

S3-Guideline on Diagnostics, Therapy and Follow-up of Malignant Ovarian Tumours

Short version 1.0 – AWMF registration number: 032/035OL, June 2013

S3-Leitlinie Diagnostik, Therapie und Nachsorge maligner Ovarialtumoren

Kurzversion 1.0 – AWMF-Registernummer: 032/035OL, Juni 2013

Authors

U. Wagner, P. Harter, F. Hilpert, S. Mahner, A. Reuß, A. du Bois, E. Petru, W. Meier, P. Ortner, K. König, K. Lindel, D. Grab, P. Piso, O. Ortmann, I. Runnebaum, J. Pfisterer, D. Lüftner, N. Frickhofen, F. Grünwald, B. O. Maier, J. Diebold, S. Hauptmann, F. Kommoss, G. Emons, B. Radeleff, M. Gebhardt, N. Arnold, G. Calaminus, I. Weisse, J. Weis, J. Sehouli, D. Fink, A. Burges, A. Hasenburg, C. Eggert

Affiliations

The affiliations are listed in chapter 1.8.1.

1 Information about this Short Version

1.1 Editors

German Guideline Programme in Oncology (OL) of the Association of the Scientific Medical Societies in Germany (AWMF), the German Cancer Society (DKG) and German Cancer Aid (DKH).

1.2 Leading professional society

Germany Society for Gynaecology and Obstetrics (DGGG).



1.3 Funding

This guideline was funded by German Cancer Aid as part of the German Guideline Programme in Oncology.

1.4 Contact

Office of the German Guideline Programme in Oncology
c/o Deutsche Krebsgesellschaft e.V.
Kuno-Fischer-Straße 8
14057 Berlin, Germany
leitlinienprogramm@krebsgesellschaft.de
www.leitlinienprogramm-onkologie.de

1.5 Citation

The German Guideline Programme in Oncology (German Cancer Society, German Cancer Aid, AWMF): S3-Guideline on Diagnostics, Therapy and Follow-up of Malignant Ovarian Tumors,

short version 1.0 (2013), AWMF registration number: 032-035OL, <http://leitlinienprogramm-onkologie.de/Leitlinien.7.0.html>

1.6 Note

Medicine is continually subject to a process of development and change so that all information, particularly all information on diagnostic and therapeutic treatments, can only reproduce the state of knowledge at the time of printing of this guideline on care. The greatest possible care was taken when compiling these recommendations on therapy and the choice and dosage of medications. Users are requested to consult the package leaflets and check the summary of product characteristics provided by manufacturers and, when in doubt, to consult a specialist. In the interests of all concerned, please contact the OL editorial office if you find discrepancies or controversial issues.

Users are responsible for all diagnostic and therapeutic applications, medications and dosages.

Registered trademarks (brand names) mentioned in this guideline have not been specifically labelled. When a specific indication lacks a trade name it should not be concluded that the brand name has not been registered. This guideline and all of its constituent parts is protected under copyright law. Any utilisation contrary to the provisions of copyright law without the written permission of the OL editorial office is prohibited and liable to prosecution. No part of this guideline may be reproduced in any form without the written permission of the OL editorial office. This applies in particular to copies, translations, microfilms and all storage, utilization and processing in electronic systems, intranets and the internet.

Bibliography

DOI <http://dx.doi.org/10.1055/s-0033-1350713>
Geburtsh Frauenheilk 2013; 73: 874-889 © Georg Thieme
Verlag KG Stuttgart · New York ·
ISSN 0016-5751

Correspondence

Prof. Dr. Uwe Wagner
Uni-Frauenklinik
Baldingerstraße
35 043 Marburg

DGGG-Leitlinienssekretariat

Prof. Dr. med. Matthias W. Beckmann, DGGG-Leitlinienbeauftragter
Frauenklinik
Universitätsklinikum Erlangen
Universitätsstraße 21-23
91054 Erlangen
Tel.: 091 31-85-335 07/44063
Fax: 091 31-85-339 51

1.7 Additional guideline documents

The contents of this short version refer to the long version of the S3-Guideline on Diagnostics, Therapy and Follow-up of Malignant Ovarian Tumours available in German on the following websites

- ▶ AWMF (<http://www.awmf.org/leitlinien/aktuelle-leitlinien.html>)
- ▶ German Guideline Programme in Oncology <http://www.leitlinienprogramm-onkologie.de/OL/leitlinien.html>
- ▶ German Cancer Society http://www.krebsgesellschaft.de/wub_llvidenzbasiert,120884.html
- ▶ German Cancer Aid (<http://www.krebshilfe.de/>)
- ▶ Guidelines International Network (www.g-i-n.net)
- ▶ Contributing German scientific medical societies (e.g. <http://www.dggg.de/leitlinien/>)

In addition to the short version, a number of other, supplementary documents are also available:

- ▶ Guideline report on the compilation of the guideline
- ▶ Long version
- ▶ Patient guideline

All of these documents will also be available on the websites listed above.

1.8 Responsibilities

1.8.1 Authors of the guideline

Editorial team

- ▶ Prof. Dr. Uwe Wagner (Co-ordinator, DGGG), Uni-Frauenklinik, Baldingerstraße, 35 043 Marburg, Germany
- ▶ Dr. Philipp Harter (DGGG), Kliniken Essen-Mitte, Henricistraße 92, 45 136 Essen, Germany
- ▶ PD Dr. Felix Hilpert (DGGG), Universitätsklinikum Schleswig Holstein, Campus Kiel, Klinik für Gynäkologie und Geburtshilfe, Arnold-Heller-Straße 3, Haus 24, 24 105 Kiel, Germany
- ▶ PD Dr. Sven Mahner (DGGG), Universitätsklinikum Hamburg-Eppendorf, Klinik für Gynäkologie, Martinistraße 52, 20 246 Hamburg, Germany
- ▶ Alexander Reuß, Koordinierungszentrum für Klinische Studien, Philipps-Universität Marburg, Karl-von Frisch-Straße 4, 35 043 Marburg, Germany

Participating scientific societies and authors

- ▶ Prof. Dr. Andreas du Bois – Arbeitsgemeinschaft Gynäkologische Onkologie e.V. (AGO) [Gynaecological Oncology Working Group]
- ▶ Prof. Dr. Edgar Petru – Arbeitsgemeinschaft für Gynäkologische Onkologie Austria (AGO AT) [Gynaecological Oncology Working Group Austria]
- ▶ Prof. Dr. Werner Meier – AGO Study Group
- ▶ Dr. Petra Ortner – Arbeitsgemeinschaft Supportive Maßnahmen in der Onkologie, Rehabilitation und Sozialmedizin (ASORS) [Working Group for Supportive Measures in Oncology, Rehabilitation and Epidemiology]
- ▶ Dr. Klaus König – Berufsverband der Frauenärzte e.V. (BVF) [Professional Organisation of German Gynaecologists]
- ▶ PD Dr. Katja Lindel – Deutsche Gesellschaft für Radioonkologie (DEGRO) [German Society for Radio-oncology]
- ▶ Prof. Dr. Dieter Grab – Deutsche Gesellschaft für Ultraschall in der Medizin e.V. (DEGUM) [German Society for Ultrasound in Medicine]
- ▶ Prof. Dr. Pompiliu Piso – Deutsche Gesellschaft für Allgemein- u. Viszeralchirurgie (DGAV) [German Society for General and Abdominal Surgery]

- ▶ Prof. Dr. Olaf Ortmann – Deutsche Gesellschaft für Endokrinologie (DGE) [German Society for Endocrinology]
- ▶ Prof. Dr. Ingo Runnebaum – Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG) [Germany Society for Gynaecology and Obstetrics]
- ▶ Prof. Dr. Jacobus Pfisterer – Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG) [Germany Society for Gynaecology and Obstetrics]
- ▶ PD Dr. Diana Lüftner – Deutsche Gesellschaft f. Hämatologie und Onkologie e.V. (DGHO) [German Society for Haematology and Oncology]
- ▶ Prof. Dr. Norbert Frickhofen – Deutsche Gesellschaft für Innere Medizin e.V. (DEGIM) [German Society for Internal Medicine]
- ▶ Prof. Dr. Frank Grünwald – Deutsche Gesellschaft für Nuklearmedizin e.V. (DGN) [German Society for Nuclear Medicine]
- ▶ Dr. Bernd Oliver Maier – Deutsche Gesellschaft für Palliativmedizin e.V. (DGP) [German Society for Palliative Medicine]
- ▶ Prof. Dr. Joachim Diebold, Prof. Dr. Steffen Hauptmann, Prof. Dr. Friedrich Kommoss – Deutsche Gesellschaft für Pathologie e.V. (DGP) [German Pathology Society]
- ▶ Prof. Dr. Günter Emons – Deutsche Menopausengesellschaft e.V. (DMG) Deutsche Gesellschaft für Pathologie [German Pathology Society]
- ▶ Dr. Boris Radeleff – Deutsche Röntgengesellschaft (DRG) [German Radiology Society]
- ▶ Marion Gebhardt (patients' representative) – Bundesverband der Frauenselbsthilfe nach Krebs e.V. [Federation of Women's Self-help after Cancer Organisations]
- ▶ Prof. Dr. Norbert Arnold – Deutsche Gesellschaft für Humangenetik (GfH) [German Society for Human Genetics]
- ▶ Dr. Gabriele Calaminus – Gesellschaft für Pädiatrische Onkologie und Hämatologie (GPOH) [Society for Paediatric Oncology and Haematology]
- ▶ Isolde Weisse – Konferenz Onkologischer Kranken- und Kinderkrankenpflege (KOK) [Conference for Oncologic Patient Care and Paediatric Patient Care]
- ▶ Prof. Dr. Joachim Weis – Arbeitsgemeinschaft für Psychosoziale Onkologie (PSO) [Psycho-social Oncology Working Group]
- ▶ Prof. Dr. Jalid Sehoul – Nord-Ostdeutsche Gesellschaft für Gynäkologische Onkologie (NOGGO) [Northeast German Society for Gynaecological Oncology]
- ▶ Prof. Dr. Daniel Fink – Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe (SGGG) [Swiss Society for Gynaecology and Obstetrics]
- ▶ Dr. Alexander Burges – as an independent expert
- ▶ Prof. Dr. Annette Hasenburg – as an independent expert
- ▶ Dr. C. Eggert from the Medizinischen Dienst der Krankenversicherung in Hessen (MDK Hessen) [Medical Service of the Health Insurance Companies in Hesse] contributed to the discussions at the Consensus Conferences as an expert without voting rights.

Methodological Support

1. The German Guideline Programme on Oncology
 - ▶ Prof. Dr. Ina Kopp, Marburg (AWMF)
 - ▶ Dr. Markus Follmann MPH MSc, Berlin (DKG) [German Cancer Society]
 - ▶ Dipl.-Soz.Wiss Thomas Langer (DKG) [German Cancer Society]

2. External agencies:

- ▶ Coordination Centre for Clinical Studies of Philipps University Marburg, A. Reuß, Dr. D. Lubbe
- ▶ Bremen Institute for Prevention Research and Epidemiology (BIPS), Dr. K. Giersiepen

3. The leading professional society:

- ▶ Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG) [German Society for Gynaecology and Obstetrics], Prof. Dr. R. Kreienberg

2 Introduction

2.1 Target audience

The guideline was compiled with the aim of providing high-risk groups with advice on diagnostics, surgical and systemic therapy in early and advanced stages of disease together with the treatment of rare histological subtypes. A lot of emphasis has been placed on follow-up care, rehabilitation, palliative therapy and psycho-oncological counselling. The recommendations are for physicians working both in hospitals and outpatient clinics, nursing staff and other medical partners involved in treating patients with malignant ovarian tumours. As it also covers the topics 'Screening' and 'Follow-up', registered physicians working in their own practice are also an important target audience of this guideline. It is additionally intended to offer guidance to affected patients and persons seeking more information as well as providing a basis for the gynaecological cancer centres currently being set up in Germany.

