**Background and importance**

**Busulfan** is a chemotherapeutic drug commonly used in preparative regimens for hematopoietic stem-cell transplantation in adults and children or a variety of malignant and non-malignant diseases. Its efficacy and safety could be affected by its narrow therapeutic margin and its great pharmacokinetic variability.

**Aim and objectives**

Quantifying the adjustments magnitude of busulfan dose made in our cohort of patients in the last ten years.

**Materials and methods**

- **Different types of variables were recorded**
  - **Demographic:** age, sex, weight, baseline disease
  - **Treatment:** type of conditioning protocol, dose by weight
  - **Drug monitoring:** need for dose modification, number of adjustments, percentage of variation between received dose and theoretical dose

- **Pharmacokinetic studies**
  - **Method:** non-linear regression with ID3 software
  - **Area under the curve target:** 55000-95000 ng/ml·h (depending on exposure target: reduced intensity or myeloablative conditioning).

**Results**

We included **45 patients** with **median age 3 years old** (range: 4 month to 16 years). In 43 cases transplantations were **allogeneic** and two of them were autologous. Baseline diseases in the allogeneic group were **23 malignant and 20 non-malignant haematological diseases** while in the autologous group were two neuroblastomas. Conditioning regimens were: **38/45 myeloablative** and **7/45 non-myeloablative**.

Busulfan initial doses ranged from **3.2 to 5.1 mg/kg/day** (related to adjusted body weight), according to the protocol and the weight band. All patients received seizures prophylaxis with phenytoin.

<table>
<thead>
<tr>
<th>Patients with dose variation</th>
<th>MYELOABLATIVE (N=39)</th>
<th>NON-MYELOABLATIVE (N=6)</th>
<th>GLOBAL (N=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose reductions</td>
<td>33</td>
<td>6</td>
<td>39</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>-7.5% (-15.1 to -4.2%)</td>
<td>-6.8% (-10.6 to -3.8%)</td>
<td>-7.1% (-15.0 to -4.0%)</td>
</tr>
<tr>
<td>Dose Increases</td>
<td>12</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>11.4% (9.1 to 17.5%)</td>
<td>10.7% (9.3 to 11.7%)</td>
<td>11.4% (8.9 to 14.8%)</td>
</tr>
</tbody>
</table>

**Eight patients presented implant failure** (seven with secondary failure). Five of them had received myeloablative conditioning.

**Four patients presented sinusoidal obstruction syndrome**, all of them had received myeloablative conditioning.

**Conclusion and relevance**

This data shows that therapeutic drug monitoring of busulfan is an essential tool that helps improving its efficacy and safety. We have observed a high variability in the direction and magnitude of dose adjustments made to optimize the exposure.