Time to Activation: Are we comparing apples-to-apples?

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Background

Time-to-activation is a key metric that the National Cancer Institute (NCI) and Sponsors use to evaluate centers when determining their ability to be successful in clinical trials. While centers aim to activate trials in 90 to 120 days, the literature reveals that majority of Centers activate trials in around six months (1). Clinical Trials Office (CTO) staff are constantly seeking learned practices from other institutions to improve time-to-activation, but it is difficult to understand where a center sits, compared to the targets, when definitions for time-to-activation, and methodologies to count days in the activation definition, differ across centers.

Methods

In February 2020, we sent a survey to the AACI-CRI *listserv* asking centers to complete a 22-question survey about their methods to calculate time-to-activation at their center.

Table 1: Responding Center Characteristics
Characteristics of centers who responded to the AACI-CRI listserv survey

Center Characteristics	N=32
NCI designation	
Comprehensive Cancer Center	80%
Cancer Center	10%
No NCI Designation	10%
Cancer center structure	
Matrix	79%
Free-standing (with or without network sites)	21%
Number of Interventional trials opened (2019)	
< 50	10%
51-75	17%
>76	73%

Activation Definitions

For industry trials, 65% of responding centers start the clock at **Protocol Review & Monitoring Committee/Scientific Review Committee (PRMC/SRC) submission** and stopped the clock at **Open to Accrual**.

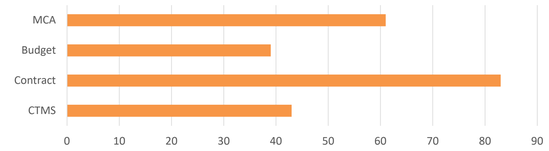
The remaining centers started at full-regulatory package received (18%), first-stage/disease committee review (6%), date of PRC/SRC acceptance (3%), date of PRC/SRC meeting (3%), and PRMC/SRC approval (3%). The end time varied between receipt of sponsor activation letter, Institutional Review Board (IRB) approval, site initiation visit, and enrolment ready.

Similar definitions are used for other sponsor trial types e.g. Investigator Initiated Trials. 94% of centers report time-to-activation in calendar days.

Centralized Activation

81% of centers (83% of matrix cancer centers) use a centralized office for pieces of the activation process. Only 44% of centers use the same activation definition as the rest of campus (i.e. centralized unit definition). Most centralized units calculate time-to-activation as intake into central unit to date contract signed, or do not track the overall metrics, and only track the time for individual components e.g. draft budget preparation and negotiation timelines.

Table 2: Centralized Resources for Matrix Cancer Centers
Percentage of responding matrix centers who use a centralized (campus) resource for components of the activation process.



Removing Studies

Centers remove trials (or a defined period) from the their time-to-calculation definition. Figures 1-3 below detail the common reasons to remove trials (or time periods) from their definitions. Other reasons include: abandon studies (remove data from metrics); extended holds causing re-review at PRMS are removed from timelines and re-started; and IITs with multiple sponsors (due to contracting difficulties).

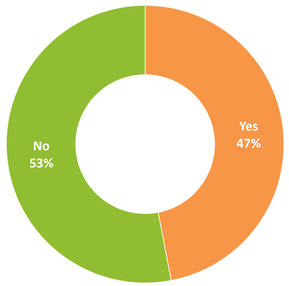


Figure 1: Extended Holds
Q. Do you remove extended holds (e.g. FDA) from the reported time-to-activation? For those centers who do remove holds, the majority of centers remove holds when the hold is outside of the cancer center's control e.g. drug delays, FDA holds, unresponsiveness from the sponsor.

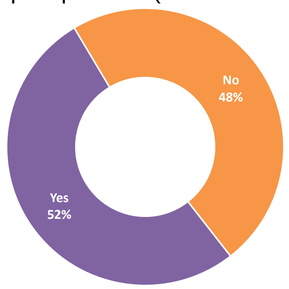


Figure 2: Exempt Studies
Q. Do you remove Protocol Review and Monitoring System (PRMS) exempt studies (e.g. registries) from your time-to-activation metric?

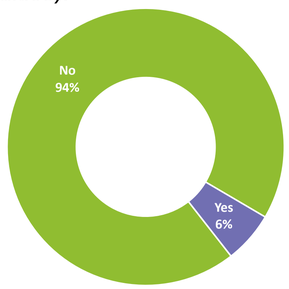


Figure 3: Mid-Activation Amendments
Q. Do you 'restart the clock' when mid-activation amendments arrive and the initial protocol has not been activated yet?

Table 3: Time to Activation Goals
Targets for time-to-activation by sponsor type

Time to Activation Goals	N=32
Industry Sponsored	
90 days	50%
90-120 days	42%
Other	8%
Institutional	
90 days	39%
90-120 days	45%
121-180 days	10%
Other	6%
National	
<90 days	52%
90 days	41%
>90 days	7%

Future Directions

Further exploration is required to understand how centers use the term "open to accrual". The data suggests that each center may interpret this phrase slightly differently e.g. time of site initiation visit, sponsor approval, or ability to accrue patients.

Given the inconsistency in time-to-activation definitions and methodologies used to count days in the activation definition, we are proposing a working group of NCI designated Cancer Centers to develop a best practice definition for time-to-activation, which can be endorsed by the NCI and reported by centers. The definition needs to use data points that are measurable at all NCI designated Cancer Centers and not be onerous on centers to collect. Additionally, the definition needs to reflect the true reality of opening a trial. Delays from all parties are inevitable and the aim should be to implement practices to reduce delays where feasible.

Reference:

[1]Stewart S and Tate W (2019). Perspectives on Cancer Community Activation Timelines. Forte Onsemble Conference. Madison, USA.