Assessing the value of an AI Platform during screening to predict adherence to study drug during treatment in an ongoing proof-of-concept study in schizophrenia

Goeldner C [1], Shafner L[2] and **Umbricht D[1]**

Roche Pharma Research and Early Development, F. Hoffmann – La Roche, Ltd., 1 Roche Innovation Center Basel, Switzerland, 2AiCure, New York, NY, USA

1 – Monitoring adherence to study treatment in psychiatry trials

- Non-adherence is a major challenge in clinical trials in psychiatric indications such as schizophrenia. Traditional methods such as pill count and self-report are not deemed sufficiently reliable.
- Accurate drug adherence data are critically needed to decrease variability and increase signal-to-noise ratio in proof-of-concept studies, which aim to show preliminary evidence of efficacy in a relatively small sample size.
- We implemented a novel AI platform (AiCure®) to monitor adherence to study treatment in an ongoing Phase 2b study of basmisanil, a $GABA_A$ a5 negative allosteric modulator, for the treatment of Cognitive Impairment Associated with Schizophrenia.
- We implemented a novel 'placebo test-phase' during the screening period in which patients had to use the AI platform in order to demonstrate the ability to use the system and adhere to prescribed treatment

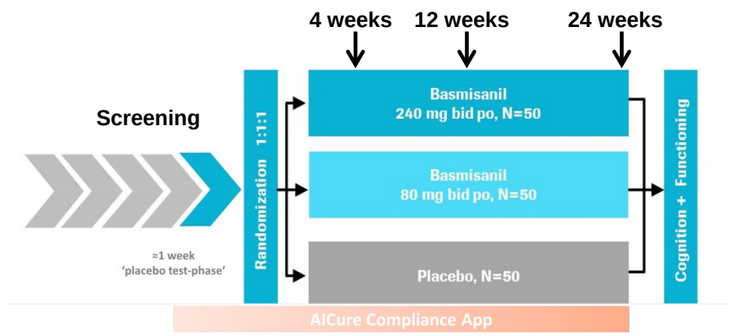
The following questions were investigated:

è **Can adherence to placebo dosing during screening be used as an accurate predictor of adherence post-randomization?**

è **Which thresholds of adherence most accurately predict non-adherence post-randomization?**

è **For which study duration can adherence post-randomization be predicted?**

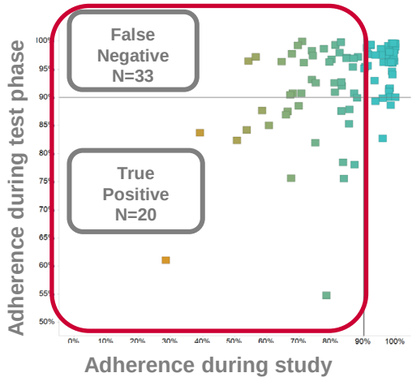
2 – Study design and monitoring of adherence to study drug



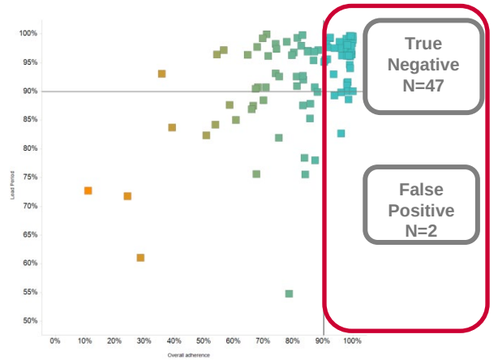
The adherence measure is based on AI platform adherence data, obtained by visual recognition and confirmation of drug ingestion by the patient, during screening (1-week placebo test-phase) and during 24 weeks of treatment

4 –Predictive validity analysis: Condition to be 'diagnosed'= *Non-Adherence*

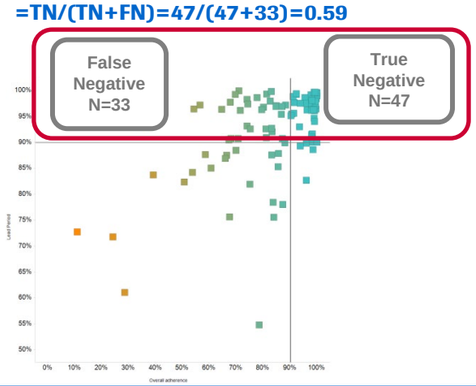
Sensitivity = Proportion of positives (**non-compliers**) that are correctly identified as such during screening.
=TP/(TP+FN)=20/(20+33)=0.38



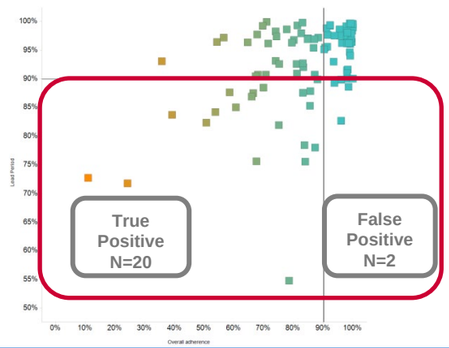
Specificity = Proportion of negatives (**compliers**) that are correctly identified as such at screening.
+FP)=47/(47+2)=0.96



Negative Predictive Value = Probability that patients are compliant during trial when screening adherence was above threshold
=TN/(TN+FN)=47/(47+33)=0.59



Positive Predictive Value = Probability that patients are non-adherent when screening adherence was below threshold
=TP/(TP+FP)=20/(20+2)=0.91



5 – Positive predictive value increases with adherence threshold

ADHERENCE PREDICTION	Threshold		
Overall adherence	**70% N=102**	**80% N=102**	**90% N=102**
Sensitivity	14	17	**38**
Specificity	99	96	**96**
PPV	75	63	**91**
NPV	82	73	**59**

6– Positive predictive value increases with treatment duration

ADHERENCE PREDICTION	Weeks of treatment		
Threshold 90%	**4w N=89**	**12w N=70**	**24w N=46**
Sensitivity	58	43	30
Specificity	92	94	96
PPV	75	77	86
NPV	84	77	64

3 – AI platform (AiCure®) to monitor adherence to study treatment

1. Patient stands in front of smartphone – facial recognition
2. Patient shows sachets (granule formulation) to the smartphone for identification - computer visionUser instructed on how to take medication
3. Patient instructed on how to take the medication - mix granule formulation into food
4. Patient instructed to consume medication in front of the smartphone, and tap button when finished
5. Dosing data are automatically logged and encrypted

7 – Conclusion

- **Adherence or non-adherence during the test phase was fairly well predictive of adherence or non-adherence during the trial.**
- **In particular, non-adherent patients during the test phase had a high chance of remaining non-adherent during the trial (PPV)**
- **Non-adherence during screening could be used as exclusion criterion**
- **However the method identifies only a small fraction of future non-adherent patients (low sensitivity).**
- **A more stringent threshold for adherence increases the proportion of non-compliers identified, as well as the probablity of correct identification –however practical considerations such as recruitment/length of study need to be taken in account.**