10th edition of perspectives in lung cancer (PILC) 2009

Highlights of the 10th edition of the perspectives in lung cancer (PILC) educational meeting, 6th – 7th March 2009, Brussels, Belgium.

Authors I. Wauters, J. Vansteenkiste

Key words Lung cancer, epidemiology and screening, staging, targeted therapy, combined modality treatment, adjuvant chemotherapy.

Summary

Perspectives in Lung Cancer is an educational meeting in the field of Respiratory Oncology. It had its celebration 10th edition in Brussels on March 6-7, 2009. The aim of this congress is to provide a concise overview of the new data of the last year. This edition was attended by approximately 750 participants. More information on the presentations given at the meeting is available at www.perspectivesinlungcancer.com.

(BJMO 2009;Vol 3;3:129-132)

Session I: Diagnosis and staging

The 7th edition of TNM classification of non-small cell lung cancer (NSCLC) was presented. This new NSCLC classification, based on survival data of 67,725 patients (1990-2000), is more accurate to predict outcome of different patient groups based on stage. Changes were made in the Tumor (T) and Metastasis (M) descriptors, while there are no changes in the N descriptors.[1] An overview is provided in *Figure 1*.

Stage is one of the major determinants of outcome in NSCLC. Optimal staging depends on the accuracy and availability of different non-invasive and invasive techniques. In addition to computed tomography (CT) scan of the chest including the upper abdomen, performing positron emission tomography with ^{18}F-fluoro-deoxy-glucose (FDG-PET) in the initial staging provides additional information especially on mediastinal and extrathoracic lesions. Esophageal (EUS) or endobronchial ultrasound (EBUS) guided aspiration nowadays permits mapping of mediastinal lymph node spread.[2] Patients with clinical IB-IIIB lung cancer with mediastinal node enlargement (discrete or extensive) and intent of curative treatment should undergo PET scan. In patients with peripheral stage I tumors, negative mediastinal findings of PET allow to omit invasive confirmation of the lymph node status before surgery. PET is also used in reassessment after induction treatment in IIIA-N2 NSCLC and provides information on both lymph node downstaging as well as primary tumor response.

With all these excellent staging tools at hand, there is growing evidence to adapt staging sequences to performance of CT, PET and E(B)US at baseline, and using a first mediastinoscopy and a PET-CT scan for restaging after induction treatment.[3]

In recent years, fine needle aspiration (FNA) cytology also became more important in the diagnosis of malignancy. These techniques often result in small samples, which is a challenge in an era where there is an increasing importance of biomarkers such as tumor histology subtype and others for treatment choices.

Session II: Surgery

Use of low dose CT scans for lung cancer screening led to an important increase in the number of detected lung nodules. It was reported that an approach of these nodules with video-assisted thoracic surgery (VATS) was as accurate but less

Table 1. Descriptors, proposed T and M categories, and proposed stage groupings for the 7th TNM edition[1]

Sixth Edition T/M Descriptor	Proposed T/M	N0	N1	N2	N3
T1 (≤ 2 cm)	T1a	IA	IIA	IIIA	IIIB
T1 (> 2-3 cm)	T1b	IA	IIA	IIIA	IIIB
T2 (≤ 5 cm)	T2a	IB	**IIA**	IIIA	IIIB
T2 (> 5-7 cm)	T2b	**IIA**	IIB	IIIA	IIIB
T2 (> 7 cm)	T3	**IIB**	**IIIA**	IIIA	IIIB
T3 invasion		IIB	IIIA	IIIA	IIIB
T4 (same lobe nodules)		**IIB**	**IIIA**	**IIIA**	IIIB
T4 (extension)	T4	**IIIA**	**IIIA**	IIIB	IIIB
M1 (ipsilateral lung)		**IIIA**	**IIIA**	**IIIB**	**IIIB**
T4 (pleural effusion)	M1a	**IV**	**IV**	**IV**	**IV**
M1 (contralateral lung)		IV	IV	IV	IV
M1 (distant)	M1b	IV	IV	IV	IV

Cells in bold indicate a change from the sixth edition for a particular TNM category.

debilitating than muscle sparing thoracotomy. Randomised studies will address the critical issue if low dose CT screening indeed reduces lung cancer related mortality.[4]

Surgery is the treatment option of choice in stages I-II, and adjuvant chemotherapy became standard treatment for stage II and probably for some patients with stage IB, with an expected 5-year survival benefit of about 5%. To improve this benefit, ongoing research focuses on better selection of patients who will benefit from adjuvant chemotherapy, and on better predictive factors to chose one therapy or another. Evidence is growing supporting the fact that gene signatures may predict survival. Different studies with customized adjuvant chemotherapy are launched, with several biomarkers of interest, such as BRCA-1, ERCC1, and others.

