Appendix A

**Simulation scenarios**

We adopted the 42 scenarios in Ji and Wang (2013) for , where scenarios for were generated by subtracting 0.03 from the original scenarios for in Ji and Wang (2013). Each scenario contains six true toxicity probabilities for all the six doses in the simulated clinical trials. They are listed as follows.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Scenarios# | Dose 1 | Dose 2 | Dose 3 | Dose 4 | Dose 5 | Dose 6 |
| 1 | 0.04 | 0.05 | 0.06 | 0.07 | 0.08 | 0.09 |
| 2 | 0.15 | 0.2 | 0.25 | 0.3 | 0.35 | 0.4 |
| 3 | 0.01 | 0.1 | 0.2 | 0.25 | 0.3 | 0.35 |
| 4 | 0.01 | 0.02 | 0.03 | 0.04 | 0.1 | 0.25 |
| 5 | 0.05 | 0.4 | 0.5 | 0.6 | 0.65 | 0.7 |
| 6 | 0.01 | 0.03 | 0.05 | 0.4 | 0.5 | 0.6 |
| 7 | 0.01 | 0.02 | 0.03 | 0.04 | 0.05 | 0.4 |
| 8 | 0.09 | 0.11 | 0.13 | 0.15 | 0.17 | 0.19 |
| 9 | 0.05 | 0.07 | 0.09 | 0.11 | 0.13 | 0.15 |
| 10 | 0.01 | 0.03 | 0.05 | 0.07 | 0.09 | 0.11 |
| 11 | 0.02 | 0.04 | 0.08 | 0.12 | 0.17 | 0.25 |
| 12 | 0.02 | 0.04 | 0.07 | 0.1 | 0.15 | 0.2 |
| 13 | 0.1 | 0.15 | 0.2 | 0.25 | 0.3 | 0.35 |
| 14 | 0.01 | 0.03 | 0.05 | 0.06 | 0.08 | 0.1 |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Scenarios# | Dose 1 | Dose 2 | Dose 3 | Dose 4 | Dose 5 | Dose 6 |
| 15 | 0 | 0.02 | 0.05 | 0.08 | 0.11 | 0.14 |
| 16 | 0.22 | 0.32 | 0.37 | 0.47 | 0.57 | 0.67 |
| 17 | 0 | 0.17 | 0.37 | 0.57 | 0.77 | 0.92 |
| 18 | 0.01 | 0.03 | 0.05 | 0.07 | 0.17 | 0.47 |
| 19 | 0.02 | 0.47 | 0.77 | 0.87 | 0.92 | 0.96 |
| 20 | 0 | 0.02 | 0.07 | 0.47 | 0.67 | 0.87 |
| 21 | 0 | 0 | 0.04 | 0.07 | 0.12 | 0.67 |
| 22 | 0.16 | 0.18 | 0.2 | 0.22 | 0.24 | 0.26 |
| 23 | 0.12 | 0.14 | 0.16 | 0.18 | 0.2 | 0.22 |
| 24 | 0.08 | 0.1 | 0.12 | 0.14 | 0.16 | 0.18 |
| 25 | 0.02 | 0.08 | 0.14 | 0.2 | 0.26 | 0.32 |
| 26 | 0.02 | 0.07 | 0.12 | 0.17 | 0.27 | 0.34 |
| 27 | 0.17 | 0.22 | 0.27 | 0.32 | 0.37 | 0.42 |
| 28 | 0.02 | 0.05 | 0.08 | 0.11 | 0.14 | 0.17 |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Scenarios# | Dose 1 | Dose 2 | Dose 3 | Dose 4 | Dose 5 | Dose 6 |
| 29 | 0.02 | 0.05 | 0.1 | 0.15 | 0.2 | 0.25 |
| 30 | 0.35 | 0.45 | 0.5 | 0.6 | 0.7 | 0.8 |
| 31 | 0.01 | 0.3 | 0.55 | 0.65 | 0.8 | 0.95 |
| 32 | 0.04 | 0.06 | 0.08 | 0.1 | 0.3 | 0.6 |
| 33 | 0.05 | 0.6 | 0.8 | 0.9 | 0.95 | 0.99 |
| 34 | 0.01 | 0.05 | 0.1 | 0.6 | 0.7 | 0.9 |
| 35 | 0.01 | 0.03 | 0.07 | 0.1 | 0.15 | 0.75 |
| 36 | 0.29 | 0.31 | 0.33 | 0.35 | 0.37 | 0.39 |
| 37 | 0.25 | 0.27 | 0.29 | 0.31 | 0.33 | 0.35 |
| 38 | 0.21 | 0.23 | 0.25 | 0.27 | 0.29 | 0.31 |
| 39 | 0.05 | 0.2 | 0.27 | 0.33 | 0.39 | 0.45 |
| 40 | 0.05 | 0.1 | 0.2 | 0.3 | 0.4 | 0.4 |
| 41 | 0.3 | 0.35 | 0.4 | 0.45 | 0.5 | 0.55 |
| 42 | 0.15 | 0.18 | 0.21 | 0.24 | 0.27 | 0.3 |

Appendix B

**Details of the CRM and BLRM design implemented in simulation study.**

*The Continuous Reassessment Method (CRM)*

In the CRM design, we used the one-parameter power model

for ,

where  is the parameter of the model, is the toxicity rate at dose , and ’s are pre-specified prior toxicity probability ('skeleton') values, monotonically increasing with . The skeleton  's reflect the initial guesses of toxicity probability at each dose. We adopted the method proposed in Lee and Cheung (2011) for selecting the skeleton based on indifference intervals. We used half-width and we used log-normal prior .

The posterior distribution of θ is given by

where are the number patients, and  are the number of patients experienced DLTs.

The CRM design starts the trial by treating the first cohort at the lowest dose . The posterior distribution of π(θ) is updated based on the accumulating information across all dose levels, and the posterior mean of π(θ) is used as the point estimate of to guide dose assignment. In particular, the next cohort will be assigned to the dose with  closest to . In our simulation, an additional no-skipping escalation rule is added in order to ensure the safety of the trial conduct. In addition, the Safety rules 1 and 2 as stated in Section 2.1 are also applied in CRM design. Lastly, no escalation is permitted if the empirical DLT rate of the most recent cohort is higher than .

*The Bayesian Logistic Regression Method (BLRM)*

BLRM assumes a two-parameter logistic model

where , are unknown parameters, is the raw dosage at dose level , and is the reference dose level. Model parameters α and β follow a multivariate log-normal prior,

, where

Let  be the hyperparameter set of the model. In the simulation, we used a default set of doses, , and the default reference dose level is the ceiling of , where  is the number of doses. In addition, we used the quantile-based non-informative prior calculator proposed by Neuenschwander et al. (2008) to obtain the values of , and use the same prior guess for the lowest and highest doses as described in Appendix A.1 in Neuenschwander et al. (2008). The posterior distribution of  is given

where are the number patients, and  are the number of patients experienced DLTs.

The BLRM starts a trial by treating the first cohort at the lowest patient. After each cohort is treated, the standard dose recommendation of BLRM relies on maximizing the probability of targeted toxicity interval . In our simulation, we used . In particular, the next cohort will be assigned to the dose whose posterior probability in the targeted toxicity interval is the largest, i.e. . The BLRM imposes an overdose control rule (Escalation with Overdose Control, EWOC) such that the probability of excessive toxicity of the recommended dose should be less than a given threshold i.e. . In our simulation, we used . In addition, the Safety rules 1 and 2 as stated in Section 2.1 are also applied in BLRM design. Besides safety rule I, if all doses violate the EWOC rule, the trial will be terminated before the maximum the sample size is reached.

Appendix C

**Operating characteristics comparing i3+3 with other phase I designs**

Six designs (mTPI2, mTPI, BOIN, CRM, BLRM and 3+3) are compared with i3+3. A sample size of 30 patients is used for each trial with a cohort size of 3. For the mTPI and mTPI-2 designs, the EI is [,]. For the BOIN design, we set = and = so that the actual intervals for decision making between BOIN and mTPI or mTPI-2 are identical. For the BLRM design, the EWOC parameter is set at 0.5. Under each simulation scenario, we generate 1,000 simulated trials.

Scenario 1

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.04 | 0.092 | 0.084 | 0.107 | 0.019 | 0.109 | 0.077 | 0.076 | 6.261 | 6.261 | 7.05 | 3.372 | | 6.888 | 5.766 | 6.102 | 0.256 | 0.249 | 0.277 | 0.133 | | | 0.275 | 0.224 | 0.259 |
| 2 | 0.05 | 0.123 | 0.119 | 0.168 | 0.035 | 0.135 | 0.235 | 0.168 | 5.916 | 5.943 | 6.081 | 3.432 | | 5.64 | 9.123 | 6.474 | 0.337 | 0.32 | 0.334 | 0.168 | | | 0.274 | 0.469 | 0.356 |
| 3 | 0.06 | 0.123 | 0.204 | 0.157 | 0.051 | 0.129 | 0.362 | 0.171 | 5.022 | 5.4 | 5.055 | 3.537 | | 4.791 | 10.011 | 5.403 | 0.288 | 0.343 | 0.322 | 0.223 | | | 0.274 | 0.637 | 0.33 |
| 4 | 0.07 | 0.218 | 0.145 | 0.162 | 0.059 | 0.174 | 0.217 | 0.172 | 4.134 | 3.969 | 3.831 | 3.444 | | 4.065 | 2.694 | 4.248 | 0.311 | 0.289 | 0.276 | 0.256 | | | 0.259 | 0.197 | 0.305 |
| 5 | 0.08 | 0.135 | 0.132 | 0.125 | 0.065 | 0.141 | 0.023 | 0.122 | 2.787 | 2.856 | 2.979 | 3.324 | | 3.378 | 0.18 | 3.042 | 0.196 | 0.225 | 0.23 | 0.271 | | | 0.286 | 0.017 | 0.243 |
| 6 | 0.09 | 0.286 | 0.291 | 0.256 | 0.75 | 0.296 | 0 | 0.266 | 5.376 | 5.01 | 4.443 | 3.003 | | 4.878 | 0.003 | 4.14 | 0.465 | 0.458 | 0.409 | 0.279 | | | 0.411 | 0 | 0.371 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | | | | |  | | | | | | | | |
| Prob. of Select MTD | | 0.885 | 0.891 | 0.868 | 0.96 | 0.875 | 0.837 | 0.899 |
| Prob. of Toxicity | | 0.063 | 0.064 | 0.063 | 0.066 | 0.06 | 0.056 | 0.063 |
| Prob. of Select Dose-over-MTD | | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Prob. of No Selection | | 0.023 | 0.025 | 0.025 | 0.021 | 0.016 | 0.086 | 0.025 |

Scenario 2 29.439 29.64 29.409

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.15 | 0.356 | 0.345 | 0.371 | 0.265 | 0.437 | 0.276 | 0.386 | 12.417 | 12.939 | 14.649 | 4.611 | | 14.403 | 10.017 | 13.743 | 1.912 | 1.969 | 2.219 | 0.684 | | | 2.089 | 1.554 | 2.082 |
| 2 | 0.2 | 0.138 | 0.145 | 0.119 | 0.233 | 0.144 | 0.104 | 0.162 | 6.339 | 6.144 | 5.058 | 3.921 | | 5.526 | 5.739 | 5.793 | 1.203 | 1.221 | 1.01 | 0.812 | | | 1.08 | 1.216 | 1.148 |
| 3 | 0.25 | 0.039 | 0.074 | 0.037 | 0.153 | 0.041 | 0.021 | 0.054 | 2.784 | 2.652 | 2.088 | 2.73 | | 2.22 | 1.326 | 2.403 | 0.732 | 0.637 | 0.507 | 0.698 | | | 0.534 | 0.322 | 0.584 |
| 4 | 0.3 | 0.014 | 0.009 | 0.007 | 0.103 | 0.012 | 0.001 | 0.01 | 0.963 | 0.963 | 0.807 | 1.662 | | 0.741 | 0.084 | 0.756 | 0.277 | 0.289 | 0.246 | 0.495 | | | 0.227 | 0.027 | 0.219 |
| 5 | 0.35 | 0.003 | 0.003 | 0.001 | 0.034 | 0.005 | 0 | 0 | 0.267 | 0.231 | 0.21 | 0.816 | | 0.243 | 0 | 0.171 | 0.102 | 0.087 | 0.081 | 0.307 | | | 0.071 | 0 | 0.069 |
| 6 | 0.4 | 0 | 0 | 0 | 0.017 | 0 | 0 | 0 | 0.069 | 0.03 | 0.039 | 0.24 | | 0.057 | 0 | 0.027 | 0.025 | 0.016 | 0.018 | 0.099 | | | 0.025 | 0 | 0.014 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.356 | 0.345 | 0.371 | 0.265 | 0.437 | 0.276 | 0.386 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | | 0.186 | 0.184 | 0.179 | 0.221 | 0.174 | 0.182 | 0.18 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.194 | 0.231 | 0.164 | 0.54 | 0.202 | 0.126 | 0.226 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | | 0.45 | 0.424 | 0.465 | 0.195 | 0.361 | 0.598 | 0.388 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 3

|  |  |  |  |
| --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | Selection Prob.  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Patients Treated  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Toxicities  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| 1 0.01 | 0.265 0.195 0.273 0.093 0.2 0.194 0.166 | 7.38 6.246 8.295 3.336 8.247 8.085 7.047 | 0.087 0.066 0.085 0.024 0.089 0.084 0.075 |
| 2 0.1 | 0.446 0.497 0.526 0.284 0.523 0.608 0.538 | 11.109 12.348 12.186 4.524 12.177 14.781 12.618 | 1.134 1.225 1.225 0.453 1.157 1.438 1.266 |
| 3 0.2  4 0.25  5 0.3  6 0.35 | 0.184 0.213 0.137 0.242 0.196 0.157 0.224  0.076 0.07 0.044 0.197 0.061 0.01 0.056  0.021 0.02 0.014 0.109 0.019 0 0.009  0.002 0.002 0.002 0.074 0 0 0.004 | 6.894 7.152 5.904 4.365 6.027 5.874 6.678  3.054 2.745 2.301 3.069 2.394 0.429 2.514  1.11 1.107 0.942 2.01 0.852 0.012 0.804  0.396 0.327 0.297 0.813 0.279 0 0.264 | 1.33 1.447 1.197 0.89 1.173 1.173 1.353  0.727 0.694 0.6 0.741 0.59 0.101 0.636  0.322 0.314 0.255 0.615 0.241 0.002 0.226  0.13 0.124 0.112 0.294 0.094 0 0.098 |
|  | i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| Prob. of Select MTD  Prob. of Toxicity  Prob. of Select Dose-over-MTD Prob. of No Selection | 0.446 0.497 0.526 0.284 0.523 0.608 0.538  0.125 0.129 0.116 0.167 0.112 0.096 0.122  0.283 0.305 0.197 0.622 0.276 0.167 0.293  0.006 0.003 0.004 0.001 0.001 0.031 0.003 |