For the first time, scientific medical societies in Switzerland and Austria were also consulted, expanding the scope of this guideline.

2.2 Methodology

The methodological approach used to compile the guideline has been described in the guideline report. The guideline report is freely available online (in German), for example on the website of the German Guideline Programme in Oncology (<http://leitlinienprogramm-onkologie.de/Leitlinien.7.0.html>) and the pages of the AWMF (<http://www.awmf.org/>).

2.2.1 SIGN level of evidence system

To classify the risk of bias or confounding in the identified studies, this guideline has used the level of evidence system of the Scottish Intercollegiate Guidelines Network (SIGN, Version 2009) (<http://www.sign.ac.uk/pdf/sign50.pdf>) as described in **Table 1** below.

2.2.2 System of grading recommendations

The OL methodology uses the grades of recommendation awarded by the authors of the guideline. The level of recommendation is decided on in a formal consensus process, using a multi-step nominal group technique moderated by the AWMF.

The guideline includes the level of evidence (SIGN, see 2.2.1) of the studies on which they are based as well as the strength of the recommendation (grade of recommendation) for all evidence-based statements (see chapter 2.2.3) and recommendations. This guideline has three different 'strength of recommendation' ratings (see **Table 2** below), which are also reflected in the formulation of the recommendation.

Table 1 SIGN system for level of evidence grading (Version 2009).

Level	Description
1++	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of case-control or cohort studies, or high quality case control or cohort studies with a very low risk of confounding or bias ("chance") and a high probability that the relationship is causal
2+	Well conducted case-control or cohort studies with a low risk of confounding or bias ("chance") and a moderate probability that the relationship is causal
2-	Case-control or cohort studies with a high risk of confounding or bias ("chance") and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Table 2 Grades of recommendations.

Grade of recommendation	Description	Syntax
A	strongly recommended/ or not recommended	must/necessary
B	recommended/ or not recommended	should
0	neither recommended nor not recommended	can

2.2.3 Statements

Statements are expositions or explanations of specific facts or issues which do not constitute a call for action. They are approved in a similar manner to that used for recommendations in a formal consensus process and may be based either on study results or expert opinions.

2.2.4 Clinical consensus (CC)

Statements/recommendations which were drawn up on the basis of a consensus of experts from the guideline group are identified by the term "clinical consensus". No symbols were used to grade the clinical consensus; the strength of the consensus is indicated by the formulations used (must, necessary/should/can) as described for the gradations in **Table 2**.

2.2.5 Independence and disclosure of possible conflicts of interest

German Cancer Aid provided the funding through the German Guideline Programme in Oncology (OL). Funds were used for staffing costs, office materials, literature and consensus conferences (costs of venue, the media technology required at conferences, catering, moderator's fees, travelling expenses of participants). Travelling expenses were reimbursed in accordance with the German law on travel expenses when on company business or according to standard practice for the DKG [German Hospital Federation]. Editorial decisions and the compilation of the guideline were carried out entirely independent of the funding organisation. During the guideline process, all members provided a written disclosure of possible conflicts of interest. The conflicts

of interest disclosed are included in the guideline report to this guideline (<http://leitlinienprogramm-onkologie.de/Leitlinien.7.0.html>). We would like to take this opportunity of thanking all contributors for their contribution to the project, which was entirely voluntary and unsalaried.

2.2.6 Period of validity and update process

This S3-guideline will remain valid until it is next updated; its estimated period of validity is 3 years. Regular updates are planned; if an urgent need for changes to the guideline occurs in between update times, these changes will be published separately. Comments and advice for the update process are expressly requested and should be sent to the following address:

Prof. Dr. Uwe Wagner, Klinik für Gynäkologie, gynäkologische Endokrinologie und Onkologie, Baldingerstraße, D-35043 Marburg, Germany; phone: 06 421-58-66 211, fax: 0642 158-68 969, e-mail: wagneru@med.uni-marburg.de.

2.3 List of abbreviations

Abbreviation	Meaning
AUC	Area under the Curve
GR	Grade of Recommendation, A = strongly recommended, B = recommended, 0 = neither recommended nor not recommended
HIPEC	Hyperthermal Intraperitoneal Chemotherapy
HT	Hormone Therapy
CC	Clinical Consensus
GL	Guideline
LoE	Level of Evidence
OL	German Guideline Programme in Oncology
OP	Operation
ST	Statement
TVS	Transvaginal sonography
WHO	World Health Organisation

3 Epidemiology, Screening and Diagnostics

3.1 Screening

No.	Recommendations/Statements	GR	LoE	Sources
3.1.	Screening with CA-125 and TVS has not resulted in any drop in mortality to date.	ST	1++	Guidelines: [1, 2] Primary studies: [3–9]
3.2.	General screening is not necessary.	A	1++	Guidelines: [1, 2] Primary studies: [3–9]
3.3.	Multidisciplinary consultation (gynaecologist and human geneticist) and genetic testing must be offered if a patient is in the at-risk population.	CC		
3.4.	Screening with CA-125 and TVS was not proven to reduce mortality in risk groups.	ST	3	Guidelines: [1] Primary studies: [10–13]
3.5.	Screening of groups at risk is not necessary.	A	3	Guidelines: [1] Primary studies: [10–13]

3.2 Diagnostics

No.	Statements	GR	LoE	Sources
3.6.	Further examinations should be initiated if the following symptoms occur repeatedly and persistently, particularly in women above the age of 50: ▶ Bloatingness ▶ Flatulence ▶ Vague abdominal pain or discomfort ▶ Increased frequency of micturition	CC		
3.7.	If there is a suspicion of an ovarian mass, pelvic examination (palpation, speculum) must be carried out, followed by transvaginal sonography.	CC		
3.8.	No diagnostic examination exists which can take the place of operative staging for ovarian cancer and give a reliable assessment of the tumour's operability.	CC		

3.3 Diagnosis of recurrence

No.	Recommendations	GR	LoE	Sources
3.9.	Asymptomatic patients: If, contrary to the recommendations of the guideline, there is a suspicion of recurrence based on increased CA-125 levels, the further procedure should be discussed with the individual patient. An early, pre-symptomatic start of treatment for recurrence is not associated with improved survival rates.	B	1+	Primary studies: [14]
3.10.	Symptomatic patients: If symptoms are present, additional diagnostic investigations can be initiated. We were unable to identify evidence which would indicate improved survival for any of the available procedures.	0	2+	Primary studies: [15–23]

4 Patient Consent and Information

No.	Statements	GR	LoE	Sources
4.1.	The information provided by the physician to the patient must include information on the disease, the results of the examination(s), the course of treatment to date, the diagnostic and therapeutic options including expected side-effects as well as the assessment of the associated prognosis and the impact on the patient's life plans and quality of life. Written materials and other suitable media can be used to help explain all of this to the patient and as aids in decision-making.	CC		
4.2.	Conveying this information and explaining it to the patient must be done based on the following principles of patient-centred communication: <ul style="list-style-type: none"> ▶ The physician must show empathy and use active listening ▶ Difficult topics must be touched upon directly and sensitively ▶ Avoid using specialised medical vocabulary; explain specialist terminology where necessary ▶ Use strategies to improve the patient's comprehension (repetition, summarising of important information, use of diagrams and graphs) ▶ Encourage the patient to ask questions ▶ Permit and encourage the patient to express her feelings, particularly her worries and fears ▶ Offer further help 	CC		
4.3.	The patient's wishes about being involved in the process of medical decision-making must be taken into account.	CC		

5 Genetics, Prevention and Risk Factors

No.	Recommendations/Statements	GR	LoE	Sources
5.1.	Bilateral salpingo-oophorectomy is the most effective method to reduce the risk of developing the disease and to reduce mortality in patients with hereditary ovarian cancer.	ST	2+	Guidelines: [1, 2] Primary studies: [11, 24–39]
5.2.	Patients with BRCA1/2 mutation should be offered prophylactic bilateral salpingo-oophorectomy; surgery should be done once the patient plans to have no more children, after the patient has either turned 40 years of age or 5 years prior to the youngest age at which a member of the patient's family developed ovarian cancer.	B	2+	Guidelines: [2] Primary studies: [11, 24–39]

6 Pathological Diagnosis and Prognostic Factors

No.	Recommendations/Statements	GR	LoE	Sources
6.1.	To date, the evidence for an association between detected biochemical parameters and prediction/prognosis has been insufficient.	ST	2+	Primary studies: [40–50]
6.2.	The established prognostic factors for ovarian cancer listed below must be used: <ul style="list-style-type: none"> ▶ Tumour stage ▶ Postoperative residual tumour ▶ Age ▶ General condition ▶ Histological type ▶ Tumour grading ▶ Guideline-based therapy 	CC		

7 Surgical Treatment

7.1 Surgical treatment of early ovarian cancer

No.	Recommendations	GR	LoE	Sources
7.1.	Optimal staging must include the following surgical steps: <ul style="list-style-type: none"> ▶ Longitudinal laparotomy ▶ Inspection and palpation of the entire abdominal cavity ▶ Peritoneal cytology ▶ Biopsies from all abnormal sites ▶ Peritoneal biopsies from unremarkable regions ▶ Bilateral excision of adnexa of uterus ▶ Hysterectomy, using an extraperitoneal approach where necessary ▶ Infracolic omentectomy ▶ Appendectomy (for mucinous/unclear tumour types) ▶ Bilateral pelvic and paraaortal lymphonodectomy 	CC		
7.2.	If ovarian cancer is unexpectedly diagnosed, this must be confirmed histologically and the extent of spread described. The definitive treatment must then be carried out by a gynaecological oncologist.	CC		
7.3.	In patients with unilateral FIGO I stage tumours, fertility-preserving surgery can be done if staging was adequate.	0	4	Primary studies: [51–65]
7.4.	Patients with early stage ovarian cancer must be informed about the increased risk associated with fertility-preserving treatment, a risk which also depends on additional prognostic factors.	CC		
7.5.	Laparoscopic staging must not be done outside of studies.	A	3	Guidelines: [2] Primary studies: [66–72]

7.2 Surgical treatment of advanced ovarian cancer

No.	Recommendations/Statements	GR	LoE	Sources
7.6.	The goal of primary surgery to treat advanced ovarian cancer must be macroscopically complete resection.	CC		
7.7.	Multivisceral resection must be carried out if complete resection (free of residual macroscopic tumour) can be achieved or if it can be used to remove an obstruction and is not contraindicated in this patient.	CC		
7.8.	If advanced ovarian cancer is unexpectedly diagnosed, this must be confirmed histologically and the extent of spread described. The definitive treatment must then be carried out by a gynaecological oncologist in a suitable facility.	A	4	Guidelines: [2] Primary studies: [73–89]
7.9.	Patients obtain no benefit from primary chemotherapy followed by interval operation.	ST	1+	Guidelines: [1] Primary studies: [90–95]
7.10.	The sequence of therapy must consist first of primary surgery followed by chemotherapy.	A	1+	Guidelines: [1] Primary studies: [90–95]
7.11.	Second-look operations must not be carried out.	CC		

8 Systemic Primary Therapy

8.1 Systemic primary therapy for early ovarian cancer

No.	Recommendations	GR	LoE	Sources
8.1.	Patients with stage IA grade 1 ovarian cancer after complete operative staging must not receive adjuvant chemotherapy.	A	1+	Primary studies: [96–104]
8.2.	Patients with stage IC or IA/B, grade 3 ovarian cancer must receive platinum-based chemotherapy (6 cycles).	A	1+	Primary studies: [96–104]
8.3.	Patients with stage IAG2, IB G1/2 ovarian cancer can be offered platinum-based chemotherapy.	0	1+	Primary studies: [96–104]
8.4.	The therapy should include carboplatin and consist of 6 cycles.	B	1+	Guidelines: [1, 2] Primary studies: [67, 99, 105–117]

8.2 Systemic primary therapy for advanced ovarian cancer

No.	Recommendations	GR	LoE	Sources
8.5.	The first-line chemotherapy for patients with advanced ovarian cancer (II b-IV) must consist of carboplatin AUC5 and paclitaxel 175 mg/m ² for 3 h i. v. over a total of 6 cycles, with one cycle every 3 weeks.	A	1++	Guidelines: [118, 119] Primary studies: [120–131]
8.6.	Additional therapy with bevacizumab can be considered in patients with advanced ovarian cancer (IIIB-IV).	0	1+	Primary studies: [132, 133]
8.7.	Changes in dose density or intensity should only be done as part of a clinical trial.	B	1+	Guidelines: [2] Primary studies: [134–146]
8.8.	No maintenance or consolidation therapies must be carried out after primary therapy has been completed.*	A	1+	Primary studies: [132, 133, 147–154]
8.9.	Systematic recording of the patient's quality of life can be helpful to identify difficulties during treatment.	CC		

* Data on the effectiveness of consolidation or maintenance therapy to increase progression-free survival (PFS) is only available for bevacizumab (see 8.6.)

