Using an artificial intelligence platform to accurately predict pharmacokinetic sampling outcomes in clinical trials

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INTRODUCTION

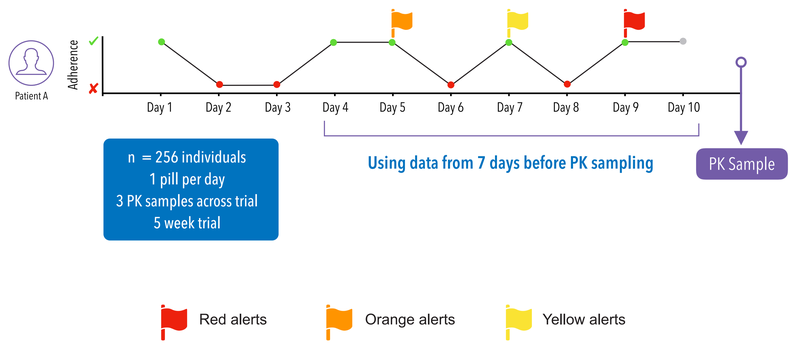
- Remote patient monitoring is critical in ensuring optimal drug exposure and accurately measuring drug intake
- It is estimated that 30-50% of CNS studies fail because subjects are not taking the study drug
- High rates of non-adherence in clinical research and the lack of a continuous and accurate measure of adherence interfere with hypothesis testing and the interpretation of trial results
- Current measures of adherence such as pill counts are inaccurate and underestimate non-adherence
- PK (pharmacokinetic) sampling, while accurate, is used sparsely in ambulatory settings and does not capture adherence in the placebo group
- An artificial intelligence (AI) platform that uses computer vision and neural networks to visually confirm ingestion and capture ingestion-related behaviors was evaluated for accuracy in predicting PK outcomes
- The AI platform is the only known modality to be able to distinguish between non-adherence and fraud
- A preliminary analysis using 6 CNS studies and 278 subjects with available PK data was conducted to assess the ability of adherence to predict PK levels
- A subsequent analysis on 256 of those subjects with available PK data was conducted to assess the ability of adherence and fraud to predict PK levels

METHODS

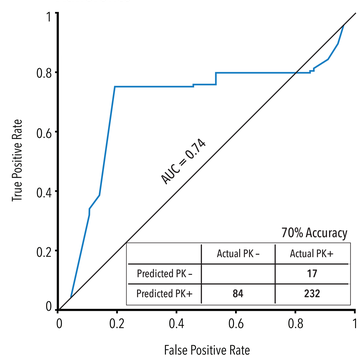
- The preliminary analysis across 6 CNS studies showed that weighted adherence 7 days prior to PK sampling was able to predict the PK outcome using a logistic regression
- Subsequent analysis on a single large CNS trial (256 subjects with 682 PK samples) was used to test the accuracy of fraud in addition to adherence in predicting PK outcomes
- Fraud is defined as a dosing event that is tagged by the AI platform as being clearly fraudulent (red alert), likely fraudulent (orange alert), or having missing information to detect fraudulent behavior (yellow alert), confirmed through human review
- A logistic regression was used to predict PK outcomes above the lower limit of quantification (LLOQ) or PK outcomes below the LLOQ using adherence and fraud in the previous 7 days as predictors
- **The following four models were tested:**
- *log odds of PK+ = β0 + β1 Adherence* —— (1)
- *log odds of PK+ = β0 + β1 Adherence + β2 Red* —— (2)
- *log odds of PK+ = β0 + β1 Adherence + β2 Red + β3 Orange* —— (3)
- *log odds of PK+ = β0 + β1 Adherence + β2 Red + β3 Orange + β4 Yellow* —— (4)

- A 70% cut-off threshold in the logistic regression provided the most accurate results. The training/testing dataset ratio was 60:40
- Due to the under-representation of subjects with PK samples below LLOQ, these subjects were upsampled to 25% of the total population, resulting in a 3:1 PK above LLOQ to PK below LLOQ ratio

DATA AND RESULTS

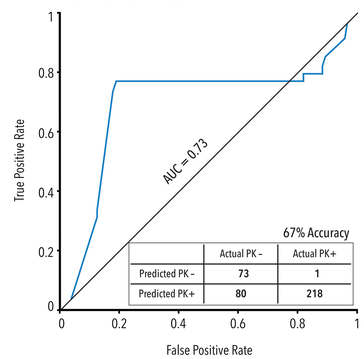


Adherence



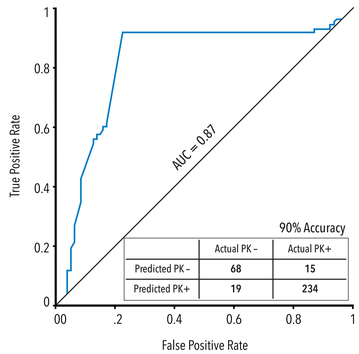
	Actual PK –	Actual PK+
Predicted PK –		17
Predicted PK+	84	232

Adherence + Red Alerts



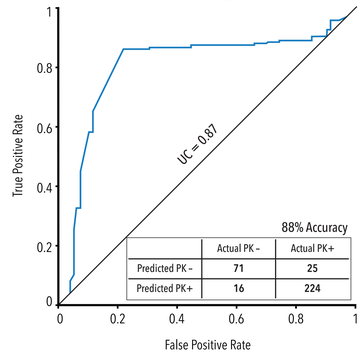
	Actual PK –	Actual PK+
Predicted PK –	73	1
Predicted PK+	80	218

Adherence + Red & Orange Alerts



	Actual PK –	Actual PK+
Predicted PK –	68	15
Predicted PK+	19	234

Adherence + Red, Orange, & Yellow Alerts

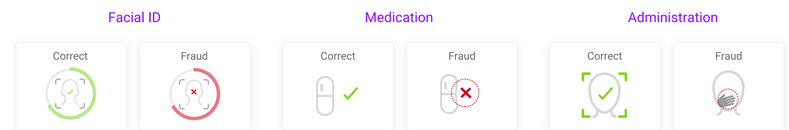


	Actual PK –	Actual PK+
Predicted PK –	71	25
Predicted PK+	16	224

CONCLUSION

- PK outcomes can be predicted with high accuracy using adherence and fraud alerts logged by the AI Platform as predictors
- A 7-day look-back window is sufficient in predicting PK with high accuracy: Increasing the window does not improve accuracy in this data subset
- Adherence alone is not a very strong predictor of PK outcome. The identification of fraud (red and orange alerts logged by the AI platform), a behavioral pattern that is separate and distinct from non-adherence, is a key contributor to the model's accuracy
- To our knowledge, this is the first time that high concordance and > 90% prediction accuracy has been demonstrated based on a remote assessment of subject behavior (adherence and fraud) using an AI Platform. By contrast, concordance between pill counts and actual pill-taking behavior is relatively poor
- Statistical implications of using an accurate and continuous measure of subject behavior, on a pill by pill basis, include: Customizing adherence thresholds; data enrichment strategies pre- and post-randomization; and using AI platform-generated data as the primary measure of adherence and a variable in determining sample size
- Data obtained from the AI platform may also be useful for quantitative pharmacometrics as a PK surrogate to augment the quality of population PK modeling. Substituting or reducing the number of PK draws with AI platform data, when PK is used as an adherence measure, could also be of interest in virtual trials, reducing cost and subject/site burden.

MEASURING ADHERENCE & CHEATING BEHAVIOR



Anzar Abbas, Arunava Samaddar, Laura Shafner, and Isaac Galatzer-Levy are employees of AiCure, New York, NY.