Alopecia as surrogate marker for chemotherapy response in patients with primary epithelial ovarian cancer: A metaanalysis of four prospective randomised phase III trials with 5114 patients

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Responds  
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Abstract  
Purpose: Alopecia is a common side-effect of chemotherapy and affects quality of life of cancer patients. Some patients and physicians believe that alopecia could be a surrogate marker for response to chemotherapy and impact on prognosis. However, this was never been tested in a sufficiently large cohort of ovarian cancer patients.

Patients and methods: We analysed retrospectively the meta-databank of four prospective randomised phase-III-trials with platinum- and taxane-based 1st-line-chemotherapy in patients with advanced epithelial ovarian cancer (EOC) regarding the impact of alopecia overall outcome.

Results: For 4705 (92.0%) of a total of 5114 EOC-patients alopecia was documented. They had received on median six cycle platinum-taxane chemotherapy (range 0–11) with 4186 (89.0%)

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having completed $\geq 6$ cycles. Worst alopecia grade was 0 in 2.4%, 1 in 2.9% and 2 in 94.7% of the patients. In a univariate analysis, including all patients, grade-0/1 alopecia was associated with significantly lower progression free survival (PFS) and overall survival (OS) compared to grade-2 alopecia. However when assessing only those patients who completed $\geq 6$ chemotherapy-cycles and hence eliminating the bias of lower total dose of treatment, alopecia failed to retain any significant impact on survival in the multivariate analysis. Merely the time point of alopecia onset was an independent prognostic factor of survival: patients who developed grade-2 alopecia up to cycle 3 had a significantly longer OS compared to patients who experienced alopecia later during therapy (hazard ratio (HR): 1.25; 95% confidence interval (CI): 1.04–1.50).

Conclusions: Within a large EOC-patient cohort with 1st-line platinum- and taxane-based chemotherapy early onset alopecia appears to be significantly associated with a more favourable outcome in those patients who completed $\geq 6$ chemotherapy cycles. It remains to be elucidated if early onset alopecia is just a surrogate marker for higher sensitivity to chemotherapy or if other biological effects are underlying.

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1. Introduction

In the context of an individual’s life, a cancer diagnosis is a major event, with an understandable emphasis on survival which patients may deem more important than their quality of life, body image and sexuality [1]. The desire to prolong survival or even achieve a cure can result in the patient accepting the complications associated with both extensive surgical interventions and the sequelae of systemic therapies [2]. Short- and long-term toxicities like polyneuropathy, fatigue and loss of appetite, tend to be the accepted and are often unavoidable consequences of effective systemic modalities [3]. Alopecia represents a typical example of such a treatment related toxicity. Interestingly, very little is known about mechanisms of apoptosis induced chemotherapy in human hair follicles. Among all chemotherapy induced side-effects, cancer patients have ranked the loss of their hair as the second most severe one [4], often experiencing this as a constant visual reminder of their disease [5,6]. Nevertheless, large surveys in women with breast cancer have demonstrated that only a relatively small proportion of the patients would decline a potentially lifesaving or life-prolonging cytotoxic treatment to avoid alopecia [7,8]. Clinical experience has shown that some patients may tend to perceive alopecia as an indirect evidence of success of their chemotherapy regimen, as it reflects successful targeting of similarly rapid-growing cells i.e. cancer cells, by the toxic chemotherapy agent [9,10]. There are no studies so far addressing this putative hypothesis in ovarian cancer patients.

Therefore, we conducted this retrospective analysis to evaluate the putative association of alopecia and chemotherapy efficacy on a sample of more than five thousand patients with primary epithelial ovarian cancer (EOC), treated with platinum- and taxane based chemotherapy regimens.

2. Patients and methods

2.1. Databases

This study was conducted using pooled single patient data from four large prospective randomised trials on platinum/paclitaxel based chemotherapy in patients with advanced primary EOC. All studies were conducted by the AGO (Arbeitsgemeinschaft Gynaekologische Onkologie)-Ovar Study Group as the leading group with cooperating groups GINECO (Groupe d’Investigateurs Nationaux pour l’Étude des Cancers Ovariens et du sein) and NSGO (Nordic Society Gynecological Oncology). Detailed characteristics of patients and treatment protocols have been described elsewhere [11–14]. We report characteristics pertaining to our present analysis. All four trials included in all arms the cytotoxic agent paclitaxel in a three-weekly regimen, with alopecia as known side-effect (Table 1).

