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Quality of pathology reports for advanced ovarian cancer: Are we missing essential information? An audit of 479 pathology reports from the EORTC-GCG 55971/NCIC-CTG OV13 neoadjuvant trial

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ARTICLE INFO

Article history:

Received 18 June 2010

Received in revised form 6 August 2010

Accepted 10 August 2010

Available online 16 September 2010

Keywords:

Ovarian cancer

Quality of health care

Surgical pathology

ABSTRACT

Objective: To assess the quality of surgical pathology reports of advanced stage ovarian, fallopian tube and primary peritoneal cancer. This quality assurance project was performed within the EORTC-GCG 55971/NCIC-CTG OV13 study comparing primary debulking surgery followed by chemotherapy with neoadjuvant chemotherapy and interval debulking surgery.

Methods: Four hundred and seventy nine pathology reports from 40 institutions in 11 different countries were checked for the following quality indicators: macroscopic description of all specimens, measuring and weighing of major specimens, description of tumour origin and differentiation.

Results: All specimens were macroscopically described in 92.3% of the reports. All major samples were measured and weighed in 59.9% of the reports. A description of the origin of the tumour was missing in 20.5% of reports of the primary debulking group and in

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doi:10.1016/j.ejca.2010.08.008

23.4% of the interval debulking group. Assessment of tumour differentiation was missing in 10% of the reports after primary debulking and in 20.8% of the reports after interval debulking. Completeness of reports is positively correlated with accrual volume and adversely with hospital volume or type of hospital (academic versus non-academic). Quality of reports differs significantly by country.

Conclusion: This audit of ovarian cancer pathology reports reveals that in a substantial number of reports basic pathologic data are missing, with possible adverse consequences for the quality of cancer care. Specialisation by pathologists and the use of standardised synoptic reports can lead to improved quality of reporting. Further research is needed to better define pre- and post-operative diagnostic criteria for ovarian cancer treated with neoadjuvant chemotherapy.

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1. Introduction

In Europe, approximately 3.2 million people are diagnosed with cancer each year.¹ When diagnosed with cancer, every patient expects to receive best treatment available to optimise the chance for survival with minimal morbidity. However, data suggest a significant variation in treatment outcome and quality of cancer care.²

Quality of care has been defined by the Institute of Medicine as 'the degree to which health services for individuals and populations increase the likelihood of desired outcomes and are consistent with current professional knowledge'.³ In oncology, best practice is based on an accurate diagnosis, staging and prognostic assessment of a tumour allowing adequate treatment decisions by multidisciplinary teams. Diagnostic and prognostic information is mainly provided by pathologic assessment of biopsies and surgical specimens. Evidently, pathologic assessment needs to be accurate and complete. However, to avoid error and suboptimal care, results also need to be well communicated to the treating physicians in a timely and comprehensible fashion. As such, the quality of the pathology report can be considered an essential part of the quality of the histopathology process.⁴

To assess the quality of pathology reporting for ovarian cancer, surgical pathology reports from cytoreductive surgery were collected within the framework of the EORTC-GCG 55971/NCIC-CTG OV 13 trial. That trial compared upfront cytoreductive surgery followed by chemotherapy with neoadjuvant chemotherapy and interval debulking surgery as treatment for advanced stage ovarian, fallopian tube and primary peritoneal cancer.⁵ This audit of pathology reports aims to serve as a basis for quality improvement and better standardisation of ovarian cancer histopathology.

2. Patients and methods

2.1. The EORTC 55971/NCIC-CTG OV13 trial

Timing of surgery in the treatment of patients with FIGO stage IIIC or IV epithelial ovarian, primary peritoneal or fallopian tube carcinoma was investigated in the EORTC-GCG 55971/NCIC-CTG OV13 randomised phase III study. Patients in the control arm underwent upfront debulking surgery followed by minimum six cycles of platinum-based chemo-

therapy. Patients in the experimental arm received three cycles of pre-operative platinum-based chemotherapy followed by cytoreductive surgery and the remainder of chemotherapy.⁵

Diagnosis had to be proven by biopsy or if no biopsy was available, all of the following criteria needed to be fulfilled:

- fine needle aspiration showing adenocarcinoma,
- presence of a pelvic (ovarian) mass,
- omental cake or other metastasis larger than two centimetre in the upper abdomen or regional lymph node metastasis or FIGO stage IV,
- serum Ca125/CEA ratio more than 25,
- if the serum Ca125/CEA ratio was lower than 25, a barium enema (or colonoscopy) and gastroscopy (or radiological examination of the stomach) should be negative for the presence of a primary tumour within six weeks before randomisation,
- normal mammography had to be obtained within 6 weeks prior to randomisation,

The trial was registered under <http://www.clinicaltrials.gov/ct2/show/NCT00003636> since November 1, 1999.