9 Treatment for Recurrence

9.1 Populations with recurrence

No.	Statement	GR	LoE	Sources
9.1.	Platinum-sensitive ovarian cancer: Disease responds primarily to platinum-based first-line chemotherapy with recurrence occurring at the earliest 6 months after conclusion of platinum-based chemotherapy. This also includes the subgroup of partially platinum-sensitive recurrences of ovarian cancer . In this subgroup, disease also responds primarily to platinum-based first-line chemotherapy but recurrence occurs between 6 and 12 months after concluding platinum-based chemotherapy. Platinum-resistant ovarian cancer: Disease recurs within the first 6 months after concluding initial platinum-based chemotherapy. This also includes the subgroup with platinum-refractory recurrence of ovarian cancer . In this subgroup, disease does not respond to platinum-based chemotherapy or disease progresses within 4 weeks after therapy has been concluded.	ST	1+	Guidelines: [1, 119] Primary studies: [14, 155–163]

9.2 Systemic therapy for recurrence

9.2.1 Platinum-resistant recurrence

No.	Recommendations/Statements	GR	LoE	Sources
9.2.	Combination therapy offers no advantages compared to monotherapy.	ST	1+	Guidelines: [119] Primary studies: [155, 156, 158, 164–171]
9.3.	Endocrine therapies are inferior to a monochemotherapy.	ST	1+	Guidelines: [119] Primary studies: [155, 156, 158, 164–171]
9.4.	Patients with platinum-resistant and/or refractory recurrence of ovarian cancer must not receive platinum-based monotherapy, if chemotherapy is indicated. The following cytostatic drugs can be used: <ul style="list-style-type: none"> ▶ pegylated liposomal doxorubicin ▶ topotecan ▶ gemcitabine ▶ paclitaxel weekly 	A	1+	Guidelines: [119] Primary studies: [155, 156, 158, 164–171]

9.2.2 Platinum-sensitive recurrence

No.	Recommendations	GR	LoE	Sources
9.5.	Patients with platinum-sensitive recurrence of ovarian cancer should have platinum-based combination therapy if chemotherapy is indicated. The following combinations can be used: <ul style="list-style-type: none"> ▶ carboplatin + gemcitabine + bevacizumab* ▶ carboplatin + pegylated liposomal doxorubicin ▶ carboplatin + paclitaxel ▶ carboplatin + gemcitabine 	CC		

* to treat patients with primary recurrence who did not have previous VEGF-targeted therapy

9.3 Surgery for recurrence

No.	Recommendations	GR	LoE	Sources
9.6.	The value of surgery to treat ovarian cancer recurrence cannot be verified by data from prospective studies with a high level of evidence, but retrospective data indicate a potential clinical benefit.	A	2+	Guidelines: [1] Primary studies: [172–177]
9.7.	The goal of surgery for recurrence should be macroscopically complete resection.	B	2+	Guidelines: [1] Primary studies: [172–177]

10 Follow-up Care, Rehabilitation, Psycho-oncology, Palliative Medicine

10.1 Follow-up care and rehabilitation

No.	Recommendations/Statements	GR	LoE	Sources
10.1.	Patients with ovarian cancer must be informed about the various options for rehabilitation and offered support from social counselling services; patients must be offered suitable options after their individual need has been assessed.	CC		
10.2.	The goal of follow-up care is to detect and treat therapy-associated side-effects, to offer rehabilitation, psychosocial care and reintegration, to improve the patient's quality of life and to detect any recurrence.	CC		
10.3.	Routine use of the determination of CA-125 does not result in longer survival.	ST	1+	Guidelines: [1] Primary studies: [14, 178, 179]
10.4.	Routine sophisticated diagnostics and determination of markers is not required during follow-up when patients are symptom-free.	A	1+	Leitlinien: [1] Primary studies: [14, 178, 179]
10.5.	Follow-up must include detailed medical history, physical examination including gynaecological examination with speculum and palpation, rectal examination and vaginal sonography.	CC		
10.6.	There is no reliable information about the safety of hormone therapy after treatment for ovarian cancer.	ST	2+	Primary studies: [180–183]
10.7.	Hormone therapy cannot be recommended after treatment for ovarian cancer. It can be considered in individual cases, particularly in patients with considerable limitations in their quality of life.	0	2+	Primary studies: [180–183]

10.2 Psycho-oncology

No.	Recommendations	GR	LoE	Sources
10.8.	Psychosocial interventions have a positive impact on the patient's quality of life, psychological condition and capacity to cope emotionally with the disease.	CC		
10.9.	Psycho-oncological care of patients with ovarian cancer is an integral part of the oncological diagnosis, therapy and follow-up care and requires an interdisciplinary approach.	CC		
10.10.	Psycho-oncological counselling and support should be offered to all patients and their family members based on their needs.	CC		
10.11.	The topic of sexuality should always be actively explored to identify when further support is required and to provide additional support as required.	CC		

10.3 Palliative medicine

No.	Recommendations	GR	LoE	Sources
10.12.	The right moment to initiate palliative medical care depends first and foremost on the patient's needs and the individual stage of disease.	CC		
10.13.	Patients who primarily require palliative medical care should be included in a programme of specialised palliative care.	CC		
10.14.	Palliative medical care includes the medical control of symptoms, palliative care and psychosocial support till death. It is offered as needed in the form of general or specialised palliative care.	CC		
10.15.	In a palliative setting all necessary measures taken must be geared to the patient's individual therapeutic aims and aims in life.	CC		

11 Borderline Tumours (BOT)

No.	Recommendations/Statements	GR	LoE	Sources
11.1.	Borderline tumours must be distinguished according to the WHO classification and categorised into subtypes. This should include the categorisation of any existing implants (invasive – non invasive) as well as information about microinvasion.	CC		[184]
11.2.	Careful surgical staging is necessary and, in addition to complete removal of the tumour (including bilateral salpingo-oophorectomy), should include inspection of the abdomen with peritoneal wash cytology, resection of all abnormal areas, peritoneal biopsies of unremarkable areas and omentectomy. In mucinous borderline tumours, metastasis of extraovarian tumours must be excluded; an appendectomy is necessary to exclude a primary appendiceal neoplasm.	B	2+	Primary studies: [185–189]
11.3.	There are some indications that performing cystectomy instead of ovariectomy and carrying out a fertility-preserving procedure instead of bilateral salpingo-oophorectomy is associated with higher rates of recurrence.	ST	2+	Primary studies: [190]
11.4.	If the patient wishes to have children/wishes to preserve endocrine functions, a fertility-preserving procedure can be carried out. The patient must be informed about the increased risk of recurrence associated with this procedure.	0	2+	Guidelines: [2] Primary studies: [191]
11.5.	There is no persuasive evidence for the effectiveness of adjuvant therapy for the treatment of borderline tumours.	ST	1+	Guidelines: [2] Primary studies: [192]
11.6.	Patients with borderline tumours must not receive adjuvant therapy.	A	1+	Guidelines: [2] Primary studies: [192]

12 Ovarian Germ Cell and Stromal Tumours

No.	Recommendations/Statements	GR	LoE	Sources
12.1.	The diagnosis of germ cell and stromal tumours must done in a similar manner as the diagnosis of ovarian cancer.	CC		
12.2.	Optimal staging must include the following procedures: <ul style="list-style-type: none"> ▶ Lower median laparotomy ▶ Inspection and palpation of the entire abdominal cavity ▶ Peritoneal cytology ▶ Removal of the tumour with salpingo-oophorectomy ▶ For potentially malignant tumours (granulosa cell tumours, Sertoli-Leydig cell tumours G2/G3 or steroid cell tumours NOS): <ul style="list-style-type: none"> ▶ Definitive operative staging analogous to that for ovarian cancer. ▶ The benefit of systematic lymphonodectomy when lymph nodes are unremarkable has not been proven. ▶ If the uterus is not removed, hysteroscopy and curettage are recommended (to exclude endometrial hyperplasias or endometrial carcinoma). 	A	2+	Primary studies: [193–196]
12.3.	Fertility-preserving procedures should be considered when treating younger patients.	B	2+	Primary studies: [53]
12.4.	The benefit of adjuvant radiotherapy, chemotherapy or endocrine therapy after complete resection has not been proven and is controversially discussed in the literature.	ST	2+	Primary studies: [197, 198]
12.5.	Platinum-based chemotherapy should be considered for tumours which are stage IC or higher or if residual tumour is still present.	B	2+	Primary studies: [199–202]

13 Ovarian Germ Cell Tumours

No.	Recommendations/Statements	GR	LoE	Sources
13.1.	The diagnosis of ovarian germ cell tumours must done in a similar manner as the diagnosis for ovarian cancer.	CC		
13.2.	The goal of surgical treatment is, in addition to histological typification, complete resection of the tumour and adequate staging while preserving fertility if the remaining genital area is unremarkable. The benefit of systematic lymphonodectomy when lymph nodes are unremarkable has not been proven.	ST	2+	Primary studies: [53, 203–212]
13.3.	No adjuvant chemotherapy is required for stage IA tumours.	A	2+	Primary studies: [213]
13.4.	For cancers > FIGO IA, platinum-based risk-adapted chemotherapy must be carried out, consisting of 2–4 cycles of 2 or 3 cytostatic drugs*.	A	2+	Primary studies: [213, 214]
13.5.	In patients with advanced stage tumours, primary chemotherapy can be administered to preserve fertility. Resection of the residual tumour and of residual metastases must be planned after 3 or 4 cycles of chemotherapy have been concluded.	CC		
13.6.	In addition to standard follow-up examinations, follow-up must also include the determination of specific tumour markers.	CC		

* Chemotherapy must always include platinum and etoposide. The 3rd cytostatic drug can be either bleomycin or ifosfamide.

