of cost-effectiveness of two or more treatment options. For example, endovascular strategy versus open repair for the management of a ruptured abdominal aortic aneurysm [11].

These are critical research questions answered by IISs which are generally outside the primary ambit of industry sponsored research for obvious resource, time & financial constraints. The main advantages or value proposition that emerges out of IISs can be summarised as below:

- Insights into real world setting and day to day challenges

- A wider patient population truly representative of the society
- Greater generalizability as more heterogeneous study population is involved as opposed to relatively homogenous populations in regulatory studies
- Helps in developing hospital/region/nation specific policies
- Helps in repurposing licensed drugs and convert sporadic off label use to guidelines or policy recommendations
- Fewer commercial conflicts of interest
- Tools to generate satisfaction and learning among medical fraternity

Examples of IIS changing the way medicine is practised

- The Anglo-Scandinavian Outcomes Trial Lipid Lowering Arm (ASCOT -LLA) is an example of an IIS, where Atorvastatin was shown to have a highly significant reduction in coronary events when compared to placebo [12]. Both British Hypertension Society IV (2004) and European Society of Hypertension guidelines (2003) changed their guidelines for management of hypertension. Both these guidelines recommended statin therapy to be used especially in hypertensive men aged over 50 years with a total cholesterol of >/3.5 mmol/L [13,14].
- An IIS multi-collaborative study called the Pulmonary Embolism Prevention (PEP) trial proved the efficacy of Aspirin in the prevention of Venous Thromboembolism (VTE) for patients undergoing arthroplasty and for those with a fracture of the hip. The PEP and similar studies led to the American College of Chest Physicians endorsing Aspirin and the American Academy of Orthopedic Surgeons to Accepting Aspirin as prophylaxis for prevention of VTE in patients undergoing arthroplasty [15].
- An IIS in India by D'Cruz et al comparing elective versus therapeutic neck dissection in node-negative oral cancer showed higher rates of overall and disease-free survival with the former. This evidence was later incorporated into the Spanish Society of Medical Oncology Clinical Guidelines [16,17].
- IIS have also played a critical role in imaging studies. The GOLMePsA study (an investigator-initiated, double-blind, parallel-group, randomised, controlled trial of GOLimumab and Methotrexate versus Methotrexate in early diagnosed psoriatic arthritis using clinical and whole body MRI outcomes) investigated the anticipated benefits of early use of biologic disease-modifying anti-rheumatic drugs leads to sustained response while on Methotrexate monotherapy and better disease control. In addition, rapid optimization of disease management lead to significant improvements in quality of life of affected individuals. Similarly, the Eudra CT study involved investigation of changes in disease activity and course of joint destruction by use of 3 tesla whole-bodies MRI, dedicated 3 tesla MRI and CT of the hand, and soluble biomarkers for rheumatoid arthritis. A subset of the trial threw important insights into tumor necrosis factor-inhibitor (Adalimumab) treatment [18-20].

Differences between industry run trial & IIS

A classic example of the differences between these two types of studies can be explained by the SPIRIT III and the TUXEDO trials. The former, initiated by Abbott, showed patients treated with Everolimus-eluting stent experienced significantly improved event-free survival at a 2-year follow-up when compared to Paclitaxel-eluting stent. The latter, an IIS, showed that in patients with diabetes mellitus and coronary artery disease undergoing percutaneous coronary intervention, Paclitaxel-eluting stents were not shown to be non-inferior to Everolimus-eluting stents, and they resulted in higher rates of target-vessel failure, myocardial infarction, stent thrombosis, and target-vessel revascularization at 1 year [21,22].The features of these two types of clinical research has been elucidated in Table 1.

Industry Initiated Trials	Investigator Initiated Studies
Regulatory input into drug development	Academic motivation
FDA gives extensive inputs to trial design, especially phase I and phase III	Support product life cycle - Might be part of product development plan
More restrictive	Will not lead to product approval, but can be cited as “supportive”
Comparator agent: approved vs. most current thought	Hypothesis generating
Treatment plan may be a compromise	Publication, presentations
Patient numbers	Less costly than industry conducted trials
Stringent inclusion, exclusion	Wider population & application

Table 1: Comparison between industry initiated trials & investigator initiated studies.

