An Analysis of Investigator Sponsored Study Cycle Times: Communication is the key for success

An Analysis of Investigator Sponsored Study Cycle Times: Communication is the key for success

Pharmaceutical companies conduct evidence generation activities within Medical Affairs through Investigator Sponsored (ISS), Company Sponsored (CSS), and Collaborative Research Studies (CRS). The timely completion of these studies is vital to generate relevant evidence for the wider scientific community; and helps to ensure that studies complete on budget.

However, many companies are concerned that studies do not progress on the timescales they expect, especially with studies where they are not the sponsor (for example ISS). Some companies find that their initial timelines are not accurate, leading to frustrations, cost over-runs, and worsened investigator-company relations, ultimately leading to lower volume of evidence being produced.

An investigation of standard study approval, study start-up, and study conduct across Medical Affairs Studies has revealed several causes for these mismatches between plans and reality.

However, in order to fully understand the differences between expectation and reality, it is vital to first understand the standard cycle times that have been observed within the industry. The following results of actual clinical study data as reported in clinicaltrials.gov show the Mean cycle time for each milestone, for Oncology studies in Ph IV studies, excluding studies more than 2 standard deviations from the median[1].

Definition of terms below[2]	Idea Receipt to FPA (Actual)[3]	FPA to FSFV (Actual)[3]	FSFV to LSFV (Actual)	LSFV to LSLV (Actual)	LSLV to CTR Publication (Actual)
Mean Cycle Time for ISS	120 – 400 days	180 – 300 days	1008.27 days (n = 398)	321.19 days (n=128)	439.47 days (n = 274)
Mean Cycle Time for CRS			1131.18 days (n = 72)	366.16 days (n = 32)	469.18 days (n = 39)
Mean Cycle Time for CSS			854.35 days (n = 405)	372.75 days (n = 289)	450.24 days (n = 325)

Table 1: Mean Medical Affairs Oncology Cycle Times

> **The key determinant factor to study cycle time is study recruitment rate**

Beyond inter-company variation in study approval and start-up times, which are dependent on internal process, the key determinant factor is study recruitment rate (once again excluding outliers that are two standard deviations from the median).

[1] Data for clinical studies finishing within the last 5 years where the study was identified as a Medical Affairs study, primary data use (no registry or database studies included), both observational and interventional studies, and therapeutic area identified as Oncology.

[2] FPA: Final Protocol Approval; FSFV: First Subject First Visit; LSFV: Last Subject First Visit; LSLV: Last Subject Last Visit; CTR Publication: Clinical Trial Report Publication.

[3] Note that for idea receipt to FPA and FPA to FSFV a benchmark of biotech, mid-size and top 10 Pharma was taken to allow for comparison within ISS.

An Analysis of Investigator Sponsored Study Cycle Times:
Communication is the key for success

Indication	Recruitment Rate Lower bound ↓ Mean Upper bound (Patients per site per month)
NSCLC	0.1 — 1.6 — 6.2
CRC	0.1 — 1.0 — 6.2
SCLC	0.2 — 0.6 — 4.6
Gastric	0.4 — 0.9 — 2.6
RCC	0.1 — 0.7 — 5.7
UC	0.1 — 0.7 — 4.1
SCCHN	0.3 — 0.9 — 4.6
RRMS	0.5 — 2.1 —

Table 2: Selected Indication Recruitment Rates for ISS

> **Investigators over-estimate their recruitment rate and underestimate the recruitment time**

However, when compared against the original plans that investigators submitted in their initial protocol, we can see a multi-fold over-estimate in recruitment rate, and underestimate in recruitment time.

An Analysis of Investigator Sponsored Study Cycle Times: Communication is the key for success

	Idea Receipt to FPA	FPA to FSFV	FSFV to LSFV (Planned)	FSFV to LSLV (Planned)	LSFV to LSLV (Planned)	LSLV to CTR Publication
Mean Cycle Time for ISS	N/A	N/A	485.1 days (n = 125)	842.92 days (n=391)	402.26 days (n=117)	N/A