14 Care Facilities

No.	Recommendations/Statements	GR	LoE	Sources
14.1.	Patients with ovarian cancer should be treated by a gynaecological oncologist (specialist) in a specialist facility which includes interdisciplinary diagnostic and therapeutic services.	CC		

15 Quality Indicators

Quality indicator	Recommendation reference	Evidence base/additional information
Quality indicator 1: Operative staging of early ovarian cancer		
Z: Number of pts. with operative staging using: ▶ laparotomy ▶ peritoneal cytology ▶ peritoneal biopsies ▶ bilateral excision of adnexa of uterus ▶ hysterectomy, using an extraperitoneal approach where necessary ▶ infracolic omentectomy ▶ bilateral pelvic and paraaortal lymphonodectomy N: All pts. with a primary diagnosis of ovarian cancer FIGO I – IIIA	7.1. Optimal staging must including the following procedures: ▶ longitudinal laparotomy ▶ inspection and palpation of the entire abdominal cavity ▶ peritoneal cytology ▶ biopsies from all abnormal sites ▶ peritoneal biopsies from unremarkable regions ▶ bilateral excision of adnexa of uterus ▶ hysterectomy, using an extraperitoneal approach where necessary ▶ infracolic omentectomy ▶ appendectomy (for mucinous/unclear tumour types) ▶ bilateral pelvic and paraaortal lymphonodectomy	a) <i>Quality target</i> Operative staging to be done as often as possible b) <i>Evidence base</i> CC Guidelines: NICE 2011 [118] Primary studies: [215–223]
Quality indicator 2: Intraoperative tumour rupture		
Z: Number of pts. with intraoperative tumour rupture N: All pts. with a primary diagnosis of ovarian cancer FIGO IA or IB	Background text to 7.5. “When an unclear ovarian carcinoma is removed laparoscopically, complete removal is important with no tumour rupture.”	a) <i>Quality target</i> No intraoperative tumour rupture b) <i>Evidence base</i> Leitlinien: [1,2] Primärstudien: [139–143]
Quality indicator 3: Macroscopically complete resection of advanced ovarian cancer		
Z: Number of pts. with macroscopically complete resection N: All pts. with a primary diagnosis of ovarian cancer ≥ FIGO IIB and surgical removal of the tumour	7.6. The goal of primary surgery must be to achieve macroscopically complete resection.	a) <i>Quality target</i> Macroscopically complete resection to be achieved as often as possible b) <i>Evidence base</i> CC Guidelines: [1, 2] Primary studies: [75, 83, 95, 174, 224–236]
Quality indicator 4: Surgery for advanced ovarian cancer		
Z: Number of pts. whose definitive surgery was done by a gynaecological oncologist N: All pts. with a primary diagnosis of ovarian cancer FIGO ≥ IIB after surgical therapy has been completed	7.8. The diagnosis for patients unexpectedly diagnosed with advanced ovarian cancer must be confirmed histologically and the extent of spread described. The definitive treatment must then be carried out by a gynaecological oncologist in a suitable facility.	a) <i>Quality target</i> Surgery to be performed as often as possible by a gynaecological oncologist b) <i>Evidence base</i> LoE 4, A Guidelines: [2] Primary studies: [73–89]
Note: Gynaecological oncologist = Medical specialist for gynaecology and obstetrics with a special focus on gynaecological oncology		
Quality indicator 5: Postoperative chemotherapy for advanced ovarian cancer		
Z: Number of pts. who received postoperative chemotherapy N: All pts. with a primary diagnosis of ovarian cancer ≥ FIGO IIB and receiving chemotherapy	7.10. The sequence of therapy must consist of primary surgery followed by chemotherapy.	a) <i>Quality target</i> Postoperative chemotherapy to be administered as often as possible in patients with advanced stage ovarian cancer b) <i>Evidence base</i> LoE 1+, A Guidelines: [1] Primary studies: [90–95]
Quality indicator 6: No adjuvant chemotherapy for early ovarian cancer		
Z: Number of pts. who received adjuvant chemotherapy N: All pts. with a primary diagnosis of ovarian cancer FIGO IA, G 1 und complete operative staging	8.1. Patients with stage IA grade 1 ovarian cancer after complete operative staging must not receive adjuvant chemotherapy.	a) <i>Quality target</i> If possible, no adjuvant chemotherapy to be administered to patients with FIGO IA, G 1 ovarian cancer who have had complete operative staging b) <i>Evidence base</i> LoE 1+, A Primary studies: [96–104]
Note: Please note that the FIGO classification has been updated! (position as of 12/2012)		

Quality indicator	Recommendation reference	Evidence base/additional information
Quality indicator 7: Platinum-based chemotherapy for early ovarian cancer		
Z: Number of pts. who received platinum-based chemotherapy N: All pts. with a primary diagnosis of ovarian cancer FIGO IC or IA/B and grade 3	8.2. Patients with stage IC or IA/B and grade 3 ovarian cancer must receive 6 cycles of platinum-based chemotherapy.	a) <i>Quality target</i> Patients with a primary diagnosis of IC or IA/B and grade 3 ovarian cancer to receive platinum-based chemotherapy as often as possible b) <i>Evidence base</i> LoE 1+, A Primary studies: [96–104]
Quality indicator 8: First-line chemotherapy for advanced ovarian cancer		
Z: Number of pts. who received 6 cycles of first-line chemotherapy carboplatin AUC5 and paclitaxel 175 mg/m ² N: All pts. with a primary diagnosis of ovarian cancer ≥ FIGO IIB	8.5. First-line chemotherapy for patients with advanced ovarian cancer (II b-IV) must consist of carboplatin AUC5 and paclitaxel 175 mg/m ² for 3 h i. v. over a total of 6 cycles, with one cycle every 3 weeks.	a) <i>Quality target</i> Patients with a primary diagnosis of ovarian cancer ≥ FIGO IIB to receive 6 cycles of first-line chemotherapy with carboplatin AUC5 and paclitaxel 175 mg/m ² as often as possible b) <i>Evidence base</i> LoE 1++, A Guidelines: NICE 2011 [118], NHS TA91 [119] Primary studies: [120–131]
Quality indicator 9: Chemotherapy for platinum-resistant and/or refractory primary recurrence		
Z: Number of pts. who received non platinum-based monotherapy with pegylated liposomal doxorubicin, topotecan, gemcitabine or paclitaxel weekly N: All pts. with platinum-resistant and/or refractory primary recurrence of ovarian cancer receiving chemotherapy for primary recurrence outside clinical trials	9.4. Patients with platinum-resistant and/or refractory recurrence of ovarian cancer must receive non platinum-based monotherapy if chemotherapy is indicated: The following cytostatic drugs can be considered: ▶ pegylated liposomal doxorubicin ▶ topotecan ▶ gemcitabine ▶ paclitaxel weekly	a) <i>Quality target</i> Non platinum-based monotherapy (s. left) to be administered as often as possible to treat patients with platinum-resistant and/or refractory primary recurrence of ovarian cancer receiving chemotherapy for primary recurrence outside clinical trials b) <i>Evidence base</i> LoE 1+, A Guidelines: NHS TA91 [119] Primary studies: [155, 156, 158, 164–171]
Note: Platinum-resistant recurrence: recurrence within 6 months after completing primary therapy		
Quality indicator 10: Combination therapy for platinum-sensitive recurrence		
Z: Number of pts. receiving platinum-based combination therapy N: All pts. with platinum-sensitive recurrence of ovarian cancer receiving chemotherapy for recurrence outside clinical trials	9.5 Patients with platinum-sensitive recurrence of ovarian cancer must receive platinum-based combination therapy, if chemotherapy is indicated. The following combinations of cytostatic drugs can be considered: ▶ carboplatin/gemcitabine/bevacizumab* ▶ carboplatin/pegylated liposomal doxorubicin ▶ carboplatin/paclitaxel ▶ carboplatin/gemcitabine	a) <i>Quality target</i> Platinum-based combination therapy to be administered as often as possible to treat patients with platinum-sensitive recurrence receiving chemotherapy for recurrence outside clinical trials b) <i>Evidence base</i> CC Guidelines: [1] Primary studies: [155, 157, 171, 237, 238]
Note: Platinum-based combination therapy: carboplatin/gemcitabine/bevacizumab*, carboplatin/pegylated liposomal doxorubicin, carboplatin/paclitaxel, carboplatin/gemcitabine		
Quality indicator 11: Counselling by social services		
Z: Number of pts who received counselling by social services N: All pts. with a primary diagnosis of ovarian cancer being treated in the facility	10.1. Patients with ovarian cancer must receive information about the available rehabilitation and support from social services and must be offered suitable support based on their individual need.	a) <i>Quality target</i> Patients with a primary diagnosis of ovarian cancer to receive counselling from social services as often as possible b) <i>Evidence base</i> CC Guidelines: [1] Primary studies: [14, 178, 179]
Quality indicator 12: No adjuvant therapy for BOT		
Z: Number of pts. with adjuvant therapy N: All pts. with a primary diagnosis of BOT	11.6. Patients with borderline tumours must not receive adjuvant therapy.	a) <i>Quality target</i> No adjuvant therapy to be given to patients with BOT b) <i>Evidence base</i> LoE 2+, A Guidelines: [2] Primary studies: [192]

* for patients with primary recurrence who did not previously receive VEGF-targeted therapy

