Chemotherapy and surgery achieve a 5-year event-free survival of 60-70% in localized osteosarcoma (OS). Little additional progress has been made since the 1980s (Figure).

- Few RCTs with a survival endpoint in localized OS are ongoing (Map). No trial in Europe or North-America.
- Clinical research in OS is hampered by a limited pipeline of new agents.
- Drug repurposing, an alternative development pathway that seeks to reuse existing drugs as the source of new treatment options, represents an interesting opportunity to solve this issue.
- Repurposing benefits from existing data on safety, dosing and clinical use.
- As of 22 May 2018, the Repurposing Drugs in Oncology – ReDO – project (Pantziarka 2014) has found 255 non-cancer drugs supported by evidence for use in cancer.

Objectives & Methods

- Objective: Estimate the number of OS repurposing opportunities of non-cancer drugs.
- Methods:
  - We started from our ReDO list of 255 non-cancer drugs with at least one peer-reviewed article showing an anticancer effect in vitro, in vivo or human trials.
  - We queried PubMed for each drug and the terms "osteosarcoma" and screened titles in search of articles reporting activity of the drug against OS. If at least one paper reported in vitro, in vivo or human data, it was considered positive. For a given drug, if all articles were about the management of disease-related or treatment-induced symptoms, it was not considered positive (e.g. antidepressant, anti-emetics).

Results

- Of the 255 ReDO drugs, 75 (29%) had at least one article reporting in vitro, in vivo or in human activity against OS.
- We have not yet fully quantified the number of repurposing opportunities of drugs approved for other cancers, which also represents an interesting source of interventions for future trials. We currently have found 12 of them.
- Combining both ReDO and non-OS cancer drugs, we selected drug candidates and grouped them according to their mechanisms of action (Table 1).

Conclusion

- The number of opportunities to repurpose non-cancer drugs in osteosarcoma is large. Adding cancer drugs to this list improves the number of candidates even further.
- Making an objective selection is difficult because of the volume and heterogeneous quality of the data. Only 2 drugs (neoadjuvant lithium & neoadjuvant zoledronic acid) are currently being tested in RCTs in localized OS.
- We have presented several other drugs that have a good rationale to be trialed in OS.
- Implementing the infrastructure for a multi-arm multi-stage platform trial would be a great service to patients. An independent drug selection committee could assess drug candidates supported by human and/or in vivo evidence and make recommendations if additional evidence is needed. We are currently looking for expression of interest to participate in (clinicians, researchers, patients advocates and fund (governments, philanthropic organizations) this effort.

Table 1: Selection of drugs grouped by their main mechanism of action & type of evidence for repurposing in OS

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Mechanism of Action</th>
<th>Type of evidence</th>
<th>MainReference(s)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>DNA alkylating</td>
<td>Case report</td>
<td>Zhou Cancer 2017</td>
<td>Also immune modulation</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>DNA alkylating</td>
<td>Case report</td>
<td>Zhou Cancer 2017</td>
<td>Also immune modulation</td>
</tr>
</tbody>
</table>

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