Bayessian hierachical models for selecting clinical trial proposals of new targeted drugs.

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The Clinical Research Unit in the Catalan Institut of Oncology received on 2007, 172 proposals for participating in drug clinical trials but only 32.5 % of them were selected according to trial theorical drug interest and protocol design. Although the expected response rate in a phase I trial is 3 %, they could provide the information to decide which are the most promising drugs. New targeted drugs (NTD) are designed to block one or more different cell mechanisms (targets). NTD end targets can be classified by families. It is possible to find some NTD that block more than one target in the same family. Therefore, the relationship between drug, target and family variables is considered as a hierarchy. A Bayesian model is proposed to analyze them and to use it as a statistical criterion to be added on the trial selection. 170 non-cytotoxic novel drug phase I studies were systematically reviewed, between 1999-2007 publications and American Society of Clinical Oncology abstracts. Combinations of drugs, well-known active drugs and hormone and immunotherapy studies were excluded. Number of radiological responses (minor included), total patient number, drug involved in the clinical trial, drug targets and drug family were recorded. A hierarchical bayesian model for binomial responses was performed for adjusting data. The Bayesian analysis has the advantage that one disposes of a posterior distribution. Then this posterior probability was used as a criteria for detecting promising targets and families as follows: Drugs, targets and families have been considered as promising if their posterior probability of having a response rate greater than 0.03 is upper than 0.95. Markov Chain Monte Carlo algorithms are used to estimate by simulating the posterior distribution of the parameters and hyperparameters of the model through WinBugs, while graphical representation of results is done through R. Using this criteria that uses posterior probabilities we have been able to detect some families and targets that according to the current experience are active drugs. The model detected VEGF family as one of the most promising ones as it has been confirmed with available clinical data.. We are currently working to perform a hierarchical model which will take into account the complex relationship between drug, target and family in order to improve the selection of NTD in clinical trials.