## Melphalan PK-PD Model – Variable Descriptions

**Continuous Covariates**

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| --- | --- | --- | --- | --- | --- |
| **Abbreviation** | **Description** | **Units** | **Lower Limit** | **Upper Limit** | **Range** |
| BSA | Body surface area | m2 |  |  | 1.37-2.50 |
| CRCL | Creatinine clearance | mL/min |  |  | 5.34-195.98 |
| FFM | Fat free mass | kg |  |  | 31.30-81.90 |
| HCT | Haematocrit | % |  |  | 20.6-44.6 |
| BUN | Blood urea nitrogen | mg/dL |  |  | 5-59 |
| ANCBASE | Baseline absolute neutrophil count | K/µL |  |  | 0.7-13.8 |
| WBC | White blood cell count | K/µL |  |  | 1.7-18.3 |
| LNP53FOLD | Log transformed data of p53 mRNA expression level change in PBMCs after treating 75ug/ml melphalan *ex vivo* versus baseline level | No unit |  |  | 0.3-42.9 |

Other questions:

What are some plausible lower and upper limits for the above? i.e., based on your patient population (that you have data for) but also the general patient population?

* I ask so that I can attached limits to the application’s widgets – i.e., sliders or numerical input so that implausible combinations of values can not be used to simulate PK-PD profiles.

How was fat free mass calculated?

|  |  |
| --- | --- |
| FFM Calculation | |
| Male | 9270\*Weight/(6680+(216\*BMI)) |
| Female | 9270\*Weight/(8780+(244\*BMI)) |

How was creatinine clearance calculated?

* From the Cockcroft-Gault equation? YES
* Did you use fat free mass or ideal body weight in the equation? We chose TBW instead of IBW
* Would you like sliders for each of it’s elements? i.e., age, serum creatinine, height, etc.?

|  |
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| Cockcroft and Gault equation using Total bodyweight: |
| CrCl = [(140 - age) x TBW] / (Scr x 72) (x 0.85 for females) |

**Categorical Covariates**

|  |  |  |  |
| --- | --- | --- | --- |
| **Abbreviation** | **Description** | **0** | **1** |
| SEX | Gender | Female | Male |
| SLC7A5 | Drug Transporter Genotype (Solute Carrier Family 7 (Amino Acid Transporter Light Chain, L System), Member 5) | AA or AG | GG |
| G-CSF | Granulocyte Colony Stimulating Factor – Filgrastim (Neupogen®) | Started on Day 1 | Started on Day 7 |

**Infusion Guidelines**

What are the guidelines around the melphalan infusion? 30 min iv infusion was scheduled ideally.

Based on the dataset, everyone has very different infusion rates. When I go to calculate the infusion duration, it varies quite a bit between half an hour to 1 hour.

Would it be best to have a slider for infusion duration if it varies between individuals and doses?