2.2. Patients

A total of 5114 patients, 18 years or older, with histologically proven primary EOC FIGO (Fédération Internationale de Gynécologie et d’Obstétrique)-stage [15] IIB–IV [16], who had not previously undergone any systemic treatment for ovarian cancer, were included in these four studies (AGO-Ovar 3, -5, -7 and -9) between
10/1995 and 06/2004. All patients were enrolled within 6 weeks following debulking surgery. The Eastern Cooperative Oncology Group (ECOG) performance status [16] ranged between 0 and 2 and all patients had initially adequate hematologic, renal and hepatic functions and received paclitaxel and platinum based chemotherapy in both arms of each study. The regimens evaluated in the experimental arms contained a third drug which was added as a triplet (epirubicin or gemcitabine) or given sequentially (topotecan). No specific protocol addressed alopecia prophylaxis such as of scalp cooling, which was not applied in the patients. The majority of the patients of our analysis were treated as inpatients.

2.3. Definition and reporting of alopecia

The grade of alopecia was documented by professional study nurses and the principle investigators. They interviewed the patients personally before applying each chemotherapy cycle and in the follow-up consultations. Definitions were stable across all centres and classified according to the National Cancer Institute Common Toxicity Criteria (CTC; version 2.0) [16,17]. Grade 0 was defined as lack of alopecia. Grade I was defined as hair thinning or development of few hair gaps. Developing many hair gaps or complete hair loss was defined as grade II.

<p>| Table 2 | Patient characteristics. |
|-----------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No of patients (%)</th>
<th>Patients with alopecia grade 0–1 (%)</th>
<th>Patients with alopecia grade 2 (%)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age; years</td>
<td>59 (19–83) 59 (25–79)</td>
<td>59 (19–83) 138 (3.1%)</td>
<td>138 (3.1%) 13 (2.8%)</td>
<td>0.077</td>
</tr>
<tr>
<td>FIGO stage</td>
<td>435 (9.2%) 414 (9.3%)</td>
<td>134 (34.6%) 13 (16.4%)</td>
<td>13 (16.4%) 13 (16.4%)</td>
<td>0.059</td>
</tr>
<tr>
<td>Serous/papillary</td>
<td>208 (4.4%) 203 (4.4%)</td>
<td>53 (1.1%) 14 (11.5%)</td>
<td>14 (11.5%) 14 (11.5%)</td>
<td>0.264</td>
</tr>
<tr>
<td>Endometrioid</td>
<td>3261 (69.3%) 3180 (71.4%)</td>
<td>23 (0.5%) 23 (0.5%)</td>
<td>23 (0.5%) 23 (0.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mucinous</td>
<td>134 (2.4%) 134 (2.4%)</td>
<td>5 (0.4%) 5 (0.4%)</td>
<td>5 (0.4%) 5 (0.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mixed</td>
<td>208 (4.4%) 208 (4.4%)</td>
<td>5 (0.4%) 5 (0.4%)</td>
<td>5 (0.4%) 5 (0.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>1373 (29.2%) 1373 (29.2%)</td>
<td>21 (8.4%) 21 (8.4%)</td>
<td>21 (8.4%) 21 (8.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clear cell</td>
<td>102 (40.8%) 102 (40.8%)</td>
<td>5 (0.4%) 5 (0.4%)</td>
<td>5 (0.4%) 5 (0.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Transitional cell</td>
<td>925 (19.7%) 925 (19.7%)</td>
<td>17 (7.6%) 17 (7.6%)</td>
<td>17 (7.6%) 17 (7.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Residual tumour</td>
<td>1688 (35.9%) 1688 (35.9%)</td>
<td>59 (23.6%) 59 (23.6%)</td>
<td>59 (23.6%) 59 (23.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Macroscopic tumour free</td>
<td>401 (34.6%) 401 (34.6%)</td>
<td>12 (16.4%) 12 (16.4%)</td>
<td>12 (16.4%) 12 (16.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Partial response</td>
<td>357 (30.8%) 357 (30.8%)</td>
<td>9 (12.8%) 9 (12.8%)</td>
<td>9 (12.8%) 9 (12.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stable disease</td>
<td>157 (13.6%) 157 (13.6%)</td>
<td>5 (6.8%) 5 (6.8%)</td>
<td>5 (6.8%) 5 (6.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>100 (8.6%) 100 (8.6%)</td>
<td>16 (21.9%) 16 (21.9%)</td>
<td>16 (21.9%) 16 (21.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Worst grade of alopecia</td>
<td>0 (2.4%) 0 (2.4%)</td>
<td>112 (2.4%) 112 (2.4%)</td>
<td>112 (2.4%) 112 (2.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Early onset (before cycle 4)</td>
<td>4237 (90.1%) 4237 (90.1%)</td>
<td>218 (4.6%) 218 (4.6%)</td>
<td>218 (4.6%) 218 (4.6%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