Industry initiated clinical trial ecosystem & its challenges

Industry initiated clinical trials are increasingly facing newer and more complex challenges. Some of these challenges have been described below [23,24].

- Spiralling costs
- Difficulty in patient enrolment and retention
- Inefficiency in protocol implementation
- Ineffectiveness in supporting the development of new medicinal products
- Selection and use of right technology
- Involvement of huge number of vendors leading to governance issues
- New classes of drugs, cell therapies, genomics, companion diagnostics and personalised treatments creating newer complexities
- Increasingly complex modern trial designs
- Constrained by complexity of regulatory guidelines
- Lack of supportive infrastructure
- Inadequate research training

- Lack of specialists

Traditional challenges in ISSs

ISSs typically provide more scientific, clinical and intellectual satisfaction to investigator sponsors. In spite of being more rewarding, there are inherent challenges in the way current ISSs are conceived and implemented. In fact, very few ideas ultimately result in research projects. Some of these challenges include:

- Inability to formulate a strong research question for a truly novel unmet need
- Half-baked research question due to incomplete literature search
- Lack of awareness for regulatory guidelines
- Inadequate training to address ethical concerns
- Lack of trained resources in areas like:

i. Biostatistics

ii. Data management

iii. Medical writing

iv. Software

v. Legal matters

vi. Finance matters

vii. Logistics

viii. Research coordination and study monitoring

- Lack of familiarity of basic research methodologies
- Improper time management between regular clinical practice and research
- Lack of project management skills – time and cost over runs
- Inadequate planning of safety monitoring and risk mitigation strategies
- Protocol deviations and inadequate adverse event reporting
- Patient dropouts
- Lack of archival system
- Lack of publication planning and study close out
- Data ownership disputes, particularly in multicentric studies
- Lack of robust and sustained funding
- Lack of transparency in funding and ownership

To further elucidate the practical challenges in improperly guided IISs, let us look at the some of the incongruences. In a systematic search publication from Portugal, it was revealed that 20% of trials were supported by industry with unclear information on the ownership of the results. Inaccuracy was found in the information about sponsors and funders. The information about funding in all resulting publications was also inconsistent between databases of the studies [25]. Herfarth et al have published their operational challenges faced during conduct of an IIS named MERIT-UC (Randomized, double blind, prospective trial investigating the efficacy of Methotrexate in induction and maintenance of steroid-free remission in ulcerative colitis) funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) [26]. An IIS involving children with epilepsy had to be stopped prematurely. The reasons for this termination were overestimation of the number of eligible drug-naive children referred by general paediatricians, personal preferences of investigators for specific antiepileptic drugs and the extensive administrative burden due to additional regulatory guidelines for children [27]. The bottom line is – in the current scenario, IISs suffer from inspirational, financial, operational and regulatory challenges. Industry and Government bodies need to step up to usher in a new era of ISSs.

Research relationship between industry and independent sponsor-investigators

In recent years, the pharmaceutical and medical devices industry is increasingly taking interest in and being receptive to fresh research ideas originating from the IIS space especially when it comes to generating additional real world evidence with novel technologies like Imaging, diagnostic tools, implantable devices etc. . Industry support is coming in many ways - in the form of funding, provision of product and aid in the study design and operational guidance. The reasons for this active involvement and support are multi-dimensional.

- Medical and scientific support to research aimed at the advancement of disease knowledge and potential treatments in therapeutic areas of interest to the industry partner.
- Better understanding of marketed products, technologies and therapies and therefore potential new applications.
- Improving the quality of care, increasing efficiency, reducing the total cost of care and therefore improving product shelf lives.
- As part of commitment to delivering innovative therapies to patients.
- Complementing ongoing research and gaining insights into future research for new innovation.
- Nurturing healthy scientific relationship with clinicians – the enablers through whom the investments and innovations of industry reach their end users, the patients.
- Creating an ecosystem of trust and value, wherein sponsor-investigators create and own their research without having to bother on financial bottlenecks.

