HOW TO DEAL WITH ELDERLY AND FRAIL PATIENTS OR INDIVIDUALS WITH COMORBIDITIES

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DISCLOSURE OF INTEREST

• Personal financial interests, honoraria for advisory role, travel grants, research grants (past 5 years): Hoffman La-Roche, Sanofi Aventis, Amgen, Merck Serono, Servier, MSD, Array Pharmaceuticals, Bristol-Myers Squibb, Pierre-Fabre

• Institutional financial interests, my institution received honoraria due to my investigator contribution in clinical trials from: Hoffman La-Roche, Sanofi Aventis, Amgen, Merck Serono, MSD, Boehringer Ingelheim, AbbVie, Array Pharmaceuticals, Pierre-Fabre, Novartis, Bristol-Myers Squibb, GlaxoSmithKline, Medimmune, Pierre-Fabre
A MATTER OF INTEREST?
SOME STATS

- Median age at diagnosis of CRC is 72 years old (~60% of patients are >70, 43% >75 and 28% >80 years)
- Considering the trend of increased life expectancy, it is expected that the number of elderly patients with CRC will also increase
SOME FACTS

• The representation of patients over 70 years old in clinical trials is low. There is a lack of generalizability of existing clinical trial data to the general older patient.

• Older patients are less likely to be properly assessed and treated on an evidence-based setting:
  • The referral of older patients for consideration of cancer treatment as well as their inclusion in multidisciplinary meetings is limited.
  • Factors such as increased co-morbidities and impaired organ function are quite often put forward as arguments for low rates of specialist referral.
LET’S START BY THE BASIS...
DEFINING THE ELDERLY

- There is no universally accepted age cut-off defining “elderly.”
- This reflects the fact that chronological age itself is less important than biological events in driving the ageing process within an individual.
- However, chronological age is a simple and practical way of defining a target population, and 70 years is currently the most commonly used cut-off for defining patients as elderly within the field of geriatric oncology.

AGEING PATHOLOGY + DISABILITY

SUCCEFUL AGEING WITH MINIMAL DISABILITY

NORMAL AGEING + SOME DISABILITY
Patients need individualized assessments to determine their biological age.

Biological age is believed to reflect a person’s remaining life expectancy and functional reserves, and will influence treatment decisions and predict treatment tolerance.

Limited by time, resources and lack of expert interpretation. One of the best clinical tools available to date is the comprehensive geriatric assessment.
44 studies reporting on the use of 17 different ST in older cancer patients.

The validity of most tools was tested against a multidimensional assessment with geriatric instruments, or an assessment by a geriatrician. G8 is one with the highest sensitivity.

None of these tools are very specific and, therefore, if positive, they need to be supplemented by a more complete GA. However, they can help to focus geriatric resources towards those patients who need them most.
### G8 Geriatric Assessment Tool - EORTC

<table>
<thead>
<tr>
<th>Item</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?</td>
<td>0= severe decrease in food intake 1= moderate decrease in food intake 2= no decrease in food</td>
</tr>
<tr>
<td>Weight loss during the last 3 months?</td>
<td>0= weight loss &gt; 3 kg 1= does not know 2= weight loss between 1 and 3 kg 3= no weight loss</td>
</tr>
<tr>
<td>Mobility?</td>
<td>0= bed or chair bound 1= able to get out of bed/chair but does not go out 2= goes out</td>
</tr>
<tr>
<td>Neuropsychological problems?</td>
<td>0= severe dementia or depression 1= mild dementia 2= no psychological problems</td>
</tr>
<tr>
<td>Body mass index?</td>
<td>0= BMI &lt; 19 1= BMI 19 to &lt; 21 2= BMI 21 to &lt; 23 3= BMI &gt; 23</td>
</tr>
<tr>
<td>Takes more than three prescription drugs per day?</td>
<td>0= yes 1= no</td>
</tr>
<tr>
<td>In comparison with other people of the same age, how does the patient consider his/her health status?</td>
<td>0= not as good 0.5= does not know 1= as good 2= better</td>
</tr>
<tr>
<td>Age</td>
<td>0= &gt; 85 1= 80-85 2= &lt; 80</td>
</tr>
</tbody>
</table>

**Total score: 17**  
**Cut off ≤ 14**
CRC IN THE ELDERLY: MANAGEMENT
MULTIDISCIPLINARY MANAGEMENT

ESMO/SIOG Cancer in the Elderly Working Group

The goal of the joint Working Group on Cancer in the Elderly is to promote education in cancer topics specific to this population.

The Cancer in the Elderly Working Group is a joint venture between ESMO and the International Society of Geriatric Oncology (SIOG) created in 2019.