Seven hundred and eighteen patients were randomised from 60 institutions. Three hundred and forty of the 361 patients randomised to the upfront debulking arm, underwent the planned upfront debulking surgery. Three hundred and fourteen of the 357 patients randomised to the neoadjuvant arm underwent interval debulking surgery.

2.2. Assessment of pathology reports

Original pathology reports of the respective cytoreductive surgery were requested to all participating centres.

Minimal standards for the pathology reports for ovarian cancer were identified in the literature.^{6–8} Apart from the histological type, at least the following items should be reported:

- detailed macroscopic description of all specimens
- weight and measurements of major samples (uterus, ovaries, omentum)
- origin of tumour
- degree of differentiation

These selected items were scored for their presence or absence in the report, a method previously reported being useful in auditing pathology reports.⁹ Items that were noted in the report as inconclusive were judged as present. For example, if the report stated that grading was not possible because of extensive necrosis after chemotherapy, we judged grade of differentiation as being reported.

All reports were assessed by one author (L.V.). For internal quality control, a randomly selected 10% of the reports were also assessed by a second author (BP), showing only minor discrepancies.

2.3. Statistical methods

We correlated the completeness of reports for all items combined to accrual volume, hospital volume, type of hospital and country.

Institutions were grouped by the number of patients entered in the trial (<20 versus 20–39 versus ≥40 patients randomized) to assess accrual volume of the centres.

Investigators were requested to report the estimated number of newly diagnosed ovarian cancer patients treated yearly at their institution to define hospital volume and were grouped accordingly (≤35, 36–80 and >80 patients per year).

Type of hospital was defined as academic or non-academic. Hospitals linked to a university for research and teaching purposes were considered as academic.

Differences in completeness on all four items were tested via multivariate analysis of variance (Manova). All tests were performed at a 2-sided 5% significance level. Because of the ongoing discussion regarding the value of grade of differentiation after chemotherapy, this item was excluded for the analyses for the patients treated with neo-adjuvant chemotherapy.

3. Results

We received 479 out of 654 (73.2%) original pathology reports; 239 from primary debulking surgery and 240 from interval debulking surgery. Forty institutions from 11 different countries (Austria, Belgium, Canada, Denmark, France, Norway, Portugal, Spain, Sweden, the Netherlands and United Kingdom) returned at least one pathology report.

Median number of reports per institution was five (range 1–121).

Results for the presence or absence of the four checked items are summarised in Table 1. Weight and measurement of the major specimens and origin of the tumour were most frequently missing in the reports being scored as present in 59.9% and 78.0%, respectively. Weight of the major specimens was more frequently missing than the size. A macroscopic examination of all received specimens was present in 92.3% of the reports.

Overall, degree of differentiation was mentioned in 84.6% but was clearly more often missing when the surgery was performed after neoadjuvant chemotherapy ($p = 0.001$). For the other items, there was no statistically significant difference between the two treatment arms.

Two hundred and seven (43.2%) reports contained information regarding all checked items. In 309 (64.5%) reports macroscopic description, degree of differentiation and origin of the tumour were mentioned. This was more often the case after primary surgery than after interval surgery.

3.1. Quality of reporting by accrual volume Fig. 1

Overall completeness of reports is correlated with the number of patients recruited in the trial. Institutions with a higher accrual produce more complete pathology reports.

3.2. Quality of reporting by hospital volume Fig. 2

Thirty-five of the 40 participating investigators reported the estimated number of newly diagnosed ovarian cancer patients treated yearly in their institution. Small volume hospitals produced the most complete reports, followed by high volume hospitals. Intermediate volume hospitals have most often missing data in the pathology reports.

3.3. Quality of reporting: academic versus non-academic Fig. 3

Overall completeness of reports is correlated with the type of hospital. Overall quality is significantly better in non-academic hospitals.

Table 1 – Frequencies and proportions of reports with items documented for whole sample and for each type of operation.

