Polypharmacy, Potential Inappropriate Medications, and Drug Interactions in older patients with ovarian cancer - Influence on treatment completion and prognosis

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Disclosure

I do not have any conflict of interest to declare.
Background

Polypharmacy (PP)

Potential Inappropriate Medication (PIM)

- ↑ Adverse drug reactions
- ↓ Evidence-based indications
- Risks > Benefits

24-54%\(^1\)

Potential Drug Interaction (PDI)

- ↑ drug effect → ↑ toxicity
- ↓ drug effect → ↑ failure

30-84%\(^1\)
30-75%\(^{2-4}\)

\(^1\)Sharma, JGO 2016; \(^2\)Girre, CROH 2011; \(^3\)Alkan, SCC 2016; \(^4\)Popa, JGO 2014
Aims

• Description of PP, PIMs, and PDIs in older patients with ovarian cancer receiving 1\textsuperscript{st} line chemotherapy (CT).

• Is there an association of PP, PIMs and/or PDIs with completion of 1\textsuperscript{st} line CT?

• Is there an association of PP, PIMs, and/or PDIs with survival?
Ovarian cancer - treatment

• Stage IA-B, grade 1 disease: cytoreductive surgery (CRS)
• All others: CRS and combination chemotherapy
Methods

**National Patient Register (NPR)**
- Comorbidity (CCIS)
- Antineoplastic treatment
  - Type
  - Dates of treatment

**Danish Gynecological Cancer Database (DGCD)**
(Epithelial Ovarian Cancer, Jan 2005-Dec 2014)
- Tumor characteristics
- Functional status (PS)
- Surgical data

**Drug Statistics Register**
- Drug use at diagnosis (PP)
- PIMs during antineoplastic treatment
- PDIs during antineoplastic treatment
- Comorbidity (CCIS)

**Register of Causes of Death**
- Date of death (Jan 2017)
- Cause of death (Dec 2015)
Methods

• Associations of PP, PIMs, and PDIs with completion of 6 cycles of chemotherapy without dose delay were analysed in a logistic regression model.
  • PIM – EU(7)-PIM list¹
  • PDI – Lexicomp, Micromedex, Stockley

• Associations of PP, PIMs, and PDIs with survival were analysed fitting a cox regression model
  • End of follow-up: January, 2017

¹Renom-Guiteras, Eur J Pharmacol (2015)
Results

Patients diagnosed with epithelial ovarian cancer in the DGCD, 2005-2014, n=4,965
Age <70: 3018 (61%) Age ≥70: 1947 (39%)

• FIGO Ia-Ib and no records of CT, n= 312
• No ct registered in the NPR, n=858 (Age <70: 229 (31%), Age ≥70: 501(69%))
Patients diagnosed with epithelial ovarian cancer in the DGCD, 2005-2014, n=4,965
Age <70: 3018 (61%) Age ≥70: 1947 (39%)

Patients with chemotherapy data registered, n=3,795
Age < 70: 2,501 (65.9%), Age ≥ 70: 1,294 (34.1%)

- FIGO Ia-Ib and no records of ct, n=312
- No ct registered, n=858

- No surgery registered, n=179
  Age <70: 66 (37%), Age ≥70:113 (63%)
- Unspec./other treatment, n=1397
  Age <70: 930 (67 %), Age ≥70:467(33 %)
Patients diagnosed with epithelial ovarian cancer in the DGCD, 2005-2014, \( n=4,965 \)

Age <70: 3018 (61%) Age \( \geq 70 \): 1947 (39%)

Patients with chemotherapy data registered, \( n=3,795 \)

Age <70: 2,501 (65.9%), Age \( \geq 70 \): 1,294 (34.1%)

- FIGO Ia-Ib and no records of ct, \( n=312 \)
- No ct registered in the NPR, \( n=858 \)

- No surgery registered, \( n=179 \)
- Unspec./other treatment, \( n=1397 \)

Patients with a date of surgery and combination chemotherapy with platinum and a taxane or platinum monotherapy, \( n=2,119 \)

Age <70: 1,505 (68%), Age \( \geq 70 \): 714 (32%)
Results - Characteristics

Age ≥ 70 years was associated with increased PP, PIMs, and PDI.

- Advanced disease stage
- Interval debulking and no surgery
- Platinum monotherapy
- Comorbidity
- Poor functional status

Higher completion rate of six cycles of platinum monotherapy!

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>PP</th>
<th>PIMs</th>
<th>PDIs</th>
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<tr>
<td>None</td>
<td>40%</td>
<td>61%</td>
<td>9%</td>
</tr>
<tr>
<td>Minor</td>
<td>43%</td>
<td>17%</td>
<td>9%</td>
</tr>
<tr>
<td>Major</td>
<td>17%</td>
<td>40%</td>
<td>9%</td>
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</tbody>
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Chemotherapy completion

Analyses adjusted for:
- FIGO stage
- Surgical regimen
- Surgical outcome*
- Chemo regimen *
- Interacting variables

Variables:
- Age 60-69
- Age 70-79
- Age ≥ 80
- Minor PP
- Major PP
- Extensive PP
- 1-2 PIMs
- ≥ 3 PIMs
- 1 PDI
- ≥ 2 PDIs
- PS=1
- PS=2
- CCIS 1-2
- CCIS 3+
Analyses adjusted for:
- FIGO stage*
- Surgical regimen*
- Surgical outcome*
- Interacting variables
Potential Inappropriate Medication

Median survival (months)

- No PIMs: 48
- 1-2 PIMs: 38
- ≥ 3 PIMs: 22
Strengths & limitations

- 10-year national cohort - Real-world data
- Long follow-up
- Linkage of multiple registers

- Insufficient registered cytostatic treatment
- Retrospective design
Conclusion

- Ovarian cancer patients ≥ 70 years are more often exposed to both PP, PIMs, and PDIs than younger patients.

- Qualitative drug use is important because:
  - PP is not independently associated with CT completion or mortality
  - ≥ 3 PIMs $\rightarrow$ ↑ mortality, HR 2.08
  - ≥ 2 PDIs $\rightarrow$ ↓ CT completion, OR 2.27
  - CT completion $\rightarrow$ ↓ mortality, HR 0.86

- Future intervention studies should focus on optimising older cancer patients’ drug use.
Acknowledgements

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Thank you!