Activities and responsibilities

- To improve management of the elderly cancer patients
- To better educate oncology professionals in issues related to elderly cancer patients
- To raise awareness on specific needs and requirements related to the management of the elderly patients with cancer

Chairs

- Demetris Papamichael, Cyprus (ESMO)
- Etienne Brain, France (SIOG)

Committee Members

- Capucine Baldini, France (SIOG)
- Laura Bignozzi, Italy (ESMO)
- Valentin Goede, Germany (SIOG)
- Ravindran Kanesvaran, Singapore (ESMO)
- Elisabeth Quoix, France (ESMO)
- Siri Rostoft, Norway (SIOG)
- Christopher Steer, Australia (ESMO)
- Hans Wildiers, Belgium (SIOG)

Treatment of colorectal cancer in older patients: International Society of Geriatric Oncology (SIOG) consensus recommendations 2013

Table 1. Treatment considerations for older patients with CRC

<table>
<thead>
<tr>
<th>Outcomes that need to be considered in relation to surgery</th>
<th>Outcomes that need to be considered in relation to chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Immediate postoperative morbidity</td>
<td>1) Toxicity (which can be divided into numerous subcategories)</td>
</tr>
<tr>
<td>2) Thirty-day postoperative morbidity and mortality</td>
<td>2) Completion of therapy</td>
</tr>
<tr>
<td>3) Length of stay</td>
<td>3) QoL</td>
</tr>
<tr>
<td>4) Discharge to nursing home</td>
<td>4) Functional status</td>
</tr>
<tr>
<td>5) One-year mortality</td>
<td>5) Progression</td>
</tr>
<tr>
<td>6) Short-term and long-term functional outcomes</td>
<td>6) Survival</td>
</tr>
<tr>
<td>7) QoL (short and long term)</td>
<td>7) Composite end points (overall treatment utility)</td>
</tr>
<tr>
<td>8) Survival</td>
<td></td>
</tr>
</tbody>
</table>

QoL, quality of life; CRC, colorectal cancer.
FIRST DECISION:
Fit older patients should be treated with systemic combination chemotherapy plus targeted agents as they derive the same benefit as younger patients (Balance OS-QoL?)

RESECTABLE DISEASE:
- To consider regardless of age
- Even though higher morbidity, the benefit of long term outcomes appears to be similar to their younger counterparts.
- Patients considered unfit for major surgery should be considered for alternative procedures
AVEX STUDY

Bevacizumab plus capecitabine versus capecitabine alone in elderly patients with previously untreated metastatic colorectal cancer (AVEX): an open-label, randomised phase 3 trial

280 patients enrolled and randomly assigned

140 allocated to bevacizumab plus capecitabine
134 received allocated treatment
6 did not receive allocated treatment

131 discontinued intervention
68 disease progression
23 adverse event
19 withdrew consent
8 deaths
7 at discretion of investigator
3 protocol violations
4 other reasons
3 remained on intervention
0 lost to follow-up

140 in intention-to-treat population
134 in safety population

140 allocated to capecitabine
136 received allocated treatment
4 did not receive allocated treatment

133 discontinued intervention
88 disease progression
13 adverse event
9 withdrew consent
12 deaths
3 at discretion of investigator
3 protocol violations
5 other reasons
1 remained on intervention
2 lost to follow-up

140 in intention-to-treat population
136 in safety population

Cunningham et al. Lancet Oncol 2013
The addition of Bevacizumab to single agent capecitabine achieved encouraging results with a significant PFS improvement over single agent capecitabine (9.1 vs. 5.1 months, \( P < .0001 \)) (20.7 vs. 16.8 months, \( P < .18 \)).

Cunningham et al, Lancet Oncology (2013)
Cetuximab in combination with FOLFIRI or FOLFOX, may provide a PFS and OS benefit in patients over 70 as well.

Panitumumab has demonstrated to be well tolerated in monotherapy in the Frail study.

Data for the use of newer agents like aflibercept, ramucirumab, TAS102 and regorafenib in older patients are still limited but several studies are on going.

**ANTI-EGFR AGENTS**

<table>
<thead>
<tr>
<th>Trial/treatment</th>
<th>Age (years)</th>
<th>N</th>
<th>Median PFS (95% CI) (months)</th>
<th>Median OS (95% CI) (months)</th>
<th>PFS HR (95% CI)</th>
<th>OS HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sastre et al.</td>
<td>≥70</td>
<td>41</td>
<td>2.9</td>
<td>11.1</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Sastre et al.</td>
<td>≥70</td>
<td>66</td>
<td>7.1 (5.3–8.4)</td>
<td>16.1 (12.0–18.8)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Polprecht et al.</td>
<td>&lt;70</td>
<td>700</td>
<td>Cet + CT: 9.0–11.5</td>
<td>Cet + CT: 23.6 (20.7–26.8)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Jonker et al.</td>
<td>≥70</td>
<td>145</td>
<td>Cet + BSC: 1.9</td>
<td>Cet + BSC: 6.1</td>
<td>0.68 (0.57–0.80)</td>
<td>0.64 (0.57–0.80)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Age <65/≥65 years was shown not to be associated with OS (P = 0.13) [109].
BSC, best standard of care; cet, cetuximab; CI, confidence interval; CT, chemotherapy; HR, hazard ratio; PFS, progression-free survival; NA, not available; OS, overall survival.

SUMMARY AND CONCLUSIONS
SUMMARY AND CONCLUSIONS

• Age is the first step to individualize treatment

• A collaboration of oncologists and geriatricians strengthened in a multidisciplinary consultation will ensure the optimal care of these patients

• The treatment challenges presented by older patients with CRC make it important to use some form of GA to inform our clinical decision making

• Investigators should be encouraged to design patient-centered assessments to expand the evidence base in the treatment of older patients with CRC

• Treatments must be targeted and adapted according to age and associated co-morbidities
THANK YOU!

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