	Primary debulking (<i>n</i> = 239)	Interval debulking (<i>n</i> = 240)	Total (<i>n</i> = 479)
Major specimens weighed and measured	143 (59.8%)	144 (60.0%)	287 (59.9%)
All specimens macroscopically described	222 (92.9%)	220 (91.7%)	442 (92.3%)
Degree of differentiation mentioned in the report	215 (90%)	190 (79.2%)	405 (84.6%)
Origin of the tumor clearly mentioned in the report	190 (79.5%)	184 (76.6%)	374 (78.0%)
Macroscopic description, degree of differentiation and origin of tumour present	162 (67.8%)	147 (61.3%)	309 (64.5%)
All four topics present	109 (45.6%)	98 (40.8%)	207 (43.2%)

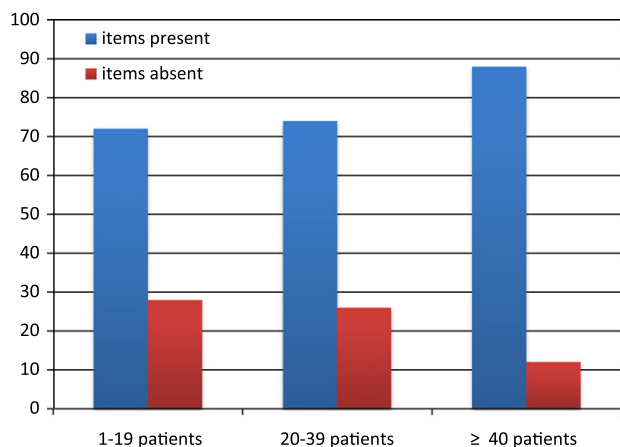


Fig. 1 – % of items present and absent (all items combined) per center accrual volume (Manova $p < 0.0001$).

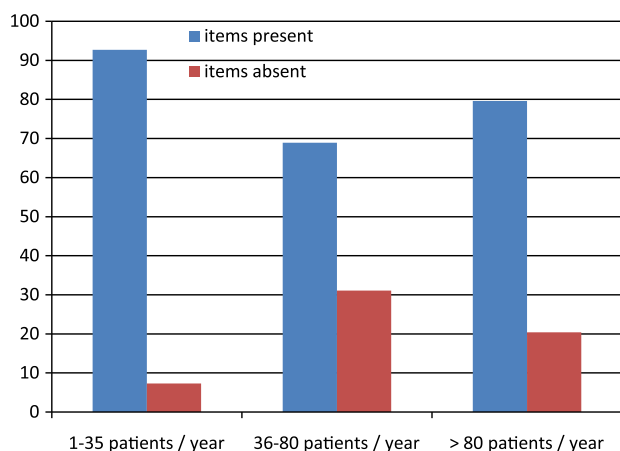


Fig. 2 – % of items present and absent (all items combined) per number of newly diagnosed ovarian cancer patients treated yearly (Manova $p < 0.0001$).

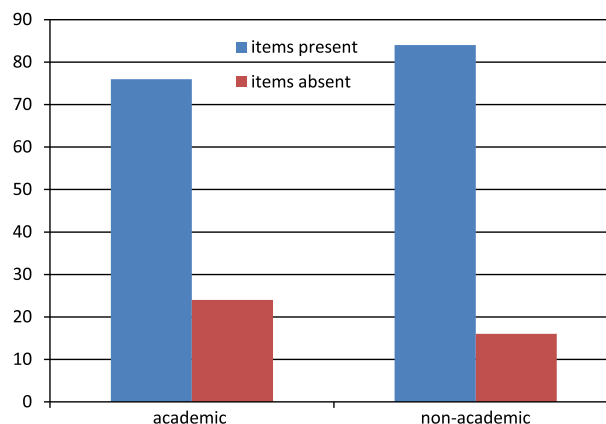


Fig. 3 – % of items present and absent (all items combined) per hospital type (Manova $p = 0.0003$).

