Monoclonal antibodies’ handling: toxicological evaluation and survey of practices in Swiss hospitals

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BACKGROUND
Monoclonal antibodies (Mabs) are often used at Geneva University Hospital (HUG). Risks taken by the handler when preparing or administering these new therapeutic agents with complex mechanisms of action are often unknown and clear official information is missing. We performed a study to evaluate how Mabs are manipulated in Swiss hospitals and to determine the toxicity related to Mabs for the handler.

OBJECTIVES
- Survey of practices of Mabs’ handling in Swiss hospitals
- Evaluation of nurses’ perception of the toxicity related to Mabs’ handling in HUG wards
- Toxicological evaluation and risk classification of Mabs

DESIGN
- Standardised questionnaires to 43 Swiss hospitals chief-pharmacists
- Semi-structured interviews of 9 nurses using frequently Mabs in their wards
- Based on literature review and recommended protective measures for the handling, a classification of 15 Mabs in 4 toxicity classes was performed by a pharmacist and a toxicologist (Fig. 1 & 2)

RESULTS
- Practices in Swiss hospitals:
  - Twelve of 43 (28%) of Swiss hospital pharmacies answered the questionnaire
  - Preparation of Mabs with oncological indications is centralized at the pharmacy in 5 (42%) hospitals. In only 1 hospital all Mabs are prepared by the pharmacy
  - Recommendations for transport or waste management differ among hospitals
  - Regular handlers’ medical examination is performed in only 25% of the hospitals
- Nurses interviews in wards using Mabs: (Tab. 1)
  - Four of 9 nurses (44%) considered Mabs as hazardous drugs (cited eg 3x rituximab, 2x trastuzumab, 1x adalimumab, 1x infliximab, 1x palivizumab)
  - Only 1 ward used rigid containers for hazardous drugs for Mabs’ waste management
  - Estimation of number of manipulations by nurses was less than 3/week/nurse in 6 (56%) wards and between 3 and 5 in 2 (22%) wards
- Toxicological evaluation and protective measures to be recommended at HUG: (Tab. 2)
  - Gemtuzumab-ozogamicin was associated with the highest handling risk (class 1), followed by cetuximab, bevacizumab, alemtuzumab and rituximab (class 2) and then infliximab (class 3). For all other Mabs, no protective measures are recommended (class 4)

CONCLUSIONS
This study highlights the lack of standardized practice in the handling of Mabs in Swiss hospitals. Mabs with oncological indications are perceived by nurses at a higher risk than other Mabs, and most of them (exception: trastuzumab) were effectively associated with some degree of potential toxicity in our evaluation. Recommendations for the Mabs’ handling should be implemented based on documented toxicological data.

This study is the first part of a major toxicological evaluation of potentially hazardous drugs in order to develop institutional protective guidelines for transport, preparation and administration of these drugs.

Table 1: Sample of nurses interview
<table>
<thead>
<tr>
<th>Wards</th>
<th>Drugs regarded as dangerous by nurses</th>
<th>Protection measures in wards</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>Rituximab, Infliximab</td>
<td>Yes</td>
</tr>
<tr>
<td>RB</td>
<td>Abciximab</td>
<td>Yes</td>
</tr>
<tr>
<td>GC</td>
<td>Rituximab, Cetuximab, Gemtuzumab-ozogamicin, Trastuzumab</td>
<td>Yes</td>
</tr>
<tr>
<td>SC</td>
<td>Siltuximab</td>
<td>Yes</td>
</tr>
<tr>
<td>VC</td>
<td>Alemtuzumab</td>
<td>Yes</td>
</tr>
<tr>
<td>FG</td>
<td>Rituximab, Trastuzumab</td>
<td>Yes</td>
</tr>
<tr>
<td>HH</td>
<td>Rituximab, Cetuximab, Alemtuzumab</td>
<td>Yes</td>
</tr>
<tr>
<td>1</td>
<td>Alemtuzumab</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Table 2: Mabs toxicological classification

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