In stage IIIA, single modality treatment with surgery or radiotherapy is not optimal. Treatment should be a multidisciplinary combination of systemic (mainly chemotherapy) and local (surgery or radiotherapy) treatment. The best prognosis after resection is seen in patients with mediastinal downstaging after induction chemotherapy and who can be offered a complete resection by performing a lobectomy.[5] If stage IIIA is due to unexpected N2 disease, adjuvant chemotherapy should be given, while the role of adjuvant radiotherapy remains unclear.

In selected T4 patients without mediastinal lymph node involvement, induction chemoradiotherapy followed by surgery can be rewarding if a complete resection can be obtained.

Session III: Radiotherapy

Concurrent chemoradiotherapy is the preferred approach in case of unresectable stage III NSCLC, but one should realise that quite some patients are not fit enough to receive this treatment modality.[6] The benefit of adding induction versus consolidation chemotherapy to the concurrent treatment is unproven and further studied, as is the role of maintenance chemotherapy after chemoradiotherapy. The effect of increasing the radiation dose to improve survival is evaluated, as the evolution to more precise radiation techniques permits to deliver higher total doses without unacceptable toxicity.

In medically inoperable patients with stage I disease, stereotactic radiotherapy could be a better alternative than standard radiotherapy.

Session IV: Pulmonary neuro-endocrine lung tumors (NET)

The pathological spectrum of neuro-endocrine lung tumors varies from typical carcinoids to small cell lung cancer (SCLC). The intermediate entities of atypical carcinoids and large cell neuro-endocrine carcinomas often make the pathologic diagnosis challenging. Correct classification, based on morphology and immunohistochemistry is important however, as survival is clearly related to the type of NET.[7]

Patients with a bronchial carcinoid tumor should be offered surgery whenever possible. In case of inoperability or distant metastasis, data on therapeutic options are limited, and these include biotherapy or chemotherapy. The results of therapy with radi-

olabelled somatostatin analogues in patients with a positive octreotide scan are promising.
For true SCLC, chemotherapy based on platinum and etoposide remains the preferred first line option. The evidence in favour of clinical benefit of second line chemotherapy in patients with relapsed SCLC remains limited. In case of relapse three or more months after having completed first line treatment, patients may benefit from re-treatment with the same regimen. Oral or intravenous topotecan is another valid second-line option, superior to best supportive care in overall survival (25.9 vs. 13.9 weeks, HR 0.64, 95%CI 0.45-0.90) and in symptom control.[8] Trials evaluating the role of amrubicin (a new anthracycline compound) and targeted therapies are ongoing.

Session V: Supportive care

Pleural effusions causing 'wet' stage T4 are associated with a worse prognosis than other T4 lung tumors. In fit patients, thoracoscopic talc poudrage remains the preferred approach to obtain durable relief of symptoms. The effect of cytokines to influence pleural effusion formation is under investigation.
Bone metastasis is another frequent problem in patients with lung cancer. The administration of zoledronic acid significantly reduces the incidence of skeletal related events.[9] Evidence for an additional positive effect of this treatment on disease recurrence and survival is growing, based on data of three studies performed in breast cancer patients.
Chemotherapy-induced anaemia can effectively be treated with erythropoietic substitution agents resulting in decrease of red blood cell transfusions and improvement of quality of life. It became clear that treatment of aneamic patients not receiving chemotherapy or targeting high haemoglobin levels to prevent anaemia may result in worse outcome. Therefore, it is important to treat patients based on existing guidelines; when doing so, there is no evidence for negative impact on survival.[10]
Interventional bronchoscopy with laser therapy and stent placement is mostly associated with bulky disease for symptom control. It also gained attention, e.g. with autofluorescence bronchoscopy, in the radical treatment of early lung cancer lesions in central airways.