Scenario 4

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.01 | 0.006 | 0.015 | 0.016 | 0.004 | 0.023 | 0.004 | 0.009 | 3.648 | 3.858 | 4.089 | 3.099 | | 4.272 | 3.786 | 3.714 | 0.036 | 0.042 | 0.045 | 0.034 | | | 0.052 | 0.034 | 0.039 |
| 2 | 0.02 | 0.036 | 0.022 | 0.076 | 0.011 | 0.066 | 0.101 | 0.044 | 4.335 | 4.404 | 4.647 | 3.207 | | 4.581 | 7.719 | 4.425 | 0.089 | 0.091 | 0.093 | 0.067 | | | 0.102 | 0.143 | 0.095 |
| 3 | 0.03 | 0.068 | 0.144 | 0.115 | 0.014 | 0.093 | 0.346 | 0.109 | 4.554 | 4.764 | 4.785 | 3.282 | | 4.581 | 12.066 | 5.007 | 0.134 | 0.125 | 0.13 | 0.1 | | | 0.123 | 0.359 | 0.135 |
| 4 | 0.04 | 0.343 | 0.245 | 0.299 | 0.091 | 0.243 | 0.472 | 0.309 | 5.307 | 5.34 | 5.811 | 3.528 | | 5.646 | 5.316 | 6.732 | 0.217 | 0.218 | 0.229 | 0.142 | | | 0.223 | 0.214 | 0.271 |
| 5 | 0.1 | 0.466 | 0.48 | 0.422 | 0.367 | 0.457 | 0.049 | 0.423 | 7.269 | 6.966 | 6.858 | 4.518 | | 6.948 | 0.42 | 6.729 | 0.7 | 0.717 | 0.701 | 0.439 | | | 0.642 | 0.046 | 0.674 |
| 6 | 0.25 | 0.079 | 0.091 | 0.069 | 0.51 | 0.117 | 0.003 | 0.103 | 4.848 | 4.593 | 3.735 | 3.804 | | 3.948 | 0.024 | 3.318 | 1.22 | 1.167 | 0.977 | 0.975 | | | 1.009 | 0.002 | 0.882 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.466 | 0.48 | 0.422 | 0.367 | 0.457 | 0.049 | 0.423 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | | 0.08 | 0.079 | 0.073 | 0.082 | 0.0718 | 0.027 | 0.07 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.079 | 0.091 | 0.069 | 0.51 | 0.117 | 0.003 | 0.103 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | | 0.002 | 0.003 | 0.003 | 0.003 | 0.001 | 0.025 | 0.003 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 5

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.05 | 0.937 | 0.939 | 0.937 | 0.742 | 0.956 | 0.681 | 0.918 | 22.308 | 22.38 | 22.926 | 5.394 | | 23.004 | 17.952 | 23.037 | 1.11 | 1.14 | 1.152 | 0.277 | | | 1.13 | 0.931 | 1.172 |
| 2 | 0.4 | 0.01 | 0.007 | 0.009 | 0.197 | 0.015 | 0.025 | 0.039 | 5.724 | 6.033 | 5.439 | 4.737 | | 5.67 | 4.986 | 5.46 | 2.29 | 2.408 | 2.194 | 1.924 | | | 2.229 | 2.035 | 2.188 |
| 3 | 0.5 | 0.001 | 0.001 | 0.001 | 0.028 | 0.003 | 0 | 0 | 0.975 | 0.648 | 0.612 | 1.314 | | 0.738 | 0.411 | 0.567 | 0.504 | 0.352 | 0.332 | 0.654 | | | 0.357 | 0.185 | 0.31 |
| 4 | 0.6 | 0 | 0 | 0 | 0.002 | 0 | 0 | 0 | 0.099 | 0.057 | 0.051 | 0.225 | | 0.084 | 0 | 0.054 | 0.056 | 0.038 | 0.036 | 0.139 | | | 0.057 | 0 | 0.037 |
| 5 | 0.65 | 0 | 0 | 0 | 0.001 | 0 | 0 | 0 | 0.006 | 0 | 0 | 0.021 | | 0.003 | 0 | 0 | 0.003 | 0 | 0 | 0.011 | | | 0.002 | 0 | 0 |
| 6 | 0.7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.003 | | 0 | 0 | 0 | 0 | 0 | 0 | 0.002 | | | 0 | 0 | 0 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.937 | 0.939 | 0.937 | 0.742 | 0.956 | 0.681 | 0.918 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | | 0.136 | 0.135 | 0.128 | 0.257 | 0.128 | 0.135 | 0.127 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.011 | 0.008 | 0.01 | 0.228 | 0.018 | 0.025 | 0.039 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | | 0.052 | 0.053 | 0.053 | 0.03 | 0.026 | 0.294 | 0.043 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 6

|  |  |  |  |
| --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | Selection Prob.  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Patients Treated  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Toxicities  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| 1 0.01  2 0.03 | 0.014 0.017 0.031 0.013 0.036 0.013 0.015  0.122 0.089 0.177 0.024 0.132 0.186 0.148 | 3.762 3.984 4.452 3.132 4.647 4.11 3.912  5.472 5.457 6.279 3.342 6.093 9.135 6.915 | 0.032 0.044 0.05 0.033 0.055 0.038 0.044  0.164 0.161 0.19 0.11 0.19 0.251 0.209 |
| 3 0.05 | 0.828 0.868 0.768 0.739 0.792 0.718 0.809 | 14.832 14.943 14.076 5.31 14.103 14.103 14.076 | 0.759 0.741 0.695 0.257 0.696 0.702 0.708 |
| 4 0.4  5 0.5  6 0.6 | 0.036 0.023 0.021 0.194 0.038 0.058 0.025  0 0 0 0.023 0.001 0 0  0 0 0 0.005 0 0 0 | 4.998 4.791 4.416 4.725 4.464 1.956 4.407  0.855 0.669 0.621 1.29 0.594 0.027 0.537  0.081 0.081 0.081 0.183 0.075 0 0.078 | 1.964 1.919 1.758 1.884 1.758 0.78 1.77  0.431 0.332 0.31 0.673 0.279 0.011 0.261  0.051 0.05 0.05 0.111 0.039 0 0.048 |
|  | i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| Prob. of Select MTD  Prob. of Toxicity  Prob. of Select Dose-over-MTD Prob. of No Selection | 0.828 0.868 0.768 0.739 0.792 0.718 0.809  0.113 0.109 0.102 0.171 0.1 0.061 0.102  0.036 0.023 0.021 0.222 0.039 0.058 0.025  0 0.003 0.003 0.002 0.001 0.025 0.003 |

Scenario 7

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.01 | 0.011 | 0.015 | 0.016 | 0.004 | 0.023 | 0.004 | 0.009 | 3.603 | 3.858 | 4.086 | 3.102 | | 4.272 | 3.786 | 3.714 | 0.026 | 0.042 | 0.045 | 0.033 | | | 0.052 | 0.034 | 0.039 |
| 2 | 0.02 | 0.025 | 0.022 | 0.075 | 0.008 | 0.066 | 0.101 | 0.044 | 4.434 | 4.404 | 4.638 | 3.225 | | 4.581 | 7.719 | 4.425 | 0.104 | 0.091 | 0.092 | 0.075 | | | 0.102 | 0.143 | 0.095 |
| 3 | 0.03 | 0.063 | 0.142 | 0.108 | 0.025 | 0.091 | 0.346 | 0.108 | 4.692 | 4.764 | 4.731 | 3.315 | | 4.512 | 12.054 | 4.935 | 0.14 | 0.125 | 0.128 | 0.096 | | | 0.123 | 0.359 | 0.13 |
| 4 | 0.04 | 0.252 | 0.144 | 0.177 | 0.029 | 0.145 | 0.464 | 0.26 | 4.68 | 4.434 | 4.716 | 3.435 | | 4.473 | 5.304 | 6.477 | 0.183 | 0.184 | 0.2 | 0.166 | | | 0.167 | 0.213 | 0.276 |
| 5 | 0.05 | 0.639 | 0.663 | 0.604 | 0.642 | 0.646 | 0.057 | 0.53 | 8.805 | 8.787 | 8.418 | 4.971 | | 8.55 | 0.441 | 7.368 | 0.439 | 0.464 | 0.429 | 0.243 | | | 0.42 | 0.025 | 0.364 |
| 6 | 0.4 | 0.01 | 0.011 | 0.017 | 0.29 | 0.028 | 0.003 | 0.046 | 3.786 | 3.678 | 3.336 | 4.038 | | 3.588 | 0.027 | 3.006 | 1.525 | 1.488 | 1.369 | 1.615 | | | 1.405 | 0.006 | 1.253 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.639 | 0.663 | 0.604 | 0.642 | 0.646 | 0.057 | 0.53 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | | 0.081 | 0.08 | 0.076 | 0.101 | 0.076 | 0.027 | 0.072 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.01 | 0.011 | 0.017 | 0.29 | 0.028 | 0.003 | 0.046 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | | 0 | 0.003 | 0.003 | 0.002 | 0.001 | 0.025 | 0.003 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 8

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.09 | 0.277 | 0.273 | 0.323 | 0.1 | 0.303 | 0.182 | 0.26 | 10.461 | 10.29 | 11.736 | 3.981 | | 11.331 | 7.842 | 10.344 | 0.948 | 0.95 | 1.075 | 0.39 | | | 1.04 | 0.704 | 0.957 |
| 2 | 0.11 | 0.188 | 0.188 | 0.195 | 0.13 | 0.198 | 0.317 | 0.247 | 6.435 | 7.056 | 6.468 | 3.774 | | 6.405 | 9.36 | 7.335 | 0.713 | 0.801 | 0.747 | 0.406 | | | 0.668 | 1.002 | 0.839 |
| 3 | 0.13 | 0.149 | 0.179 | 0.144 | 0.121 | 0.149 | 0.181 | 0.163 | 4.659 | 4.656 | 4.317 | 3.447 | | 4.293 | 5.202 | 4.668 | 0.594 | 0.596 | 0.543 | 0.474 | | | 0.526 | 0.673 | 0.589 |
| 4 | 0.15 | 0.143 | 0.103 | 0.096 | 0.137 | 0.106 | 0.033 | 0.107 | 2.994 | 2.76 | 2.496 | 3 | | 2.652 | 0.765 | 2.805 | 0.436 | 0.41 | 0.372 | 0.442 | | | 0.395 | 0.12 | 0.411 |
| 5 | 0.17 | 0.069 | 0.074 | 0.057 | 0.111 | 0.061 | 0.004 | 0.067 | 1.542 | 1.533 | 1.47 | 2.523 | | 1.554 | 0.042 | 1.485 | 0.275 | 0.256 | 0.237 | 0.446 | | | 0.237 | 0.003 | 0.24 |
| 6 | 0.19 | 0.029 | 0.046 | 0.031 | 0.306 | 0.05 | 0 | 0.041 | 1.338 | 1.329 | 1.071 | 1.752 | | 1.095 | 0 | 0.981 | 0.251 | 0.244 | 0.202 | 0.338 | | | 0.184 | 0 | 0.188 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.757 | 0.743 | 0.758 | 0.488 | 0.756 | 0.713 | 0.777 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | | 0.117 | 0.118 | 0.115 | 0.135 | 0.112 | 0.108 | 0.117 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.098 | 0.12 | 0.088 | 0.417 | 0.366 | 0.004 | 0.108 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | | 0.145 | 0.137 | 0.154 | 0.095 | 0.133 | 0.283 | 0.115 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 9

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.05 | 0.16 | 0.149 | 0.186 | 0.047 | 0.174 | 0.097 | 0.128 | 7.446 | 7.584 | 8.721 | 3.537 | | 8.61 | 6.285 | 7.326 | 0.364 | 0.379 | 0.432 | 0.18 | | | 0.415 | 0.328 | 0.366 |
| 2 | 0.07 | 0.171 | 0.173 | 0.229 | 0.071 | 0.221 | 0.317 | 0.229 | 6.516 | 6.945 | 6.969 | 3.63 | | 6.942 | 10.161 | 7.5 | 0.495 | 0.519 | 0.513 | 0.244 | | | 0.489 | 0.678 | 0.551 |
| 3 | 0.09 | 0.164 | 0.26 | 0.202 | 0.11 | 0.177 | 0.329 | 0.239 | 5.511 | 5.619 | 5.208 | 3.75 | | 5.34 | 8.346 | 5.757 | 0.478 | 0.483 | 0.468 | 0.346 | | | 0.467 | 0.769 | 0.497 |
| 4 | 0.11 | 0.225 | 0.146 | 0.158 | 0.111 | 0.181 | 0.11 | 0.149 | 4.116 | 4.059 | 3.789 | 3.543 | | 3.834 | 1.647 | 4.215 | 0.432 | 0.493 | 0.448 | 0.42 | | | 0.441 | 0.167 | 0.513 |
| 5 | 0.13 | 0.149 | 0.119 | 0.096 | 0.122 | 0.104 | 0.01 | 0.114 | 2.943 | 2.418 | 2.391 | 3.18 | | 2.427 | 0.111 | 2.427 | 0.379 | 0.328 | 0.329 | 0.409 | | | 0.315 | 0.023 | 0.323 |
| 6 | 0.15 | 0.094 | 0.12 | 0.094 | 0.513 | 0.119 | 0 | 0.109 | 2.76 | 2.634 | 2.181 | 2.514 | | 2.346 | 0 | 2.034 | 0.437 | 0.381 | 0.313 | 0.382 | | | 0.334 | 0 | 0.295 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | | | | |  | | | | | | | | |
| Prob. of Select MTD | | 0.963 | 0.967 | 0.965 | 0.974 | 0.976 | 0.863 | 0.968 |
| Prob. of Toxicity | | 0.088 | 0.088 | 0.086 | 0.098 | 0.083 | 0.074 | 0.087 |
| Prob. of Select Dose-over-MTD | | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Prob. of No Selection | | 0.037 | 0.033 | 0.035 | 0.026 | 0.024 | 0.137 | 0.032 |

