Package 'UBCRM'

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Type Package

Title Functions to Simulate and Conduct Dose-Escalation Phase I Studies

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Description Two Phase I designs are implemented in the package: the classical 3+3 and the Continual Reassessment Method. Simulations tools are also available to estimate the operating characteristics of the methods with several user-dependent options.

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UBCRM-package *UBCRM is a package containing functions to simulate and conduct dose escalation phase I studies*

Description

Two designs are implemented in the package: the classical 3+3 and the Continual Reassessment Method. Simulations tools are also available to estimate the operating characteristics of the methods with several user-dependent options.

Details

Package:	UBCRM
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Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. Biometrics 46, 33-48.

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. Biometrics 52, 673-684.

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. Statistics in Medecine 28, 3012-3028.

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

Examples

```
data<- CreData(4)
prior<-c(.05,.1,.15,.2)
```

```
# One study simulation
simCrm(prior=prior, firstdose = 2, truerate = prior, cohortsize = 3, target = 1/3,
nptmax = 18, nmaxmtd = 6, nmaxdose = 18, sd = 1.34, approach = "bayes", model = "power",
method = "fpost", nextlevel = "ntarget", upskipping = TRUE, downskipping = FALSE,
lastdose = NA, graphic = FALSE, seed = 20130110)

# N simulations with CRM
# Power model, no up skipping, start at dose 2
res1<- ssimCrm(prior=prior, 100, firstdose = 2, truerate = prior, cohortsize = 3,
target = 1/3, nptmax = 18, nmaxmtd = 6, nmaxdose = 18, sd = 1.34, approach = "bayes",
method = "fpost", model = "power", nextlevel = "ntarget", upskipping = TRUE,
downskipping = FALSE, r = 2, seed=20130110)
res1

# Simulations with 3+3 design
res2<- ssim3p3(truerate=prior, 100, r = 2, seed=20130110)
res2
```

`aip` *Functions to calculate the appropriate dose level singletons*

Description

Pool of functions to calculate dose level singletons values: aip, ail2 and ait2 calculate sgl in order that E[psy] = prior, ail1 and ait1 calculate sgl in order that psy(sgl,1) = prior.

Usage

```
aip(p_prior, sd = 1.34)
ait1(p_prior, a=1)
ail1(p_prior, a=1)
ait2(p_prior)
ail2(p_prior)
```

Arguments

`p_prior`	Prior toxicity probability.
`sd`	Standard deviation in case of normal distribution for the parameter.
`a`	Rate in case of exponential distribution for the parameter.

Value

Numeric length(p-prior)-vector.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. Biometrics 46, 33-48.

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. Biometrics 52, 673-684.

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. Statistics in Medecine 28, 3012-3028.

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

CreData *Creates a CRM dataframe*

Description

Creates a n-row summary dataframe indicating the number of treated patients and observed DLTs at each of the n dose-levels. This is the dataframe structure that will be needed in the different functions of the UBCRM package.

Usage

```
CreData(ndose = 3, dosenames = paste("dose", 1:ndose, sep = " "))
```

Arguments

ndose	Number of dose levels.
dosenames	A ndose-length character vector of labels for the dose levels.

Value

A ndose * 3 dataframe containing:

dose	Integer value 1..ndose ordering the doses.
npt	Integer count of the treated patients at dose i.
ndlt	Integer count of the observed DLT at dose i.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. Biometrics 46, 33-48.

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. Biometrics 52, 673-684.

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. Statistics in Medecine 28, 3012-3028.

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

See Also

updata

Examples

```
data<- CreData(5,c("5 mg/m2","7 mg/m2","10 mg/m2","15 mg/m2","20 mg/m2"))
data
```

Crm *Dose-escalation with the Continual Reassessment Method*

Description

The function gives the next level to include patients following a model-based design. Needs an updated input dataframe with the CreData() structure.