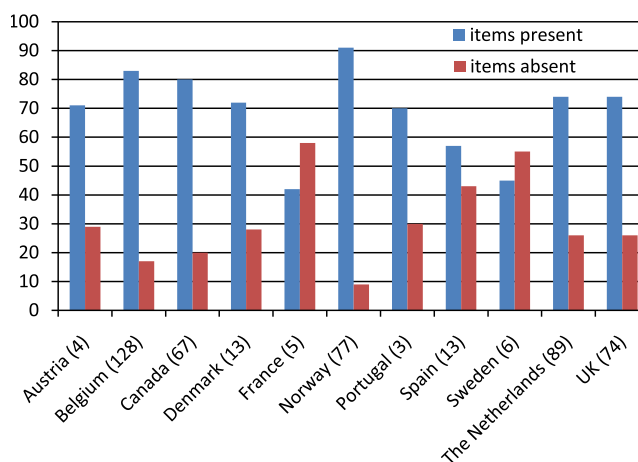


Fig. 4 – % of items present and absent (all items combined) per country (Manova $p < 0.0001$). Numbers between () indicate the number of reports received per country.

3.4. Quality of reporting by country Fig. 4

Overall completeness of reports is correlated with country of origin. The on average most complete reports were found in Norway and Belgium, missing data were found most frequently in France and Sweden.

4. Discussion

This quality assurance project assessed the completeness of histopathology reports of cytoreductive surgery for advanced stage ovarian, fallopian tube and primary peritoneal cancer. Although only minimal requirements were checked, important deficiencies were identified. This is in line with findings for other tumour types and studies performed in different settings. Also for e.g. breast cancer and head and neck cancer, it was noted that information essential for clinical decision making is too often missing or unclear in pathology reports.^{10–12} This is of concern as the report is essential not only for communication to treating physicians but also for data

collection within clinical trials, for review by a second pathologist or when unforeseen problems arise and reassessment is needed later on. Hence, a short summary of the conclusions is insufficient and every step needs to be reported in a complete and unambiguous way.

A first step in the histopathological process is the macroscopic description and sampling of the specimens. A clear description of the specimens and the way samples are taken is essential in case of unexpected findings or expert review. In these cases, certainly when additional biopsies are needed, the original presentation of the specimens must be easily reproducible.¹³ Although the current staging of ovarian cancer is essentially a surgical staging, macroscopic and microscopic pathologic findings are necessary to define the final FIGO stage of a given tumour. Both surgery and pathology report are thus important for staging and prognostic assessment.¹⁴ Furthermore, macroscopic assessment of specimens plays a significant role in the determination of the primary origin of the tumour, e.g. the differential diagnosis between primary peritoneal cancer and carcinoma of the ovary is

mainly based on macroscopic features.¹⁵ Seidman and colleagues found that the origin of mucinous tumours can be correctly classified by the size and laterality alone. Other macroscopic features, e.g. a smooth capsule and evenly distributed solid and cystic areas help to refine the distinction between primary tumours and extra-ovarian tumours metastatic to the ovary.¹⁶

In the Western world, it is estimated that approximately 6–7% of malignant ovarian masses are metastatic rather than primary ovarian tumours, but the proportion of secondary tumours can be much higher in other parts of the world.¹⁷ Although other gynaecological tumours may be treated in the same way as advanced epithelial ovarian cancer,^{15,18} the determination of the origin of the tumour has major consequences for treatment decisions and assessment of prognosis.¹⁹ The distinction between primary ovarian and metastatic tumours is based on the interpretation of a complex combination of macroscopic, microscopic and biochemical data and requires a lot of expertise.²⁰ Consequently, the final diagnosis is made by the pathologist. The pathologist's conclusions should be stated in the report separately even when the narrative of the report is considered to be obvious to the pathologists. It has been shown that if active interpretation by clinicians is needed, the risk of communication errors increases.²¹ In more than one-fifth of the reports of our study, the pathologist did not report his or her final conclusion about the origin of the tumour. We do not know if this reflects limited attention to the differential diagnosis for origin of the tumour or the assumption that the final diagnosis is clear to the reader from the narrative.

Guidelines on the reporting of ovarian pathology recommend the determination of histological grade, although its prognostic value for the advanced stages of ovarian cancer is still under discussion.²² Histological grade was reported in 90% of the reports after primary debulking, but in only 79% of the reports after neo-adjuvant chemotherapy. As stated in some of the reports and as became clear from informal discussion with investigators, some pathologists consider degree of differentiation more difficult to interpret after neoadjuvant therapy. The feasibility of tumour grading after neo-adjuvant therapy has indeed been questioned because chemotherapy-induced changes (e.g. no glandular formation and reduced mitotic activity) can make the criteria for tumour grading unreliable.²³ However, other authors have been able to grade ovarian tumours after chemotherapy and even reported a good concordance with grading of pre-chemotherapy biopsies.^{24,25} Similar issues with grading after neoadjuvant treatment have been reported for other tumour types and the most common approach seems to be to grade pre-operatively treated tumours whenever possible.²⁶