Scenario 10

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1  2 | 0.01  0.03 | 0.021  0.082 | 0.017  0.069 | 0.025  0.145 | 0.014  0.018 | 0.035  0.112 | 0.013  0.179 | 0.011  0.086 | 4.041  5.169 | 3.984  5.394 | 4.404  5.781 | 3.129  3.306 | | 4.629  5.643 | 4.11  9 | 3.879  5.421 | 0.049  0.164 | 0.044  0.158 | 0.05  0.168 | 0.031  0.105 | | | 0.055  0.18 | 0.038  0.247 | 0.044  0.158 |
| 3 | 0.05 | 0.143 | 0.223 | 0.182 | 0.049 | 0.162 | 0.421 | 0.193 | 5.724 | 5.853 | 5.772 | 3.489 | | 5.643 | 11.862 | 6.072 | 0.283 | 0.288 | 0.281 | 0.168 | | | 0.272 | 0.595 | 0.301 |
| 4 | 0.07 | 0.292 | 0.176 | 0.197 | 0.076 | 0.178 | 0.326 | 0.221 | 5.301 | 5.01 | 4.902 | 3.609 | | 4.695 | 4.092 | 5.592 | 0.397 | 0.361 | 0.354 | 0.251 | | | 0.321 | 0.259 | 0.396 |
| 5 | 0.09 | 0.212 | 0.219 | 0.215 | 0.094 | 0.203 | 0.035 | 0.224 | 4.134 | 4.035 | 4.224 | 3.615 | | 4.194 | 0.252 | 4.392 | 0.385 | 0.351 | 0.372 | 0.327 | | | 0.338 | 0.021 | 0.386 |
| 6 | 0.11 | 0.248 | 0.293 | 0.233 | 0.748 | 0.309 | 0.001 | 0.262 | 5.58 | 5.649 | 4.842 | 3.207 | | 5.172 | 0.015 | 4.569 | 0.669 | 0.672 | 0.587 | 0.36 | | | 0.54 | 0.001 | 0.554 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | | | | |  | | | | | | | | |
| Prob. of Select MTD | | 0.895 | 0.911 | 0.827 | 0.967 | 0.852 | 0.783 | 0.9 |
| Prob. of Toxicity | | 0.065 | 0.063 | 0.061 | 0.061 | 0.057 | 0.04 | 0.061 |
| Prob. of Select Dose-over-MTD | | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Prob. of No Selection | | 0.002 | 0.003 | 0.003 | 0.001 | 0.001 | 0.025 | 0.003 |

Scenario 11

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1  2 | 0.02  0.04 | 0.052  0.169 | 0.03  0.146 | 0.043  0.238 | 0.012  0.071 | 0.063  0.193 | 0.041  0.282 | 0.023  0.179 | 4.728  6.357 | 4.566  6.573 | 5.178  7.158 | 3.183  3.525 | | 5.613  6.912 | 4.854  10.56 | 4.431  6.882 | 0.101  0.286 | 0.087  0.273 | 0.099  0.275 | 0.058  0.15 | | | 0.119  0.272 | 0.103  0.417 | 0.086  0.284 |
| 3  4 | 0.08  0.12 | 0.265  0.312 | 0.374  0.223 | 0.334  0.218 | 0.134  0.193 | 0.259  0.27 | 0.457  0.154 | 0.331  0.272 | 7.152  5.817 | 7.578  5.547 | 7.422  5.214 | 3.915  3.975 | | 6.822  5.304 | 10.908  2.061 | 7.932  6.051 | 0.556  0.722 | 0.579  0.706 | 0.568  0.674 | 0.327  0.502 | | | 0.543  0.581 | 0.864  0.258 | 0.629  0.764 |
| 5 | 0.17 | 0.151 | 0.174 | 0.126 | 0.232 | 0.162 | 0.01 | 0.146 | 3.429 | 3.498 | 3.156 | 3.669 | | 3.462 | 0.12 | 3.024 | 0.595 | 0.593 | 0.529 | 0.639 | | | 0.584 | 0.019 | 0.509 |
| 6 | 0.25 | 0.043 | 0.045 | 0.033 | 0.351 | 0.048 | 0 | 0.041 | 2.313 | 2.052 | 1.686 | 2.472 | | 1.773 | 0 | 1.494 | 0.544 | 0.481 | 0.404 | 0.623 | | | 0.429 | 0 | 0.36 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.577 | 0.597 | 0.552 | 0.327 | 0.529 | 0.611 | 0.603 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | | 0.094 | 0.091 | 0.085 | 0.111 | 0.085 | 0.058 | 0.088 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.194 | 0.219 | 0.159 | 0.583 | 0.21 | 0.01 | 0.187 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | | 0.008 | 0.008 | 0.008 | 0.007 | 0.005 | 0.056 | 0.008 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 12

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1  2 | 0.02  0.04 | 0.042  0.136 | 0.029  0.12 | 0.041  0.206 | 0.017  0.05 | 0.063  0.164 | 0.04  0.242 | 0.021  0.155 | 4.632  5.91 | 4.554  6.234 | 5.154  6.696 | 3.216  3.456 | | 5.607  6.393 | 4.827  10.137 | 4.407  6.474 | 0.085  0.264 | 0.087  0.257 | 0.099  0.261 | 0.063  0.146 | | | 0.119  0.258 | 0.1  0.404 | 0.085  0.268 |
| 3 | 0.07 | 0.234 | 0.332 | 0.295 | 0.086 | 0.214 | 0.443 | 0.287 | 6.582 | 7.071 | 6.978 | 3.726 | | 6.288 | 10.914 | 7.425 | 0.435 | 0.46 | 0.454 | 0.268 | | | 0.426 | 0.738 | 0.5 |
| 4 | 0.1 | 0.341 | 0.234 | 0.238 | 0.158 | 0.282 | 0.2 | 0.288 | 5.958 | 5.532 | 5.334 | 3.864 | | 5.367 | 2.451 | 6.135 | 0.635 | 0.603 | 0.593 | 0.397 | | | 0.477 | 0.236 | 0.664 |
| 5 | 0.15 | 0.165 | 0.186 | 0.144 | 0.206 | 0.174 | 0.019 | 0.156 | 3.909 | 3.735 | 3.408 | 3.81 | | 3.783 | 0.171 | 3.333 | 0.605 | 0.573 | 0.52 | 0.555 | | | 0.565 | 0.023 | 0.518 |
| 6 | 0.2 | 0.076 | 0.091 | 0.068 | 0.476 | 0.098 | 0 | 0.085 | 2.865 | 2.688 | 2.244 | 2.859 | | 2.448 | 0.003 | 2.04 | 0.567 | 0.527 | 0.446 | 0.601 | | | 0.459 | 0 | 0.399 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.74 | 0.752 | 0.677 | 0.45 | 0.67 | 0.662 | 0.731 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | | 0.087 | 0.084 | 0.08 | 0.097 | 0.077 | 0.053 | 0.082 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.076 | 0.091 | 0.068 | 0.476 | 0.098 | 0 | 0.085 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | | 0.006 | 0.008 | 0.008 | 0.007 | 0.005 | 0.056 | 0.008 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 13

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.1 | 0.385 | 0.378 | 0.442 | 0.176 | 0.42 | 0.297 | 0.376 | 11.769 | 11.838 | 14.001 | 4.173 | | 13.614 | 9.834 | 12.312 | 1.21 | 1.215 | 1.409 | 0.422 | | | 1.4 | 0.979 | 1.269 |
| 2 | 0.15 | 0.262 | 0.247 | 0.213 | 0.227 | 0.241 | 0.282 | 0.3 | 8.172 | 8.361 | 7.26 | 4.152 | | 7.326 | 8.856 | 8.424 | 1.224 | 1.233 | 1.109 | 0.63 | | | 1.042 | 1.335 | 1.234 |
| 3 | 0.2 | 0.092 | 0.141 | 0.093 | 0.187 | 0.102 | 0.074 | 0.125 | 4.254 | 4.095 | 3.438 | 3.522 | | 3.483 | 3.243 | 3.912 | 0.885 | 0.812 | 0.665 | 0.736 | | | 0.673 | 0.606 | 0.81 |
| 4 | 0.25 | 0.032 | 0.038 | 0.03 | 0.179 | 0.049 | 0.01 | 0.025 | 1.617 | 1.839 | 1.476 | 2.55 | | 1.494 | 0.291 | 1.566 | 0.434 | 0.458 | 0.359 | 0.594 | | | 0.36 | 0.065 | 0.389 |
| 5 | 0.3 | 0.013 | 0.012 | 0.01 | 0.073 | 0.008 | 0 | 0.009 | 0.684 | 0.591 | 0.519 | 1.563 | | 0.537 | 0.015 | 0.462 | 0.18 | 0.172 | 0.154 | 0.528 | | | 0.154 | 0.005 | 0.134 |
| 6 | 0.35 | 0.003 | 0.001 | 0.001 | 0.055 | 0 | 0 | 0.003 | 0.231 | 0.183 | 0.153 | 0.579 | | 0.159 | 0 | 0.141 | 0.08 | 0.061 | 0.046 | 0.199 | | | 0.052 | 0 | 0.042 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.647 | 0.625 | 0.655 | 0.403 | 0.661 | 0.579 | 0.676 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | | 0.15 | 0.147 | 0.139 | 0.188 | 0.138 | 0.134 | 0.145 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.14 | 0.192 | 0.134 | 0.494 | 0.159 | 0.084 | 0.162 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | | 0.213 | 0.183 | 0.211 | 0.103 | 0.18 | 0.337 | 0.162 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 14

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.1  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1  2 | 0.01  0.03 | 0.014  0.071 | 0.017  0.068 | 0.025  0.143 | 0.014  0.023 | 0.035  0.112 | 0.013  0.179 | 0.011  0.085 | 3.789  5.136 | 3.984  5.379 | 4.404  5.742 | 3.132  3.312 | | 4.629  5.634 | 4.11  8.997 | 3.879  5.394 | 0.033  0.151 | 0.044  0.157 | 0.05  0.167 | 0.033  0.101 | | | 0.055  0.18 | 0.038  0.247 | 0.044  0.157 |
| 3 | 0.05 | 0.101 | 0.202 | 0.154 | 0.033 | 0.15 | 0.403 | 0.167 | 5.4 | 5.616 | 5.472 | 3.447 | | 5.391 | 11.769 | 5.793 | 0.257 | 0.273 | 0.266 | 0.175 | | | 0.261 | 0.588 | 0.284 |
| 4 | 0.06 | 0.299 | 0.172 | 0.19 | 0.058 | 0.161 | 0.341 | 0.216 | 5.226 | 4.818 | 4.782 | 3.486 | | 4.47 | 4.161 | 5.412 | 0.297 | 0.293 | 0.285 | 0.204 | | | 0.266 | 0.221 | 0.324 |
| 5 | 0.08 | 0.22 | 0.201 | 0.208 | 0.078 | 0.19 | 0.037 | 0.212 | 4.26 | 4.05 | 4.257 | 3.567 | | 4.137 | 0.276 | 4.467 | 0.327 | 0.328 | 0.34 | 0.288 | | | 0.301 | 0.023 | 0.355 |
| 6 | 0.1 | 0.295 | 0.337 | 0.277 | 0.792 | 0.351 | 0.002 | 0.306 | 6.189 | 6.078 | 5.268 | 3.252 | | 5.715 | 0.018 | 4.98 | 0.661 | 0.638 | 0.566 | 0.327 | | | 0.54 | 0.001 | 0.534 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | | | | |  | | | | | | | | |
| Prob. of Select MTD | | 0.915 | 0.912 | 0.829 | 0.961 | 0.852 | 0.783 | 0.901 |
| Prob. of Toxicity | | 0.058 | 0.058 | 0.056 | 0.056 | 0.053 | 0.038 | 0.057 |
| Prob. of Select Dose-over-MTD | | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Prob. of No Selection | | 0 | 0.003 | 0.003 | 0.002 | 0.001 | 0.025 | 0.003 |

Scenario 1

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.01 | 0.003 | 0.001 | 0.001 | 0.012 | 0.002 | 0.001 | 0.001 | 3.081 | 3.33 | 3.507 | 3.105 | | 3.267 | 3.3 | 3.249 | 0 | 0.034 | 0.035 | 0.027 | | | 0 | 0.036 | 0.034 |
| 2 | 0.02 | 0.015 | 0.015 | 0.028 | 0.015 | 0.015 | 0.017 | 0.015 | 3.606 | 3.759 | 4.428 | 3.216 | | 4.149 | 4.656 | 3.606 | 0.064 | 0.069 | 0.086 | 0.075 | | | 0.08 | 0.096 | 0.068 |
| 3 | 0.05 | 0.066 | 0.058 | 0.121 | 0.068 | 0.064 | 0.17 | 0.059 | 4.638 | 5.085 | 5.829 | 3.492 | | 5.337 | 9.126 | 4.701 | 0.227 | 0.279 | 0.299 | 0.147 | | | 0.261 | 0.45 | 0.254 |
| 4 | 0.08 | 0.16 | 0.212 | 0.239 | 0.109 | 0.184 | 0.361 | 0.181 | 5.643 | 5.604 | 5.736 | 3.822 | | 5.913 | 7.776 | 6.195 | 0.47 | 0.418 | 0.441 | 0.327 | | | 0.469 | 0.636 | 0.463 |
| 5 | 0.11 | 0.262 | 0.194 | 0.237 | 0.136 | 0.251 | 0.25 | 0.268 | 5.145 | 4.713 | 4.881 | 3.732 | | 4.887 | 3.276 | 5.373 | 0.584 | 0.491 | 0.527 | 0.414 | | | 0.533 | 0.351 | 0.563 |
| 6 | 0.14 | 0.494 | 0.52 | 0.374 | 0.658 | 0.484 | 0.192 | 0.476 | 7.887 | 7.509 | 5.619 | 3.168 | | 6.447 | 1.623 | 6.876 | 1.098 | 1.105 | 0.837 | 0.464 | | | 0.822 | 0.209 | 1.006 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | | | | |  | | | | | | | | |
| Prob. of Select MTD | | 0.494  0.081  0  0 | 0.52  0.08  0  0 | 0.374  0.074  0  0 | 0.658  0.071  0  0.002 | 0.484  0.072  0  0 | 0.192  0.06  0  0.009 | 0.476  0.08  0  0 |
| Prob. of Toxicity | |
| Prob. of Select Dose-over-MTD | |
| Prob. of No Selection | |