Usage

```
Crm(Dk, prior, target = 1/3, nptmax = 24, nmaxmtd = 6, nmaxdose = nptmax, sd = 1.34,
approach = "bayes", model = "power", method = "fpost", nextlevel = "ntarget",
upskipping = F, downskipping = F, lastdose = NA)
```

Arguments

Dk	Study dataframe with CreData() structure.
prior	Numeric vector of prior DLTs probabilities.
target	Target used for the MTD determination.
nptmax	Maximum number of patients to include in the study.
nmaxmtd	Maximum number of patients to be treated at the designated MTD. Assign a high value (=nptmax) to avoid such a stopping rule.
nmaxdose	Maximum number of patients to be treated at the same dose. Assign a high value (=nptmax) to avoid such a stopping rule.

sd	Standard deviation used in case of a normal distribution assumption for the parameter.
approach	Character indicating the estimation method: "bayes" (default value) for CRM or "mle" for CRML.
model	Character indicating the dose-DLT relationship model: "power", "tangent" or "logistic". More informations in the details section.
method	Estimation method for the posterior probabilities. "fpost" (default) estimates the mean of the posterior distribution of the parameter alpha (hat_alpha=E[alpha]) and uses it in psy(hat_alpha,...). "ppostp" and "pposts" directly estimate the mean of the posterior DLT probability. "ppostp" uses prior as singletons whereas "pposts" calculates appropriates singletons (see ail, ait or aip functions).
nextlevel	Character option used for determining the next dose level. "ntarget" (default) if the next level is chosen as the closest level to the desired target (may be higher than target). "utarget" if the next level is the closest level with the restriction to be lower than the target value.
upskipping	Boolean option used for determining the next dose level. If TRUE no level skip in escalation will be allowed. If FALSE (default) the level skips will be permitted.
downskipping	Boolean option used for determining the next dose level. If TRUE no level skip in desescalation will be allowed. If FALSE (default) the level skips will be permitted.
lastdose	Integer representing the last experimented dose level.

Details

Details of the 3 dose-DLT relationship proposed models: "power" for the power model psy(s,a)=s^exp(a), "tangent" for the hyperbolic tangent model psy(s,a)= ((tanh(s)+1)/2)**a, "logistic" for the logistic model psy(s,a) = exp(3+a*s)/(1+exp(3+a*s)). Note: power and tangent models are equivalent after an appropriate transformation on the parameter.

Value

nextdose	An integer representing the next recommended dose to experiment.
mtd	If reached, an integer representing the MTD.
prob	Posterior DLTs probabilities.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. Biometrics 46, 33-48.

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. Biometrics 52, 673-684.

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. Statistics in Medecine 28, 3012-3028.

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

See Also

simCrm, ssimCrm

Examples

```
data<- CreData(5)
data<- updata(data,1,3,0)
data<- updata(data,2,3,1)
data<- updata(data,2,3,1)
data
Crm(data,prior=c(0.1,0.15,0.25,0.35,0.45),target=0.3,nextlevel="ntarget",nptmax=24,nmaxmtd=6)
data<- updata(data,3,3,2)
data
Crm(data,prior=c(0.1,0.15,0.25,0.35,0.45),target=0.3,nextlevel="ntarget",nptmax=24,nmaxmtd=6)
```

---

fp *Density functions*

Description

Density functions for the model parameter. fp(a,sd) is the normal density: 1/(sd*sqrt(2*pi))*exp(-(a^2)/(2*sd^2)). ft and fl are the exponential density (with a fixed rate = 1): exp(-a).

Usage

```
fp(a, sd)
ft(a)
fl(a)
```

Arguments

a	Parameter.
sd	Standard deviation.

Value

Numeric value of the computed density.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. Biometrics 46, 33-48.

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. Biometrics 52, 673-684.

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. Statistics in Medecine 28, 3012-3028.

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

`Lp` *Likelihood functions*

Description

Lp is the likelihood function for the power model psy(s,a)=s^exp(a). Lt is the likelihood function for the hyperbolic tangent model psy(s,a)= ((tanh(s)+1)/2)**a. Ll is the likelihood function for the logistic model psy(s,a) = exp(3+a*s)/(1+exp(3+a*s)).

Usage

```
Lp(a, data, sgl)
Lt(a, data, sgl)
Ll(a, data, sgl)
```

Arguments

`a`	Parameter.
`data`	CRM dataframe with a CreData() structure.
`sgl`	Dose level singleton.