Data on the histopathological examination of ovarian cancer after chemotherapy are still very scarce. Changes induced by neoadjuvant chemotherapy can obscure the diagnosis of origin and cell type; especially clear cell changes are mentioned in this regard.²⁷ As a consequence of these architectural and cellular changes after chemotherapy, diagnosis more and more relies on pre-treatment biopsies or cytology and immunohistochemistry techniques on the specimens.²⁶ Immunohistochemistry appears to be useful in these cases. Small studies have shown a good concordance of biomarker expression on

diagnostic biopsies and surgical specimens after neoadjuvant chemotherapy.^{28,29} Further research on the use of immunohistochemistry on pre-treatment biopsies and cytology would be of much interest in attempts to improve diagnostic accuracy and, in times of targeted therapies, to individualise treatment. For both biopsies and post-chemotherapy specimens however, more research on the value of diagnostic and prognostic markers is warranted.

The reasons for the observed incompleteness of reports are unclear. Several explanations can be considered.

First, some pathologists may have limited knowledge of ovarian pathology. Experience and expertise have been linked with better diagnostic accuracy and improved quality of reporting, as reflected in the positive relationship between accrual volume and the quality of reports.³⁰ However, other local factors such as training activities and work load constraints probably play a role, as academic centres and high volume hospitals did not deliver superior reports. Furthermore, we were not able to assess the experience of individual pathologists. We also do not know if the smaller, non-academic hospitals participating in this trial are representative for community hospitals in general.

Second, it is possible that pathologists are insufficiently familiar with existing guidelines for ovarian cancer pathology reporting,^{8,31} do not fully agree with every item of the guideline or consider some parts as less important.³¹ In the current era of immunohistochemistry and other modern technology, the value of a gross description and measurements may sometimes be underestimated. Weighing the specimens may be considered not essential and be omitted to save precious time.³² Pathologists may omit to assess degree of differentiation because of the ongoing discussion on its value and reproducibility.

Third, local logistic factors such as work load and the use of standardised formats may explain some of the variability in the quality of reports. We don't know which of the participating centres are using some form of content checklists or structured formats, but no full synoptic reports were received.

Finally, used language and reporting style may be less clear to the clinician than expected by the pathologist. A study has shown a discrepancy rate of 30% between pathologists' intended meaning and the interpretation by surgeons.²¹ It is thus possible that items considered clear from the narrative by the pathologist are scored absent by the assessing clinicians. The problems of interpretation errors and missing data have been noted before within the framework of a clinical trial. In a study by Nagtegaal and colleagues, only one-third of case report forms (CRFs) were complete and correct when compared with the hospital pathology reports.¹²

Hence, to improve the quality of pathology reports of ovarian cancer, several actions can be taken. Centralising care in comprehensive cancer centres with sufficient case load makes it possible for pathologists to specialise in a specific domain.^{30,33,34} Within these cancer centres, multidisciplinary team meetings can serve as a first fail-safe mechanism to correct possible errors or incomplete data.^{35,36} Quality improvement projects have shown the benefit of standardised and synoptic reporting for several other tumour types. Synoptic reports have significantly less missing data and are better readable and preferred by physicians.^{10,37–40} To use

the advantage of synoptic reports at full length, guidelines for the processing and reporting of pre-operative biopsies in cases of suspected ovarian cancer and for specimens removed after neoadjuvant chemotherapy will need to be developed by experts.

Standardised pathology processes are also important in the framework of clinical trials. To reduce variability and errors with possible influence on trial results, a pathology section with clear guidelines should be included in each trial protocol.^{12,13,41}

The quality of surgical pathology and the quality of interdisciplinary communication must of course be placed in a broader context. Assessment of pathology reports in our study was limited to the presence or absence of four basic items only. Clarity of language could not be assessed as the original reports were written in the native language. Other important data such as the appropriate use of biomarkers were not evaluated, which is another limitation of this audit.

Quality of pathology reports includes besides completeness also timeliness and accuracy of diagnosis.^{37,42} Central review of specimens is a very useful tool to test accuracy of diagnosis and prognostic factors in order to improve data quality in clinical trials and daily practice.^{33,42–44} Unfortunately, in this study, resources for central pathology review were not available.

