Figure 1. Dose response curves for five scenarios

Chart, line chart

Description automatically generated

Dose response curves for toxicity (black), efficacy (blue), and utility (red). True MTD and MED are noted on two curves, respectively.

Table 1 Dose recommendation percentage of each dose level for 4 designs under 5 scenarios.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **S1: Extremely Good** | **Dose Level** | | | | | |
| **1** | **2** | **3** | **4** | **5** | None |
| Probability of DLT/NETS | 0.03 | 0.06 | 0.11 | 0.2 | 0.33 | NA |
| Probability of Efficacy | 0.08 | 0.3 | 0.68 | 0.91 | 0.98 | NA |
| Utility | -0.01 | 0.12 | 0.35 | 0.31 | -0.02 | NA |
| EWOC | 0.20 | 0.60 | 3.50 | 50.30 | 45.40 | 0.00 |
| EWOUC-NW | 0.00 | 0.90 | 49.60 | 47.30 | 0.80 | 1.40 |
| EWOUC-Comp | 0.00 | 1.40 | 91.90 | 6.10 | 0.10 | 0.50 |
| EWOUC-NETS-NW | 0.00 | 0.10 | 27.40 | 72..20 | 0.00 | 0.00 |
| EWOUC-NETS-Comp | 0.00 | 0.00 | 26.90 | 72.70 | 0.40 | 0.00 |
| **S2: Good** | **Dose Level** | | | | | |
| **1** | **2** | **3** | **4** | **5** | None |
| Probability of DLT/NETS | 0.03 | 0.07 | 0.16 | 0.33 | 0.56 | NA |
| Probability of Efficacy | 0.08 | 0.3 | 0.68 | 0.91 | 0.98 | NA |
| Utility | -0.01 | 0.08 | 0.18 | -0.09 | -0.69 | NA |
| EWOC | 0.40 | 1.80 | 29.00 | 64.80 | 4.00 | 0.00 |
| EWOUC-NW | 0.00 | 2.40 | 67.40 | 25.90 | 0.00 | 4.30 |
| EWOUC-Comp | 0.20 | 3.60 | 91.00 | 4.40 | 0.00 | 0.80 |
| EWOUC-NETS-NW | 0.00 | 1.20 | 54.70 | 44.10 | 0.00 | 0.00 |
| EWOUC-NETS-Comp | 0.00 | 0.00 | 56.80 | 43.20 | 0.00 | 0.00 |
| **S3: Moderate** | **Dose Level** | | | | | |
| **1** | **2** | **3** | **4** | **5** | None |
| Probability of DLT/NETS | 0.03 | 0.06 | 0.11 | 0.2 | 0.33 | NA |
| Probability of Efficacy | 0.08 | 0.16 | 0.3 | 0.49 | 0.68 | NA |
| Utility | －0.01 | 0.01 | 0.09 | 0.19 | －0.31 | NA |
| EWOC | 0.10 | 0.20 | 0.10 | 26.00 | 73.60 | 0.00 |
| EWOUC-NW | 0.00 | 0.00 | 3.40 | 54.90 | 40.60 | 1.10 |
| EWOUC-Comp | 0.00 | 0.10 | 28.50 | 67.90 | 2.60 | 0.90 |
| EWOUC-NETS-NW | 0.00 | 0.00 | 11.70 | 83.70 | 4.60 | 0.00 |
| EWOUC-NETS-Comp | 0.00 | 0.00 | 11.70 | 83.00 | 5.30 | 0.00 |
| **S4: Bad** | **Dose Level** | | | | | |
| **1** | 2 | **3** | **4** | **5** | None |
| Probability of DLT/NETS | 0.03 | 0.33 | 0.89 | 0.99 | 1 | NA |
| Probability of Efficacy | 0.08 | 0.13 | 0.2 | 0.3 | 0.42 | NA |
| Utility | -0.01 | -0.87 | -2.47 | -2.68 | -2.58 | NA |
| EWOC | 53.00 | 43.30 | 3.70 | 0.00 | 0.00 | 0.00 |
| EWOUC-NW | 0.30 | 0.60 | 0.00 | 0.00 | 0.00 | 99.10 |
| EWOUC-Comp | 0.40 | 3.70 | 0.10 | 0.00 | 0.00 | 95.80 |
| EWOUC-NETS-NW | 1.30 | 6.00 | 0.10 | 0.00 | 0.00 | 92.60 |
| EWOUC-NETS-Comp | 1.30 | 6.30 | 0.10 | 0.00 | 0.00 | 92.30 |
| **S5: Extremely Bad** | **Dose Level** | | | | | |
| **1** | **2** | **3** | **4** | **5** | None |
| Probability of DLT/NETS | 0.03 | 0.33 | 0.89 | 0.99 | 1 | NA |
| Probability of Efficacy | 0.08 | 0.11 | 0.16 | 0.22 | 0.3 | NA |
| Utility | -0.01 | -0.88 | -2.51 | -2.75 | -2.7 | NA |
| EWOC | 53.40 | 42.70 | 3.90 | 0.00 | 0.00 | 0.00 |
| EWOUC-NW | 0.10 | 0.40 | 0.10 | 0.00 | 0.00 | 99.40 |
| EWOUC-Comp | 0.10 | 1.60 | 0.20 | 0.00 | 0.00 | 98.10 |
| EWOUC-NETS-NW | 1.20 | 6.50 | 0.10 | 0.00 | 0.00 | 92.30 |
| EWOUC-NETS-Comp | 1.30 | 6.30 | 0.10 | 0.00 | 0.00 | 92.40 |

