InSilicoTrials

Drug Safety Suite

Solution Brief

Introduction

Regulatory bodies are recommending an enhanced assessment of drug-induced proarrhythmic risks and Torsade de Pointes in drug candidates early screening.

The ICH S7B and ICH E14 guidelines will be soon replaced by one that will regulate both the preclinical and clinical studies.

The Comprehensive In Vitro Proarrhythmya Assay (**CiPA**) initiative has the goal of increasing early detection of drug induced cardiac safety liabilities and and it recommends testing on 7 ionic channels instead of one and the use of Modelling and Simulation. This can lead to a huge increase of R&D costs and time in a traditional industrial setting.

Why is In Silico so Crucial

Regulators recommend in silico to complement in vitro evidence.

The CiPA initiative aims to mitigate risks through an approach based on modelling and simulation to complement in vitro studies, increasing insights on the effects of compound drugs on the functioning of the heart.

Data Generated by ion current blocking in vitro test are used as input for in silico testing and risk assessment, to screen as early as possible drug candidates on potential cardiotoxicity liabilities, and to predict their effects on the cardiac action potential at the cellular level.

In silico testing helps to identify also the drug compound safety window, through virtual screening of multiple concentrations, guiding in vitro and in vivo testing and resulting in a drastic reduction of risks and investments.

InSilicoTrials Highlights

- Based on innovative and validated models, created by top researchers and by regulatory bodies.
- Cloud based platform, accessible from anywhere in the world.
- Simplified interface, to be used by non simulation experts.
- Developed according to the latest cybersecurity standards.
- Pay per use: no need to invest on software or IT.

Validated Models

Made by top scientists and universities
Supported by scientific evidences and publications
Locked to ensure integrity.

Unified Interface

Simplified UI
One interface for multiple models
Guided workflows
Ready to use reports

Cloud-Based

Embedded simulation engines
Unlimited and flexible
Multiple solvers embedded
Resilient and accessible
Cybersecure
Turnkey ready

84%

Of companies never or rarely use in silico studies to evaluate drug effects on the Cardiac Action Potential (1)

75%

Of researchers considers human induced stem cells drived cardio-myocytes (hiPSa-CMs) a valuable addiction to proarrhythmia screen-ing assays (1)

500 days
20% costs (2)

Of companies never or rarely use in silico studies to evaluate drug effects on the Cardiac Action Potential (1)

1. Based Proarrhythmia liability assessment and CiPA survey
2. McKinsey & Co - The pursuit of excellence in new-drug development

Complement standard and complex in vitro testing through validated models without software and IT investments and without specific simulation knowledge.

QT/TdP

Risk Screen

A unique tool able to calculate safety markers and estimate clinical risks following CredibleMeds classification for multiple concentrations of a compound with respect to the four most relevant ion currents, and in minutes.

Input: 2 standard in vitro parameters for up to 4 ion currents and the concentration range of interest.
Validation: 109 drugs (51 torsadogenic)
Output: Safety markers and clinical risk

CIPA InSilico

A tool based on the FDA standards, to calculate the safety marker qNet on up to 7 ion currents at different concentrations.

Input: drug-hERG kinetics, IC50 and Hill parameters for up to 7 ion currents and the concentration range of interest.
Validation: 16 drugs (4 torsadogenic)
Output: Safety markers

STrhiPs

A tool to conduct in silico safety trials on a population of human induced pluripotential stem cells, for 7 ion currents and at different concentrations.

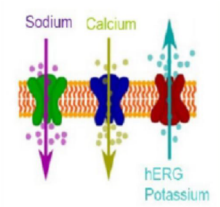
Input: IC50 and Hill parameters for up to 7 ion currents and the concentration range of interest.
Validation: 4 drugs (Paci 2018); the 12 CiPA training set drugs (SPSAnnual Meeting 2020)
Output: Safety markers

Drastically reduce your R&D timelines and costs by running multiple models and:

Disqualify early in the process the unsafe molecules and concentrations. Cut the risks by increasing the accuracy of your decisions through cross results.

01. EVALUATION

Standard and complex protocols



In vitro assessment of drug effects on multiple channels

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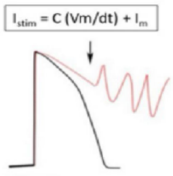
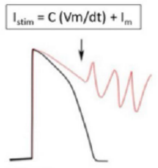
CiPA In Silico



Computer Modeling to predict markers

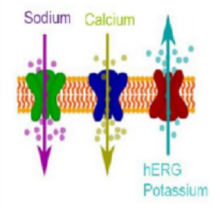
QT/TdP Risk Screen



Computer Modeling to predict risk

← CredibleMeds® +

Standard protocol



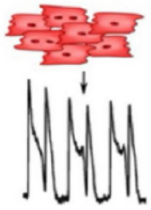
In vitro assessment of drug effects on multiple channels

qNet Clinical Risk

OUTCOME

02. CONFIRMATION

Standard protocol



Effects in human stem cell-derived cardiomyocytes

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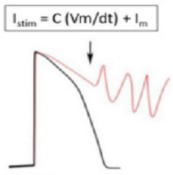
STrhiPS



Computer Modeling to predict markers

Safety Markers

↑↑ **ACCURACY**

↑↑ **SENSITIVITY**

↑↑ **SPECIFICITY**

Contact us: info@insilicotrials.com
Ask for a demo and a free test