Session VI: Advanced NSCLC

A large phase III trial recently showed that treatment of advanced NSCLC with cisplatin-pemetrexed resulted in non-inferior overall survival compared to cisplatin-gemcitabine. Moreover, there was a statistically significant better overall survival for patients with adenocarcinoma or large cell carcinoma when treated with cisplatin-pemetrexed.[11] The reverse was true for patients with squamous cell carcinoma. A major advantage of pemetrexed is its mild toxicity profile for a chemotherapeutic agent.
In a selected group of patients (non-squamous histology, no major cardiovascular problems, no haemoptysis), addition of bevacizumab (an anti vascular endothelial growth factor antibody) to cisplatin-gemcitabine provided modest benefit in progression-free survival, without difference in overall survival.[12]
The other recent advance is cetuximab, a monoclonal antibody against the epidermal growth factor receptor (EGFR). In the large phase III FLEX study, the combination of cetuximab and cisplatin-vinorelbine resulted in significantly better overall survival compared to chemotherapy alone in patients with EGFR expressing advanced NSCLC. This benefit was independent of histology.[13]

Session VII: Biomarkers

Gender, histology, smoking history and ethnicity are known clinical predictive factors for response to EGFR tyrosine kinase inhibitors (TKIs). EGFR activating mutations and EGFR high gene copy number or amplification as assessed by fluorescence in situ hybridisation are the biomarkers of interest. Ongoing research is elucidating the prognostic and predictive value of these biomarkers, and how they may guide optimal treatment for NSCLC with EGFR-TKIs.

Session VIII: Mesothelioma

Patients with advanced mesothelioma should receive a combination of platinum and pemetrexed, which can also be considered in case of sensitive relapse (i.e. at least 3 months after the end of 1st line therapy). Palliative radiotherapy has its indication in pain relief in case of chest wall infiltration. Selected early stage patients can be considered for radical multi-modality treatment in dedicated centres or clinical trials. In this setting, induction chemotherapy followed by extrapleural pneumonectomy is associated with better survival outcomes than upfront surgery followed by adjuvant therapy. The role of adjuvant radiotherapy is not defined yet. In regard to multimodality treat-

ment, it should be noted that an important number of the patients initially considered for this approach, are not able to complete the whole therapy.
As the overall improvement in outcome of mesothelioma patients remains very modest, a better understanding of the biology of the disease and of biomarkers is warranted.

References

1. Goldstraw P, Crowley J, Chansky K, Giroux DJ, Groome PA, Rami-Porta R, Postmus PE, Rusch V, Sobin L. The IASLC lung cancer staging project: proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumors. J Thorac Oncol 2007;2:706-714.

2. Herth FJ, Rabe KF, Gasparini S, Annema JT. Transbronchial and transoesophageal (ultrasound-guided) needle aspirations for the analysis of mediastinal lesions. Eur Respir J 2006;28:1264-75.

3. Dooms C, Verbeken E, Stroobants S, Nackaerts K, De Leyn P, Vansteenkiste J. Prognostic stratification of stage IIIA-N2 non-small cell lung cancer after induction chemotherapy: a model based on the combination of morphometric-pathologic response in mediastinal nodes and primary tumor response on serial 18-fluoro-2-deoxy-glucose positron emission tomography. J Clin Oncol 2008;26:1128-34.

4. Nackaerts K, Vansteenkiste J. Low-dose CT screening for lung cancer: trial and error? J Thorac Oncol 2009;4:563-4.

5. Albain KS, Swann RS, Rusch VW, Turrisi AT, Shepherd FA, Smith CJ, Gandara DR, Johnson DH, Green MR, Miller RC, North American Lung Cancer Intergroup. Phase III study of concurrent chemotherapy and radiotherapy (CT/RT) vs CT/RT followed by surgical resection for stage IIIA(pN2) non-small cell lung cancer: Outcomes update of North-American Intergroup 0139 (RTOG 9309) [Abstract]. J Clin Oncol 2005;23 Suppl 1:624S.

6. De Ruysscher D, Botterweck A, Dirx M, Pijls-Johannesma M, Wanders R, Hochstenbag M, Dingemans AM, Bootsma G, Geraedts W, Simons J, Pitz C, Lambin P. Eligibility for concurrent chemotherapy and radiotherapy of locally advanced lung cancer patients: a prospective, population-based study. Ann Oncol 2009;20:98-102.

7. Gustafsson BI, Kidd M, Chan A, Malfertheiner MV, Modlin IM. Bronchopulmonary neuroendocrine tumors. Cancer 2008;113:5-21.