2.4. Statistical analysis

The chi-square test or Fisher’s exact test was used to assess differences in the frequencies of qualitative variables. Crude odds ratios (ORs) with the corresponding 95%-confidence intervals (95%-CI) were obtained using logistic regression analysis. Estimates of median overall survival and progression free survival were calculated using the Kaplan–Meier method. Logrank tests were used for univariate statistical comparisons. Adjusted hazard ratios (HRs) were estimated with the Cox proportional hazards model. All data were analysed using the IBM SPSS Statistics 21.0 (SPSS Inc., Chicago, IL) and \( p < 0.05 \) was considered statistically significant.

3. Results

4705 (92.0%) patients with documented grade of alopecia out of a total of 5114 patients were included in this analysis. Median age was 59 years (range: 19–83) including 1096 (23.3%) patients older than 65 years. FIGO-stage IIIC–IV was present in 3413 (72.5%) of the patients.

Total macroscopic tumour clearance was accomplished in 1688 patients (35.9%). Altogether more than 31,000 cycles were applied, with a median of six cycles (range: 0–11) in each patient. All received at least one chemotherapy cycle, while 4186 (89.0%) patients received 6–11 cycles. Maximal 6–11 cycles of adjuvant chemotherapy were applied, according to the chemotherapy regimen of each study group. Demographics and tumour related characteristics of the patients are summarised in Table 2.

4. Incidence and timing of alopecia

A hundred and twelve patients (2.4%) did not experience alopecia at all (grade 0). A hundred and thirty-eight patients (2.9%) experienced grade 1 alopecia. In 218 patients (4.6%) the worst grade of alopecia was observed only after the 4th cycle of chemotherapy – as a late onset alopecia, while the vast majority of the patients experienced an early onset alopecia by cycle 4. None of the patients discontinued chemotherapy due to alopecia alone. No significant differences were noted between patients with grade 0/1 versus grade 2 alopecia regarding tumour stage and histological subtype. Patients with grade 2 alopecia had significantly higher rates of no macroscopic tumour residual after surgery (36.6% versus 23.6%, \( p < 0.001 \)). As expected the proportion of

<table>
<thead>
<tr>
<th>Worst grade of alopecia</th>
<th>Overall survival</th>
<th>95%-CI</th>
<th>Progression free survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>28.1</td>
<td>22.3 – 33.9</td>
<td>13.8</td>
</tr>
<tr>
<td>1</td>
<td>33.9</td>
<td>24.2 – 43.6</td>
<td>14.2</td>
</tr>
<tr>
<td>2</td>
<td>48.7</td>
<td>46.9 – 50.5</td>
<td>18.9</td>
</tr>
<tr>
<td>Total</td>
<td>47.6</td>
<td>45.9 – 49.3</td>
<td>18.7</td>
</tr>
</tbody>
</table>

Fig. 1. Overall- and progression free survival according to the grade of alopecia.
patients who completed more than three cycles had higher rates of grade 2 alopecia (96.1% versus 44.4%, \( p < 0.001 \)). Details are presented in Table 2.

