Challenges to improve clinical trials for the elderly

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Why are so few patients included in clinical trials?

How can we improve this trend?
Why are so few patients included in clinical trials?

- Physicians?
- Family?
- Patients?
- Clinical trial design?

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Why are so few patients included in clinical trials? Physicians: Primary care practitioners (PcP)

- 2,240 questionnaires - Referral to oncologist?
- response rate, 24% (of which 93% were assessable)
- 86% refer older patients with early-stage cancers
- only 65% refer those with advanced-stage cancers.

C. Townsley - J Clin Oncol, 2003

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Why are so few patients included in clinical trials?

PCPs role

- The factors that most influence referral decisions of PCPs are
  - patient’s desire to be referred (69%),
  - type (54%) and stage (49%) of cancer
  - severity of cancer symptoms (49%).

- Age do not seem to influence the referral decision.

- 9% of respondents found difficult to refer older cancer patients to oncology specialists,
  - the length of waiting lists,
  - mandatory tissue diagnosis before referral,
  - And the belief that oncologists seldom relate to PCPs.

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Most of the decline in radiotherapy use observed with increasing age was explained by a decline in referral to cancer centres.


In a retrospective cohort study of the SEERS data in the United States, age did not significantly influence the referral of lung cancer patients to oncologists.

(Earle CC, J Clin Oncol, 2002)

However, after patients were seen by oncologists, increasing age was associated with a lower likelihood of receiving chemotherapy!
Why are so few patients included in clinical trials?

Physicians: Oncologists

- **Ethical considerations**
  - Fears for more toxicities
  - To avoid coercion and exploitation of vulnerable patients in research
  - Dilemmas in deciding about choice of treatment, continuation of treatments, events near the end of life, conflicts of interest, and risk management

*(Smith TJ, JCO 1995)*

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Why are so few patients included in clinical trials?
Physicians: oncologists

- Ethical considerations

clinical benefit or cost-effectiveness?
Why are so few patients included in clinical trials? The family…?

- The majority of the patients consider their families as the main source of support in the disease experience (86.5%),

- wish to have a family member participating in oncology consultation (79.1%)

(Repetto, Eur J Cancer 2008)

- Not aware of different kinds of treatments

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Why are so few patients included in clinical trials?

The family…?

- Fears for treatment’s toxicities and side effects
- Fears for pain for their parent
- Fears that the parent becomes a “guinea pig”
- Fears not to be able to handle the burden of heavy treatment
Why are so few patients included in clinical trials?

- Elderly patients often do not receive any treatment and are less likely to undergo a combination of therapeutic modalities
  \((de\ Rijke\ -\ Ann\ Oncol\ 1996)\)

- Elderly patients are willing to be treated
  \((Extermann,\ JCO\ 2004)\)

- And willing to be included in clinical trials as are the younger ones

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Why are so few patients included in clinical trials?

Patients...?

Paternalistic relationship between physicians and elderly patients.

Cognitive/affective and specialist-related determinants might have an impact on the patient’s treatment preference. 

(Jensen, JCO 2004)

Everybody...
Why are so few patients included in clinical trials? Patients…?.

Repetto - *Eur J Cancer*. 2008 Oct 4

- Structured interviews
- Patients age ≥ 65 y receiving chemotherapy
  - information on diagnosis and prognosis disclosure
  - satisfaction with information
  - compliance to disease experience
  - willingness to receiving more information and ability to cope

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622 patients completed the interviews and were evaluated.

66% were informed,
34% were not informed

Information was associated with
- Age
- Geographical area,
- Tumour site
- Patient’s perception of being supported in the disease experience.
- Degree of education
- ECOG-PS,
- Family composition

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Importance of communication

Receiving adequate information facilitates a better patient–health professional relationship for 84.8% of the patients.

(Repetto, Eur J Cancer. 2008 Oct 4)
Why are so few patients included in clinical trials?

**Clinical trials**

- Patients with comorbidity are not treated according to guidelines  

- Less extensive treatment for a breast cancer patient with comorbidity is responsible for inferior prognosis  
  *(Louwman, Eur J Cancer, 2005)*

- In addition to the influence on treatment, comorbidity has been demonstrated to lower 3-year survival rates  
  *(Satariano, Ann Intern Med, 1994)*

Importance to develop clinical trials for vulnerable patients
Clinical trial design

- Inclusion/ exclusion criteria
  - Age cut off, or if no cut off, few patients 75-85 yo (“real old”)
  - Performance status: not relevant criteria
  - Heart function
  - Biological data too strict: creatinine clearance etc..
  - No data for patients with cognition troubles
  - Informed consent not easy to read (visual deficiency)

Elderly =

Not a homogeneous population!

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Age is a common barrier for accrual to cancer treatment trials, even when reimbursement for healthcare costs is not an issue.
How can we improve this trend to increase clinical trials’ validity and reliability, and avoid pre-emptive exclusion of such groups in the research design?
How can we improve this trend?

Older cancer patients are encouraged to ask their doctors about the standard of care for their type and stage of cancer, regardless of their age.

Inquiries should be made about their eligibility for standard treatments or for clinical trials.

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How can we improve this trend?
The Patients/Family….

Increase patients/family awareness

- with seminars: seminar for the elderly population

- with flyers, TV advertising focused on the old ones not only the 50+

- via the practitioner’s awareness, flyers in the practice.

- conducting personalized interviews of older patients with and without cancer to gain insights into their perspectives

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“You say life is suffering, but isn’t it also complaining?”
How can we improve this trend? The practitioners....

Increase practitioners' awareness and kind of awareness required:

- What prevents them from informing their patients about clinical trials?
- Improve the referral to oncologists even if it's advanced cancer, even if the conclusion could be “no specific treatment”.

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Primary care practitioners need more information about making appropriate referrals to oncologists.

Example: establishing focus groups among PCPs from different practice settings to obtain a more complete understanding of the findings in the study.

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How can we improve this trend? Clinical trial design?

- Geriatric component, geriatric assessment trials

- End point: « classical »: DFS, OS, response, dose intensity… but also functional status, QoL, including willingness test, cost-effectiveness…

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How can we improve this trend? Clinical trial design?

- Trials for vulnerable or frail patients (not only for ECOG/PS 2!)

  but we need to define "vulnerable"!

Importance to have the same language

- Trials for every kind of cancer (gastric, esophageal...)

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How can we improve this trend? Clinical trial design?

- New drug, targeted treatment

  drug companies support

- PK studies age specific

- Phase I and II

- Phase III: older specific or not

- Include biological data, translational research

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How can we improve this trend? Clinical trial design?

- Collaboration between geriatricians and oncologists (medical, radiotherapist, surgeons…)

- Cooperative group to have enough patients and to share our ideas!
Conclusion (1)

• Be aware of the possibility to treat elderly, even “vulnerable” patients

• Try to inform patients and family about modalities of treatment and the importance to participate to such clinical trials,

• Include them in treatment decision making

• Open inclusion/exclusion criteria

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Conclusion (2)

- Choice of end points of the study: clinical benefit, quality of life, functional status …

- Open study in every kind of cancers

- Collaboration between geriatricians and oncologists and between different groups

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Thank you

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