8. Eckardt JR, Von Pawel J, Pujol JL, Papai Z, Quoix E, Ardizzoni A, Poulin R, Preston AJ, Dane G, Ross G. Phase III study of oral compared with intravenous topotecan as second-line therapy in small cell lung cancer. J Clin Oncol 2007;25:2086-92.

9. Aapro M, Abrahamsson PA, Body JJ, Coleman RE, Colomer R, Costa L, Crino L, Dirix L, Gnant M, Gralow J, Hadji P, Hortobagyi GN, Jonat W, Lipton A, Monnier A, Paterson AH, Rizzoli R, Saad F, Thurlimann B. Guidance on the use of bisphosphonates in solid tumors: recommendations of an international expert panel. Ann Oncol 2008; 19:420-32

10. Wauters I, Vansteenkiste J. Darbepoetin alfa in the treatment of chemotherapy-induced anaemia. Expert Opin Biol Ther 2009; 9:221-30

11. Scagliotti G, Parikh P, Von Pawel J, Biesma B, Vansteenkiste J, Manegold C, Serwatowski P, Gatzemeier U, Digumarthy SR, Zukin M, Lee JS, Mellemgaard A, Park B, Patil S, Rolski J, Goksel T, De Marinis F, Simms L, Sugarman K, Gandara D. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naive patients with advanced stage non-small cell lung cancer. J Clin Oncol 2008;26:3543-51.

12. Reck M, Von Pawel J, Zatloukal P, Ramlau R, Gorbounova V, Hirsh V, Leighl N, Mezger J, Archer V, Moore N, Manegold C. Phase III trial of cisplatin plus gemcitabine with either placebo or bevacizumab as first-line therapy for nonsquamous non-small cell lung cancer: AVAiL. J Clin Oncol 2009;27:1227-34.

13. Pirker R, Szczesna A, Von Pawel J, Krzakowski M, Ramlau R, Park K, Gatzemeier U, Bajetta E, Emig M, Pereira JR. FLEX: A randomized, multicenter, phase III study of cetuximab in combination with cisplatin/vinorelbine (CV) versus CV alone in the first-line treatment of patients with advanced non-small cell lung cancer (NSCLC) [Abstract]. J Clin Oncol 2009; 26 Suppl:5S.

Correspondence address

Authors: I. Wauters, J. Vansteenkiste
Respiratory Oncology Unit (Pulmonology) and Leuven Lung Cancer Group, University Hospital Gasthuisberg, Leuven, Belgium

Please send all correspondence to:
J. Vansteenkiste
Respiratory Oncology Unit (Pulmonology) and Leuven Lung Cancer Group
University Hospital Gasthuisberg
Herestraat 49
B-3000 Leuven
Belgium
Tel: 0032 (0)16 346802
Fax: 0032 (0)16 346803
johan.vansteenkiste@uz.kuleuven.ac.be
http://www.LLCG.be

Conflicts of interest: the authors have nothing to disclose and indicate no potential conflicts of interest.

7th International symposium on advanced ovarian cancer: update on optimal therapy

Highlights of the 7th Valencia Ovarian cancer Meeting, February 27 2009, Valencia, Spain

Authors J. B. Vermorken and A. Poveda

Key words Epithelial ovarian cancer, biomarkers, early detection, primary disease, recurrent disease, surgery, systemic therapies

Summary

This was the seventh time in 13 years that this intensive one-day symposium on advanced ovarian cancer was held in Valencia. The symposium was organized, as every other year, by *GEICO* (*Grupo Español de investigación de Cáncer de Ovario, the Spanish Ovarian Cancer group*), but now for the first time together with *ESMO* (*European Society for Medical Oncology*). The meeting was held under the auspicies of the *Spanish Society of Medical Oncology* (*SEOM*), the *Gynecologic Cancer InterGroup* (*GCIG*) and *ESMO*. Crucial for the success of these meetings has been the selectively chosen speakers, all keyplayers in the field of ovarian cancer and the participation of most active cooperative groups from around the globe. Moreover, from the 2nd edition (1999) onwards, nearly all presentations have been published as full papers in the *International Journal of Gynecological Cancer* (*IJCS*). Illustrative for the success of this meeting is the steadily increasing number of attendees to these meetings: from 157 in 1996 to 360 in 2009.