16 References

- 1 *Scottish Intercollegiate Guidelines Network*. SIGN #75: Epithelial ovarian cancer. A national clinical guideline. Scottish Intercollegiate Guidelines Network; 2003
- 2 *The Australian Cancer Network and National Breast Cancer Centre*. Clinical practice guidelines for the management of women with epithelial ovarian cancer. Camperdown, NSW: National Breast Cancer Centre; 2004
- 3 *Menon U et al*. Sensitivity and specificity of multimodal and ultrasound screening for ovarian cancer, and stage distribution of detected cancers: results of the prevalence screen of the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS). *Lancet Oncol* 2009; 10: 327–340
- 4 *Kobayashi H et al*. A randomized study of screening for ovarian cancer: a multicenter study in Japan. *Int J Gynecol Cancer* 2008; 18: 414–420
- 5 *Buys SS et al*. Effect of screening on ovarian cancer mortality: the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Randomized Controlled Trial. *JAMA* 2011; 305: 2295–2303
- 6 *Fung MF et al*. Screening postmenopausal women for ovarian cancer: a systematic review. *J Obstet Gynaecol Can* 2004; 26: 717–728
- 7 *van Nagell Jr. JR et al*. Long-term survival of women with epithelial ovarian cancer detected by ultrasonographic screening. *Obstet Gynecol* 2011; 118: 1212–1221
- 8 *Timmerman D et al*. Simple ultrasound-based rules for the diagnosis of ovarian cancer. *Ultrasound Obstet Gynecol* 2008; 31: 681–690
- 9 *Timmerman D et al*. Terms, definitions and measurements to describe the sonographic features of adnexal tumors: a consensus opinion from the International Ovarian Tumor Analysis (IOTA) Group. *Ultrasound Obstet Gynecol* 2000; 16: 500–505
- 10 *Karlan BY et al*. Peritoneal serous papillary carcinoma, a phenotypic variant of familial ovarian cancer: implications for ovarian cancer screening. *Am J Obstet Gynecol* 1999; 180: 917–928
- 11 *Moller P et al*. The BRCA1 syndrome and other inherited breast or breast-ovarian cancers in a Norwegian prospective series. *Eur J Cancer* 2001; 37: 1027–1032
- 12 *Taylor L, Schwarz H*. Identification of a soluble OX40 isoform: development of a specific and quantitative immunoassay. *J Immunol Methods* 2001; 255: 67–72
- 13 *van der Velde NM et al*. Time to stop ovarian cancer screening in BRCA1/2 mutation carriers? *Int J Cancer* 2009; 124: 919–923
- 14 *Rustin GJ et al*. Early versus delayed treatment of relapsed ovarian cancer (MRC OV05/EORTC55955): a randomised trial. *Lancet* 2010; 376: 1155–1163
- 15 *Forstner R et al*. ESUR guidelines: ovarian cancer staging and follow-up. *Eur Radiol* 2010; 20: 2773–2780
- 16 *Peng NJ et al*. Early detection of recurrent ovarian cancer in patients with low-level increases in serum CA-125 levels by 2-[F-18]fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography. *Cancer Biother Radiopharm* 2011; 26: 175–181
- 17 *Gu P et al*. CA 125, PET alone, PET-CT, CT and MRI in diagnosing recurrent ovarian carcinoma: a systematic review and meta-analysis. *Eur J Radiol* 2009; 71: 164–174
- 18 *Partridge EE, Barnes MN*. Epithelial ovarian cancer: prevention, diagnosis, and treatment. *CA Cancer J Clin* 1999; 49: 297–320
- 19 *ESMO*. ESMO minimum clinical recommendations for diagnosis, treatment and follow-up of ovarian cancer. *Ann Oncol* 2001; 12: 1205–1207
- 20 *Jacobs I, Bast Jr. RC*. The CA 125 tumour-associated antigen: a review of the literature. *Hum Reprod* 1989; 4: 1–12
- 21 *IQWiG*. Positronemissionstomographie (PET) und PET/CT bei Ovarialkarzinom. 2011. www.iqwig.de
- 22 *Torizuka T et al*. Ovarian cancer recurrence: role of whole-body positron emission tomography using 2-[fluorine-18]-fluoro-2-deoxy-D-glucose. *Eur J Nucl Med Mol Imaging* 2002; 29: 797–803
- 23 *Takekuma M et al*. Positron emission tomography with 18F-fluoro-2-deoxyglucose for the detection of recurrent ovarian cancer. *Int J Clin Oncol* 2005; 10: 177–181
- 24 *Rebbeck TR et al*. Prophylactic oophorectomy in carriers of BRCA1 or BRCA2 mutations. *N Engl J Med* 2002; 346: 1616–1622
- 25 *Kauff ND et al*. Risk-reducing salpingo-oophorectomy in women with a BRCA1 or BRCA2 mutation. *N Engl J Med* 2002; 346: 1609–1615
- 26 *Haber D*. Prophylactic oophorectomy to reduce the risk of ovarian and breast cancer in carriers of BRCA mutations. *N Engl J Med* 2002; 346: 1660–1662
- 27 *Finch A et al*. Salpingo-oophorectomy and the risk of ovarian, fallopian tube, and peritoneal cancers in women with a BRCA1 or BRCA2 Mutation. *JAMA* 2006; 296: 185–192
- 28 *Rebbeck TR et al.; PROSE Study Group*. Effect of short-term hormone replacement therapy on breast cancer risk reduction after bilateral prophylactic oophorectomy in BRCA1 and BRCA2 mutation carriers: the PROSE Study Group. *J Clin Oncol* 2005; 23: 7804–7810
- 29 *Madalinska JB et al*. The impact of hormone replacement therapy on menopausal symptoms in younger high-risk women after prophylactic salpingo-oophorectomy. *J Clin Oncol* 2006; 24: 3576–3582
- 30 *Parker WH et al*. Ovarian conservation at the time of hysterectomy and long-term health outcomes in the nurses' health study. *Obstet Gynecol* 2009; 113: 1027–1037
- 31 *Madalinska JB et al*. Quality-of-life effects of prophylactic salpingo-oophorectomy versus gynecologic screening among women at increased risk of hereditary ovarian cancer. *J Clin Oncol* 2005; 23: 6890–6898
- 32 *Wagner TM et al*. Attitude towards prophylactic surgery and effects of genetic counselling in families with BRCA mutations. *Austrian Hereditary Breast and Ovarian Cancer Group*. *Br J Cancer* 2000; 82: 1249–1253
- 33 *Hallowell N*. A qualitative study of the information needs of high-risk women undergoing prophylactic oophorectomy. *Psychooncology* 2000; 9: 486–495
- 34 *Fry A et al*. Prophylactic oophorectomy versus screening: psychosocial outcomes in women at increased risk of ovarian cancer. *Psychooncology* 2001; 10: 231–241
- 35 *Antoniou A et al*. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case Series unselected for family history: a combined analysis of 22 studies. *Am J Hum Genet* 2003; 72: 1117–1130
- 36 *Bonadona V et al*. Cancer risks associated with germline mutations in MLH1, MSH2, and MSH6 genes in Lynch syndrome. *JAMA* 2011; 305: 2304–2310
- 37 *Chen S et al*. Characterization of BRCA1 and BRCA2 mutations in a large United States sample. *J Clin Oncol* 2006; 24: 863–871
- 38 *Dreyer G*. Screening for gynaecologic cancers in genetically predisposed women. *Best Pract Res Clin Obstet Gynaecol* 2012; 26: 267–282
- 39 *Tinelli A et al*. Hereditary ovarian cancers: from BRCA mutations to clinical management. A modern appraisal. *Cancer Metastasis Rev* 2010; 29: 339–350
- 40 *Malamou-Mitsi V et al*. Prognostic significance of HER-2, p53 and Bcl-2 in patients with epithelial ovarian cancer. *Anticancer Res* 2007; 27: 1157–1165
- 41 *Kommoss S et al*. Independent prognostic significance of cell cycle regulator proteins p16(INK4a) and pRb in advanced-stage ovarian carcinoma including optimally debulked patients: a translational research subprotocol of a randomised study of the Arbeitsgemeinschaft Gynaekologische Onkologie Ovarian Cancer Study Group. *Br J Cancer* 2007; 96: 306–313
- 42 *Secord AA et al*. Co-expression of angiogenic markers and associations with prognosis in advanced epithelial ovarian cancer: a Gynecologic Oncology Group study. *Gynecol Oncol* 2007; 106: 221–232
- 43 *Bellati F et al*. Immunology of gynecologic neoplasms: analysis of the prognostic significance of the immune status. *Curr Cancer Drug Targets* 2009; 9: 541–565
- 44 *Cree IA*. Chemosensitivity and chemoresistance testing in ovarian cancer. *Curr Opin Obstet Gynecol* 2009; 21: 39–43
- 45 *Harry VN, Gilbert FJ, Parkin DE*. Predicting the response of advanced cervical and ovarian tumors to therapy. *Obstet Gynecol Surv* 2009; 64: 548–560
- 46 *Itamochi H, Kigawa J, Terakawa N*. Mechanisms of chemoresistance and poor prognosis in ovarian clear cell carcinoma. *Cancer Sci* 2008; 99: 653–658
- 47 *Liu N, Wang X, Sheng X*. 'Triple negative' epithelial ovarian cancer and pathologic markers for prognosis. *Curr Opin Obstet Gynecol* 2011; 23: 19–23
- 48 *Sabatier R et al*. Gene expression profiling and prediction of clinical outcome in ovarian cancer. *Crit Rev Oncol Hematol* 2009; 72: 98–109
- 49 *Tian C et al*. CA-125 change after chemotherapy in prediction of treatment outcome among advanced mucinous and clear cell epithelial ovarian cancers: a Gynecologic Oncology Group study. *Cancer* 2009; 115: 1395–1403
- 50 *Trainer AH et al*. Moving toward personalized medicine: treatment-focused genetic testing of women newly diagnosed with ovarian cancer. *Int J Gynecol Cancer* 2010; 20: 704–716

