Asian perspective: the JCOG initiative

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There are no financial relationships to disclose
Life Expectancy in Japan

<table>
<thead>
<tr>
<th>Year</th>
<th>Male</th>
<th>Female</th>
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<tbody>
<tr>
<td>1955</td>
<td>63.60</td>
<td>67.75</td>
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<tr>
<td>1960</td>
<td>65.32</td>
<td>70.19</td>
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<tr>
<td>1965</td>
<td>67.74</td>
<td>72.92</td>
</tr>
<tr>
<td>1970</td>
<td>69.31</td>
<td>74.66</td>
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<tr>
<td>1975</td>
<td>71.73</td>
<td>76.89</td>
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<tr>
<td>1980</td>
<td>73.35</td>
<td>78.76</td>
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<td>1985</td>
<td>74.78</td>
<td>80.48</td>
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<td>1990</td>
<td>75.92</td>
<td>81.90</td>
</tr>
<tr>
<td>1995</td>
<td>76.38</td>
<td>82.85</td>
</tr>
<tr>
<td>2000</td>
<td>77.72</td>
<td>84.60</td>
</tr>
<tr>
<td>2005</td>
<td>78.56</td>
<td>85.52</td>
</tr>
<tr>
<td>2010</td>
<td>79.55</td>
<td>86.30</td>
</tr>
<tr>
<td>2015</td>
<td>80.75</td>
<td>86.99</td>
</tr>
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</table>
Causes of death in Japan

Cancer
Heart disease
CVD
Pneumonia

VITAL STATISTICS OF JAPAN 2018
The lack of reliable evidences

- Older pts tend to be excluded in clinical trials
  - High incidence of organ dysfunction and co-morbidities
  - The high risk of death from other causes

Geriatric research methodologies have not been established

- Clinical research focused on older pts with cancer is urgently needed...
Japan Clinical Oncology Group (JCOG)

- **The largest cooperative group in Japan**
  - Primarily funded and headquartered by National Cancer Center and the Japanese national funding agency
  - Multi-disease, Multi-disciplinary treatment
  - Multi-center phase II / phase III trials

- **MISSION of JCOG**
  - To establish effective standard treatments for various types of cancers by conducting nationwide multicenter clinical trials
## JCOG geriatric research; 1st generation

<table>
<thead>
<tr>
<th>Trial name</th>
<th>Group</th>
<th>Subject</th>
<th>Age</th>
<th>Standard treatment</th>
<th>Test treatment</th>
<th>Primary endpoint</th>
<th>Status</th>
<th>Publication</th>
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<tbody>
<tr>
<td>JCOG9203</td>
<td>Lymphoma</td>
<td>NHL</td>
<td>70-75</td>
<td>--</td>
<td>VEPA&amp;FEPP</td>
<td>CR rate</td>
<td>Completed</td>
<td>Int J Hematol 2006</td>
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<td>JCOG9702</td>
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<td>SCLC PS0-2</td>
<td>≥ 70</td>
<td>CBDCA + VP-16</td>
<td>CDDP + VP-16</td>
<td>OS</td>
<td>Completed</td>
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<td>JCOG0207</td>
<td>Lung</td>
<td>NSCLC PS0-1</td>
<td>≥ 70</td>
<td>DOC Weekly</td>
<td>DOC+CDDP Weekly</td>
<td>OS</td>
<td>Completed</td>
<td>JJCO 2015</td>
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<tr>
<td>JCOG0301</td>
<td>Lung</td>
<td>NSCLC PS0-2</td>
<td>≥ 71</td>
<td>RT alone</td>
<td>CBDCA + RT</td>
<td>OS</td>
<td>Completed</td>
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<tr>
<td>JCOG0803</td>
<td>Lung</td>
<td>NSCLC PS0-1</td>
<td>≥ 70</td>
<td>DOC Every 3 week</td>
<td>DOC+CDDP Weekly</td>
<td>OS</td>
<td>Completed</td>
<td>JCO 2014</td>
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<tr>
<td>JCOG1018</td>
<td>Colon</td>
<td>Colon cancer</td>
<td>≥ 75</td>
<td>FU+BEV</td>
<td>FOLFOX+BEV</td>
<td>PFS</td>
<td>Follow-up</td>
<td>-</td>
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<td>JCOG1105</td>
<td>Lymphoma</td>
<td>Myeloma PS0-2</td>
<td>65-79</td>
<td>--</td>
<td>Modified MPB JCOG MPB</td>
<td>CR rate</td>
<td>Follow-up</td>
<td>-</td>
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<tr>
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<td>ED-SCLC PS0-2</td>
<td>≥ 71</td>
<td>CBDCA + ETP</td>
<td>CBDCA + CPT-11</td>
<td>OS</td>
<td>Follow-up</td>
<td>-</td>
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<tr>
<td>JCOG1210</td>
<td>Lung</td>
<td>NSCLC PS0-1</td>
<td>≥ 75</td>
<td>DOC Every 3 week</td>
<td>CBDCA + PEM</td>
<td>OS</td>
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</table>
RCT for older pts with unresectable NSCLC

JCOG0301

Key Eligibility Criteria

- Stage IIIA or IIIB
- NSCLC
- Age ≥ 71 years old
- ECOG PS of 0 or 1
- Unable to receive cisplatin-based combination chemotherapy

N=200

RT arm:
TRT 60 Gy/30 fr
Day 1 8 15 22 29 36

CRT arm:
CBDCA 30 mg/m^2 x 20 times + TRT 60 Gy/30 fr
Day 1 CBDCA

RCT for older pts with unresectable NSCLC

Who the older patients that precluded cisplatin-based combination chemotherapy were?