5. Impact of alopecia on overall and progression free survival

Of the patients eligible for response evaluation (\( N = 1157 \)), the majority showed complete or partial response (34.6% and 30.8% resp.) at completion of chemotherapy, while 100 patients (8.4%) showed progressive disease. Complete response and no evidence of disease at imaging were not significantly more often in patients with grade 2 alopecia versus grade 0 or 1 (OR = 1.28, 95% CI 0.70–2.35). Median overall survival (OS) in the entire patient cohort was 47.6 months (95% CI: 45.9–49.3). With a median of 48.8 months (95% CI: 47.0–50.5 months) OS was significantly longer in the grade 2 alopecia group than the median OS of 28.1 months (22.3–33.9 months) in the patient group who did not experience alopecia at all (\( p < 0.001 \)). Similarly, progression free survival (PFS) rates were higher in the patients with higher grade of alopecia. Median PFS was 19.0 months (95% CI: 18.2–19.7) versus 13.8 months (95% CI: 12.2–15.3) in the grade 2 versus 0/1 alopecia group, respectively (\( p = 0.001 \)). However, when performing a survival analysis including only those patients who completed six or more cycles of chemotherapy the differences in survival between alopecia grade 0/1 and grade 2 were not retained: \( p = 0.436 \) (OS) and \( p = 0.499 \) (PFS) (Fig. 1).

After excluding patients with early termination (due to toxicity or progress or patients wish) of chemotherapy before cycle 6, the risk for death was higher for patients who experienced alopecia later during therapy (HR 1.25, 95% CI: 1.04–1.50) compared to patients with early onset of alopecia. In the multivariate analysis grade 2 alopecia failed to have any prognostic impact on survival, but early onset of grade 2 alopecia appeared to be an independent prognostic factor for longer OS (Fig. 2). Other risk factors in this multivariate analysis were higher age (HR per ten years = 1.15; 95% CI: 1.11–1.20).

![Fig. 2. Risk factors for mortality – multivariate analysis (Cox regression) in epithelial ovarian cancer (EOC)-patients who completed at least six cycles of 1st line platinum and taxane based chemotherapy (\( n = 4183 \)).](image-url)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio</th>
<th>95% Confidence interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per ten years)</td>
<td>1.15</td>
<td>1.11–1.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FIGO stage I* (vs. FIGO IV)</td>
<td>0.12</td>
<td>0.06 – 0.23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FIGO stage II* (vs. FIGO IV)</td>
<td>0.34</td>
<td>0.27 – 0.43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FIGO stage IIIa/b* (vs. FIGO IV)</td>
<td>0.56</td>
<td>0.48 – 0.66</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FIGO stage IIIc* (vs. FIGO IV)</td>
<td>0.77</td>
<td>0.69 – 0.85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mucinous histology (vs. serous)</td>
<td>1.79</td>
<td>1.46 – 2.20</td>
<td>0.001</td>
</tr>
<tr>
<td>Tumor residuals &gt;1cm (vs. no tumor residuals)</td>
<td>2.48</td>
<td>2.19 – 2.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tumor residuals ≤1cm (vs. no tumor residuals)</td>
<td>2.19</td>
<td>1.94 – 2.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alopecia grade 2 late onset (versus grade 2 early onset)</td>
<td>1.25</td>
<td>1.04 – 1.50</td>
<td>0.018</td>
</tr>
<tr>
<td>Alopecia grade 0 (versus grade 2 early onset)</td>
<td>1.13</td>
<td>0.74 – 1.74</td>
<td>0.565</td>
</tr>
<tr>
<td>Alopecia grade 1 (versus grade 2 early onset)</td>
<td>0.94</td>
<td>0.68 – 1.31</td>
<td>0.728</td>
</tr>
</tbody>
</table>

*protective
1.11–1.20), mucinous histology (HR = 1.79; 95% CI: 1.46–2.20) and postoperative tumour residuals >1 cm (HR = 2.48; 95% CI: 1.94–2.46) compared to no residuals.

