Using R For Flexible Modeling Of Pre-Clinical Combination Studies

Chris Harbron

1. Discovery Statistics, AstraZeneca
* Contact author:Chris.Harbron@AstraZeneca.Com

Keywords: Combinations, Synergy, Non-linear models.

There is a strong and increasing interest in the development of drug combination therapies within the pharmaceutical industry, so a robust evaluation of the potential for compounds to interact synergistically at an early stage within the pharmaceutical pipeline is clearly of great value.

I will describe a newly developed unified approach for assessing synergy which allows a number of different assessments to be made and compared under a common framework, powerfully and flexibly using all the available experimental data and giving a complete description of the studied combination space with statements of confidence. The method is applicable over wide classes of experimental design and response patterns and is backed up with informative graphical displays.

The R language, using the *nls()* function provides a powerful environment to implement these assessments, although due to the functional form of the models and the variety of data scenarios encountered, some adaptations are required. Features of this implementation ensuring that these models can be implemented reliably, robustly and efficiently will be highlighted and discussed.