Top companies have made conscious financial policies and streamlined process efficiency to support IIS. The industry understands that they can either be facilitators or direct funding sources for innovative research ideas originating directly from the community.

- Facilitating Funds: The industry can co-fund or facilitate funding from Government agencies like NIH (National Institute of Health, US), NHS (National Health Services, UK), NHMRC (National Health and Medical Research Council, Australia), Major Research Charities (Cancer Research, UK) and ICMR (Indian Council of Medical

Research). However, the process can be cumbersome and needs improvement in efficiency.

- Direct Funding: Increasingly, there have been great success stories in industry-clinician partnership in the IIS arena. Proof of concept studies in drug eluting stents for in-stent restenosis and saphenous vein graft; head on comparison studies like PRE-COMBAT, BEST and PREVENT trials as well as use of new technology and treatment studies like FAME and DAPT trials are testimony to industry support for research projects undertaken at academic medical centers are part of the drug or device development process [28-33].

The future of effective industry: ISS partnership

The Key to Success: Effective future collaborations lie in identifying and pursuing mutually synergistic goals of generating high quality research and data for specific disease states of high importance, which can benefit the industry and clinician community alike. In the order to do that, the vision and roles and responsibilities for both the parties need to be crystallised at the onset. Table 2 summarises the demarcation of roles and responsibilities for both the parties.

Expectations & responsibilities	
Industry	**Sponsor-investigator**
Robust medical and scientific governance	Rigorous ethical and scientific standards – unsolicited from industry without any conflict of interest
No undue interference from sales & marketing	Development of research idea & study protocol
Financial transparency	Comply with regulatory requirements like EC, Govt. agencies, CT registry, etc
Contractual commitment	Implementation & monitoring of research in adherence with all ethical & regulatory requirements
Training & mentoring	Coordination with multiple stakeholders like other sites, vendors, laboratories, logistics
Review and suggestions on improving protocol implementation efficiency	Maintain sufficient resource bank
Provide products	Continuous professional up gradation
Distribution of updated product information	Review & submission of protocol amendments
Provide insurance coverage to study subjects	Maintaining study records
Comprehensive and sustained funding at fair market value	Adherence to itemised study budget
Provide legal and financial services support	Safety reporting
Provide non test-item medication support if needed	Analysis of interim & final study results
Liaise with and facilitate companion diagnostics support for investigator-sponsors	Report study results to all stakeholders
Provide technical support	Publish study results
Inspire and motivate investigator-sponsors	Coordinate and communicate with industry partner at every stage for updates & help
Create sustainable policies for IIS support	Display research rigor & tenacity

Table 2: Roles and responsibilities of industry & sponsor-investigator.

Recommendation from the Industry: Experts from industry recommend the following to potential sponsor-investigators:

- Take ownership
- Devote sufficient time and initiative
- Don't lose focus of the objective
- Ask yourself – "Do I really want to do this?"
- Work with Research Dept. & Biostatistics
- Work with the IRB
- Plan for the long-haul
- Manage risks
- Identify critical resources like co-investigators, research coordinators, laboratory and diagnostic services, project management & regulatory experts, patient recruitment plan, pharmacy, computer and facility maintenance support

One key aspect of IIS is to get a buy in from the institute or hospital. There is a lot at stake for them. The most obvious are academic gains like novel research, publications, podium presence and attracting new trials. But the bigger gain is evolution into a centre of excellence inspite of being cost neutral. This not only makes the centre a preferred partner for research, but also augurs well for regular commercial operations. Since these aspects may not be realized instinctively by hospital management because they are not direct measures of return on investment, it is the responsibility of clinicians to convince the management on the dire need of industry-IIS collaboration aligned with the vision of the management. In fact, 46% of hospital executives don't know if their research programs are profitable, breaking even or even losing money. When utilized successfully, clinical trials offer additional revenue [34,35]. The success measures for buy-in from management can be estimated and quantified using the matrix provided in Table 3.