- 51 Shaw MC *et al.* Development of an evidence-based algorithm for the management of ovarian cancer. *Eur J Gynaecol Oncol* 2003; 24: 117–125
- 52 Ayhan A *et al.* Oncologic and reproductive outcome after fertility-sparing surgery in ovarian cancer. *Eur J Gynaecol Oncol* 2003; 24: 223–232
- 53 Gershenson DM. Fertility-sparing surgery for malignancies in women. *J Natl Cancer Inst Monogr* 2005; 34: 43–47
- 54 Morice P *et al.* Conservative treatment in epithelial ovarian cancer: results of a multicentre study of the GCLCC (Groupe des Chirurgiens de Centre de Lutte Contre le Cancer) and SFOG (Societe Francaise d'Oncologie Gynecologique). *Hum Reprod* 2005; 20: 1379–1385
- 55 Leitao Jr. MM, Chi DS. Fertility-sparing options for patients with gynecologic malignancies. *Oncologist* 2005; 10: 613–622
- 56 Dexeus S, Labastida R, Dexeus D. Conservative management of epithelial ovarian cancer. *Eur J Gynaecol Oncol* 2005; 26: 473–478
- 57 Monk BJ, Disaia PJ. What is the role of conservative primary surgical management of epithelial ovarian cancer: the United States experience and debate. *Int J Gynecol Cancer* 2005; 15 (Suppl. 3): 199–205
- 58 Colombo N *et al.* Role of conservative surgery in ovarian cancer: the European experience. *Int J Gynecol Cancer* 2005; 15 (Suppl. 3): 206–211
- 59 Marhrom E, Cohen I. Fertility preservation options for women with malignancies. *Obstet Gynecol Surv* 2007; 62: 58–72
- 60 Denschlag D *et al.* Clinical recommendation on fertility preservation in borderline ovarian neoplasm: ovarian stimulation and oocyte retrieval after conservative surgery. *Gynecol Obstet Invest* 2010; 70: 160–165
- 61 Sarnacki S, Brisse H. Surgery of ovarian tumors in children. *Horm Res Paediatr* 2011; 75: 220–224
- 62 Zanetta G *et al.* Conservative surgery for stage I ovarian carcinoma in women of childbearing age. *Br J Obstet Gynaecol* 1997; 104: 1030–1035
- 63 Schilder JM *et al.* Outcome of reproductive age women with stage IA or IC invasive epithelial ovarian cancer treated with fertility-sparing therapy. *Gynecol Oncol* 2002; 87: 1–7
- 64 Morice P *et al.* Results of conservative management of epithelial malignant and borderline ovarian tumours. *Hum Reprod Update* 2003; 9: 185–192
- 65 Duska LR *et al.* Epithelial ovarian carcinoma in the reproductive age group. *Cancer* 1999; 85: 2623–2629
- 66 Medeiros LR *et al.* Laparoscopy versus laparotomy for FIGO Stage I ovarian cancer. *Cochrane Database Syst Rev* 2008; (4): CD005344
- 67 Trope C, Kaern J. Adjuvant chemotherapy for early-stage ovarian cancer: review of the literature. *J Clin Oncol* 2007; 25: 2909–2920
- 68 Panici PB *et al.* Laparoscopy compared with laparoscopically guided minilaparotomy for large adnexal masses: a randomized controlled trial. *Obstet Gynecol* 2007; 110 (2 Pt 1): 241–248
- 69 Ghezzi F *et al.* Should adnexal mass size influence surgical approach? A series of 186 laparoscopically managed large adnexal masses. *BJOG* 2008; 115: 1020–1027
- 70 Fagotti A *et al.* Should laparoscopy be included in the work-up of advanced ovarian cancer patients attempting interval debulking surgery? *Gynecol Oncol* 2010; 116: 72–77
- 71 Kindermann G, Maassen V, Kuhn W. Laparoscopic management of ovarian tumors subsequently diagnosed as malignant: a survey from 127 German departments of obstetrics and gynecology. *J Pelvic Surgery* 1996; 2: 245–251
- 72 Canis M *et al.* Laparoscopic management of adnexal masses: a gold standard? *Curr Opin Obstet Gynecol* 2002; 14: 423–428
- 73 Randall TC, Rubin SC. Surgical management of ovarian cancer. *Semin Surg Oncol* 1999; 17: 173–180
- 74 Axtell AE *et al.* Multi-institutional reciprocal validation study of computed tomography predictors of suboptimal primary cytoreduction in patients with advanced ovarian cancer. *J Clin Oncol* 2007; 25: 384–389
- 75 Wimberger P *et al.* Influence of residual tumor on outcome in ovarian cancer patients with FIGO stage IV disease: an exploratory analysis of the AGO-OVAR (Arbeitsgemeinschaft Gynaekologische Onkologie Ovarian Cancer Study Group). *Ann Surg Oncol* 2010; 17: 1642–1648
- 76 Gadducci A *et al.* Relationship between time interval from primary surgery to the start of taxane- plus platinum-based chemotherapy and clinical outcome of patients with advanced epithelial ovarian cancer: results of a multicenter retrospective Italian study. *J Clin Oncol* 2005; 23: 751–758
- 77 Trope C, Kaern J. Primary surgery for ovarian cancer. *Eur J Surg Oncol* 2006; 32: 844–852
- 78 Bristow RE *et al.* Delaying the primary surgical effort for advanced ovarian cancer: a systematic review of neoadjuvant chemotherapy and interval cytoreduction. *Gynecol Oncol* 2007; 104: 480–490
- 79 Wimberger P *et al.* Prognostic factors for complete debulking in advanced ovarian cancer and its impact on survival. An exploratory analysis of a prospectively randomized phase III study of the Arbeitsgemeinschaft Gynaekologische Onkologie Ovarian Cancer Study Group (AGO-OVAR). *Gynecol Oncol* 2007; 106: 69–74
- 80 Vernooij F *et al.* The outcomes of ovarian cancer treatment are better when provided by gynecologic oncologists and in specialized hospitals: a systematic review. *Gynecol Oncol* 2007; 105: 801–812
- 81 Elit LM *et al.* Surgical outcomes in women with ovarian cancer. *Can J Surg* 2008; 51: 346–354
- 82 Gerstein CG *et al.* The prediction of progression-free and overall survival in women with an advanced stage of epithelial ovarian carcinoma. *BJOG* 2009; 116: 372–380
- 83 du Bois A *et al.* Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: a combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials: by the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom (AGO-OVAR) and the Groupe d'Investigateurs Nationaux Pour les Etudes des Cancers de l'Ovaire (GINECO). *Cancer* 2009; 115: 1234–1244
- 84 Gerstein CG *et al.* Causes of postoperative mortality after surgery for ovarian cancer. *Eur J Cancer* 2009; 45: 2799–2803
- 85 Einkenkel J *et al.* Characteristics and management of diaphragm involvement in patients with primary advanced-stage ovarian, fallopian tube, or peritoneal cancer. *Int J Gynecol Cancer* 2009; 19: 1288–1297
- 86 Tixier H *et al.* Evaluation of pelvic posterior exenteration in the management of advanced-stage ovarian cancer. *Arch Gynecol Obstet* 2010; 281: 505–510
- 87 Gerstein CG *et al.* Prediction of residual disease after primary cytoreductive surgery for advanced-stage ovarian cancer: accuracy of clinical judgment. *Int J Gynecol Cancer* 2009; 19: 1511–1515
- 88 Aletti GD *et al.* Identification of patient groups at highest risk from traditional approach to ovarian cancer treatment. *Gynecol Oncol* 2011; 120: 23–28
- 89 du Bois A *et al.* Variations in institutional infrastructure, physician specialization and experience, and outcome in ovarian cancer: a systematic review. *Gynecol Oncol* 2009; 112: 422–436
- 90 Vergote I *et al.* Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *N Engl J Med* 2010; 363: 943–953
- 91 Schwartz PE *et al.* Neoadjuvant chemotherapy for advanced ovarian cancer: long-term survival. *Gynecol Oncol* 1999; 72: 93–99
- 92 van der Burg ME *et al.* The effect of debulking surgery after induction chemotherapy on the prognosis in advanced epithelial ovarian cancer. Gynecological Cancer Cooperative Group of the European Organization for Research and Treatment of Cancer. *N Engl J Med* 1995; 332: 629–634
- 93 Rose PG *et al.*; *Gynecologic Oncology Group*. Secondary surgical cytoreduction for advanced ovarian carcinoma. *N Engl J Med* 2004; 351: 2489–2497
- 94 Redman CW *et al.* Intervention debulking surgery in advanced epithelial ovarian cancer. *Br J Obstet Gynaecol* 1994; 101: 142–146
- 95 Tangjitgamol S *et al.* Interval debulking surgery for advanced epithelial ovarian cancer. *Cochrane Database Syst Rev* 2010; (10): CD006014
- 96 Winter-Roach BA, Kitchener HC, Dickinson HO. Adjuvant (post-surgery) chemotherapy for early stage epithelial ovarian cancer. *Cochrane Database Syst Rev* 2009; (3): CD004706
- 97 Young RC *et al.* Adjuvant therapy in stage I and stage II epithelial ovarian cancer. Results of two prospective randomized trials. *N Engl J Med* 1990; 322: 1021–1027
- 98 Trope C *et al.* Are borderline tumors of the ovary overtreated both surgically and systemically? A review of four prospective randomized trials including 253 patients with borderline tumors. *Gynecol Oncol* 1993; 51: 236–243
- 99 Trimbos JB *et al.* Impact of adjuvant chemotherapy and surgical staging in early-stage ovarian carcinoma: European Organisation for Research and Treatment of Cancer-Adjuvant Chemotherapy in Ovarian Neoplasm trial. *J Natl Cancer Inst* 2003; 95: 113–125

- 100 Timmers PJ *et al.* Clear cell carcinoma compared to serous carcinoma in early ovarian cancer: same prognosis in a large randomized trial. *Int J Gynecol Cancer* 2009; 19: 88–93
- 101 Trimbos B *et al.* Surgical staging and treatment of early ovarian cancer: long-term analysis from a randomized trial. *J Natl Cancer Inst* 2010; 102: 982–987
- 102 Adams G *et al.* Platinum-based adjuvant chemotherapy for early-stage epithelial ovarian cancer: single or combination chemotherapy? *BJOG* 2010; 117: 1459–1467
- 103 Takano M *et al.* Less impact of adjuvant chemotherapy for stage I clear cell carcinoma of the ovary: a retrospective Japan Clear Cell Carcinoma Study. *Int J Gynecol Cancer* 2010; 20: 1506–1510
- 104 Garcia-Saenz JA *et al.* Platinum-based adjuvant chemotherapy on moderate- and high-risk stage I and II epithelial ovarian cancer patients. Long-term single institution experience and literature review. *Clin Transl Oncol* 2011; 13: 121–132
- 105 Trimbos JB *et al.* International Collaborative Ovarian Neoplasm trial 1 and Adjuvant ChemoTherapy In Ovarian Neoplasm trial: two parallel randomized phase III trials of adjuvant chemotherapy in patients with early-stage ovarian carcinoma. *J Natl Cancer Inst* 2003; 95: 105–112
- 106 Colombo N *et al.* International Collaborative Ovarian Neoplasm trial 1: a randomized trial of adjuvant chemotherapy in women with early-stage ovarian cancer. *J Natl Cancer Inst* 2003; 95: 125–132
- 107 Vergote I *et al.* Prognostic importance of degree of differentiation and cyst rupture in stage I invasive epithelial ovarian carcinoma. *Lancet* 2001; 357: 176–182
- 108 Ho CM *et al.* Evaluation of complete surgical staging with pelvic and para-aortic lymphadenectomy and paclitaxel plus carboplatin chemotherapy for improvement of survival in stage I ovarian clear cell carcinoma. *Gynecol Oncol* 2003; 88: 394–399
- 109 Kitchener HC. Adjuvant chemotherapy improves survival after resection of stage 1 ovarian cancer. *Cancer Treat Rev* 2005; 31: 323–327
- 110 Shimada M *et al.* Outcome of patients with early ovarian cancer undergoing three courses of adjuvant chemotherapy following complete surgical staging. *Int J Gynecol Cancer* 2005; 15: 601–605
- 111 Bell J *et al.* Randomized phase III trial of three versus six cycles of adjuvant carboplatin and paclitaxel in early stage epithelial ovarian carcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol* 2006; 102: 432–439
- 112 Obermair A *et al.* A new prognostic model for FIGO stage 1 epithelial ovarian cancer. *Gynecol Oncol* 2007; 104: 607–611
- 113 Skirnisdottir I, Sorbe B. Survival and prognostic factors in early-stage epithelial ovarian carcinoma treated with taxane-based adjuvant chemotherapy. *Int J Gynecol Cancer* 2007; 17: 1231–1237
- 114 Chan JK *et al.* Prognostic factors for high-risk early-stage epithelial ovarian cancer: a Gynecologic Oncology Group study. *Cancer* 2008; 112: 2202–2210
- 115 Takano M *et al.* Clear cell carcinoma of the ovary: a retrospective multicentre experience of 254 patients with complete surgical staging. *Br J Cancer* 2006; 94: 1369–1374
- 116 Chan JK *et al.* The potential benefit of 6 vs. 3 cycles of chemotherapy in subsets of women with early-stage high-risk epithelial ovarian cancer: an exploratory analysis of a Gynecologic Oncology Group study. *Gynecol Oncol* 2010; 116: 301–306
- 117 Mannel RS *et al.* A randomized phase III trial of IV carboplatin and paclitaxel × 3 courses followed by observation versus weekly maintenance low-dose paclitaxel in patients with early-stage ovarian carcinoma: a Gynecologic Oncology Group Study. *Gynecol Oncol* 2011; 122: 89–94
- 118 NICE. NICE clinical guideline 122. The recognition and initial management of ovarian cancer. 2011 [cited 2012 September 7]. <http://guidance.nice.org.uk/CG122>; Stand: 07.09.2012
- 119 NHS National Institute for Health and Clinical Excellence. Technology Appraisal Guidance 91 Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer. 2005 [cited 2012 September 7]. <http://www.nice.org.uk/TA091>; Stand: 07.09.2012
- 120 ICON Collaborators. ICON2: randomised trial of single-agent carboplatin against three-drug combination of CAP (cyclophosphamide, doxorubicin, and cisplatin) in women with ovarian cancer. ICON Collaborators. International Collaborative Ovarian Neoplasm Study. *Lancet* 1998; 352: 1571–1576
- 121 ICON Collaborators. Paclitaxel plus carboplatin versus standard chemotherapy with either single-agent carboplatin or cyclophosphamide, doxorubicin, and cisplatin in women with ovarian cancer: the ICON3 randomised trial. *Lancet* 2002; 360: 505–515
- 122 McGuire WP *et al.* Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and stage IV ovarian cancer. *N Engl J Med* 1996; 334: 1–6
- 123 Muggia FM *et al.* Phase III randomized study of cisplatin versus paclitaxel versus cisplatin and paclitaxel in patients with suboptimal stage III or IV ovarian cancer: a gynecologic oncology group study. *J Clin Oncol* 2000; 18: 106–115
- 124 Neijt JP *et al.* Exploratory phase III study of paclitaxel and cisplatin versus paclitaxel and carboplatin in advanced ovarian cancer. *J Clin Oncol* 2000; 18: 3084–3092
- 125 Piccart MJ *et al.* Randomized intergroup trial of cisplatin-paclitaxel versus cisplatin-cyclophosphamide in women with advanced epithelial ovarian cancer: three-year results. *J Natl Cancer Inst* 2000; 92: 699–708
- 126 West RJ, Zweig SF. Meta-analysis of chemotherapy regimens for ovarian carcinoma: a reassessment of cisplatin, cyclophosphamide and doxorubicin versus cisplatin and cyclophosphamide. *Eur J Gynaecol Oncol* 1997; 18: 343–348
- 127 Ozols RF. Chemotherapy for ovarian cancer. *Semin Oncol* 1999; 26 (6 Suppl. 18): 34–40
- 128 du Bois A, Neijt JP, Thigpen JT. First line chemotherapy with carboplatin plus paclitaxel in advanced ovarian cancer – a new standard of care? *Ann Oncol* 1999; 10 (Suppl. 1): 35–41
- 129 Aabo K *et al.* Chemotherapy in advanced ovarian cancer: four systematic meta-analyses of individual patient data from 37 randomized trials. Advanced Ovarian Cancer Trialists' Group. *Br J Cancer* 1998; 78: 1479–1487
- 130 du Bois A *et al.* A randomized clinical trial of cisplatin/paclitaxel versus carboplatin/paclitaxel as first-line treatment of ovarian cancer. *J Natl Cancer Inst* 2003; 95: 1320–1329
- 131 Ozols RF *et al.* Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. *J Clin Oncol* 2003; 21: 3194–3200
- 132 Burger RA *et al.* Incorporation of bevacizumab in the primary treatment of ovarian cancer. *N Engl J Med* 2011; 365: 2473–2483
- 133 Perren TJ *et al.* A phase 3 trial of bevacizumab in ovarian cancer. *N Engl J Med* 2011; 365: 2484–2496
- 134 McGuire WP 3rd. High-dose chemotherapeutic approaches to ovarian cancer management. *Semin Oncol* 2000; 27(3 Suppl. 7): 41–46
- 135 Mobus V *et al.* Phase III trial of high-dose sequential chemotherapy with peripheral blood stem cell support compared with standard dose chemotherapy for first-line treatment of advanced ovarian cancer: intergroup trial of the AGO-Ovar/AIO and EBMT. *J Clin Oncol* 2007; 25: 4187–4193
- 136 Katsumata N *et al.* Dose-dense paclitaxel once a week in combination with carboplatin every 3 weeks for advanced ovarian cancer: a phase 3, open-label, randomised controlled trial. *Lancet* 2009; 374: 1331–1338
- 137 Hoskins P *et al.* Advanced ovarian cancer: phase III randomized study of sequential cisplatin-topotecan and carboplatin-paclitaxel vs. carboplatin-paclitaxel. *J Natl Cancer Inst* 2010; 102: 1547–1556
- 138 Jaaback K, Johnson N. Intraperitoneal chemotherapy for the initial management of primary epithelial ovarian cancer. *Cochrane Database Syst Rev* 2006; (1): CD005340
- 139 Buyse M *et al.* Using the expected survival to explain differences between the results of randomized trials: a case in advanced ovarian cancer. *J Clin Oncol* 2003; 21: 1682–1687
- 140 Aravantinos G *et al.* Paclitaxel plus carboplatin versus paclitaxel plus alternating carboplatin and cisplatin for initial treatment of advanced ovarian cancer: long-term efficacy results: a Hellenic Cooperative Oncology Group (HeCOG) study. *Ann Oncol* 2005; 16: 1116–1122
- 141 Dizon DS *et al.* Two for good measure: six versus eight cycles of carboplatin and paclitaxel as adjuvant treatment for epithelial ovarian cancer. *Gynecol Oncol* 2006; 100: 417–421
- 142 Armstrong DK *et al.* Intraperitoneal cisplatin and paclitaxel in ovarian cancer. *N Engl J Med* 2006; 354: 34–43
- 143 Grenman S *et al.* A randomised phase III study comparing high-dose chemotherapy to conventionally dosed chemotherapy for stage III ovarian cancer: the Finnish Ovarian Cancer (FINOVA) study. *Eur J Cancer* 2006; 42: 2196–2199

