From Publication to Protocol: Increasing Awareness of Nonadherence Working Group Recommendations

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ABSTRACT

Nonadherence (NA) is a substantial problem in clinical trials and contributes to study failure.1,2 This working group (WG) has published its recommendations on ways to mitigate the effects of nonadherence in clinical trials. However, such recommendations can only be effective if stakeholders are made aware of them in a way that facilitates their implementation. The Nonadherence Working Group presented its paper at the February 2016 ISCTM meeting and agreed to continue for two or three more meetings to promote awareness of the recommendations.

BACKGROUND & METHODS: WORKING GROUP SUGGESTIONS TO PROMOTE AWARENESS OF RECOMMENDATIONS

On September 26, 2016 WG members convened to discuss ways to promote NA recommendations. The following were suggested:

- Send out e-mails to all attendees asking for additional suggestions
- Promote Nonadherence white paper recently published in J Clin Pharmacol3
- Enlist Pharma to share NA data (draft clear request statement to Pharma/NIH?)
- Utilize clinicalstudydatarequest.com
- Develop a simple Best Practices statement
- Enlist the help of CROs
- Make the NA Working Group available to consult on adding NA measures to protocols
- Promote WG recommendations to FDA
- Continue the WG for at least one more meeting
- Present poster at February 2017 ISCTM
- Interface with other Societies

NONADHERENCE WORKING GROUP RECOMMENDATIONS

1. At site selection, eliminate requirements that the majority of Phase 2-4 subjects should come from internal databases.
2. Set limits on the number of previous studies a (Phase 2-4) subject has participated in over a specified time period (e.g. no more than x studies during the past 24 months).
3. Provide PK and treatment assignment information from previous studies in a timely manner to investigators.
4. Utilize an available subject registry to identify and eliminate duplicate and professional subjects.
5. Eliminate overly restrictive screen-fail ratios, which adversely incentivize investigators.
6. Monitor ratings consistency, diary compliance and subject adherence, and consider an outside adjudication process at screen to improve the patient sample.
7. Consider performing PK sampling on background treatments and consider a biomarker or medication adherence technology during run-in.
8. Pre-specify who will be included in the final analysis based on information available on subjects prior to randomization.
9. Monitor individual subject adherence with a medication adherence technology, not pill counts alone.
10. Provide subjects and investigators with prompt feedback when nonadherence is detected.
11. Promptly discontinuing subjects who are deceptive, duplicate or egregiously nonadherent may be desirable in order to minimize the impact of the subject’s data (MMRM).
12. Consider stratification of subpopulations based on adherence and behavior.
13. Utilize adherence data to inform protocol design and go/no-go decisions in later studies.

PROGRESS TO DATE

- Emails to WG attendees elicited few additional suggestions.
- CRO members of the WG have promoted WG recommendations within INC, Quintiles, and PPD.
- Shiovitz/McCann presented the NA paper to over 40 members of the ACCP Journal Club on January 18, 2017.
- Recent efforts to obtain new data from sponsors to address WG interests yielded minimal success.
- Feasibility of making WG available for consultation TBD by ISCTM Executive Committee.
- Further steps were discussed at the February 21, 2017 ISCTM workshop.

CONCLUSIONS

- Recommendations alone are not enough to change current practices.
- More work needs to be done to continue to make stakeholders aware of the benefits of adding NA mitigation to studies.
- Promoting papers and presenting at other societies/meetings are two clear strategies.

REFERENCES