Measure	**Example**
Number and skill level of clinical and basic scientists engaged in generating new knowledge	•How many studies resulted in manuscripts, presentations and follow-up grants?
	•Were we able to increase the number of publication by investigators
	•Did we contribute toward an increase in the research portfolio (number of studies, amount of research dollars awarded)
Cost efficiency of the conduct of research	Was the unit able to recoup the cost of managing the study? (The cost to the Department
Avoidance of costly pitfalls of research including underestimating budgets,	How many studies stayed within the estimated study cost?

and non-adherence to regulatory requirements	
Number of recruited protocol-specific participants	How many studies achieved enrolment goal?
Number of investigators served (new and returning)	•How many new investigators have we introduced to research?
	•What was the number of return clients/investigators?
Levels of outcomes, safety, and service	•How many quality studies are we undertaking, how many protocol deviations/violations warnings
	•How many and what type of audits are we experiencing

Table 3: Success measures with examples-management perspective.

Manish Narang success measures with examples-management perspective.

Conclusion

IISs are critical in generating evidence that is outside the scope of industry initiated clinical trials. They can drive policy decisions leading to tremendous advances in medical science and improvement in patient outcomes. In today's era of COVID-19 global pandemic, we are witnessing more and more impactful collaboration between the industry and the clinicians. The key is to forge such collaborations based on mutual trust and respect but fostering the relationship outside the commercial interests of regular operations. It is time to develop a clinical research culture deeply ingrained into the healthcare delivery system. We as drivers of industry and supporters of clinicians must inculcate the mind-set of inquiry into observations in practice and have the zeal and craving for answers. The problems are out there in the real world. The answers must come from there.

References

1. Bhatt A. Evolution of clinical research: A history before and beyond james lind. Perspect Clin Res. 2010; 1(1):6-10.
2. Collier R. Legumes, lemons and streptomycin: A short history of the clinical trial. CMAJ. 2009; 180(1):23-24.
3. Research: Definition, Meaning, Importance Types and Qualities of Research. 2020.
4. Tunis S, Korn A, Institute of Medicine (US) Clinical Research Roundtable, et al. The Role of Purchasers and Payers in the Clinical Research Enterprise: Workshop Summary. Washington (DC): National Academies Press (US); 2002.
5. Vijayananthan A, Nawawi O. The importance of Good Clinical Practice guidelines and its role in clinical trials. Biomed Imaging Interv J. 2008;4(1):e5.
6. Konwar M, Bose D, Gogtay NJ, Thatte UM. Investigator-initiated studies: Challenges and solutions. Perspect Clin Res. 2018;9(4):179-83.
7. IIT made easy, investigator initiated trials made easy. 2020.
8. Investigator responsibilities – regulation and clinical trials. 2020.1-78.
9. Tufail A, Patel PJ, Egan C, et al. Bevacizumab for neovascular age related macular degeneration (ABC Trial): multicentre randomised double masked study. BMJ. 2010;340:c2459.
10. Han Y, Guo J, Zheng Y, et al. Bivalirudin vs. heparin with or without tirofiban during primary percutaneous coronary intervention in acute myocardial infarction: the BRIGHT randomized clinical trial. JAMA. 2015;313(3):1336-46.
11. Powell JT. Comparative clinical effectiveness and cost effectiveness of endovascular strategy v open repair for ruptured abdominal aortic aneurysm: Three year results of the IMPROVE randomised trial. BMJ. 2017;359:j4859
12. Sever PS, Poulter NR, Dahlöf B, et al. Reduction in cardiovascular events with atorvastatin in 2,532 patients with type 2 diabetes: Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm (ASCOT-LLA). Diabetes Care. 2005;28(5):1151-7.
13. Williams B, Poulter NR, Brown MJ, et al. British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary. BMJ. 2004;328(7440):634-40.
14. European Society of Hypertension-European Society of Cardiology Guidelines Committee. European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens. 2003;21(6):1011-53.
15. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. Lancet. 2000;355(9212):1295-302.
16. D'Cruz AK, Vaish R, Kapre N, et al. Elective versus therapeutic neck dissection in node-negative oral cancer. N Engl J Med. 2015;373:521-9.
17. Iglesias DLC, Arrazubi AV, Baste RN, et al. SEOM clinical guidelines for the treatment of head and neck cancer (2017). Clin Transl Oncol. 2018;20(1):75-83.
18. De Marco G, Helliwell P, McGonagle D, Emery P, Coates LC, Hensor EMA, et al. The GOLMePsA study protocol: An investigator-initiated, double-blind, parallel-group, randomised, controlled trial of GOLimumab and methotrexate versus methotrexate in early diagnosed psoriatic arthritis using clinical and whole body MRI outcomes. BMC Musculoskelet Disord. 2017;18(1):303.
19. Adalimumab in Rheumatoid Arthritis. An Investigation of Wholebody MRI, Conventional MRI, CT and Circulating Biomarkers. 2020.
20. Ng SN, Axelsen MB, Østergaard M, et al. Whole-body magnetic resonance imaging assessment of joint inflammation in rheumatoid arthritis-agreement with ultrasonography and clinical evaluation. Front Med (Lausanne). 2020;7:285.
21. Stone GW, Midei M, Newman W, et al. Randomized comparison of everolimus-eluting and paclitaxel-eluting stents: two-year clinical follow-up from the Clinical Evaluation of the Xience V Everolimus Eluting Coronary Stent System in the Treatment of Patients with de novo