Details

# Power model Lp<- function(a, data, sgl) npt<- data$npt ndlt<- data$ndlt sapply(a,FUN=function(a)prod((psip(sgl,a)^ndlt)*(
psip(sgl,a))^(npt-ndlt))))

# Hyperbolic tangent model Lt<- function(a, data, sgl) npt<- data$npt ndlt<- data$ndlt sapply(a,FUN=function(a)prod((psit(sg
psit(sgl,a))^(npt-ndlt))))

# Logistic model Ll<- function(a, data, sgl) npt<- data$npt ndlt<- data$ndlt sapply(a,FUN=function(a)prod((psil(sgl,a)^ndlt)*
psil(sgl,a))^(npt-ndlt))))

Value

Numeric value of the computed likelihood.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. Biometrics 46, 33-48.

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. Biometrics 52, 673-684.

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. Statistics in Medecine 28, 3012-3028.

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

`psip` *Dose-Toxicity modelisation functions*

Description

psip corresponds to the power model psy(s,a)=s^exp(a). psit corresponds to the hyperbolic tangent model psy(s,a)= ((tanh(s)+1)/2)**a. psil corresponds to the logistic model psy(s,a) = exp(3+a*s)/(1+exp(3+a*s)).

Usage

```
psip(sgl,a)
psit(sgl,a)
psil(sgl,a)
```

Arguments

`sgl`	Dose level singleton.
`a`	Parameter.

Value

Numeric value of the computed function.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. Biometrics 46, 33-48.

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. Biometrics 52, 673-684.

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. Statistics in Medecine 28, 3012-3028.

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

`sim3p3` *Simulation of one dose-escalation study with the classical 3+3 design*

Description

Given a true rates vector of DLT probabilities, the function simulate a 3+3 dose-escalation design.

Usage

```
sim3p3(truerate, seed = NULL)
```

Arguments

`truerate`	A nlevel-length vector of true rates for the DLTs.
`seed`	If not empty, the seed to use for random generation.

Value

`data`	Study data.
`mtd`	If reached, an integer representing the MTD level.
`lastdose`	An integer representing the last experimented dose.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. Biometrics 46, 33-48.

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. Biometrics 52, 673-684.

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. Statistics in Medecine 28, 3012-3028.

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

See Also

troisPtrois, ssim3p3

Examples

```
# A 3-dose study with 10%, 20% and 30% of true rates for toxicity
sim3p3(c(0.1,0.2,0.3))
```

`simCrm` *Simulation of one dose-escalation study with the Continual Reassessment Method*

Description

Given prior and true rates vectors of DLT probabilities, the function simulates a CRM dose-escalation design.

Usage

```
simCrm(prior, firstdose = NA, truerate = prior, cohortsize = 3, target = 1/3,nptmax = 24,
nmaxmtd = nptmax, nmaxdose = nptmax, sd = 1.34, approach = "bayes", model = "power",
method = "fpost", nextlevel = "ntarget", upskipping = F, downskipping = F, lastdose = NA,
graphic = F, seed = NULL)
```

Arguments

`prior`	Numeric vector of prior DLT probabilities.
`firstdose`	Integer representing the dose at which the first cohort will be treated.
`truerate`	A nlevel-length vector of true rates for the DLTs.
`cohortsize`	Size of the cohort. Default value = 3.
`target`	Target used for the MTD determination.
`nptmax`	Maximum number of patients to include in the study.