In the multivariate analysis for PFS in the subgroup of the patients who had completed ≥6 cycles of chemotherapy alopecia 0/1 versus 2 and early versus late onset alopecia did not appear to have any significant impact on PFS. Here, significance was only observed for higher age (HR per ten years = 1.08; 95% CI: 1.04–1.12), mucinous histology (HR = 1.46; 95% CI: 1.22–1.76) and postoperative tumour residuals >1 cm (HR = 2.40; 95% CI: 2.17–2.66) and ≤1 cm (HR = 2.09; 95% CI: 1.90–2.31). Earlier FIGO stages appeared to have a protective effect against recurrence with hazard ratios between 0.12 (95% CI: 0.08–0.18) for stage I and 0.78 (95% CI: 0.71–0.86) for stage IIIC compared to stage IV (Fig. 3).

### Variable Hazard ratio 95% Confidence interval p-value

- **Age (per ten years)**
  - 1.08
  - 1.04–1.12
  - < 0.001
- **FIGO stage I**
  - (vs. FIGO IV)
  - 0.12
  - 0.08–0.18
  - < 0.001
- **FIGO stage II**
  - (vs. FIGO IV)
  - 0.33
  - 0.27–0.40
  - < 0.001
- **FIGO stage IIIa/b**
  - (vs. FIGO IV)
  - 0.57
  - 0.50–0.65
  - < 0.001
- **FIGO stage IIIc**
  - (vs. FIGO IV)
  - 0.78
  - 0.71–0.86
  - < 0.001
- **Mucinous histology**
  - (vs. serous)
  - 1.45
  - 1.22–1.76
  - < 0.001
- **Tumor residuals >1 cm**
  - (vs. no tumor residuals)
  - 2.40
  - 2.17–2.66
  - < 0.001
- **Tumor residuals ≤1 cm**
  - (vs. no tumor residuals)
  - 2.09
  - 1.90–2.31
  - < 0.001
- **Alopecia grade 2 late onset**
  - (versus grade 2 early onset)
  - 1.08
  - 0.92–1.27
  - 0.375
- **Alopecia grade 0**
  - (versus grade 2 early onset)
  - 1.04
  - 0.71–1.52
  - 0.841
- **Alopecia grade 1**
  - (versus grade 2 early onset)
  - 0.89
  - 0.67–1.18
  - 0.425

*protective

Fig. 3. Risk factors for ovarian cancer recurrence – multivariate analysis (Cox regression) in epithelial ovarian cancer (EOC)-patients who completed at least six cycles of 1st line platinum and taxane based chemotherapy (n = 4185).

6. Discussion

The present study aimed to assess the value of alopecia as surrogate marker for chemotherapy response in a large cohort of 1st line advanced ovarian cancer patients. We observed that patients with absent or mild alopecia had poorer remission rates and less favourable overall and progression-free survival compared to patients who experienced grade 2 alopecia, but this may well be attributed to the fact that patients with grade 0/1 alopecia were administered significantly less chemotherapy cycles. In the subgroup of patients who had completed at least six cycles of chemotherapy (86.7% of the entire cohort) alopecia failed to retain any prognostic value for both PFS and OS. Nevertheless, patients with early onset alopecia, before cycle four, experienced significantly higher PFS and OS compared to those with later onset alopecia, even after stratification of common clinicopathological
features such as advanced FIGO stage, mucinous histology and postoperative tumour residuals. This is the first time to reveal an association of alopecia with chemotherapy response rates and survival in patients with advanced EOC. However there are two major limitations of the present analysis: only 5% of all the patients and 2.8% of those patients who completed ≥ 6 cycles did not experience grade 2 alopecia and hence an extrapolation of the results to a less alopecia inducing chemoregimen is questionable. Second, due to the retrospective design of the study there is a considerable possibility of under- or over-reporting alopecia and hence limiting the value of our results even further.

Even though our results are important and serve to further enlighten the associations between toxicity and efficacy of cytotoxic chemotherapy, the exact underlying mechanisms and pathways can only be speculative. It is unclear whether early onset alopecia is just a surrogate marker for higher sensitivity to chemotherapy and therefore associated with a more favourable outcome or if other biological effects are underlying that correlate survival through unidentified pathways with hair toxicity.