Native Coronary Artery Lesions (SPIRIT) III trial. Circulation. 2009;119(5):680-6.

22. Kaul U, Bangalore S, Seth A, et al. Paclitaxel-eluting versus everolimus-eluting coronary stents in diabetes. N Engl J Med. 2015;373:1709-19.
23. Rebecca A, Lebovitz Y, and Giffin RB. Institute of Medicine (US) forum on drug discovery, development, and translation. transforming clinical research in the united states: challenges and opportunities: Workshop summary. Washington (DC): National Academies Press (US); 2010. 3 Challenges in Clinical Research.
24. Burrows A. REPORT: The 8 biggest challenges facing clinical trial professionals.
25. Madeira C, Santos F, Kubiak C, et al. Transparency and accuracy in funding investigator-initiated clinical trials: a systematic search in clinical trials databases. BMJ Open 2019;9(5):e023394.
26. Herfarth HH, Jackson S, Schliebe BG, et al. Investigator-Initiated IBD Trials in the United States: Facts, obstacles, and answers. Inflamm Bowel Dis. 2017;23(1):14-22.
27. Weijenberg A, Callenbach PMC, LEV-VPA Study Group, et al. Investigator-initiated randomized controlled trials in children with epilepsy: Mission impossible?. Epilepsia Open. 2016;2(1):32-8.
28. Liou k, Jepson N, Cao C, et al. Drug-eluting Balloon Versus Second Generation Drug Eluting Stents in the Treatment of In-stent Restenosis: A Systematic Review and Meta-analysis. Heart Lung Circ. 2016;25(12):1184-94
29. Park SJ, Kim YH, Park DW, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease. N Engl J Med. 2011;364(18):1718-27.
30. Park SJ, Ahn JM, Kim YH, et al. Trial of everolimus-eluting stents or bypass surgery for coronary disease. N Engl J Med. 2015;372(13):1204-12.
31. Prevention of Recurrent Venous Thromboembolism (PREVENT).2000.
32. Heyndrickx GR, Tóth GG. The FAME Trials: Impact on Clinical Decision Making. Interv Cardiol. 2016;11(2): 116-9.
33. The Dual Antiplatelet Therapy Study (DAPT Study). 2020.
34. Suvarna V. Investigator initiated trials (IITs). Perspect Clin Res. 2012;3(4):119-21.
35. Investigator Initiated Trials (IIT) – Considerations and Guidance from the perspective of clinical trial supplies and GMP. 2020.

*Correspondence to:

Manish Narang

Department of Medical Affairs,

Amity Institute of Pharmaceutical Sciences, Amity University,

Noida, India

Tel: +919810268685

E-mail: manish.narang@abbott.com; manish1901@yahoo.com