- 144 *Spriggs DR et al.* Phase III randomized trial of intravenous cisplatin plus a 24- or 96-hour infusion of paclitaxel in epithelial ovarian cancer: a Gynecologic Oncology Group Study. *J Clin Oncol* 2007; 25: 4466–4471
- 145 *Lhomme C et al.* Phase III study of valsopodar (PSC833) combined with paclitaxel and carboplatin compared with paclitaxel and carboplatin alone in patients with stage IV or suboptimally debulked stage III epithelial ovarian cancer or primary peritoneal cancer. *J Clin Oncol* 2008; 26: 2674–2682
- 146 *Safra T et al.* Combined weekly carboplatin and paclitaxel as primary treatment of advanced epithelial ovarian carcinoma. *Gynecol Oncol* 2009; 114: 215–218
- 147 *Lambert HE et al.* A randomized trial of five versus eight courses of cisplatin or carboplatin in advanced epithelial ovarian carcinoma. A North Thames Ovary Group Study. *Ann Oncol* 1997 8: 327–333
- 148 *Sorbe B; Swedish-Norwegian Ovarian Cancer Study Group.* Consolidation treatment of advanced (FIGO stage III) ovarian carcinoma in complete surgical remission after induction chemotherapy: a randomized, controlled, clinical trial comparing whole abdominal radiotherapy, chemotherapy, and no further treatment. *Int J Gynecol Cancer* 2003; 13: 278–286
- 149 *Mei L et al.* Maintenance chemotherapy for ovarian cancer. *Cochrane Database Syst Rev* 2010; (9): CD007414
- 150 *Berek J et al.* Oregovomab maintenance monoimmunotherapy does not improve outcomes in advanced ovarian cancer. *J Clin Oncol* 2009; 27: 418–425
- 151 *Pecorelli S et al.* Phase III trial of observation versus six courses of paclitaxel in patients with advanced epithelial ovarian cancer in complete response after six courses of paclitaxel/platinum-based chemotherapy: final results of the After-6 protocol 1. *J Clin Oncol* 2009; 27: 4642–4648
- 152 *Penson RT et al.* Phase II study of carboplatin, paclitaxel, and bevacizumab with maintenance bevacizumab as first-line chemotherapy for advanced mullerian tumors. *J Clin Oncol* 2010; 28: 154–159
- 153 *Pomel C et al.* Hyperthermic intra-peritoneal chemotherapy using oxaliplatin as consolidation therapy for advanced epithelial ovarian carcinoma. Results of a phase II prospective multicentre trial. CHIPOVAC study. *Eur J Surg Oncol* 2010; 36: 589–593
- 154 *Hess LM et al.* Continued chemotherapy after complete response to primary therapy among women with advanced ovarian cancer: a meta-analysis. *Cancer* 2010; 116: 5251–5260
- 155 *Williams C, Simera I, Bryant A.* Tamoxifen for relapse of ovarian cancer. *Cochrane Database Syst Rev* 2010; (3): CD001034
- 156 *ten Bokkel Huinink W et al.* Topotecan versus paclitaxel for the treatment of recurrent epithelial ovarian cancer. *J Clin Oncol* 1997; 15: 2183–2193
- 157 *Parmar MK et al.* Paclitaxel plus platinum-based chemotherapy versus conventional platinum-based chemotherapy in women with relapsed ovarian cancer: the ICON4/AGO-OVAR-2.2 trial. *Lancet* 2003; 361: 2099–2106
- 158 *Gordon AN et al.* Recurrent epithelial ovarian carcinoma: a randomized phase III study of pegylated liposomal doxorubicin versus topotecan. *J Clin Oncol* 2001; 19: 3312–3322
- 159 *Cantu MG et al.* Randomized controlled trial of single-agent paclitaxel versus cyclophosphamide, doxorubicin, and cisplatin in patients with recurrent ovarian cancer who responded to first-line platinum-based regimens. *J Clin Oncol* 2002; 20: 1232–1237
- 160 *Blackledge G et al.* Response of patients in phase II studies of chemotherapy in ovarian cancer: implications for patient treatment and the design of phase II trials. *Br J Cancer* 1989; 59: 650–653
- 161 *Eisenhauer EA et al.* New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer* 2009; 45: 228–247
- 162 *Rustin GJ et al.* Definitions for response and progression in ovarian cancer clinical trials incorporating RECIST 1.1 and CA 125 agreed by the Gynecological Cancer Intergroup (GCGI). *Int J Gynecol Cancer* 2011; 21: 419–423
- 163 *Friedlander M et al.; Gynecologic Cancer InterGroup.* Clinical trials in recurrent ovarian cancer. *Int J Gynecol Cancer* 2011; 21: 771–775
- 164 *Meier W et al.* Topotecan versus treosulfan, an alkylating agent, in patients with epithelial ovarian cancer and relapse within 12 months following 1st-line platinum/paclitaxel chemotherapy. A prospectively randomized phase III trial by the Arbeitsgemeinschaft Gynaekologische Onkologie Ovarian Cancer Study Group (AGO-OVAR). *Gynecol Oncol* 2009; 114: 199–205
- 165 *ten Bokkel Huinink W, Lane SR, Ross GA.* Long-term survival in a phase III, randomised study of topotecan versus paclitaxel in advanced epithelial ovarian carcinoma. *Ann Oncol* 2004; 15: 100–103
- 166 *Vergote I et al.* Phase 3 randomised study of canfosamide (Telcyta, TLK286) versus pegylated liposomal doxorubicin or topotecan as third-line therapy in patients with platinum-refractory or -resistant ovarian cancer. 2009 (1879-0852 [Electronic])
- 167 *Ferrandina G et al.* Phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in progressive or recurrent ovarian cancer. *J Clin Oncol* 2008; 26: 890–896
- 168 *Mutch DG et al.* Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinum-resistant ovarian cancer. *J Clin Oncol* 2007; 25: 2811–2818
- 169 *du Bois A et al.* Chemotherapy versus hormonal treatment in platinum- and paclitaxel-refractory ovarian cancer: a randomised trial of the German Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) Study Group Ovarian Cancer. *Ann Oncol* 2002; 13: 251–257
- 170 *Sehouli J et al.* Nonplatinum topotecan combinations versus topotecan alone for recurrent ovarian cancer: results of a phase III study of the North-Eastern German Society of Gynecological Oncology Ovarian Cancer Study Group. *J Clin Oncol* 2008; 26: 3176–3182
- 171 *Peng LH, Chen XY, Wu TX.* Topotecan for ovarian cancer. *Cochrane Database Syst Rev* 2008; 2: CD005589; DOI: 10.1002/14651858.CD005589.pub2
- 172 *Eisenkop SM, Friedman RL, Spirtos NM.* The role of secondary cytoreductive surgery in the treatment of patients with recurrent epithelial ovarian carcinoma. *Cancer* 2000; 88: 144–153
- 173 *Harter P et al.; Arbeitsgemeinschaft Gynaekologische Onkologie Ovarian Committee; AGO Ovarian Cancer Study Group.* Surgery in recurrent ovarian cancer: the Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) DESKTOP OVAR trial. *Ann Surg Oncol* 2006; 13: 1702–1710
- 174 *Sehouli J et al.* Role of secondary cytoreductive surgery in ovarian cancer relapse: who will benefit? A systematic analysis of 240 consecutive patients. *J Surg Oncol* 2010; 102: 656–662
- 175 *Galaal K et al.* Cytoreductive surgery plus chemotherapy versus chemotherapy alone for recurrent epithelial ovarian cancer. *Cochrane Database Syst Rev* 2010; (6): CD007822
- 176 *Bristow RE, Puri I, Chi DS.* Cytoreductive surgery for recurrent ovarian cancer: a meta-analysis. *Gynecol Oncol* 2009; 112: 265–274
- 177 *Harter P et al.* Prospective validation study of a predictive score for operability of recurrent ovarian cancer: the Multicenter Intergroup Study DESKTOP II. A project of the AGO Kommission OVAR, AGO Study Group, NOGGO, AGO-Austria, and MITO. *Int J Gynecol Cancer* 2011; 21: 289–295
- 178 *Kew F et al.* Evaluation of follow-up strategies for patients with epithelial ovarian cancer following completion of primary treatment. *Cochrane Database Syst Rev* 2011; (6): CD006119
- 179 *Gadducci A et al.* Surveillance procedures for patients treated for epithelial ovarian cancer: a review of the literature. *Int J Gynecol Cancer* 2007; 17: 21–31
- 180 *Guidozzi F, Daponte A.* Estrogen replacement therapy for ovarian carcinoma survivors: A randomized controlled trial. *Cancer* 1999; 86: 1013–1018
- 181 *Eeles RA et al.* Hormone replacement therapy and survival after surgery for ovarian cancer. *BMJ* 1991; 302: 259–262
- 182 *Ursic-Vrscaj M, Bebar S, Zakelj MP.* Hormone replacement therapy after invasive ovarian serous cystadenocarcinoma treatment: the effect on survival. *Menopause* 2001; 8: 70–75
- 183 *Mascarenhas C et al.* Use of hormone replacement therapy before and after ovarian cancer diagnosis and ovarian cancer survival. *Int J Cancer* 2006; 119: 2907–2915
- 184 *WHO.* Classification of Tumours. Pathology and Genetics of Tumours of the Breast and female genital Organs. 3rd ed. Switzerland: WHO-Press; 2003
- 185 *Kaern J, Trope CG, Abeler VM.* A retrospective study of 370 borderline tumors of the ovary treated at the Norwegian Radium Hospital from 1970 to 1982. A review of clinicopathologic features and treatment modalities. *Cancer* 1993; 71: 1810–1820
- 186 *Leake JF et al.* Long-term follow-up of serous ovarian tumors of low malignant potential. *Gynecol Oncol* 1992; 47: 150–158
- 187 *Odegaard E et al.* Surgery of borderline tumors of the ovary: retrospective comparison of short-term outcome after laparoscopy or laparotomy. *Acta Obstet Gynecol Scand* 2007; 86: 620–626

