Impact of muscle loss and sarcopenia on dose limiting toxicities in metastatic colorectal cancer patients receiving palliative systemic treatment

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Abstract #2-42

Introduction

- Evidence on the link between skeletal muscle (SM) depletion and poor outcome in metastatic cancer patients is increasing.
- We recently found, using data of the randomized phase 3 CAIRO3 study1, that SM loss was significantly related to shorter overall survival (OS) (Table 2).

Aim

As a potential risk factor for reduced survival we explored whether muscle loss was associated with dose limiting toxicities (DLT) during palliative systemic treatment.

Methods

- Secondary analysis of the randomized phase 3 CAIRO3 study2 (Figure 1).
- DLT = dose delay, reduction, or discontinuation of systemic treatment because of reported CTCAE (v3.0) toxicities.
- The association between DLT, sarcopenia and muscle loss was studied within periods with available data on DLT (Figure 1).

Skeletal muscle analysis

- 1355 CT scans of 450 pts were analyzed for skeletal muscle by Slice-o-matic (Tomovision, version 5.0) at the L3 level using thresholds in Hounsfield Units (-150; -29).
- Per patient, repeated CT-scan were rotated and fused with a rigid fusion method (MeVisLab, version 2.7.1) and L3 as a bony landmark to reduce measurement errors due to variation in the positioning of patients over time.
- Skeletal muscle index (SMI) = skeletal muscle area (cm²) adjusted for height (m²).
- Sarcopenia was determined by applying published cut off points3 (Table 2).

Patient characteristics total group (Table 1)

<table>
<thead>
<tr>
<th></th>
<th>Sarcopenia at randomization</th>
<th>Non sarcopenic at randomization</th>
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<tbody>
<tr>
<td>Age, mean in years (±SD)</td>
<td>64.2 ±9</td>
<td>63.1 ±8</td>
</tr>
<tr>
<td>Male, %</td>
<td>59</td>
<td>68</td>
</tr>
<tr>
<td>BMI, mean (±SD)</td>
<td>25.0 ±3.9</td>
<td>26.6 ±2.4</td>
</tr>
<tr>
<td>WHO performance score, %</td>
<td>60 / 40</td>
<td>62 / 38</td>
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<tr>
<td>Treatment arm after randomization, %</td>
<td>49 / 51</td>
<td>51 / 49</td>
</tr>
<tr>
<td>Reintroduction treatment, %</td>
<td>57 / 43</td>
<td>58 / 42</td>
</tr>
</tbody>
</table>

Primary endpoint

- Sarcopenia at randomization: Time to PD1, Time to PD2, Time to death
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- SM loss during ∆ SMI per 2 units: Time to PD1, Time to PD2, Time to death
- SM loss during ∆ SMI per 2 units: Time to PD1, Time to PD2, Time to death

Dose limiting toxicities during systemic treatment (Figure 2)

- Sarcopenia at randomization: Risk ratio (RR) determined by Cox models adjusted for age, sex, WHO PS, stage, primary tumor site, resection primary tumor, response to induction treatment, LDH at randomization, synchronous vs metachronous mCRC, dose reduction during induction treatment. Sarcopenia males SM <43 if BMI ≥25 or BMI <30 if BMI ≥25, females SM <41 any BMI. NA = not applicable. * indicate statistically significant RR.

In blue: time periods with available data on dose limiting toxicities

In blue: time periods with available data on dose limiting toxicities

Conclusions

- In metastatic colorectal cancer patients during palliative systemic treatment, sarcopenia and/or muscle loss is associated with an increased risk of experiencing dose limiting toxicities, which may contribute to the worse survival in this group of patients.
- These data suggest that skeletal muscle preservation may be a therapeutic goal.

References


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