Geriatric Study Committee of JCOG

Geriatric Research Policy:
Japan Clinical Oncology Group (JCOG) policy

Published in 2016

- Patients Selection Policy
- Typical study design
- Recommended GA tools
Summary of geriatric research policy

- **Patients Selection Policy**
  - Defined the pts selection policy based on treatment tolerance and chronological age.
  - Older pts are categorized into three conceptual groups; fit, vulnerable and frail pts.

- **Study Design and Endpoints**
  - Study endpoints should include both survival and functional endpoints.
  - Study design will differ depending on the clinical question.
  - RCT is the gold standard when the clinical question asks which treatment is better.
  - An observational study is applicable for investigating actual conditions of older pts.

- **Geriatric Assessment**
  - G8, a geriatric screening tool, is to be used in all JCOG geriatric research.
  - IADL, CCI, MINI-COG and the social situation are also strongly recommended.
  - Other appropriate tools can be applied depending on the purpose of each study.
## JCOG geriatric research; 2\textsuperscript{nd} generation

<table>
<thead>
<tr>
<th>Trial name</th>
<th>Group</th>
<th>Subject</th>
<th>Age</th>
<th>Standard treatment</th>
<th>Test treatment</th>
<th>Primary endpoint</th>
<th>Status</th>
<th>Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>JCOG1408</td>
<td>Radiation</td>
<td>NSCLC c-stage IA</td>
<td>Inoperable</td>
<td>SBRT 42 Gy</td>
<td>SBRT 55 Gy</td>
<td>OS</td>
<td>Recruiting</td>
<td>RCT superiority</td>
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<tr>
<td>JCOG1507</td>
<td>Gastric</td>
<td>Gastric Ca p-stage II-III</td>
<td>≥ 80</td>
<td>Surgery alone</td>
<td>Modified S-1 for adjuvant</td>
<td>OS</td>
<td>Recruiting</td>
<td>RCT superiority</td>
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<tr>
<td>JCOG1607</td>
<td>Lung</td>
<td>MBC HER2 +</td>
<td>≥ 65</td>
<td>HPD</td>
<td>T-DM1</td>
<td>OS</td>
<td>Recruiting</td>
<td>RCT non-inferiority</td>
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<tr>
<td>JCOG1710A</td>
<td>Lung</td>
<td>NSCLC c stage 0-III</td>
<td>≥ 75</td>
<td>Radical operation</td>
<td>-</td>
<td>IADL</td>
<td>Recruiting</td>
<td>Observational</td>
</tr>
</tbody>
</table>

Nine other researches are being planned

The 2\textsuperscript{nd} generation geriatric research are conducted based on JCOG geriatric research policy
RCT for vulnerable older pts with GC

JCOG1507

Key Eligibility Criteria
- Gastric cancer
- p-Stage II/III
- Age ≥ 80 years old
- R0 resection
- Vulnerable pts

Surgery alone
No treatment after surgery

Modified S-1 treatment
4 weeks on and 2 weeks off

N=370

UMIN-CTR: UMIN000025742

Clinical trial notes
Jpn J Clin Oncol. 2018 Dec 1;48(12):1101-1104
How can we define vulnerable pts?

- The Stomach Cancer Study Group of JCOG conducted a questionnaire survey on older patients aged ≥80 years.

Questionnaire survey on adjuvant chemotherapy for elderly patients after gastrectomy indicates their vulnerabilities.

N=15,573

- The most influential factors for the compliance of S-1 are as follows:
  - Renal function
  - Body weight loss
  - Type of operation

Gastric Cancer. 2019 Jan;22(1):130-137.
### Vulnerable older pts in JCOG1507

<table>
<thead>
<tr>
<th></th>
<th>Body weight loss*</th>
<th>Ccr** &lt; 30</th>
<th>30 ≤ Ccr &lt; 80</th>
<th>Ccr ≥ 80</th>
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</thead>
<tbody>
<tr>
<td><strong>Non-total gastrectomy</strong></td>
<td>15%</td>
<td>Frail</td>
<td>Vulnerable</td>
<td>Fit</td>
</tr>
<tr>
<td>≥ 15%</td>
<td>Frail</td>
<td>Frail</td>
<td>Frail</td>
<td>Frail</td>
</tr>
<tr>
<td><strong>Total gastrectomy</strong></td>
<td>15%</td>
<td>Frail</td>
<td>Vulnerable</td>
<td>Vulnerable</td>
</tr>
<tr>
<td>≥ 15%</td>
<td>Frail</td>
<td>Frail</td>
<td>Frail</td>
<td>Frail</td>
</tr>
</tbody>
</table>

* Body weight loss is defined as the proportion of body weight loss during 1 month after surgery

** Creatinine clearance (Ccr) is calculated using the Cockcroft–Gault equation

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Gastric Cancer. 2019 Jan;22(1):130-137.
Conclusions

- This JCOG Geriatric Research Policy identified various issues, which commonly occur in geriatric research.

- This policy is expected to serve as a practical framework in planning future geriatric oncology research.

- Geriatric research is not profitable, so academic groups like SIOG or JCOG should conduct such research!

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