- 188 *Camatte S et al.* Impact of surgical staging in patients with macroscopic "stage I" ovarian borderline tumours: analysis of a continuous series of 101 cases. *Eur J Cancer* 2004; 40: 1842–1849
- 189 *Menczer J, Chetrit A, Sadetzki S.* The effect of hysterectomy on survival of patients with borderline ovarian tumors. *Gynecol Oncol* 2012; 125: 372–375
- 190 *du Bois A, Ewald-Riegler N.* Borderline-Tumoren des Ovars – eine systematische Übersicht. *Geburtsh Frauenheilk* 2009; 69: 807–833
- 191 *Morice P et al.* Recommendations of the Fertility Task Force of the European Society of Gynecologic Oncology about the conservative management of ovarian malignant tumors. *Int J Gynecol Cancer* 2011; 21: 951–963
- 192 *Faluyi O et al.* Interventions for the treatment of borderline ovarian tumours. *Cochrane Database Syst Rev* 2010; (9): CD007696
- 193 *Miller BE et al.* Prognostic factors in adult granulosa cell tumor of the ovary. *Cancer* 1997; 79: 1951–1955
- 194 *Nosov V et al.* Predictors of recurrence of ovarian granulosa cell tumors. *Int J Gynecol Cancer* 2009; 19: 628–633
- 195 *Colombo N et al.* Management of ovarian stromal cell tumors. *J Clin Oncol* 2007; 25: 2944–2951
- 196 *Sehouli J et al.* Granulosa cell tumor of the ovary: 10 years follow-up data of 65 patients. *Anticancer Res* 2004; 24 (2C): 1223–1229
- 197 *Zanagnolo V, Pasinetti B, Sartori E.* Clinical review of 63 cases of sex cord stromal tumors. *Eur J Gynaecol Oncol* 2004; 25: 431–438
- 198 *Evans AT 3rd et al.* Clinicopathologic review of 118 granulosa and 82 theca cell tumors. *Obstet Gynecol* 1980; 55: 231–238
- 199 *Zhang M et al.* Prognostic factors responsible for survival in sex cord stromal tumors of the ovary – an analysis of 376 women. *Gynecol Oncol* 2007; 104: 396–400
- 200 *Fotopoulou C et al.* Adult granulosa cell tumors of the ovary: tumor dissemination pattern at primary and recurrent situation, surgical outcome. *Gynecol Oncol* 2010; 119: 285–290
- 201 *Zambetti M et al.* cis-platinum/vinblastine/bleomycin combination chemotherapy in advanced or recurrent granulosa cell tumors of the ovary. *Gynecol Oncol* 1990; 36: 317–320
- 202 *Colombo N et al.* Cisplatin, vinblastine, and bleomycin combination chemotherapy in metastatic granulosa cell tumor of the ovary. *Obstet Gynecol* 1986; 67: 265–268
- 203 *Mahdi H et al.* Prognostic impact of lymphadenectomy in clinically early stage malignant germ cell tumour of the ovary. *Br J Cancer* 2011; 105: 493–497
- 204 *Gershenson DM.* Management of ovarian germ cell tumors. *J Clin Oncol* 2007; 25: 2938–2943.
- 205 *Pectasides D, Pectasides E, Kassanos D.* Germ cell tumors of the ovary. *Cancer Treat Rev* 2008; 34: 427–441
- 206 *Kumar S et al.* The prevalence and prognostic impact of lymph node metastasis in malignant germ cell tumors of the ovary. *Gynecol Oncol* 2008; 110: 125–132
- 207 *Oltmann SC et al.* Pediatric ovarian malignancies: how efficacious are current staging practices? *J Pediatr Surg* 2010; 45: 1096–1102
- 208 *Gobel U et al.* Treatment of germ cell tumors in children: results of European trials for testicular and non-testicular primary sites. *Crit Rev Oncol Hematol* 1990; 10: 89–98
- 209 *Marina NM et al.* Complete surgical excision is effective treatment for children with immature teratomas with or without malignant elements: a Pediatric Oncology Group/Children's Cancer Group Inter-group Study. *J Clin Oncol* 1999; 17: 2137–2143
- 210 *Gershenson DM et al.* Second-look laparotomy in the management of malignant germ cell tumors of the ovary. *Obstet Gynecol* 1986; 67: 789–793
- 211 *Billmire D et al.* Outcome and staging evaluation in malignant germ cell tumors of the ovary in children and adolescents: an intergroup study. *J Pediatr Surg* 2004; 39: 424–429; discussion 424–429
- 212 *Beiner ME et al.* Cystectomy for immature teratoma of the ovary. *Gynecol Oncol* 2004; 93: 381–384
- 213 *Cushing B et al.* Surgical resection alone is effective treatment for ovarian immature teratoma in children and adolescents: a report of the Pediatric Oncology Group and the Children's Cancer Group. *Am J Obstet Gynecol* 1999; 181: 353–358
- 214 *Kang H et al.* Outcome and reproductive function after cumulative high-dose combination chemotherapy with bleomycin, etoposide and cisplatin (BEP) for patients with ovarian endodermal sinus tumor. *Gynecol Oncol* 2008; 111: 106–110
- 215 *Chan JK et al.* Association of lymphadenectomy and survival in stage I ovarian cancer patients. *Obstet Gynecol* 2007; 109: 12–19
- 216 *Kim HS et al.* Systematic lymphadenectomy for survival in epithelial ovarian cancer: a meta-analysis. *Int J Gynecol Cancer* 2010; 20: 520–528
- 217 *Maggioni A et al.* Randomised study of systematic lymphadenectomy in patients with epithelial ovarian cancer macroscopically confined to the pelvis. *Br J Cancer* 2006; 95: 699–704
- 218 *Suzuki S et al.* Is there any association between retroperitoneal lymphadenectomy and survival benefit in ovarian clear cell carcinoma patients? *Ann Oncol* 2008; 19: 1284–1287
- 219 *Yang X et al.* Prognosis in epithelial ovarian cancer: clinical analysis of 287 pelvic and para-aortic lymphadenectomy. *Chinese-German Journal of Clinical Oncology* 2007; 6: 492–496
- 220 *Yokoyama Y et al.* Evaluation of cytoreductive surgery with pelvic and paraaortic lymphadenectomy and intermittent cisplatin-based combination chemotherapy for improvement of long-term survival in ovarian cancer. *Eur J Gynaecol Oncol* 1999; 20: 361–366
- 221 *Young RC et al.* Staging laparotomy in early ovarian cancer. *JAMA* 1983; 250: 3072–3076
- 222 *Piver MS, Barlow JJ, Lele SB.* Incidence of subclinical metastasis in stage I and II ovarian carcinoma. *Obstet Gynecol* 1978; 52: 100–104
- 223 *Buchsbaum HJ et al.* Surgical staging of carcinoma of the ovaries. *Surg Gynecol Obstet* 1989; 169: 226–232
- 224 *Griffiths CT.* Surgical resection of tumor bulk in the primary treatment of ovarian carcinoma. *Natl Cancer Inst Monogr* 1975; 42: 101–104
- 225 *Hoskins WJ et al.* The influence of cytoreductive surgery on recurrence-free interval and survival in small-volume stage III epithelial ovarian cancer: a Gynecologic Oncology Group study. *Gynecol Oncol* 1992; 47: 159–166
- 226 *Hacker NF et al.* Primary cytoreductive surgery for epithelial ovarian cancer. *Obstet Gynecol* 1983; 61: 413–420
- 227 *Hunter RW, Alexander ND, Soutter WP.* Meta-analysis of surgery in advanced ovarian carcinoma: is maximum cytoreductive surgery an independent determinant of prognosis? *Am J Obstet Gynecol* 1992; 166: 504–511
- 228 *Allen DG, Heintz AP, Touw FW.* A meta-analysis of residual disease and survival in stage III and IV carcinoma of the ovary. *Eur J Gynaecol Oncol* 1995; 16: 349–356
- 229 *Voest EE, van Houwelingen JC, Neijt JP.* A meta-analysis of prognostic factors in advanced ovarian cancer with median survival and overall survival (measured with the log (relative risk) as main objectives. *Eur J Cancer Clin Oncol* 1989; 25: 711–720
- 230 *Nguyen HN et al.* National survey of ovarian carcinoma. Part V. The impact of physician's specialty on patients' survival. *Cancer* 1993; 72: 3663–3670
- 231 *Junor EJ et al.* Specialist gynaecologists and survival outcome in ovarian cancer: a Scottish national study of 1866 patients. *Br J Obstet Gynaecol* 1999; 106: 1130–1136
- 232 *Bristow RE et al.* Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *J Clin Oncol* 2002; 20: 1248–1259
- 233 *Elattar A et al.* Optimal primary surgical treatment for advanced epithelial ovarian cancer. *Cochrane Database Syst Rev* 2011; (8): CD007565
- 234 *Ang C et al.* Ultra-radical (extensive) surgery versus standard surgery for the primary cytoreduction of advanced epithelial ovarian cancer. *Cochrane Database Syst Rev* 2011; 4: CD007697
- 235 *Bashir S et al.* Surgical technique of diaphragm full-thickness resection and trans-diaphragmatic decompression of pneumothorax during cytoreductive surgery for ovarian cancer. *Gynecol Oncol* 2010; 119: 255–258
- 236 *Sehouli J et al.* Primary versus interval debulking surgery in advanced ovarian cancer: results from a systematic single-center analysis. *Int J Gynecol Cancer* 2010; 20: 1331–1340
- 237 *Pfisterer J et al.* Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: an intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG. *J Clin Oncol* 2006; 24: 4699–4707
- 238 *Pujade-Lauraine E et al.* Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. *J Clin Oncol* 2010; 28: 3323–3329

Deutschsprachige Zusatzinformationen online abrufbar unter:
www.thieme-connect.de/ejournals/toc/gebfra.