Scenario 2

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.22 | 0.386 | 0.44 | 0.393 | 0.37 | 0.506 | 0.305 | 0.5 | 16.035 | 15.411 | 17.79 | 5.061 | | 17.469 | 11.472 | 16.134 | 3.614 | 3.404 | 3.944 | 1.125 | | | 3.799 | 2.535 | 3.568 |
| 2 | 0.32 | 0.076 | 0.074 | 0.056 | 0.149 | 0.114 | 0.081 | 0.098 | 5.037 | 5.919 | 4.017 | 3.237 | | 4.545 | 4.971 | 5.004 | 1.635 | 1.894 | 1.268 | 1.081 | | | 1.441 | 1.598 | 1.617 |
| 3 | 0.37 | 0.018 | 0.019 | 0.012 | 0.078 | 0.011 | 0.009 | 0.021 | 1.389 | 1.524 | 0.951 | 1.461 | | 1.182 | 1.131 | 1.551 | 0.528 | 0.55 | 0.336 | 0.529 | | | 0.427 | 0.397 | 0.546 |
| 4 | 0.47 | 0.001 | 0 | 0 | 0.011 | 0.001 | 0.001 | 0 | 0.288 | 0.264 | 0.171 | 0.51 | | 0.231 | 0.129 | 0.234 | 0.125 | 0.14 | 0.097 | 0.258 | | | 0.109 | 0.043 | 0.128 |
| 5 | 0.57 | 0 | 0 | 0 | 0.001 | 0 | 0 | 0 | 0.033 | 0.036 | 0.027 | 0.06 | | 0.042 | 0.003 | 0.033 | 0.021 | 0.018 | 0.013 | 0.035 | | | 0.019 | 0.002 | 0.016 |
| 6 | 0.67 | 0 | 0 | 0 | 0.001 | 0 | 0 | 0 | 0 | 0.003 | 0.003 | 0.009 | | 0 | 0 | 0.003 | 0 | 0.002 | 0.002 | 0.004 | | | 0 | 0 | 0.002 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.386  0.26  0.095  0.519 | 0.44  0.259  0.093  0.467 | 0.393  0.247  0.068  0.539 | 0.37  0.293  0.24  0.39 | 0.506  0.247  0.126  0.368 | 0.305  0.258  0.091  0.604 | 0.5  0.256  0.119  0.381 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 3

|  |  |  |  |
| --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | Selection Prob.  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Patients Treated  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Toxicities  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| 1 0.01 | 0.356 0.293 0.362 0.255 0.166 0.245 0.213 | 7.65 6.363 9.372 3.828 9.249 8.1 7.848 | 0 0.065 0.101 0.039 0 0.083 0.079 |
| 2 0.17 | 0.592 0.648 0.608 0.545 0.725 0.669 0.692 | 15.402 16.503 15.768 5.334 15.138 16.107 15.372 | 2.621 2.763 2.639 0.88 2.526 2.709 2.595 |
| 3 0.37  4 0.57  5 0.77  6 0.92 | 0.052 0.059 0.03 0.186 0.109 0.076 0.095  0 0 0 0.013 0 0 0  0 0 0 0 0 0 0  0 0 0 0 0 0 0 | 5.979 6.414 4.341 3.9 4.974 5.148 6.036  0.9 0.669 0.477 1.11 0.615 0.387 0.705  0.069 0.051 0.042 0.111 0.024 0.009 0.039  0 0 0 0.003 0 0 0 | 2.233 2.398 1.631 1.507 1.799 1.871 2.257  0.489 0.385 0.277 0.653 0.376 0.233 0.404  0.052 0.043 0.036 0.086 0.02 0.009 0.033  0 0 0 0.003 0 0 0 |
|  | i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| Prob. of Select MTD  Prob. of Toxicity  Prob. of Select Dose-over-MTD Prob. of No Selection | 0.592 0.648 0.608 0.545 0.725 0.669 0.692  0.18 0.188 0.156 0.222 0.157 0.165 0.179  0.052 0.059 0.03 0.199 0.109 0.076 0.095  0 0 0 0.001 0 0.01 0 |

Scenario 4

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.01 | 0.001 | 0.001 | 0.001 | 0.008 | 0.002 | 0.003 | 0.001 | 3.246 | 3.33 | 3.594 | 3.102 | | 3.552 | 3.363 | 3.273 | 0.03 | 0.034 | 0.036 | 0.029 | | | 0.025 | 0.036 | 0.034 |
| 2 | 0.03 | 0.018 | 0.02 | 0.035 | 0.031 | 0.022 | 0.024 | 0.016 | 4.026 | 4.05 | 4.686 | 3.387 | | 4.428 | 5.016 | 3.75 | 0.128 | 0.103 | 0.122 | 0.117 | | | 0.13 | 0.152 | 0.098 |
| 3 | 0.05 | 0.049 | 0.054 | 0.112 | 0.054 | 0.069 | 0.161 | 0.064 | 4.278 | 4.977 | 5.502 | 3.519 | | 5.1 | 8.835 | 4.716 | 0.193 | 0.269 | 0.279 | 0.188 | | | 0.25 | 0.429 | 0.25 |
| 4 | 0.07 | 0.364 | 0.363 | 0.395 | 0.246 | 0.307 | 0.46 | 0.32 | 6.177 | 5.751 | 6.873 | 4.038 | | 7.05 | 8.121 | 7.365 | 0.394 | 0.365 | 0.476 | 0.292 | | | 0.494 | 0.575 | 0.487 |
| 5 | 0.17 | 0.546 | 0.532 | 0.429 | 0.525 | 0.561 | 0.308 | 0.552 | 9.012 | 8.547 | 7.104 | 4.863 | | 7.329 | 3.588 | 8.214 | 1.53 | 1.42 | 1.208 | 0.824 | | | 1.239 | 0.602 | 1.385 |
| 6 | 0.47 | 0.022 | 0.03 | 0.028 | 0.133 | 0.039 | 0.035 | 0.047 | 3.261 | 3.345 | 2.241 | 2.928 | | 2.541 | 0.834 | 2.682 | 1.515 | 1.603 | 1.058 | 1.375 | | | 1.159 | 0.396 | 1.278 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.546  0.126  0.022  0 | 0.532  0.126  0.03  0 | 0.429  0.106  0.028  0 | 0.525  0.129  0.133  0.003 | 0.561  0.11  0.039  0 | 0.308  0.074  0.035  0.009 | 0.552  0.118  0.047  0 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 5

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.02 | 0.995 | 0.991 | 0.991 | 0.862 | 0.934 | 0.88 | 0.92 | 22.272 | 22.077 | 22.5 | 5.622 | | 22.746 | 21.528 | 22.671 | 0.415 | 0.437 | 0.438 | 0.114 | | | 0.45 | 0.444 | 0.436 |
| 2 | 0.47 | 0.004 | 0.007 | 0.007 | 0.132 | 0.064 | 0.057 | 0.078 | 7.131 | 7.392 | 7.017 | 4.56 | | 6.726 | 6.516 | 6.675 | 3.368 | 3.466 | 3.285 | 2.173 | | | 3.199 | 3.024 | 3.152 |
| 3 | 0.77 | 0 | 0 | 0 | 0.002 | 0 | 0 | 0 | 0.585 | 0.471 | 0.423 | 0.705 | | 0.468 | 0.444 | 0.594 | 0.449 | 0.365 | 0.326 | 0.539 | | | 0.358 | 0.339 | 0.461 |
| 4 | 0.87 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.012 | 0.006 | 0.006 | 0.018 | | 0.006 | 0 | 0.006 | 0.012 | 0.005 | 0.005 | 0.015 | | | 0.004 | 0 | 0.005 |
| 5 | 0.92 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | 0 | 0 | 0 |
| 6 | 0.96 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | 0 | 0 | 0 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.995  0.141  0.004  0.001 | 0.991  0.143  0.007  0.002 | 0.991  0.135  0.007  0.002 | 0.862  0.261  0.134  0.004 | 0.934  0.134  0.064  0.002 | 0.88  0.134  0.057  0.063 | 0.92  0.135  0.078  0.002 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 6

|  |  |  |  |
| --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | Selection Prob.  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Patients Treated  i3+3 mTPI mTPI-2 3+3 BLRM CRM | # of Toxicities  i3+3 mTPI mTPI-2 3+3 BLRM CRM |
| 1 0.01  2 0.02 | 0 0.001 0.001 0.009 0.002 0.001 0.001  0.035 0.043 0.077 0.057 0.032 0.05 0.045 | 3.003 3.33 3.51 3.12 3.27 3.3 3.252  3.735 3.999 5.139 3.357 4.881 5.388 4.62 | 0 0.034 0.035 0.033 0 0.036 0.034  0.053 0.074 0.106 0.08 0.095 0.115 0.095 |
| 3 0.07 | 0.945 0.932 0.895 0.806 0.898 0.861 0.877 | 16.353 15.771 15.831 5.571 15.75 16.797 15.78 | 1.108 1.114 1.097 0.391 1.077 1.161 1.106 |
| 4 0.47  5 0.67  6 0.87 | 0.02 0.024 0.025 0.122 0.066 0.078 0.077  0 0 0.002 0.004 0.002 0.001 0  0 0 0 0 0 0 0 | 6.273 6.366 5.1 4.317 5.592 4.131 5.871  0.612 0.519 0.405 0.732 0.48 0.141 0.468  0.024 0.015 0.015 0.018 0.027 0 0.009 | 2.915 2.937 2.413 2.062 2.586 1.964 2.696  0.404 0.362 0.279 0.483 0.319 0.097 0.326  0.021 0.013 0.013 0.015 0.022 0 0.008 |
|  | i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| Prob. of Select MTD  Prob. of Toxicity  Prob. of Select Dose-over-MTD Prob. of No Selection | 0.945 0.932 0.895 0.806 0.898 0.861 0.877  0.15 0.151 0.131 0.179 0.137 0.113 0.142  0.02 0.024 0.027 0.126 0.068 0.079 0.077  0 0 0 0.002 0 0.009 0 |

Scenario 7

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.01 | 0 | 0 | 0 | 0.001 | 0 | 0 | 0 | 3 | 3.306 | 3.402 | 3.084 | | 3 | 3.249 | 3.21 | 0 | 0.034 | 0.034 | 0.03 | | | 0 | 0.036 | 0.034 |
| 2 | 0.01 | 0.002 | 0.008 | 0.014 | 0.017 | 0.006 | 0.009 | 0.011 | 3.078 | 3.435 | 3.975 | 3.12 | | 3.561 | 4.212 | 3.396 | 0 | 0.032 | 0.04 | 0.029 | | | 0 | 0.042 | 0.032 |
| 3 | 0.04 | 0.035 | 0.043 | 0.099 | 0.064 | 0.048 | 0.126 | 0.042 | 4.143 | 4.731 | 5.397 | 3.504 | | 5.097 | 8.607 | 4.338 | 0.132 | 0.214 | 0.232 | 0.145 | | | 0.203 | 0.345 | 0.191 |
| 4 | 0.07 | 0.224 | 0.235 | 0.268 | 0.14 | 0.206 | 0.479 | 0.275 | 5.679 | 5.436 | 6.231 | 3.834 | | 6.354 | 8.793 | 7.41 | 0.384 | 0.344 | 0.433 | 0.3 | | | 0.456 | 0.632 | 0.498 |
| 5 | 0.12 | 0.738 | 0.71 | 0.61 | 0.746 | 0.738 | 0.356 | 0.651 | 11.223 | 10.434 | 8.661 | 5.322 | | 9.498 | 3.879 | 9.279 | 1.361 | 1.28 | 1.052 | 0.642 | | | 1.072 | 0.455 | 1.126 |
| 6 | 0.67 | 0.001 | 0.004 | 0.009 | 0.029 | 0.002 | 0.021 | 0.021 | 2.877 | 2.658 | 2.334 | 2.934 | | 2.49 | 1.017 | 2.367 | 1.894 | 1.803 | 1.562 | 1.972 | | | 1.675 | 0.685 | 1.604 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.738  0.126  0.001  0 | 0.71  0.124  0.004  0 | 0.61  0.112  0.009  0 | 0.746  0.143  0.029  0.003 | 0.738  0.112  0.002  0 | 0.356  0.074  0.021  0.009 | 0.651  0.116  0.021  0 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 8

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.16 | 0.291 | 0.325 | 0.399 | 0.203 | 0.317 | 0.248 | 0.31 | 11.928 | 11.901 | 15.285 | 4.497 | | 13.077 | 9.639 | 12.231 | 1.938 | 1.92 | 2.449 | 0.731 | | | 2.061 | 1.495 | 1.965 |
| 2 | 0.18 | 0.198 | 0.193 | 0.185 | 0.174 | 0.229 | 0.251 | 0.219 | 6.762 | 7.458 | 6.189 | 3.603 | | 6.78 | 7.971 | 6.516 | 1.186 | 1.333 | 1.127 | 0.655 | | | 1.205 | 1.456 | 1.173 |
| 3 | 0.2 | 0.143 | 0.156 | 0.107 | 0.146 | 0.15 | 0.148 | 0.183 | 4.125 | 4.194 | 3.234 | 2.754 | | 3.753 | 4.398 | 4.758 | 0.828 | 0.819 | 0.628 | 0.556 | | | 0.72 | 0.848 | 0.901 |
| 4 | 0.22 | 0.08 | 0.088 | 0.058 | 0.085 | 0.077 | 0.051 | 0.101 | 2.364 | 2.22 | 1.449 | 1.884 | | 1.869 | 1.101 | 2.436 | 0.537 | 0.492 | 0.313 | 0.439 | | | 0.412 | 0.251 | 0.539 |
| 5 | 0.24 | 0.06 | 0.04 | 0.024 | 0.076 | 0.052 | 0.01 | 0.039 | 1.047 | 0.891 | 0.63 | 1.272 | | 0.9 | 0.231 | 0.933 | 0.259 | 0.213 | 0.149 | 0.291 | | | 0.197 | 0.047 | 0.227 |
| 6 | 0.26 | 0.021 | 0.015 | 0.007 | 0.089 | 0.024 | 0.005 | 0.014 | 0.579 | 0.429 | 0.273 | 0.759 | | 0.495 | 0.057 | 0.339 | 0.157 | 0.123 | 0.081 | 0.211 | | | 0.128 | 0.008 | 0.1 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.712  0.183  0.081  0.207 | 0.762  0.181  0.055  0.183 | 0.749  0.175  0.031  0.22 | 0.608  0.195  0.165  0.227 | 0.773  0.176  0.076  0.151 | 0.698  0.175  0.015  0.287 | 0.813  0.18  0.053  0.134 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 9

