

Claims

1. A system for determining a personalized dose of a pharmaceutical for an individual, the system comprising:

5 an input port configured to receive:

first data representative of one or more characteristics of the individual prior to administration of the pharmaceutical, wherein the characteristics of the individual include at least one of sex, age, weight, race, disease stage, disease status, prior therapy, concomitant
10 diseases, demographic information, and laboratory test result information; and

second data representative of a measurement of a physiological parameter of the individual after administration of the pharmaceutical, wherein the physiological parameter is a measured concentration time profile of the pharmaceutical or a biomarker in the individual's blood, tissue, or cells; and

15 a computer processor in communication with the input port and an electronic database having information that represents a computational model to predict an effect of the pharmaceutical on the individual's body, the computational model being a function of response profiles for a population of patients and patient factor covariates corresponding to the characteristics of the individual, the computation model including a pharmacokinetic component including a
20 pharmacokinetic clearance and a pharmacodynamic component including a pharmacodynamic response, the computational model describing an interrelation between the pharmacokinetic component and the pharmacodynamic component wherein the pharmacokinetic clearance is modified to include a diminishing effect of the pharmacodynamic response on the pharmacokinetic clearance over time, and the computer processor being configured to:

25 generate, based on the first data and the computational model, a first target concentration and one or more first doses determined by Bayesian analysis to likely achieve

the first target concentration for the pharmaceutical in the individual's body;

after receiving the second data, compute, based on the second data, a Bayesian
5 update to the pharmacokinetic component and the pharmacodynamic component of the
computational model to obtain an updated computational model that reflects the
measurement of the physiological parameter of the individual, wherein the second data
indicates a response by the individual to the one or more first doses; and

generate, based on the updated computational model, a second target concentration
10 and one or more second doses determined by Bayesian analysis to likely achieve the second
target concentration for the pharmaceutical in the individual's body, wherein the update to
the pharmacodynamic component of the computational model is used to predict that the
second target concentration will have a therapeutic effect on the individual.

15 2. The system of claim 1, wherein the pharmacokinetic component of the computational
model includes a compartmental model, and the computer processor is configured to use the
pharmacokinetic component to predict a concentration time profile of the pharmaceutical in at least
one compartment in the compartmental model.

20 3. The system of claim 2, wherein the predicted concentration time profile is predicted by
using a first differential equation that describes a flow rate of the pharmaceutical into and out of the
at least one compartment in the compartmental model.

25 4. The system of claim 3, wherein:
the pharmacodynamic component of the computational model includes a synthesis rate
30 parameter representative of a synthesis rate of a pharmacodynamic marker and a degradation rate
parameter representative of a degradation rate of the pharmacodynamic marker; and

the synthesis rate parameter and the degradation rate parameter are used in a second differential equation that predicts the individual's response to the pharmaceutical.

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5. The system of any of claims 2-4, wherein Bayesian analysis comprises comparing the measured concentration time profile to the predicted concentration time profile.

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6. The system of claim 5, wherein Bayesian analysis further comprises performing an optimization technique to minimize a difference between the measured concentration time profile and the predicted concentration time profile.

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7. The system of any of the above claims, wherein the pharmaceutical is infliximab, and the pharmacodynamic component of the computational model reflects an effect of infliximab on the individual's body.

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8. The system of claim 7, wherein the flow rate accounts for the individual's predicted response to the infliximab as the individual heals.

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9. The system of any of the above claims, wherein the first target concentration and the second target concentration each corresponds to a concentration that is predicted to cause an effect in the individual's body that is at least half of a predicted maximal effect.

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10. The system of any of the above claims, wherein the first data and the second data each include an anonymized identifier for the individual.

11. A method for determining a personalized dose of a pharmaceutical for an individual, the method comprising:

receiving, at an input port, first data representative of one or more characteristics of the individual prior to administration of the pharmaceutical, wherein the characteristics of the individual include at least one of sex, age, weight, race, disease stage, disease status, prior therapy, concomitant diseases, demographic information, and laboratory test result information;

generate, at a computer processor, based on the first data and a computational model, a first target concentration and one or more first doses determined by Bayesian analysis to likely achieve the first target concentration for the pharmaceutical in the individual's body, wherein the computer processor is in communication with the input port and an electronic database having information that represents the computational model to predict an effect of the pharmaceutical on the individual's body, the computational model being a function of response profiles for a population of patients and patient factor covariates corresponding to the characteristics of the individual, the computation model including a pharmacokinetic component including a pharmacokinetic clearance and a pharmacodynamic component including a pharmacodynamic response, the computational model describing an interrelation between the pharmacokinetic component and the pharmacodynamic component wherein the pharmacokinetic clearance is modified to include a diminishing effect of the pharmacodynamic response on the pharmacokinetic clearance over time;

receiving, at the input port, second data representative of a measurement of a physiological parameter of the individual after administration of the pharmaceutical, wherein the physiological parameter is a measured concentration time profile of the pharmaceutical or a biomarker in the individual's blood, tissue, or cells, wherein the second data indicates a response by the individual to the one or more first doses;

computing, based on the second data, a Bayesian update to the pharmacokinetic component and the pharmacodynamic component of the computational model to obtain an updated

computational model that reflects the measurement of the physiological parameter of the individual;
and

generating, based on the updated computational model, a second target concentration and
5 one or more second doses determined by Bayesian analysis to likely achieve the second target
concentration for the pharmaceutical in the individual's body, wherein the update to the
pharmacodynamic component of the computational model is used to predict that the second target
concentration will have a therapeutic effect on the individual.

10 12. The method of claim 11, wherein the pharmacokinetic component of the computational
model includes a compartmental model, and the method further comprises using the
pharmacokinetic component to predict a concentration time profile of the pharmaceutical in at least
one compartment in the compartmental model.

15 13. The method of any of claims 11-12, further comprising predicting the predicted
concentration time profile by using a first differential equation that describes a flow rate of the
pharmaceutical into and out of the at least one compartment in the compartmental model.

20 14. The method of claim 13, wherein:

the pharmacodynamic component of the computational model includes a synthesis rate
25 parameter representative of a synthesis rate of a pharmacodynamic marker and a degradation rate
parameter representative of a degradation rate of the pharmacodynamic marker; and

the synthesis rate parameter and the degradation rate parameter are used in a second
differential equation that predicts the individual's response to the pharmaceutical, and, optionally, at
least one of:

30 wherein the physiological parameter is a measured concentration time profile of the

pharmaceutical in the individual's blood, tissue, or cells, and Bayesian analysis comprises comparing the measured concentration time profile to the predicted concentration time profile;

5 wherein Bayesian analysis further comprises performing an optimization technique to minimize a difference between the measured concentration time profile and the predicted concentration;

wherein the pharmaceutical is infliximab, and the pharmacodynamic component of the computational model reflects an effect of infliximab on the individual's body;

10 wherein the flow rate accounts for the individual's predicted response to the infliximab as the individual heals; and

wherein the first target concentration and the second target concentration each corresponds to a concentration that is predicted to cause an effect in the individual's body that is at least half of a predicted maximal effect.

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