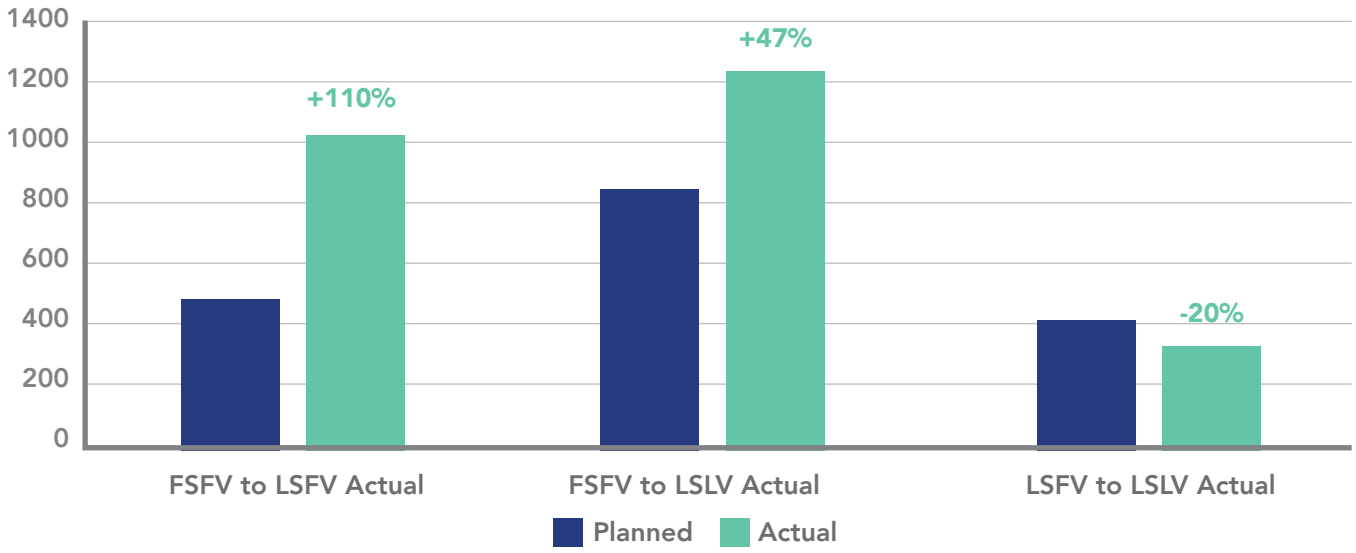

Figure 1: Planned ISS Cycle times and comparison to Actual times

A question that a head of clinical operations or Medical Affairs may be asking is "why are there so many differences between plans and reality", or perhaps more controversially, "why do investigators get it so wrong?" Unfortunately, this situation is, in part, driven by mis-matched expectations, and the understanding of how investigators and the industry work together.

Medical Affairs is aware that they cannot influence protocol design for studies which are investigator sponsored, however, investigators also know that if they submit timelines which are too long, there is a strong possibility their proposal for funding will not be chosen, in favour of investigators who are seen to deliver in shorter timescales. Unfortunately, at first glance, it is difficult to identify whether a timeline is realistic.

> **Key areas to maximise the success of investigator sponsored clinical studies: Open communication around approval and start-up times**

In addition, due to the necessary separation of funder and sponsor, investigators cannot see the internal processes required to approve a study by a pharmaceutical company. Hence, when an investigator believes that a first site initiation within six months is possible, there can be limited scope for a company to challenge this belief, for fear of looking inefficient or uninterested.

An Analysis of Investigator Sponsored Study Cycle Times: Communication is the key for success

In examining these issues, we have identified three key areas to focus on to maximise the success of investigator sponsored clinical studies:

1) Open communication around the expected approval and start-up times for a typical study; early and frequent communication ensures an investigator feels appreciated, knows a company is committed, and decreases frustration felt by both company and investigator

   In addition, communication of industry standard recruitment rates, perhaps even from this paper, allow investigators to adequately tailor their ideas and proposals to an achievable timeline

2) Adequate internal communication around expected timelines and recruitment rates; a company with an internal knowledge of expected recruitment rates will set its own expectations, and assess proposed ideas from investigators on their merits, rather than on potentially unrealistic timelines

3) Fostering an internal culture of collaboration, allowing transparency between Clinical Operations teams, Medical Affairs teams, Governance teams, and even Scientific

   Communications teams, allows for:

   a. full visibility of upcoming proposals
   b. creates opportunities for course corrections without one function being pitted against another or seen as a blocker
   c. greatly improves the opportunity to plan evidence generation to support product lifecycle based on realistic timelines.

   These improved timelines allow better study selection to ensure that the evidence that is expected to be generated is still going to be relevant by the time the study completes.

The greater communication and collaboration can be additionally strengthened by building capabilities within clinical trial feasibility. An assessment of previously funded studies, along with a robust feasibility analysis (or even access to databases of industry standards) can allow the right study ideas to be funded, while avoiding mis-matched expectations.

> **A successful company will focus on ensuring their culture is set up to enable successful collaboration, and their teams have the right capabilities (both hard and soft skills) to foster communication and cooperation**

An Analysis of Investigator Sponsored Study Cycle Times: Communication is the key for success

In Protagoras' experience, an important pitfall to avoid is to focus on a new system, process, or tool to act as a panacea for evidence generation. A successful company will focus on ensuring their culture is set up to enable successful collaboration, and their teams have the right capabilities (both hard and soft skills) to foster communication and cooperation. With the right foundations, a new enabling system, or overhauled process can certainly bring benefits. Without them however, a new system or process just creates a financial and change burden, which can stress already stretched teams without ever resolving the root cause.

> **The key differentiator we found for successful improvement was an openness and willingness to address the culture and capabilities, before investing into new systems**

Across projects with several companies aiming to adapt and improve their evidence generation approaches, the key differentiator we found for successful improvement was an openness and willingness to address the culture and capabilities, before investing into new systems and devising new processes. Whilst a new system is certainly a tangible and demonstrable outcome, the reduction in governance reviews, improvement in study timeliness compared to plan, and overall improvement in evidence quality is a highly desired and equally tangible outcome.

Some companies have already taken steps within these focus areas and are recognising improved efficiency within their ISS. This drives a virtuous circle where the right studies are funded for the right reasons, evidence is successfully generated, and learnings are incorporated into future study idea selections. In conclusion, perhaps the question is less "why do investigators get it so wrong", and more "how does my company compare?" to drive better evidence generation.

Contact

George Simon, Director, Advisory Services
george.simon@protagorasgroup.com

Roumteen Keshe, Director, Advisory Services,
roumteen.keshe@protagorasgroup.com