Table 2. Toxicity and expected utility under each design for the 5 scenarios

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Scenario of Drug Characteristic | DLT | | | |  | Expected utility | | | |  |
| EWOC | EWOUC-Comp | EWOUC-NW | EWOUC-NETS-Comp | EWOUC-NETS-NW | EWOC | EWOUC-Comp | EWOUC-NW | EWOUC-NETS-Comp | EWOUC-NETS-NW |
| S1: Extremely Good | 0.17 | 0.10 | 0.15 | 0.04 | 0.04 | 0.21 | 0.28 | 0.26 | 0.63 | 0.12 |
| S2: Good | 0.21 | 0.14 | 0.21 | 0.21 | 0.21 | 0.03 | 0.14 | 0.04 | 0.45 | -0.20 |
| S3: Moderate | 0.16 | 0.08 | 0.15 | 0.05 | 0.05 | -0.04 | 0.10 | -0.00 | 0.21 | -0.04 |
| S4: Bad | 0.22 | 0.32 | 0.32 | 0.39 | 0.40 | -0.54 | -0.84 | -0.86 | -0.34 | -1.03 |
| S5: Extremely Bad | 0.21 | 0.32 | 0.32 | 0.39 | 0.40 | -0.54 | -0.85 | -0.86 | -0.36 | -1.04 |

Table 3. Percentage of patients treated at each dose level for the 4 designs under 5 scenarios

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **S1: Extremely Good** | **Dose Level** | | | | |
| **1** | **2** | **3** | **4** | **5** |
| EWOC | 8.80 | 11.96 | 20.83 | 40.46 | 17.95 |
| EWOUC-NW | 8.59 | 10.86 | 28.94 | 46.36 | 5.26 |
| EWOUC-Comp | 8.70 | 13.32 | 73.01 | 4.95 | 0.03 |
| EWOUC-NETS-NW | 8.33 | 8.49 | 31.47 | 51.57 | 0.14 |
| EWOUC-NETS-Comp | 8.33 | 8.44 | 31.27 | 51.78 | 0.18 |
| **S2: Good** | **Dose Level** | | | | |
| **1** | **2** | **3** | 4 | **5** |
| EWOC | 9.15 | 14.82 | 35.64 | 37.71 | 2.68 |
| EWOUC-NW | 8.75 | 12.21 | 38.76 | 38.88 | 1.41 |
| EWOUC-Comp | 9.06 | 16.29 | 70.81 | 3.84 | 0.00 |
| EWOUC-NETS-NW | 8.33 | 8.60 | 42.90 | 40.17 | 0.00 |
| EWOUC-NETS-Comp | 8.33 | 8.43 | 43.78 | 39.46 | 0.00 |
| **S3: Moderate** | **Dose Level** | | | | |
| **1** | **2** | **3** | **4** | **5** |
| EWOC | 8.62 | 10.00 | 11.37 | 33.51 | 36.51 |
| EWOUC-NW | 8.48 | 10.67 | 12.07 | 40.17 | 28.62 |
| EWOUC-Comp | 8.53 | 10.52 | 29.43 | 47.73 | 3.78 |
| EWOUC-NETS-NW | 8.33 | 8.44 | 24.86 | 57.18 | 1.20 |
| EWOUC-NETS-Comp | 8.33 | 8.47 | 24.63 | 57.36 | 1.22 |
| **S4: Bad** | **Dose Level** | | | | |
| **1** | **2** | **3** | **4** | **5** |
| EWOC | 47.42 | 47.75 | 4.83 | 0.00 | 0.00 |
| EWOUC-NW | 30.07 | 54.47 | 15.44 | 0.02 | 0.00 |
| EWOUC-Comp | 29.20 | 56.68 | 14.13 | 0.00 | 0.00 |
| EWOUC-NETS-NW | 26.56 | 68.30 | 5.14 | 0.00 | 0.00 |
| EWOUC-NETS-Comp | 26.05 | 68.77 | 5.18 | 0.00 | 0.00 |
| **S5: Extremely Bad** | **Dose Level** | | | | |
| **1** | **2** | **3** | **4** | **5** |
| EWOC | 48.18 | 47.02 | 4.80 | 0.00 | 0.00 |
| EWOUC-NW | 30.82 | 53.78 | 15.40 | 0.00 | 0.00 |
| EWOUC-Comp | 30.30 | 55.61 | 14.09 | 0.00 | 0.00 |
| EWOUC-NETS-NW | 26.57 | 68.40 | 5.03 | 0.00 | 0.00 |
| EWOUC-NETS-Comp | 26.28 | 68.66 | 5.06 | 0.00 | 0.00 |

Table 4. Expected time for a trial (months) under different assessment time periods and mean inter-cohort arrival times for 12 cohorts under scenario 1

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Mean Inter-arrival time (Month) | Assessment Period (Month) | EWOC-NETS-Comp (Month) | EWOUC-NETS-NW (Month) | Change |
| 0.25 | 3 | 28.05 | 5.99 | -78.65% |
| 0.5 | 3 | 28.27 | 8.98 | -68.23% |
| 1 | 3 | 28.36 | 14.96 | -47.25% |
| 2 | 3 | 34.65 | 26.92 | -22.31% |
| 3 | 3 | 42.37 | 38.88 | -8.24% |