However, this large multinational audit reveals weaknesses in pathology reporting with possible important consequences for inter-professional communication and thus patient care. This audit of pathology reports aims to serve as an incentive for further research on ovarian cancer pathology and future quality improvement projects in multi-disciplinary cancer care.

5. Conclusion

In conclusion, this large audit of ovarian cancer pathology reports from 11 different countries reveals that in a substantial number of reports basic pathologic data are missing with possible adverse consequences for the quality of cancer care. Specialisation by pathologists and the use of standardised synoptic reports can possibly improve the quality of reporting. Further research is needed to better define pre- and post-operative diagnostic criteria for patients with presumed ovarian cancer who are treated with neo-adjuvant chemotherapy.

Conflict of interest statement

None declared.

Acknowledgements

This publication was supported by Grant Nos. 2U10 CA11488-28–2U10 CA011488-36 from the National Cancer Institute (Bethesda, MD, USA). Its content is solely the responsibility of the authors and does not necessarily reflect the official views of the National Cancer Institute. We also acknowledge Fonds Cancer (FOCA) from Belgium for supporting the Research fellowship of Dr. Leen Verleye.

We thank all investigators and their data managers who participated in this quality assurance project: J.B. Vermorken, University Hospital Antwerpen, Belgium. J. De Greve, University Hospital Brussels, Belgium. I. Vergote, University Hospital Gasthuisberg, Leuven, European Union. A. Floquet, Institut Bergonie, Bordeaux, France. L. Massuger, Radboud University, Nijmegen, the Netherlands. M. Van Baal, Free University, Amsterdam, the Netherlands. B. De Valk, Onze Lieve Vrouw Gasthuis, Amsterdam, the Netherlands. J.B. Trimbos, Leiden University Medical Centre, Leiden, the Netherlands. A. Honkoop, Sophie Hospital, Zwolle, the Netherlands. M.E.L. van der Burg, Erasmus MC, Rotterdam, the Netherlands. J. van der Velden, AMC, Amsterdam, the Netherlands. C. Mendiola, Hospital Universitario 12 de Octubre, Madrid, Spain. B. Mosgaard, Herlev Hospital, Copenhagen, Denmark. L. Elit, Hamilton Health Sciences, Juravinski Cancer centre, Hamilton, Canada. G. Rustin, Mount Vernon Cancer Center, Northwood Middlesex, UK. N. Reed, Beatson Oncology Centre, Glasgow, UK. J.A. Green, Clatterbridge Centre for Oncology, Liverpool, UK. N. Johnson, Royal United Hospital, Bath, UK. P. Gauthier, Hopital Notre-Dame du CHUM, Montreal, Canada. C. Dittrich, Kaiser Franz Josef Spital, Vienna, Austria. G.B. Kristensen, Norwegian Radium Hospital, Oslo, Norway. E. Gerdin, Akademiska Sjukhuset, Uppsala, Sweden. R. Lotocki, CancerCare Manitoba CA, Winnipeg, Canada. T. Ehlen, BCCA – Vancouver Cancer Centre, Vancouver, Canada. R. Grimshaw, Nova Scotia Cancer Centre, Halifax, Canada. C. Marth, Innsbruck Universitaetsklinik, Innsbruck, Austria. P. Debruyne, AZ Groeninghe, Kortrijk, Belgium. P. Ghatage, Tom Baker Cancer Centre, Calgary, Canada. M. Plante, Chuq-Pavillon Hotel-Dieu de Quebec, Canada. P. Bessette, Centre Hospitalier Universitaire de Sherbrooke CA, Fleurimont, Canada. W. Gotlieb, McGill University, Montreal, Canada. C. Popadiuk, Dr. H. Bliss Murphy Cancer Centre, Canada. U. Lee, BCCA – Fraser Valley Cancer Centre, Surrey, Canada. P. Desjardin, Hopital Charles Lemoyne, Canada. R. Sandvei, Haukeland Hospital University of Bergen, Bergen, Norway. F. Mota, Hospitais da Universidade de Coimbra, Coimbra, Portugal. S. Chan, Nottingham City Hospital, UK. J. Nevin, the James Cook University Hospital, Cleveland, UK. J. Summers, Mid Kent Oncology Centre, Maidstone, UK. A. Nordin, Queen Elizabeth the Queen Mother Hospital, Margate (Kent), UK.

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