nmaxmtd	Maximum number of patients to be treated at the designated MTD. Assign a high value (=nptmax) to avoid such a stopping rule.
nmaxdose	Maximum number of patients to be treated at the same dose. Assign a high value (=nptmax) to avoid such a stopping rule.
sd	Standard deviation used in case of a normal distribution assumption for the parameter.
approach	Character indicating the estimation method: "bayes" (default value) for CRM or "mle" for CRML.
model	Character indicating the dose-DLT relationship model: "power", "tangent" or "logistic".
method	Estimation method for the posterior probabilities. "fpost" (default) estimates the mean of the posterior distribution of the paramater alpha (hat_alpha=E[alpha]) and uses it in psy(hat_alpha,...). "ppostp" and "pposts" directly estimate the mean of the posterior DLT probability. "ppostp" uses prior as singletons whereas "pposts" calculates appropriate singletons (see ail, ait or aip functions).
nextlevel	Character option used for determining the next dose level. "ntarget" (default) if the next level is chosen as the closest level to the desired target (may be higher than target). "utarget" if the next level is the closest level with the restriction to be lower than the target value.
upskipping	Boolean option used for determining the next dose level. If TRUE no level skip in escalation will be allowed. If FALSE (default) the level skips will be permitted.
downskipping	Boolean option used for determining the next dose level. If TRUE no level skip in desescalation will be allowed. If FALSE (default) the level skips will be permitted.
lastdose	Integer representing the last experimented dose level.
graphic	Boolean option for graphic generation.
seed	If not empty, the seed to use for random generation.

Value

data	Study data.
dose	Integer vector representing for each cohort the experimented dose levels.
nDLT	Integer vector representing for each cohort the number of observed DLTs.
mtd	If reached, an integer representing the MTD level.
lastdose	An integer representing the last experimented dose.
prob	Posterior DLT probabilities.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. Biometrics 46, 33-48.

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. Biometrics 52, 673-684.

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. Statistics in Medecine 28, 3012-3028.

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

See Also

Crm, ssimCrm

Examples

```
simCrm(c(0.1,0.2,0.3,0.35,0.45),firstdose=1,target=0.33)
```

`ssim3p3` *Simulation of n dose-escalation study with the 3+3 design*

Description

The ssim3p3 function simulates n dose-escalation study with the 3+3 design and provides summarized results.

Usage

```
ssim3p3(truerate, n, r = 2, seed = NULL)
```

Arguments

`truerate`	A nlevel-length vector of true rates for the DLTs.
`n`	Number of studies to simulate.
`r`	Integer, number of digits for percentages in output.
`seed`	If not empty, the seed to use for random generation.

Value

`data`	Summarized result in a "np1" view.
`norecommendation`	Percentage of studies with no recommendation for the MTD (in case of the first level is considered as toxic).
`mean.npt`	Mean number of enrolled patients.
`mean.ndlt`	Mean number of observed DLTs.
`mean.lastdose`	Mean last experimented dose level.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. Biometrics 46, 33-48.

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. Biometrics 52, 673-684.

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. Statistics in Medecine 28, 3012-3028.

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

See Also

`troisPtrois`, `sim3p3`

Examples

```
ssim3p3(c(0.1,0.2,0.25,0.35),100)
```

`ssimCrm` *Simulation of n dose-escalation study with the Continual Reassessment Method*

Description

The ssimCrm function simulates n dose-escalation study with the CRM and provides summarized results.

Usage

```
ssimCrm(prior, n, firstdose = NA, truerate = prior, cohortsize = 3, target = 1/3,
nptmax = 24, nmaxmtd = nptmax, nmaxdose = nptmax, sd = 1.34, approach = "bayes",
method = "fpost", model = "power", nextlevel = "ntarget", upskipping = F,
downskipping = F, r = 2, seed = NULL)
```