There has so far been one more study addressing the correlation of alopecia and response to chemotherapy, evaluating 66 patients with Hodgkin lymphoma treated with at least six cycles of doxorubicin-containing chemotherapy [10]. In this study alopecia was shown to be associated with significantly higher rates of remission (OR 8.48, 95% CI: 2.77–25.95), along with more frequent episodes of bone marrow suppression defined as neutropenia, leukopenia, delays in scheduled treatments and number of courses with dose reduction. The authors concluded that the absence of alopecia in such patients should alert clinicians to the possibility of treatment failure [10]. As opposed to our study half of the patients here lost their hair and half did not under the doxorubicin treatment, which is known to be less toxic in terms of alopecia than paclitaxel and hence allowing a clearer frame for association analysis [10,18]. By evaluating a highly alopecia inducing cytotoxic agent like paclitaxel, we have eliminated the possibility of filtering patients with more borderline response and who would not necessarily lose their hair in a less alopecia inducing treatment regimen.

The finding that the absence of alopecia and in extension severity of toxicity does not correlate with a more dismal outcome can also be encompassed with the outcome of the recently published large phase III randomised trial by Pignata et al. [19]. In an open label phase III design, the MITO group found that while a lower-dose weekly carboplatin/paclitaxel regimen did not improve PFS compared with standard three weekly carboplatin and paclitaxel as first line treatment of advanced EOC, it appeared to correlate with significantly better quality of life, less neuropathy, neutropenia, febrile neutropenia, thrombocytopenia, renal toxicity and lower rates of alopecia: 28% versus. 58% grade 2 alopecia (p < 0.001). This study dissolves clearly in a prospective design the assumption that the cytotoxic efficacy of chemotherapy has to unequivocally be associated with a more severe toxicity profile. The original results of the studies analysed here also clearly show that the use of a more toxic triplet combination chemotherapy regimen at 1st line failed to improve survival and response rates [12–14] indicating that higher toxicity does not always correlate with higher efficacy. Our finding that the timing of complete alopecia appears to be a significant surrogate marker of response and outcome will need to be further validated before drawing any clinically relevant projections and treatment decisions.

The characterisation of surrogate markers to evaluate the effects of chemotherapy is still a crucial issue of the development of chemotherapy in addition to targeted therapies taking into consideration that chemotherapy is still the mainstay of treatment of ovarian cancer and many solid tumours. Skin and nail alterations have been hypothesised to be potential surrogate markers for molecular-targeted therapies, but also for low-dose metronomic chemotherapy.

A recent report published by Soveri et al. based on two prospective randomised adjuvant trials in patients with stage II or III colon cancer has suggested that haematological and non-haematological adverse events were associated with disease-free survival or overall survival. Patients who did not experience predefined toxicity had the worst outcome [20].

A number of studies have suggested that a lack of drug-specific toxicities is associated with rather poor survival outcomes and it seems that early onset of chemotherapy-induced fatigue and weight loss could be an independent predictor of poor time to progression and overall survival [21]. Therefore finding surrogate markers of chemotherapy efficacy is still an interesting and potentially useful line of research. Unfortunately, most of these studies have been retrospective or have been shown to have limitations. The value of surrogate markers of haematological and non-haematological toxicities is therefore warranted to be prospectively assessed in future trials.

With the emotional, social and sexual consequences of cancer treatment continuing to present constant challenges in patients’ lives, evidence indicates that a smoother toxicity profile of a treatment regimen dose by no means has to be exchanged with lower treatment efficacy, supporting our efforts not only to develop effective supportive care but also design more efficacious and at the same time less toxic therapeutic approaches.

7. Conclusion

In conclusion, the absence of alopecia at 1st line paclitaxel- and platinum-based chemotherapy for EOC
was not found to be associated with higher remission and survival rates in a pooled analysis of 5114 mostly advanced EOC patients. However, when adjusting for the common clinicopathologic features such as postoperative tumour residuals, histology and FIGO stage, early onset – up to cycle 4 – grade 2 alopecia appeared to significantly correlate with a more favourable OS, but not PFS. It needs to be further elucidated whether early onset alopecia is just a surrogate marker for higher sensitivity to chemotherapy and hence associated with a longer survival or if other unidentified biological pathways are underlying that correlate alopecia with cytotoxicity and survival.

Conflict of interest statement
None declared.

References


