Using a Subject Registry to Create a Duplicate-Free Corridor for Conducting Clinical Trials

Shiovitz TS1, Wilcox CS3, Govorgyan L2, Mehra V4, Mangano TC1,2
1CTDatabase LLC, Beverly Hills, CA; 2California Neuroscience Research, Sherman Oaks, CA; 3Pharmacology Research Institute, Encino, Newport Beach, Los Alamitos, CA; 4Artemis Institute for San Diego, CA

ABSTRACT

Background: Duplicate subjects are an increasingly recognized problem in CNS studies. Within a single pharmaceutical company, duplicates may represent as high as 10% of randomized subjects.1 Subject registries and other tools attempt to identify duplicate enrollees.2

These duplicate subjects may increase placebo response, may not take study medication and almost certainly contribute to failed studies. Subject registries attempt to identify duplicate and professional subjects before randomization.

Methods: Twenty-eight Southern California CNS sites joined together to obtain IRB approval of a Subject Database Authorization and enter partial identifiers of subjects presented for clinical trial prescreening into the CTStadatabase (excluding same site matches) registry between October 31, 2011 and October 31, 2013. Sites were notified immediately when virtually certain matches (<10% likelihood of matching by chance) or Probable matches (<1 in 3M likelihood of matching by chance) occurred between sites. CTStadatabase facilitated inter-site communication in order to determine if the matched prescreener had been entered into studies.

Results: 422 virtually certain matches representing 844 potential duplicate subjects were found among 5382 prescreened subjects. 602 matches which occurred at the same site were excluded from the data set. The number and percent of matched subjects increased substantially as the number of participating sites increased. Bringing together competing local sites for a common cause meant overcoming resistance and mistrust among several sites and required prompt access to and cooperation from the matching sites when duplicates were found. More duplicate subjects changed their personal identifiers and/or traveled to sites that were 25, 50 or even 100 miles apart.

Conclusion: While use of a subject registry is best integrated into study protocols to ensure site participation and overcome the need for sites to communicate with each other in the case of matches, Southern California has made great strides in providing a Duplicate-Free Corridor for conducting CNS studies. This model may be applied to other metropolitan and suburban areas with large numbers of duplicate subjects, with the goal of markedly reducing the number of inappropriate subjects entering studies, allowing more CNS studies to succeed.

BACKGROUND & METHODS

• Duplicate subjects are an increasingly recognized problem in CNS studies. Within a single pharmaceutical company, duplicates may represent as high as 10% of randomized subjects.1

• Subject registries and other tools attempt to identify duplicate enrollees.2

• These duplicate subjects may increase placebo response, may not take study medication and almost certainly contribute to failed studies. Subject registries attempt to identify duplicate and professional subjects before randomization.

• Twenty-eight Southern California CNS sites joined together to obtain IRB approval of a Subject Database Authorization and enter partial identifiers of consenting subjects who presented for clinical trial prescreening into the CTStadatabase registry between October 31, 2011 and October 31, 2013 (Figure 2).

• The CTStadatabase registry allows for communication of when, where and for what indication matching subjects have previously prescreened or participated in studies.

• Sites were notified immediately when virtually certain matches (<10% likelihood of matching by chance) or Probable matches (<1 in 3M likelihood of chance matching) occurred between sites.

• Subjects that were re-entered at the same site, i.e. not true duplicate subjects, were excluded from the data set (n = 602).

• CTStadatabase facilitated inter-site communication in order to determine if the matched prescreener had actually entered studies.

RESULTS

• Bringing together competing local sites for a common cause meant overcoming resistance and mistrust among several sites and required prompt access to and cooperation from the matching sites when duplicates were found.

• Some sites immediately joined the collaboration. Other sites took more than 15 months and 30 contacts before agreeing to join the effort. Now, all but a handful of major CNS sites from Los Angeles to San Diego have joined the collaboration to prevent duplicate enrollment at prescreen.

• Initial resistances to join included competitive and financial as well as legal and privacy concerns.

• Some sites claimed that registry costs, or site workloads and bureaucracies inhibited participation.

• As more sites participated, the percentage of duplicates rose steadily. 422 virtually certain matches representing 844 potential duplicate subjects were found among 5382 prescreened entered. Of these, (11.4%) prescreened at a second site within 180 days (Figure 2).

• Duplicate subjects changed their personal identifiers and/or traveled to sites that were 25, 50 or even 100 miles apart (Figures 2 and 4).

• 25% of matching subjects changed their indication/diagnosis between sites. The most common changes were between depression and Bipolar (6%), depression and anxiety (3%) depression and schizophrenia (5%) and schizophrenia and bipolar (5%).

DISCUSSION

• When creating a duplicate-free zone through local site collaboration at prescreen, sites are not required to participate and professional subjects are free to shift to non-participating sites.

• By contrast, when use of a subject registry is integrated into a protocol, sites must enter subjects to prevent a protocol violation. However, all sponsors must use the registry as part of the screening process for it to be fully effective.

• A subject registry can also have a deterrent effect, whether used at prescreen or as part of a protocol.4

• This successful site collaboration was worth the efforts to get competitor sites to participate and communicate with each other during prescreen visits.

• While investigators and patients (as well as sponsors and vendors) are incentivized for enrolling quantity, there are not adequate incentives (or safeguards) for quality enrollment of subjects that reflect symptomatic patients in the general population.5

• Sponsors could help reduce duplicate enrollment by requiring sites to check a registry as a protocol procedure or by reimbursing sites for the time and modest cost of using a registry at prescreen.

CONCLUSIONS

• With collaboration and communication, 28 participating Southern California sites have made great strides in creating a Duplicate-Free Corridor for conducting CNS studies.

• This model may be applied to other metropolitan and suburban areas with large numbers of duplicate subjects, with the goal of markedly reducing the number of inappropriate subjects entering studies, allowing more CNS studies to succeed.

• A subject database can be utilized at prescreen in collaborative corridors and/or integrated into protocols to maximize detection of duplicate and professional subjects.

REFERENCES


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Figure 1: Cumulative subjects entered (excluding same site matches), and number of active sites. (December 2013 data point is extrapolated).

Figure 2: Cumulative percentage of duplicate subjects, by number of days between matches.

Figure 3: Distances in miles between sites for subjects matching within 60 days. Three subjects traveled to sites more than 100 miles apart.

Figure 4: Percentage of changed key identifiers over total matched subjects.