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.12 | 0.196 | 0.25 | 0.315 | 0.142 | 0.224 | 0.155 | 0.19 | 9.285 | 10.005 | 12.327 | 4.191 | | 10.686 | 7.749 | 9.531 | 1.164 | 1.189 | 1.472 | 0.519 | | | 1.253 | 0.907 | 1.152 |
| 2 | 0.14 | 0.19 | 0.201 | 0.224 | 0.148 | 0.224 | 0.266 | 0.234 | 6.834 | 7.638 | 7.302 | 3.726 | | 7.122 | 8.52 | 7.239 | 0.9 | 1.079 | 1.053 | 0.513 | | | 1.011 | 1.182 | 1.008 |
| 3 | 0.16 | 0.187 | 0.201 | 0.167 | 0.15 | 0.196 | 0.232 | 0.209 | 5.295 | 5.208 | 4.311 | 3.189 | | 4.983 | 6.405 | 5.589 | 0.815 | 0.846 | 0.684 | 0.508 | | | 0.758 | 1.009 | 0.921 |
| 4 | 0.18 | 0.149 | 0.145 | 0.095 | 0.122 | 0.117 | 0.124 | 0.165 | 3.582 | 3.165 | 2.496 | 2.568 | | 2.913 | 2.301 | 3.576 | 0.64 | 0.577 | 0.44 | 0.48 | | | 0.516 | 0.41 | 0.62 |
| 5 | 0.2 | 0.115 | 0.063 | 0.067 | 0.104 | 0.103 | 0.03 | 0.083 | 2.043 | 1.623 | 1.296 | 2.007 | | 1.569 | 0.441 | 1.686 | 0.408 | 0.334 | 0.252 | 0.413 | | | 0.283 | 0.1 | 0.349 |
| 6 | 0.22 | 0.067 | 0.064 | 0.038 | 0.185 | 0.064 | 0.005 | 0.047 | 1.488 | 1.026 | 0.753 | 1.278 | | 1.002 | 0.09 | 0.804 | 0.351 | 0.221 | 0.171 | 0.304 | | | 0.213 | 0.026 | 0.174 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | | | | |  | | | | | | | | |
| Prob. of Select MTD | | 0.904  0.15  0  0.096 | 0.924  0.148  0  0.076 | 0.906  0.143  0  0.094 | 0.851  0.161  0  0.149 | 0.928  0.143  0  0.072 | 0.812  0.142  0  0.188 | 0.928  0.149  0  0.072 |
| Prob. of Toxicity | |
| Prob. of Select Dose-over-MTD | |
| Prob. of No Selection | |

Scenario 10

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1  2 | 0.08  0.1 | 0.112  0.157 | 0.125  0.171 | 0.179  0.226 | 0.075  0.125 | 0.082  0.171 | 0.054  0.213 | 0.083  0.184 | 6.78  6.759 | 7.362  7.266 | 9.39  7.542 | 3.834  3.765 | | 7.404  6.984 | 5.649  8.229 | 6.927  6.663 | 0.528  0.703 | 0.589  0.723 | 0.735  0.787 | 0.336  0.352 | | | 0.568  0.672 | 0.443  0.765 | 0.559  0.672 |
| 3 | 0.12 | 0.166 | 0.202 | 0.224 | 0.125 | 0.213 | 0.298 | 0.236 | 5.454 | 5.76 | 5.4 | 3.585 | | 5.718 | 8.265 | 6.639 | 0.642 | 0.7 | 0.635 | 0.463 | | | 0.667 | 0.971 | 0.798 |
| 4 | 0.14 | 0.182 | 0.221 | 0.155 | 0.126 | 0.179 | 0.209 | 0.208 | 4.38 | 4.236 | 3.522 | 3.114 | | 4.218 | 3.966 | 4.722 | 0.609 | 0.6 | 0.539 | 0.45 | | | 0.594 | 0.543 | 0.665 |
| 5 | 0.16 | 0.204 | 0.101 | 0.086 | 0.118 | 0.164 | 0.095 | 0.145 | 3.192 | 2.463 | 1.974 | 2.745 | | 2.793 | 1.245 | 2.577 | 0.521 | 0.395 | 0.314 | 0.442 | | | 0.448 | 0.209 | 0.425 |
| 6 | 0.18 | 0.158 | 0.162 | 0.111 | 0.355 | 0.164 | 0.037 | 0.126 | 2.892 | 2.442 | 1.701 | 1.932 | | 2.226 | 0.348 | 2.001 | 0.523 | 0.445 | 0.305 | 0.346 | | | 0.399 | 0.067 | 0.356 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | | | | |  | | | | | | | | |
| Prob. of Select MTD | | 0.71  0.12  0  0.021 | 0.686  0.117  0  0.018 | 0.576  0.112  0  0.019 | 0.724  0.126  0  0.076 | 0.72  0.114  0  0.027 | 0.639  0.108  0  0.094 | 0.715  0.118  0  0.018 |
| Prob. of Toxicity | |
| Prob. of Select Dose-over-MTD | |
| Prob. of No Selection | |

Scenario 11

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1  2 | 0.02  0.08 | 0.034  0.195 | 0.036  0.188 | 0.066  0.317 | 0.06  0.187 | 0.034  0.193 | 0.027  0.263 | 0.031  0.142 | 4.017  7.059 | 4.107  7.554 | 5.454  9.138 | 3.309  4.104 | | 5.409  8.427 | 4.374  9.513 | 4.167  6.558 | 0.067  0.531 | 0.071  0.609 | 0.106  0.749 | 0.056  0.348 | | | 0.103  0.695 | 0.093  0.733 | 0.072  0.551 |
| 3  4 | 0.14  0.2 | 0.335  0.262 | 0.329  0.304 | 0.323  0.196 | 0.22  0.238 | 0.347  0.247 | 0.412  0.223 | 0.346  0.319 | 8.313  6.081 | 7.863  6.27 | 7.866  4.863 | 4.23  3.648 | | 7.824  5.028 | 10.479  4.32 | 8.601  6.819 | 1.128  1.246 | 1.12  1.211 | 1.127  0.948 | 0.627  0.716 | | | 1.042  0.979 | 1.436  0.789 | 1.166  1.3 |
| 5 | 0.26 | 0.137 | 0.107 | 0.076 | 0.155 | 0.141 | 0.056 | 0.126 | 3.144 | 3.087 | 1.995 | 2.715 | | 2.322 | 0.771 | 2.979 | 0.819 | 0.811 | 0.516 | 0.721 | | | 0.577 | 0.194 | 0.798 |
| 6 | 0.32 | 0.036 | 0.034 | 0.02 | 0.136 | 0.036 | 0.005 | 0.034 | 1.359 | 1.065 | 0.63 | 1.305 | | 0.936 | 0.171 | 0.822 | 0.435 | 0.339 | 0.197 | 0.437 | | | 0.303 | 0.054 | 0.259 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.597  0.141  0.173  0.001 | 0.633  0.139  0.141  0.002 | 0.519  0.122  0.096  0.002 | 0.458  0.15  0.291  0.004 | 0.594  0.124  0.177  0.002 | 0.635  0.111  0.061  0.014 | 0.665  0.138  0.16  0.002 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 12

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1  2 | 0.02  0.07 | 0.027  0.151 | 0.027  0.138 | 0.049  0.258 | 0.046  0.157 | 0.026  0.154 | 0.023  0.188 | 0.024  0.103 | 3.969  6.273 | 3.969  6.87 | 5.127  8.196 | 3.279  3.96 | | 5.043  7.71 | 4.215  8.325 | 3.969  5.907 | 0.078  0.429 | 0.07  0.498 | 0.102  0.585 | 0.063  0.286 | | | 0.097  0.554 | 0.09  0.559 | 0.071  0.446 |
| 3  4 | 0.12  0.17 | 0.27  0.357 | 0.282  0.389 | 0.295  0.286 | 0.188  0.281 | 0.304  0.308 | 0.394  0.303 | 0.294  0.376 | 7.443  6.756 | 7.14  6.897 | 7.56  5.856 | 4.143  3.834 | | 7.47  5.757 | 10.521  5.289 | 7.89  7.677 | 0.915  1.114 | 0.877  1.123 | 0.941  0.955 | 0.56  0.649 | | | 0.888  0.943 | 1.223  0.838 | 0.922  1.244 |
| 5 | 0.27 | 0.152 | 0.126 | 0.086 | 0.187 | 0.171 | 0.069 | 0.172 | 3.87 | 3.882 | 2.514 | 3.105 | | 2.901 | 1.098 | 3.657 | 1.063 | 1.057 | 0.686 | 0.848 | | | 0.754 | 0.297 | 1.014 |
| 6 | 0.34 | 0.042 | 0.036 | 0.024 | 0.134 | 0.035 | 0.009 | 0.029 | 1.662 | 1.188 | 0.693 | 1.425 | | 1.065 | 0.18 | 0.846 | 0.554 | 0.41 | 0.237 | 0.51 | | | 0.353 | 0.058 | 0.292 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.627  0.139  0.194  0.001 | 0.671  0.135  0.162  0.002 | 0.581  0.117  0.11  0.002 | 0.469  0.148  0.321  0.007 | 0.612  0.12  0.206  0.002 | 0.697  0.103  0.078  0.014 | 0.67  0.133  0.201  0.002 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 13

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.17 | 0.404 | 0.404 | 0.47 | 0.266 | 0.441 | 0.298 | 0.394 | 13.401 | 12.771 | 16.626 | 4.686 | | 15.072 | 10.566 | 13.311 | 2.215 | 2.134 | 2.801 | 0.8 | | | 2.496 | 1.718 | 2.243 |
| 2 | 0.22 | 0.223 | 0.229 | 0.178 | 0.231 | 0.236 | 0.252 | 0.277 | 7.683 | 8.265 | 6.288 | 3.792 | | 7.11 | 7.908 | 7.65 | 1.714 | 1.814 | 1.387 | 0.851 | | | 1.561 | 1.688 | 1.68 |
| 3 | 0.27 | 0.099 | 0.105 | 0.061 | 0.145 | 0.116 | 0.094 | 0.117 | 3.855 | 3.663 | 2.499 | 2.505 | | 3.054 | 3.27 | 3.882 | 1.031 | 1.004 | 0.667 | 0.695 | | | 0.822 | 0.837 | 1.029 |
| 4 | 0.32 | 0.039 | 0.029 | 0.015 | 0.073 | 0.038 | 0.008 | 0.032 | 1.419 | 1.278 | 0.735 | 1.365 | | 1.101 | 0.477 | 1.317 | 0.471 | 0.416 | 0.245 | 0.44 | | | 0.345 | 0.151 | 0.403 |
| 5 | 0.37 | 0.008 | 0.008 | 0.002 | 0.025 | 0.004 | 0.002 | 0.008 | 0.432 | 0.321 | 0.174 | 0.639 | | 0.285 | 0.027 | 0.267 | 0.158 | 0.112 | 0.059 | 0.242 | | | 0.113 | 0.008 | 0.099 |
| 6 | 0.42 | 0 | 0 | 0 | 0.013 | 0 | 0 | 0 | 0.078 | 0.057 | 0.033 | 0.165 | | 0.042 | 0.012 | 0.048 | 0.04 | 0.028 | 0.014 | 0.07 | | | 0.015 | 0.005 | 0.024 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select MTD | | 0.627  0.21  0.146  0.227 | 0.633  0.209  0.142  0.225 | 0.648  0.196  0.078  0.274 | 0.497  0.236  0.256  0.247 | 0.677  0.2  0.158  0.165 | 0.55  0.198  0.104  0.346 | 0.671  0.207  0.157  0.172 |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Toxicity | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of Select Dose-over-MTD | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |
| Prob. of No Selection | |  |  |  |  | |  |  |  |  |  |  |  | | |  |  |  |

Scenario 14

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.17  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | #  mTPI-2 | of | Patients Treated  3+3 BOIN | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of | Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.02 | 0.01 | 0.012 | 0.015 | 0.024 | 0.014 | 0.008 | 0.011 | 3.744 | 3.72 | 4.416 | 3.207 | | 4.488 | 3.843 | 3.636 | 0.083 | 0.066 | 0.084 | 0.058 | | | 0.087 | 0.085 | 0.066 |
| 2 | 0.05 | 0.053 | 0.044 | 0.11 | 0.06 | 0.074 | 0.081 | 0.036 | 4.653 | 5.22 | 6.111 | 3.54 | | 5.952 | 6.405 | 4.464 | 0.214 | 0.275 | 0.311 | 0.18 | | | 0.324 | 0.308 | 0.238 |
| 3 | 0.08 | 0.119 | 0.147 | 0.204 | 0.109 | 0.157 | 0.256 | 0.143 | 5.691 | 5.784 | 6.39 | 3.876 | | 6.135 | 9.354 | 6.183 | 0.441 | 0.428 | 0.498 | 0.326 | | | 0.482 | 0.674 | 0.457 |
| 4 | 0.11 | 0.2 | 0.275 | 0.257 | 0.128 | 0.241 | 0.338 | 0.277 | 5.616 | 5.76 | 5.637 | 3.798 | | 5.454 | 6.633 | 6.618 | 0.618 | 0.614 | 0.615 | 0.441 | | | 0.579 | 0.677 | 0.709 |
| 5 | 0.14 | 0.288 | 0.199 | 0.198 | 0.153 | 0.23 | 0.199 | 0.256 | 4.749 | 4.68 | 4.101 | 3.504 | | 3.954 | 2.499 | 4.881 | 0.624 | 0.696 | 0.601 | 0.475 | | | 0.536 | 0.347 | 0.7 |
| 6 | 0.17 | 0.33 | 0.321 | 0.214 | 0.518 | 0.282 | 0.104 | 0.275 | 5.547 | 4.782 | 3.291 | 2.709 | | 3.963 | 0.894 | 4.164 | 0.954 | 0.809 | 0.567 | 0.473 | | | 0.638 | 0.146 | 0.719 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | | | | |  | | | | | | | | |
| Prob. of Select MTD | | 0.618  0.098  0  0 | 0.52  0.096  0  0.002 | 0.412  0.089  0  0.002 | 0.671  0.095  0  0.008 | 0.512  0.088  0  0.002 | 0.303  0.076  0  0.014 | 0.531  0.096  0  0.002 |
| Prob. of Toxicity | |
| Prob. of Select Dose-over-MTD | |
| Prob. of No Selection | |