Arguments

prior	Numeric vector of prior DLT probabilities.
n	Number of studies to simulate.
firstdose	Integer representing the dose at which the first cohort will be treated.
truerate	A nlevel-length vector of true rates for the DLTs.
cohortsize	Size of the cohort. Default value = 3.
target	Target used for the MTD determination.
nptmax	Maximum number of patients to include in the study.
nmaxmtd	Maximum number of patients to be treated at the designated MTD. Assign a high value (=nptmax) to avoid such a stopping rule.
nmaxdose	Maximum number of patients to be treated at the same dose. Assign a high value (=nptmax) to avoid such a stopping rule.
sd	Standard deviation used in case of a normal distribution assumption for the parameter.
approach	Character indicating the estimation method: "bayes" (default value) for CRM or "mle" for CRML.
model	Character indicating the dose-DLT relationship model: "power", "tangent" or "logistic".
method	Estimation method for the posterior probabilities. "fpost" (default) estimates the mean of the posterior distribution of the paramater alpha (hat_alpha=E[alpha]) and uses it in psy(hat_alpha,...). "ppostp" and "pposts" directly estimate the mean of the posterior DLT probability. "ppostp" uses prior as singletons whereas "pposts" calculates appropriate singletons (see ail, ait or aip functions).
nextlevel	Character option used for determining the next dose level. "ntarget" (default) if the next level is chosen as the closest level to the desired target (may be higher than target). "utarget" if the next level is the closest level with the restriction to be lower than the target value.
upskipping	Boolean option used for determining the next dose level. If TRUE no level skip in escalation will be allowed. If FALSE (default) the level skips will be permitted.
downskipping	Boolean option used for determining the next dose level. If TRUE no level skip in desescalation will be allowed. If FALSE (default) the level skips will be permitted.
r	Integer, number of digits for percentages in output.
seed	If not empty, the seed to use for random generation.

Value

`data`	Summarized result in a "np1" view.
`norecommendation`	Percentage of studies with no recommendation for the MTD (in case of the first level is considered as toxic).
`mean.npt`	Mean number of enrolled patients.
`mean.ndlt`	Mean number of observed DLTs.
`mean.lastdose`	Mean last experimented dose level.
`mean.prob`	Mean of posterior DLT probabilities.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

O'Quigley J., Pepe M., Fisher L. (1990). Continual Reassessment Method: a practical design for Phase I clinical trials in cancer. Biometrics 46, 33-48.

O'Quigley J., Shen LZ. (1996). Continual Reassessment Method: a likelihood approach. Biometrics 52, 673-684.

Paoletti X., Kramar A. (2009). A comparison of model choices for the Continual Reassessment Method in phase I cancer trials. Statistics in Medecine 28, 3012-3028.

Chamorey Emmanuel. (2009). Methodologie des essais de phase precoce en cancerologie: evolution des schemas et apport de la pharmacologie. These.

Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

See Also

`Crm`, `simCrm`

Examples

```
ssimCrm(c(0.1,0.2,0.3,0.35,0.45),firstdose=1,target=0.33,n=100)
```

`troisPtrois` *Dose escalation with the 3+3 design*

Description

The function gives the next level to include patients following a 3+3 design. Needs an updated input dataframe with the CreData() structure.

Usage

```
troisPtrois(data = data, lastdose)
```

Arguments

data	Study dataframe with CreData() structure.
lastdose	Integer representing the last experimented dose level.

Value

nextdose	An integer representing the next recommended dose to experiment.
mtd	If reached, an integer representing the MTD.

Author(s)

Benjamin Esterni, Baboukar Mane. Unite de Biostatistique et de Methodologie, Institut Paoli-Calmettes, Marseille, France.

References

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See Also

sim3p3, ssim3p3

Examples

```
# Study initialization
data<- CreData(5,c("5 mg/m2","7 mg/m2","10 mg/m2","15 mg/m2","20 mg/m2"))
data

# Three patients are treated at the dose 1, without any observed DLT:
data<- updata(data,lastdose=1,npt=3,ndlt=0)
data

# 3+3 design
troisPtrois(data,lastdose=1)
```

updata *Update the CRM dataframe after new patients' collected data*

Description

This function uptdates the CRM dataframe (result of the CreData routine) with new treated patients or observed DLTs.

Usage

```
updata(data = data, lastdose, npt, ndlt)
```

Arguments

data	Dataframe to be updated.
lastdose	Integer representing the dose to be updated.
npt	Number of new treated patients.
ndlt	Number of DLTs among the npt patients.

Value

Updated dataframe.

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Garret-Mayer Elizabeth. (2006). The Continual Reassessment Method for dose-finding studies: a tutorial. Clinical Trials: 57-71.

See Also

CreData

Examples

```
# Study initialization
data<- CreData(5,c("5 mg/m2","7 mg/m2","10 mg/m2","15 mg/m2","20 mg/m2"))
data

# Three patients are treated at the dose 1, without any observed DLT:
data<- updata(data,lastdose=1,npt=3,ndlt=0)
data
```

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