At the 2009 meeting, five different sessions covered relevant topics: 1) biomarkers and early detection, 2) surgical issues, 3) primary ovarian cancer, 4) recurrent ovarian cancer and 5) trials with impact on clinical management. *(BJMO 2009;Vol 3;3:133-135)*

Session I: Biomarkers and early detection

Early diagnosis is the keystone to increase cure rates in ovarian cancer. However, at present still only one third of the patients are diagnosed in an early stage and adequate screening methods are still lacking. *Dr. Elise Kohn* (*Medical Oncology Branch, NCI, Bethesda, USA*) discussed the potential role of proteomic profiling. She made clear that advancing proteomics technologies can be used for improved diagnosis, definition, prediction, and prognostication of ovarian cancer and so, better understand ovarian cancer and its subtypes. Powered and validated analyses are needed for this. Protein profiling can also be used for characterization of therapeutic targets, confirmation of the role of these targets, stratification for therapeutic interventions, demonstration of target modulation and prediction of therapeutic benefit and so, may improve targeted therapy on an individual basis.

CA125 has been used as a biologic marker in screening programs and two-stage strategies (annual evaluation of CA125 and in case of rise performing a transvaginal sonography) has shown promising results, both in the US (*Dr. Robert Bast Jr, MD Anderson Cancer Center, Houston, USA*) and in the United Kingdom (*Dr. Ian Jacobs, Institute for Women's Health, London, UK*). However, only the UK study (*UKCTOCS*) is adequately powered (> 200.000 participating women) and enables to demonstrate an improvement in survival. These data are not available yet.

Sessions II: Surgical Issues

Dr. Fabio Ghezzi (*University of Insubria, Del Ponte Hospital, Varese, Italy*) reviewed the potential of the laparoscopic approach. He concluded that there is a growing body of evidence suggesting that laparoscopic comprehensive surgical staging of early ovarian cancer

is as safe and adequate as the standard surgical staging performed through laparotomy, provided that the surgeon is demonstrably competent in the safe application of laparoscopic techniques and the basic prerequisites of surgical oncology are fulfilled. Large prospective trials on laparoscopic vs open staging are needed to assess whether survival are similar with these two approaches and whether the assumed advantages of the laparoscopic approach over open surgery (eg. shorter hospital stay, faster recovery, improved quality of life, shorter interval to adjuvant treatment) is also true for early ovarian cancer patients.

The importance of laparoscopy prior to debulking surgery was also identified by *Dr. Ignace Vergote* (*University Hospital Leuven, Leuven, Belgium*) as an important technique to ascertain the diagnosis, and to evaluate operability of advanced ovarian cancer, when he discussed in session III the ongoing EORTC-GCG/NCIC-CTG study comparing neoadjuvant chemotherapy followed by interval debulking surgery (NACT→IDS) with primary debulking surgery (PDS). That large randomized trial (n=718) showed that NACT→IDS might be a good alternative for PDS in patients with extensive stage IIIc or IV ovarian carcinoma, with less per- and postoperative complications. Optimal surgery proved to be the most important prognostic factor. The outcome of the trial is not applicable to patients with lower stages of disease or patients with relative limited stages IIIc or IV. For these patients PDS remains the preferred recommended option. Criticism on the surgical performance in this trial is anticipated. This was also to some extent eluded to by *Dr. Philipp Harter* (*Dr. Horst Schmidt Klinik, Wiesbaden, Germany*) in his presentation on prognostic factors for complete debulking in first and second line. He indicated that imaging, serological models and laparoscopy do not identify adequate candidates sufficiently for NACT, and stressed the importance of surgical training. He also strongly recommended to change our old aim of optimal debulking with residual disease up to 1cm to the real optimal debulking, i.e. complete resection (no macroscopic tumor left). Complete debulking to no residual disease also has prognostic influence in the recurrent disease setting. Independent factors for complete resection in that setting were a good performance status (ECOG 0), complete resection at primary surgery, and the absence of ascites. The *AGO group* has developed a scoring system for that, which will be further studied in a randomized trial (*DESKTOP III*). *Dr. Jonathan Berek* (*Stanford University School of medicine, Stanford, USA*) summarized the literature on N+Stage IIIc ovarian cancer and concluded that, because of its better outcome, this could/should be seen as a separate entity and may have implications for our staging system (further stratification). He also elaborated on resection of retroperitoneal lymph nodes during primary surgery and concluded that systemic lymphadenectomy in that setting did not improve survival, but that resection of isolated recurrences in nodes may be associated with a survival benefit.