Scenario 1

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | # of Patients Treated  mTPI-2 3+3 BOIN | | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.02 | 0 | 0.001 | 0.001 | 0.02 | 0 | 0.002 | 0.001 | 3.249 | 3.255 | 3.246 | 3.21 | 3.219 | 3.189 | 3.228 | 0.077 | 0.069 | 0.069 | 0.064 | | 0.062 | 0.069 | 0.069 |
| 2 | 0.05 | 0.005 | 0.002 | 0.004 | 0.108 | 0.004 | 0.002 | 0.002 | 3.66 | 3.747 | 3.708 | 3.651 | 3.813 | 3.678 | 3.114 | 0.176 | 0.181 | 0.18 | 0.183 | | 0.195 | 0.166 | 0.147 |
| 3 | 0.1 | 0.03 | 0.051 | 0.04 | 0.165 | 0.026 | 0.066 | 0.016 | 4.74 | 5.154 | 4.866 | 4.044 | 4.893 | 6.141 | 3.711 | 0.479 | 0.543 | 0.512 | 0.417 | | 0.503 | 0.586 | 0.4 |
| 4 | 0.15 | 0.134 | 0.178 | 0.145 | 0.228 | 0.126 | 0.204 | 0.089 | 5.898 | 5.886 | 5.676 | 3.921 | 5.901 | 7.059 | 5.037 | 0.846 | 0.841 | 0.808 | 0.586 | | 0.895 | 1.053 | 0.744 |
| 5 | 0.2 | 0.279 | 0.273 | 0.272 | 0.174 | 0.258 | 0.296 | 0.269 | 5.694 | 5.724 | 5.832 | 3.375 | 5.616 | 5.289 | 6.15 | 1.131 | 1.171 | 1.186 | 0.711 | | 1.099 | 1.045 | 1.209 |
| 6 | 0.25 | 0.552 | 0.495 | 0.538 | 0.297 | 0.586 | 0.43 | 0.623 | 6.759 | 6.234 | 6.672 | 2.028 | 6.558 | 4.644 | 8.76 | 1.684 | 1.533 | 1.64 | 0.499 | | 1.59 | 1.149 | 2.17 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | | | |  | | | | | | | |
| Prob. of Select MTD | | 0.552 | 0.495 | 0.538 | 0.297 | 0.586 | 0.43 | 0.623 |
| Prob. of Toxicity | | 0.146 | 0.145 | 0.147 | 0.122 | 0.145 | 0.136 | 0.158 |
| Prob. of Select Dose-over-MTD | | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Prob. of No Selection | | 0 | 0 | 0 | 0.008 | 0 | 0 | 0 |

Scenario 2

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | # of Patients Treated  mTPI-2 3+3 BOIN | | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.35 | 0.432 | 0.45 | 0.436 | 0.265 | 0.533 | 0.292 | 0.539 | 17.847 | 17.625 | 17.964 | 5.046 | 17.607 | 11.922 | 17.415 | 6.228 | 6.134 | 6.249 | 1.73 | | 6.143 | 4.248 | 6.041 |
| 2 | 0.45 | 0.086 | 0.087 | 0.087 | 0.057 | 0.11 | 0.055 | 0.118 | 5.19 | 5.607 | 5.172 | 1.875 | 5.067 | 4.203 | 5.004 | 2.313 | 2.495 | 2.306 | 0.847 | | 2.265 | 1.975 | 2.236 |
| 3 | 0.5 | 0.018 | 0.013 | 0.02 | 0.01 | 0.026 | 0.011 | 0.027 | 1.08 | 0.933 | 1.011 | 0.459 | 1.212 | 0.72 | 1.698 | 0.554 | 0.476 | 0.517 | 0.233 | | 0.592 | 0.377 | 0.844 |
| 4 | 0.6 | 0.001 | 0 | 0.001 | 0 | 0.004 | 0 | 0 | 0.15 | 0.114 | 0.138 | 0.069 | 0.21 | 0.087 | 0.309 | 0.092 | 0.075 | 0.088 | 0.046 | | 0.116 | 0.048 | 0.195 |
| 5 | 0.7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.006 | 0 | 0.003 | 0.009 | 0.015 | 0 | 0.027 | 0.005 | 0 | 0.003 | 0.005 | | 0.012 | 0 | 0.019 |
| 6 | 0.8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select MTD | | 0.432 | 0.45 | 0.436 | 0.265 | 0.533 | 0.292 | 0.539 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Toxicity | | 0.379 | 0.378 | 0.377 | 0.384 | 0.379 | 0.393 | 0.382 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.105 | 0.1 | 0.108 | 0.067 | 0.14 | 0.066 | 0.145 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of No Selection | | 0.463 | 0.45 | 0.456 | 0.668 | 0.327 | 0.642 | 0.316 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |

Scenario 3

|  |  |  |  |
| --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | Selection Prob.  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Patients Treated  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Toxicities  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| 1 0.01 | 0.319 0.309 0.333 0.604 0.164 0.217 0.184 | 7.737 6.573 8.259 4.839 8.043 7.257 7.212 | 0.065 0.069 0.087 0.047 0.075 0.071 0.071 |
| 2 0.3 | 0.636 0.656 0.627 0.358 0.753 0.747 0.73 | 16.647 18.315 16.524 5.253 16.572 17.859 15.114 | 4.919 5.448 4.916 1.632 4.918 5.336 4.512 |
| 3 0.55  4 0.65  5 0.8  6 0.95 | 0.043 0.033 0.037 0.036 0.079 0.036 0.086  0.002 0.002 0.003 0.002 0.004 0 0  0 0 0 0 0 0 0  0 0 0 0 0 0 0 | 5.088 4.737 4.836 2.049 4.974 4.551 6.66  0.516 0.357 0.363 0.258 0.396 0.315 0.945  0.012 0.018 0.018 0.015 0.015 0.018 0.069  0 0 0 0 0 0 0 | 2.797 2.63 2.673 1.121 2.737 2.554 3.664  0.329 0.23 0.234 0.174 0.258 0.196 0.636  0.008 0.012 0.012 0.011 0.014 0.016 0.053  0 0 0 0 0 0 0 |
|  | i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| Prob. of Select MTD  Prob. of Toxicity  Prob. of Select Dose-over-MTD Prob. of No Selection | 0.66 0.656 0.627 0.358 0.753 0.747 0.73  0.271 0.28 0.264 0.24 0.267 0.272 0.298  0.045 0.035 0.04 0.038 0.083 0.036 0.086  0 0 0 0 0 0 0 |

Scenario 4

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | # of Patients Treated  mTPI-2 3+3 BOIN | | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.04 | 0.002 | 0.001 | 0.001 | 0.031 | 0 | 0 | 0.001 | 3.492 | 3.558 | 3.522 | 3.414 | 3.438 | 3.303 | 3.474 | 0.139 | 0.152 | 0.149 | 0.133 | | 0.128 | 0.12 | 0.148 |
| 2 | 0.06 | 0.003 | 0.002 | 0.003 | 0.064 | 0.003 | 0.002 | 0.002 | 3.858 | 3.927 | 3.807 | 3.591 | 3.864 | 3.642 | 3.162 | 0.249 | 0.242 | 0.242 | 0.211 | | 0.238 | 0.173 | 0.197 |
| 3 | 0.08 | 0.011 | 0.022 | 0.011 | 0.089 | 0.011 | 0.028 | 0.01 | 4.185 | 4.431 | 4.161 | 3.687 | 4.17 | 5.178 | 3.6 | 0.356 | 0.37 | 0.341 | 0.305 | | 0.343 | 0.414 | 0.303 |
| 4 | 0.1 | 0.323 | 0.304 | 0.323 | 0.436 | 0.197 | 0.337 | 0.214 | 6.348 | 5.739 | 6.279 | 4.422 | 6.393 | 8.208 | 6.09 | 0.615 | 0.57 | 0.622 | 0.456 | | 0.61 | 0.777 | 0.607 |
| 5 | 0.3 | 0.616 | 0.626 | 0.614 | 0.324 | 0.696 | 0.538 | 0.697 | 9.123 | 9.372 | 9.078 | 4.224 | 9.081 | 7.158 | 9.87 | 2.734 | 2.75 | 2.655 | 1.228 | | 2.717 | 2.161 | 2.899 |
| 6 | 0.6 | 0.045 | 0.045 | 0.048 | 0.038 | 0.093 | 0.09 | 0.076 | 2.994 | 2.973 | 3.153 | 1.578 | 3.054 | 2.379 | 3.804 | 1.797 | 1.773 | 1.886 | 0.967 | | 1.807 | 1.437 | 2.293 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select MTD | | 0.616 | 0.626 | 0.614 | 0.324 | 0.696 | 0.538 | 0.697 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Toxicity | | 0.196 | 0.195 | 0.197 | 0.158 | 0.195 | 0.17 | 0.215 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.045 | 0.045 | 0.048 | 0.038 | 0.093 | 0.09 | 0.076 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of No Selection | | 0 | 0 | 0 | 0.018 | 0 | 0.005 | 0 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |

Scenario 5

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | # of Patients Treated  mTPI-2 3+3 BOIN | | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.05 | 0.991 | 0.99 | 0.982 | 0.929 | 0.886 | 0.93 | 0.919 | 21.477 | 20.826 | 21.345 | 5.88 | 20.922 | 20.937 | 20.436 | 1.075 | 1.102 | 1.114 | 0.287 | | 1.005 | 1.011 | 1.052 |
| 2 | 0.6 | 0.009 | 0.009 | 0.017 | 0.042 | 0.114 | 0.049 | 0.08 | 8.121 | 8.739 | 8.226 | 3.924 | 8.682 | 7.842 | 8.199 | 4.884 | 5.258 | 4.943 | 2.4 | | 5.155 | 4.73 | 4.915 |
| 3 | 0.8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.402 | 0.411 | 0.405 | 0.255 | 0.396 | 0.72 | 1.317 | 0.319 | 0.327 | 0.321 | 0.197 | | 0.315 | 0.569 | 1.057 |
| 4 | 0.9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.006 | 0.006 | 0.003 | 0 | 0.009 | 0.03 | 0 | 0.006 | 0.006 | 0.003 | | 0 | 0.009 | 0.029 |
| 5 | 0.95 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 |
| 6 | 0.99 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | |  | |  |  |  |  | |  |  |  |
| Prob. of Select MTD | | 0.991 | 0.99 | 0.982 | 0.929 | 0.886 | 0.93 | 0.919 |  | | | | | | |  |  |  |  | |  |  |  |
| Prob. of Toxicity | | 0.209 | 0.223 | 0.213 | 0.287 | 0.216 | 0.214 | 0.235 |  |  |  |  | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.009 | 0.009 | 0.017 | 0.042 | 0.114 | 0.049 | 0.08 |  |  |  |  | |  |  |  |
| Prob. of No Selection | | 0 | 0.001 | 0.001 | 0.029 | 0 | 0.021 | 0.001 |  |  |  |  | |  |  |  |

Scenario 6

|  |  |  |  |
| --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | Selection Prob.  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Patients Treated  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Toxicities  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| 1 0.01  2 0.05 | 0.001 0.001 0.001 0.025 0 0.012 0.001  0.003 0.003 0.006 0.126 0.005 0.003 0.006 | 3.144 3.147 3.147 3.153 3.102 3.132 3.129  3.732 3.75 3.732 3.765 3.819 3.789 3.258 | 0.032 0.034 0.034 0.03 0.023 0.036 0.034  0.201 0.177 0.178 0.191 0.196 0.17 0.151 |
| 3 0.1 | 0.963 0.952 0.96 0.814 0.826 0.845 0.878 | 15.45 14.934 15.357 5.685 15.414 16.728 14.763 | 1.488 1.53 1.566 0.602 1.49 1.616 1.517 |
| 4 0.6  5 0.7  6 0.9 | 0.033 0.042 0.032 0.032 0.169 0.14 0.114  0 0.002 0.001 0.001 0 0 0.001  0 0 0 0 0 0 0 | 7.254 7.719 7.35 3.495 7.335 6.024 7.737  0.405 0.435 0.399 0.237 0.324 0.318 1.062  0.015 0.015 0.015 0.006 0.006 0.009 0.051 | 4.382 4.605 4.403 2.121 4.388 3.624 4.627  0.29 0.299 0.277 0.164 0.238 0.228 0.769  0.015 0.012 0.012 0.005 0.005 0.009 0.04 |
|  | i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| Prob. of Select MTD  Prob. of Toxicity  Prob. of Select Dose-over-MTD Prob. of No Selection | 0.963 0.952 0.96 0.814 0.826 0.845 0.878  0.214 0.222 0.216 0.191 0.211 0.189 0.238  0.033 0.044 0.033 0.033 0.169 0.14 0.115  0 0 0 0.002 0 0 0 |

Scenario 7

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | # of Patients Treated  mTPI-2 3+3 BOIN | | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.01 | 0 | 0.001 | 0.001 | 0.011 | 0 | 0 | 0.001 | 3.132 | 3.132 | 3.126 | 3.114 | 3.075 | 3.102 | 3.129 | 0.04 | 0.034 | 0.034 | 0.033 | | 0.023 | 0.036 | 0.034 |
| 2 | 0.03 | 0.001 | 0 | 0 | 0.051 | 0.001 | 0.002 | 0.001 | 3.399 | 3.327 | 3.321 | 3.408 | 3.387 | 3.399 | 3.027 | 0.11 | 0.084 | 0.083 | 0.111 | | 0.1 | 0.099 | 0.07 |
| 3 | 0.07 | 0.007 | 0.015 | 0.009 | 0.092 | 0.005 | 0.014 | 0.002 | 4.032 | 4.248 | 4.041 | 3.828 | 4.005 | 4.83 | 3.231 | 0.295 | 0.317 | 0.303 | 0.292 | | 0.289 | 0.321 | 0.259 |
| 4 | 0.1 | 0.061 | 0.079 | 0.058 | 0.187 | 0.031 | 0.187 | 0.034 | 4.692 | 4.728 | 4.671 | 3.942 | 4.704 | 6.966 | 4.08 | 0.454 | 0.455 | 0.45 | 0.399 | | 0.465 | 0.639 | 0.404 |
| 5 | 0.15 | 0.913 | 0.891 | 0.92 | 0.648 | 0.922 | 0.712 | 0.92 | 10.554 | 10.761 | 10.839 | 4.884 | 10.707 | 8.373 | 12.159 | 1.602 | 1.6 | 1.612 | 0.748 | | 1.583 | 1.237 | 1.779 |
| 6 | 0.75 | 0.018 | 0.014 | 0.012 | 0.007 | 0.041 | 0.085 | 0.042 | 4.191 | 3.804 | 4.002 | 2.37 | 4.122 | 3.33 | 4.374 | 3.068 | 2.854 | 3.001 | 1.788 | | 3.089 | 2.487 | 3.291 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select MTD | | 0.913 | 0.891 | 0.92 | 0.648 | 0.922 | 0.712 | 0.92 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Toxicity | | 0.186 | 0.178 | 0.183 | 0.156 | 0.185 | 0.161 | 0.195 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.018 | 0.014 | 0.012 | 0.007 | 0.041 | 0.085 | 0.042 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of No Selection | | 0 | 0 | 0 | 0.004 | 0 | 0 | 0 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |

Scenario 8

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | # of Patients Treated  mTPI-2 3+3 BOIN | | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.29 | 0.351 | 0.38 | 0.346 | 0.256 | 0.356 | 0.22 | 0.344 | 14.202 | 14.883 | 14.487 | 4.968 | 14.16 | 9.213 | 13.362 | 4.038 | 4.274 | 4.164 | 1.421 | | 4.101 | 2.694 | 3.895 |
| 2 | 0.31 | 0.197 | 0.199 | 0.185 | 0.118 | 0.224 | 0.236 | 0.2 | 7.164 | 7.119 | 7.044 | 2.595 | 6.894 | 7.716 | 6.282 | 2.289 | 2.236 | 2.201 | 0.834 | | 2.104 | 2.344 | 1.945 |
| 3 | 0.33 | 0.118 | 0.123 | 0.144 | 0.07 | 0.131 | 0.124 | 0.182 | 3.315 | 3.435 | 3.588 | 1.182 | 3.597 | 3.645 | 4.557 | 1.087 | 1.073 | 1.136 | 0.383 | | 1.182 | 1.193 | 1.443 |
| 4 | 0.35 | 0.063 | 0.052 | 0.07 | 0.017 | 0.079 | 0.038 | 0.091 | 1.41 | 1.284 | 1.56 | 0.558 | 1.611 | 1.017 | 2.166 | 0.495 | 0.456 | 0.558 | 0.22 | | 0.557 | 0.36 | 0.75 |
| 5 | 0.37 | 0.028 | 0.027 | 0.026 | 0.005 | 0.036 | 0.009 | 0.038 | 0.498 | 0.426 | 0.477 | 0.171 | 0.588 | 0.243 | 0.801 | 0.186 | 0.157 | 0.172 | 0.064 | | 0.212 | 0.08 | 0.302 |
| 6 | 0.39 | 0.014 | 0.007 | 0.016 | 0.005 | 0.017 | 0.014 | 0.008 | 0.123 | 0.102 | 0.159 | 0.045 | 0.195 | 0.132 | 0.177 | 0.046 | 0.048 | 0.066 | 0.016 | | 0.076 | 0.046 | 0.079 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select MTD | | 0.729 | 0.754 | 0.745 | 0.461 | 0.79 | 0.618 | 0.817 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Toxicity | | 0.305 | 0.303 | 0.304 | 0.309 | 0.304 | 0.306 | 0.308 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.042 | 0.034 | 0.042 | 0.01 | 0.053 | 0.023 | 0.046 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of No Selection | | 0.229 | 0.212 | 0.213 | 0.529 | 0.157 | 0.359 | 0.137 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |

Scenario 9

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | # of Patients Treated  mTPI-2 3+3 BOIN | | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.25 | 0.27 | 0.329 | 0.286 | 0.247 | 0.256 | 0.209 | 0.218 | 12.093 | 13.023 | 12.438 | 4.872 | 11.829 | 9.207 | 11.019 | 3.015 | 3.198 | 3.031 | 1.229 | | 2.888 | 2.266 | 2.708 |
| 2 | 0.27 | 0.219 | 0.252 | 0.23 | 0.161 | 0.217 | 0.273 | 0.258 | 7.749 | 8.34 | 7.914 | 2.925 | 7.71 | 8.361 | 7.275 | 2.079 | 2.311 | 2.209 | 0.809 | | 2.095 | 2.282 | 1.999 |
| 3 | 0.29 | 0.166 | 0.152 | 0.164 | 0.077 | 0.2 | 0.165 | 0.204 | 4.464 | 4.11 | 4.431 | 1.623 | 4.737 | 4.749 | 5.235 | 1.272 | 1.169 | 1.282 | 0.496 | | 1.365 | 1.428 | 1.514 |
| 4 | 0.31 | 0.125 | 0.086 | 0.108 | 0.037 | 0.126 | 0.078 | 0.141 | 2.415 | 1.809 | 2.151 | 0.78 | 2.37 | 1.758 | 3.111 | 0.751 | 0.551 | 0.655 | 0.258 | | 0.723 | 0.546 | 0.948 |
| 5 | 0.33 | 0.065 | 0.042 | 0.058 | 0.016 | 0.071 | 0.03 | 0.069 | 0.948 | 0.738 | 1.029 | 0.36 | 1.137 | 0.489 | 1.209 | 0.335 | 0.23 | 0.328 | 0.12 | | 0.365 | 0.15 | 0.388 |
| 6 | 0.35 | 0.029 | 0.028 | 0.045 | 0.013 | 0.044 | 0.02 | 0.033 | 0.351 | 0.354 | 0.441 | 0.135 | 0.501 | 0.219 | 0.555 | 0.133 | 0.124 | 0.148 | 0.05 | | 0.187 | 0.076 | 0.186 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | | | |  | | | | | | | |
| Prob. of Select MTD | | 0.874 | 0.889 | 0.891 | 0.551 | 0.914 | 0.775 | 0.923 |
| Prob. of Toxicity | | 0.271 | 0.267 | 0.269 | 0.277 | 0.27 | 0.272 | 0.273 |
| Prob. of Select Dose-over-MTD | | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Prob. of No Selection | | 0.126 | 0.111 | 0.109 | 0.449 | 0.086 | 0.225 | 0.077 |

Scenario 10

|  |  |  |  |
| --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | Selection Prob.  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Patients Treated  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM | # of Toxicities  i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |
| 1 0.21  2 0.23 | 0.158 0.218 0.163 0.244 0.151 0.14 0.126  0.203 0.247 0.209 0.153 0.202 0.232 0.21 | 9.444 10.587 9.552 4.767 9.564 7.551 8.622  7.551 8.31 7.851 3.27 7.596 8.271 6.879 | 1.95 2.161 1.967 1.027 1.983 1.539 1.765  1.715 1.925 1.799 0.788 1.699 1.927 1.602 |
| 3 0.25  4 0.27  5 0.29  6 0.31 | 0.199 0.211 0.215 0.11 0.204 0.231 0.233  0.179 0.138 0.152 0.072 0.174 0.148 0.185  0.107 0.071 0.124 0.031 0.127 0.058 0.133  0.089 0.067 0.09 0.034 0.109 0.049 0.078 | 5.616 5.361 5.706 2.031 5.643 6.288 6.231  3.561 2.811 3.411 1.281 3.618 2.856 4.044  1.797 1.338 1.68 0.696 1.8 0.981 2.205  0.912 0.783 0.99 0.288 1.089 0.624 1.209 | 1.403 1.349 1.429 0.493 1.403 1.552 1.575  0.981 0.767 0.939 0.35 0.979 0.802 1.087  0.548 0.39 0.469 0.214 0.512 0.288 0.63  0.297 0.241 0.313 0.088 0.362 0.213 0.364 |
|  | i3+3 mTPI mTPI-2 3+3 BOIN BLRM CRM |  |  |
| Prob. of Select MTD  Prob. of Toxicity  Prob. of Select Dose-over-MTD Prob. of No Selection | 0.574 0.487 0.581 0.247 0.614 0.486 0.629  0.239 0.234 0.237 0.24 0.237 0.238 0.241  0 0 0 0 0 0 0  0.065 0.048 0.047 0.356 0.033 0.142 0.035 |

Scenario 11

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | # of Patients Treated  mTPI-2 3+3 BOIN | | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.05 | 0.067 | 0.057 | 0.071 | 0.328 | 0.042 | 0.032 | 0.043 | 4.986 | 4.641 | 5.16 | 4.269 | 5.085 | 4.434 | 4.521 | 0.236 | 0.243 | 0.263 | 0.199 | | 0.244 | 0.189 | 0.233 |
| 2 | 0.2 | 0.274 | 0.276 | 0.252 | 0.298 | 0.207 | 0.309 | 0.163 | 9.543 | 9.933 | 9.273 | 4.761 | 9.183 | 9.969 | 6.66 | 1.947 | 2.013 | 1.89 | 0.986 | | 1.812 | 1.969 | 1.374 |
| 3 | 0.27 | 0.329 | 0.338 | 0.309 | 0.204 | 0.352 | 0.4 | 0.318 | 8.466 | 8.529 | 8.064 | 3.366 | 8.265 | 9.807 | 8.763 | 2.337 | 2.259 | 2.141 | 0.91 | | 2.208 | 2.679 | 2.408 |
| 4 | 0.33 | 0.196 | 0.228 | 0.232 | 0.107 | 0.243 | 0.185 | 0.309 | 4.704 | 4.548 | 4.848 | 1.932 | 4.995 | 4.221 | 6.201 | 1.589 | 1.469 | 1.562 | 0.639 | | 1.656 | 1.385 | 1.979 |
| 5 | 0.39 | 0.099 | 0.079 | 0.101 | 0.035 | 0.116 | 0.051 | 0.137 | 1.734 | 1.911 | 2.097 | 0.831 | 1.968 | 1.149 | 2.964 | 0.66 | 0.745 | 0.826 | 0.337 | | 0.735 | 0.452 | 1.126 |
| 6 | 0.45 | 0.035 | 0.021 | 0.034 | 0.004 | 0.04 | 0.017 | 0.03 | 0.567 | 0.42 | 0.54 | 0.24 | 0.504 | 0.261 | 0.891 | 0.243 | 0.191 | 0.241 | 0.121 | | 0.229 | 0.123 | 0.413 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select MTD | | 0.525 | 0.566 | 0.541 | 0.311 | 0.595 | 0.585 | 0.627 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Toxicity | | 0.234 | 0.231 | 0.231 | 0.207 | 0.229 | 0.228 | 0.251 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.134 | 0.1 | 0.135 | 0.039 | 0.156 | 0.068 | 0.167 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of No Selection | | 0 | 0.001 | 0.001 | 0.024 | 0 | 0.006 | 0 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |

Scenario 12

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | # of Patients Treated  mTPI-2 3+3 BOIN | | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.05 | 0.007 | 0.004 | 0.005 | 0.087 | 0.002 | 0.001 | 0.004 | 3.864 | 3.834 | 3.81 | 3.615 | 3.711 | 3.477 | 3.693 | 0.21 | 0.201 | 0.2 | 0.188 | | 0.178 | 0.147 | 0.195 |
| 2 | 0.1 | 0.071 | 0.068 | 0.072 | 0.29 | 0.04 | 0.086 | 0.034 | 5.517 | 5.55 | 5.562 | 4.392 | 5.604 | 5.802 | 4.053 | 0.555 | 0.565 | 0.571 | 0.43 | | 0.552 | 0.54 | 0.422 |
| 3 | 0.2 | 0.337 | 0.382 | 0.354 | 0.308 | 0.297 | 0.408 | 0.237 | 8.346 | 9.312 | 8.793 | 4.428 | 8.583 | 10.845 | 7.368 | 1.625 | 1.893 | 1.743 | 0.912 | | 1.664 | 2.22 | 1.483 |
| 4 | 0.3 | 0.362 | 0.373 | 0.357 | 0.218 | 0.406 | 0.383 | 0.455 | 7.764 | 7.425 | 7.536 | 3.153 | 7.752 | 7.119 | 8.883 | 2.341 | 2.212 | 2.269 | 0.93 | | 2.321 | 2.119 | 2.61 |
| 5 | 0.4 | 0.146 | 0.144 | 0.17 | 0.053 | 0.173 | 0.098 | 0.232 | 3.42 | 3.132 | 3.384 | 1.53 | 3.333 | 2.133 | 4.68 | 1.376 | 1.24 | 1.347 | 0.629 | | 1.317 | 0.89 | 1.869 |
| 6 | 0.5 | 0.077 | 0.029 | 0.042 | 0.012 | 0.082 | 0.018 | 0.038 | 1.089 | 0.747 | 0.915 | 0.366 | 1.017 | 0.465 | 1.323 | 0.421 | 0.356 | 0.452 | 0.199 | | 0.393 | 0.235 | 0.665 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select MTD | | 0.362 | 0.373 | 0.357 | 0.218 | 0.406 | 0.383 | 0.455 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Toxicity | | 0.218 | 0.216 | 0.219 | 0.188 | 0.214 | 0.206 | 0.241 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.223 | 0.173 | 0.212 | 0.065 | 0.255 | 0.116 | 0.27 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of No Selection | | 0 | 0 | 0 | 0.032 | 0 | 0.006 | 0 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |

Scenario 13

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | # of Patients Treated  mTPI-2 3+3 BOIN | | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.3 | 0.447 | 0.427 | 0.408 | 0.288 | 0.447 | 0.297 | 0.421 | 16.26 | 15.867 | 15.981 | 5.055 | 15.576 | 10.725 | 14.733 | 4.939 | 4.754 | 4.779 | 1.488 | | 4.592 | 3.284 | 4.41 |
| 2 | 0.35 | 0.168 | 0.225 | 0.214 | 0.105 | 0.247 | 0.199 | 0.258 | 6.717 | 7.653 | 7.263 | 2.469 | 7.443 | 6.855 | 6.906 | 2.406 | 2.655 | 2.532 | 0.894 | | 2.604 | 2.454 | 2.401 |
| 3 | 0.4 | 0.091 | 0.069 | 0.103 | 0.042 | 0.099 | 0.068 | 0.119 | 2.619 | 2.592 | 2.898 | 0.918 | 2.73 | 2.496 | 3.9 | 1.01 | 1.031 | 1.129 | 0.37 | | 1.107 | 0.999 | 1.53 |
| 4 | 0.45 | 0.023 | 0.02 | 0.021 | 0.008 | 0.028 | 0.009 | 0.034 | 0.768 | 0.657 | 0.768 | 0.291 | 0.828 | 0.492 | 1.125 | 0.344 | 0.295 | 0.369 | 0.139 | | 0.362 | 0.218 | 0.533 |
| 5 | 0.5 | 0.006 | 0.001 | 0.002 | 0.001 | 0.01 | 0.003 | 0.003 | 0.168 | 0.117 | 0.12 | 0.051 | 0.189 | 0.096 | 0.267 | 0.077 | 0.068 | 0.062 | 0.026 | | 0.086 | 0.05 | 0.133 |
| 6 | 0.55 | 0.002 | 0 | 0 | 0 | 0 | 0 | 0 | 0.024 | 0 | 0.003 | 0.003 | 0.012 | 0.009 | 0.015 | 0.011 | 0 | 0.002 | 0.002 | | 0.009 | 0.005 | 0.011 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select MTD | | 0.615 | 0.652 | 0.622 | 0.393 | 0.694 | 0.496 | 0.679 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Toxicity | | 0.331 | 0.327 | 0.328 | 0.332 | 0.327 | 0.339 | 0.335 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of Select Dose-over-MTD | | 0.122 | 0.09 | 0.126 | 0.051 | 0.137 | 0.08 | 0.156 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |
| Prob. of No Selection | | 0.263 | 0.258 | 0.252 | 0.556 | 0.169 | 0.424 | 0.165 |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |

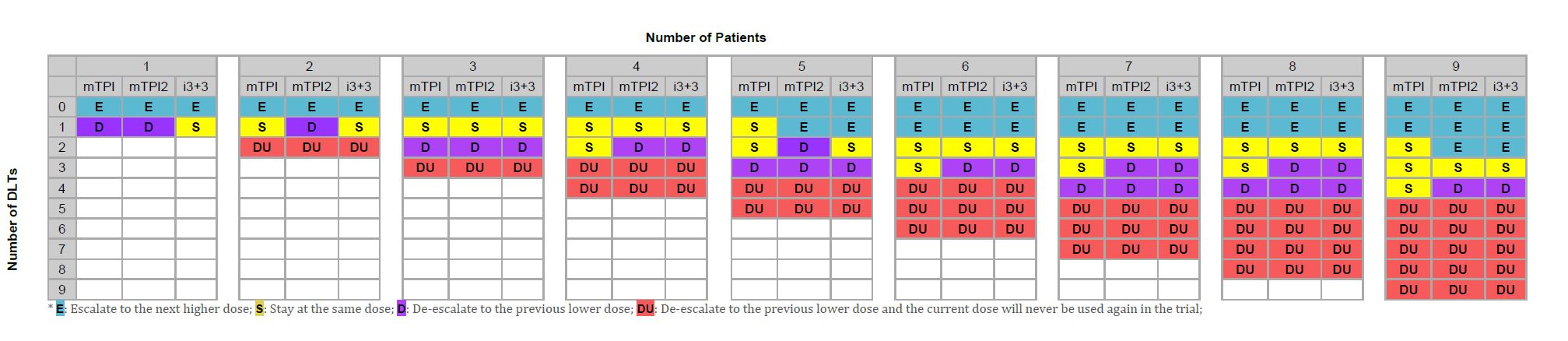
Scenario 14

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Target Toxicity Prob. = 0.3  Dose Level True Tox Prob. | | i3+3 | mTPI | mTPI-2 | Selection Prob.  3+3 | BOIN | BLRM | CRM | i3+3 | mTPI | # of Patients Treated  mTPI-2 3+3 BOIN | | | BLRM | CRM | i3+3 | mTPI | mTPI-2 | # | of Toxicities  3+3 | BOIN | BLRM | CRM |
| 1 | 0.15 | 0.057 | 0.082 | 0.061 | 0.212 | 0.054 | 0.053 | 0.041 | 6.633 | 7.461 | 6.801 | 4.494 | 6.573 | 5.517 | 6.18 | 1.017 | 1.115 | 1.026 | 0.676 | | 0.966 | 0.774 | 0.931 |
| 2 | 0.18 | 0.15 | 0.171 | 0.153 | 0.194 | 0.128 | 0.164 | 0.128 | 7.005 | 7.074 | 7.029 | 3.741 | 7.122 | 7.851 | 5.841 | 1.258 | 1.205 | 1.225 | 0.689 | | 1.259 | 1.411 | 1.022 |
| 3 | 0.21 | 0.202 | 0.24 | 0.207 | 0.151 | 0.208 | 0.266 | 0.217 | 6.387 | 6.774 | 6.36 | 2.862 | 6.333 | 7.686 | 6.417 | 1.353 | 1.469 | 1.357 | 0.606 | | 1.321 | 1.59 | 1.363 |
| 4 | 0.24 | 0.198 | 0.227 | 0.21 | 0.111 | 0.221 | 0.232 | 0.247 | 4.584 | 4.62 | 4.833 | 1.938 | 4.923 | 4.377 | 5.484 | 1.061 | 1.105 | 1.168 | 0.466 | | 1.169 | 1.034 | 1.323 |
| 5 | 0.27 | 0.192 | 0.137 | 0.18 | 0.069 | 0.183 | 0.118 | 0.204 | 2.997 | 2.334 | 2.934 | 1.251 | 2.952 | 1.962 | 3.657 | 0.767 | 0.59 | 0.771 | 0.338 | | 0.789 | 0.532 | 0.981 |
| 6 | 0.3 | 0.181 | 0.134 | 0.18 | 0.06 | 0.198 | 0.114 | 0.155 | 1.932 | 1.542 | 1.848 | 0.594 | 1.902 | 1.239 | 2.226 | 0.592 | 0.445 | 0.522 | 0.193 | | 0.553 | 0.353 | 0.642 |
|  | | i3+3 | mTPI | mTPI-2 | 3+3 | BOIN | BLRM | CRM |  | | | | | | |  | | | | | | | |
| Prob. of Select MTD | | 0.373 | 0.271 | 0.36 | 0.129 | 0.381 | 0.232 | 0.359 |
| Prob. of Toxicity | | 0.205 | 0.199 | 0.204 | 0.199 | 0.203 | 0.119 | 0.21 |
| Prob. of Select Dose-over-MTD | | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Prob. of No Selection | | 0.02 | 0.009 | 0.009 | 0.203 | 0.008 | 0.053 | 0.008 |

Appendix D

**Comparison of decision tables for different designs**

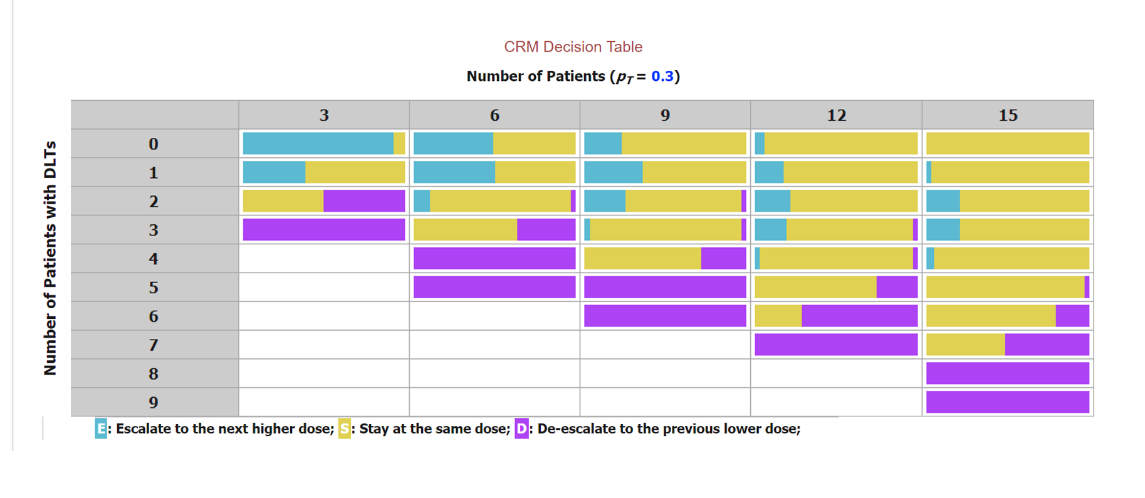
We provide a quick comparison of decision tables among the i3+3, mTPI, and mTPI-2 designs, since all three designs require the same input of the target toxicity probability and the EI. Figure A1 provides a side-by-side comparison based on and EI [0.25, 0.35] for up to 9 patients. The dose assignment decisions for i3+3 seems to be more reasonable than mTPI or mTPI-2. For example, when 1 out of 2 patients experiences DLT, the decision is “S” under i3+3 and mTPI, compared with the decision “D” under mTPI-2. Here, one could argue that when only 2 patients have been treated at a dose, 1 DLT does not provide sufficient information to warrant a de-escalation decision. Investigators might want to wait for further information to make a dose change decision. In this case, i3+3 agrees with mTPI, not mTPI-2. As a contrasting example, when 3 out of 6 patients experiences DLTs, the decision is “D” under i3+3 and mTPI-2, compared with the decision “S” under mTPI. Again, one could argue that “S” is more sensible according to our earlier discussion. Therefore, i3+3 here agrees with mTPI-2, not mTPI. In general, we can see that i3+3 seems to take more sound and ethically acceptable decisions, often complementing the mTPI and mTPI-2 designs.

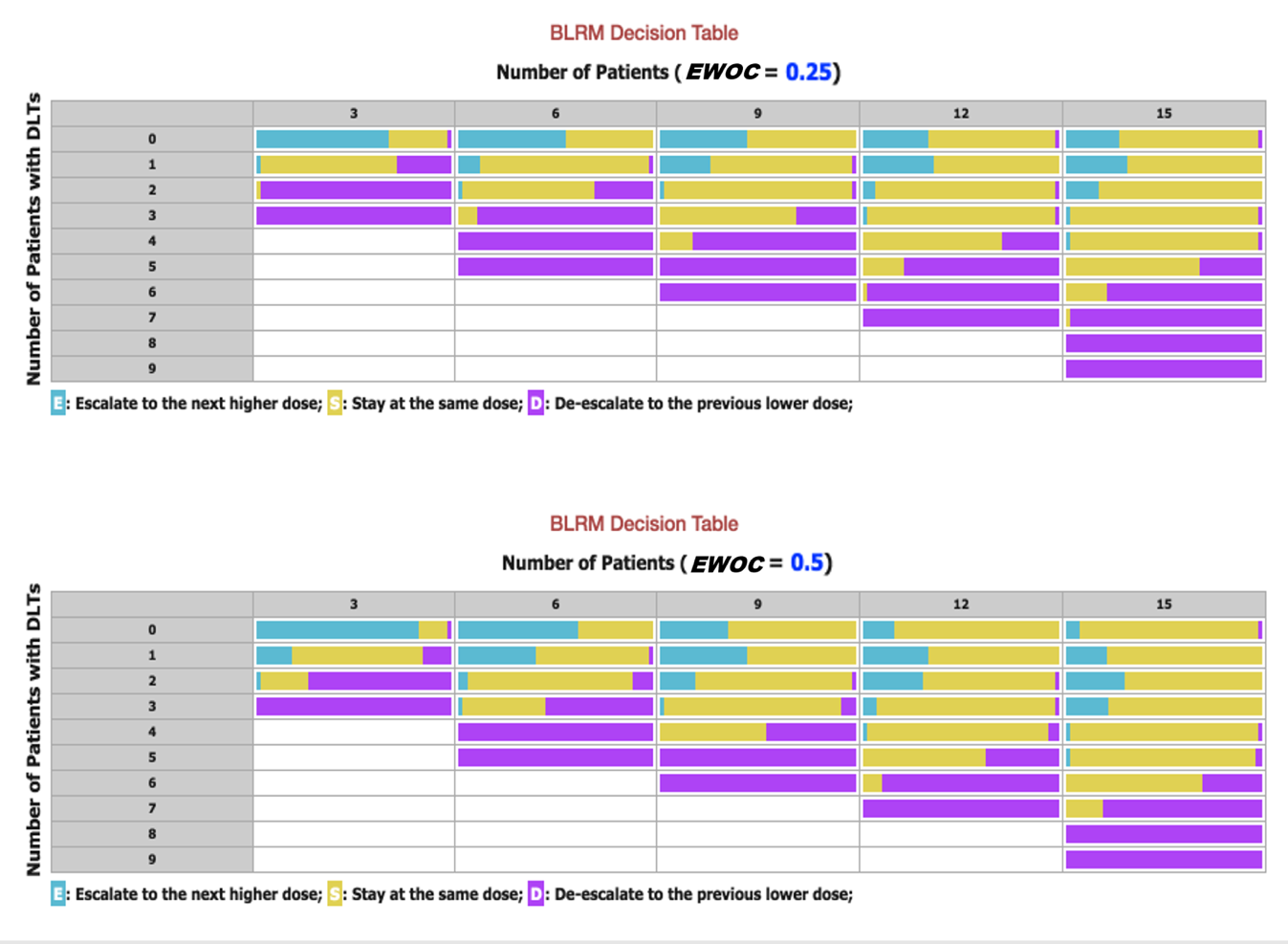


**Figure A1:** Comparison of the decision tables for i3+3, mTPI and mTPI-2. For each “Number of Patients” (column), there are three subcolumns listing the decisions of i3+3, mTPI, and mTPI-2 side-by-side corresponding to the “Number of DLTs” (row). Here, the target toxicity probability and EI (0.25, 0.35).

Other than the slightly different decision tables, all three designs use the same statistical models and inference to select the MTD. As the mTPI and mTPI-2 designs have been well established in the literature with desirable performance (Ji et al., 2010; Guo et al., 2017; Ji and Yang, 2018; Zhou et al, 2018), we decide not to conduct more and larger simulations. The i3+3 design is expected to perform at a similar level as the mTPI and mTPI-2 designs due to its similar but slightly improved decision table, which puts i3+3 in par with other major model-based designs.

While the decisions of the i3+3 design can be calculated and tabulated prior to the trial onset, the decisions of the model-based design such as CRM and BLRM require intensive computation and simulation to investigate. In particular, for each row and column in Figure A2, while the decision of i3+3 is fixed, that of CRM and BLRM is random and takes “D”, “S”, or “E” following a probability distribution. See Ji and Yang (2018) for a detailed discussion. To investigate the behavior of the CRM and BLRM designs, we summarize the empirical distribution of the random decisions by computing the frequencies of “D”, “S”, “E” for each column and row value given the observed toxicity data corresponding to the row and column numbers. The frequencies of the three decisions are plotted in terms of horizontal color bars shown in Figure A2, with the bar length proportional to the frequency.



****

**Figure A2**: Decision tables under the CRM and BLRM design for *pT = 0.3*. Each column represents *n* number of patients treated at the current dose and each row represents *x* number of patients with DLTs. For each entry, the decisions E, S, and D are colored blue, yellow, and purple, respectively. The length of the colored segments within each bar are proportional to the three proportions of the three decisions taken by CRM and BLRM for a given *(x; n)* data point from a simulation study using the 14 scenarios in Appendix B and 10,000 simulated trials per scenarios.

It can be seen from the table that more than half of the times the CRM design would stay, and about one fifth of the times the BLRM (with EWOC=0.5) design would de-escalate when 1 out of 3 patients experienced DLT at a given dose. When 3 out of 6 patients experienced DLT, about half of the times CRM and BLRM (with EWOC=0.5) would de-escalate but the other half of the times it would stay. These decisions may not pass safety review committees in real-world clinical trialsn real-world clinical trials.