Session III: Primary Ovarian Cancer

Genomic profiling can provide prognostic/predictive gene signatures for ovarian cancer. However, validation of these signatures is critical and not available at present. Within these signatures there are potential therapeutic targets. *Dr. Michael Birrer* (*NCI/US*) concluded that future development of all these markers will depend upon careful validation in independent sets of tumors. Another interesting but still undefined path is the pharmacogenetic assessment of toxicity and outcome. *Dr. Sharon Marsh* (*Pharmacogenomics Center, Montreal, Canada*) mentioned that the pharmacogenetic basis for the variability in response and toxicity to taxane-platinum therapy in ovarian cancer is still unclear, reflecting the lack of true understanding of the regulation of chemotherapy action. Further studies in this interesting field are clearly needed (see also the report on IP therapy later). As mentioned above, *Dr. Vergote* discussed the large *EORTC-GCG/NCIC-CTG trial* in this session. The last presentation in this session was from *Dr. Paul Sabbatini* (*Memorial Sloan kettering Cancer center, new York, USA*) on consolidation therapies. No randomized consolidation study in ovarian cancer has so far shown a statistically significant improvement in overall survival. However, as treatment options move beyond classic cytotoxic chemotherapy to hormones, immune interventions and targeted therapies, the consolidation strategy is regaining interest. He stated that "positive" phase II studies are not predictive to date, so that therefore randomized trials are essential. In that, current strategies with impending data are 1) immune targeted (phase III with abagovomab, a murine anti-idiotypic monoclonal antibody which functionally mimics the CA-125 antigen), and 2) anti-vascular (phase III VEGF targeted studies). He also indicated that the second remission population is ideal to further develop this strategy.

Session IV: Recurrent Ovarian Cancer

Dr. Maurie Markman (*M.D. Anderson Cancer Center, Houston, USA*) followed up on his important messages on how to treat patients with recurrent ovarian cancer. Thereby, one should focus on realistic goals for the indi-

vidual patient at a particular time in the natural history of her own illness and realizing that ovarian cancer is becoming more and more a chronic disease process and that decisions made today, in particular in the 2nd line setting, may impact on a substantial portion of the remainder of this patient's life. *Dr. Michael Friedlander* (*Prince of Wales Hospital, Sydney, Australia*) mentioned that there is a clear need to develop better measures of the benefit of palliative chemotherapy in women with platinum resistant/refractory ovarian cancer and in patients receiving three or more lines of treatment. In this, one can not rely on objective response criteria alone. It is essential that we also measure subjective benefit of treatment and carefully evaluate quality of life. A prospective *GCIG study* has been set up to evaluate this. *Dr. Bradley J. Monk* (*University of California, Irvine medical center, Orange, USA*) summarized the available data on angiogenesis inhibition. Tyrosine kinase inhibitors (sorafinib, sunitinib and pazopanib) have shown activity in the recurrent disease setting. The same is true for the monoclonal antibody bevacizumab, which is now being studied in randomized trials in first line (addition to front-line chemotherapy: *GOG 218* and *ICON 7 trial*) and second line (addition to second-line chemotherapy: *GOG 213* and *OCEANS trials*). *ICON 6*, a second-line European trial is studying the addition of AZD 2171 to second-line chemotherapy. Other molecular pathways were discussed by *Dr. Amit Oza* (*Princess Margaret Hospital, Toronto, Canada*). Of interest are EGFR targeting, poly (ADP-ribose) polymerase inhibition (parp inhibition), Src inhibition, PI3 Kinase-AKT-mTOR, epigenetic mechanisms (HDAC inhibitors), and stem cell targeting agents and tumor micro-environment (Hedgehog pathway). Although single agent studies are being performed, synergy of some with others is being looked for as well as the combination with chemotherapy. As mentioned earlier in session III, these agents are also of interest for consolidation and maintenance strategies.

Session V: Trials with impact on clinical management

Drs. Michael Bookman (*Fox Chase Cancer center, Philadelphia, USA*), *Bradley J. Monk* and *Jan B. Vermorken* (*Antwerp University Hospital, Edegem, Belgium*) summarized the present status of such trials in respectively, first-line, second-line and intraperitoneal chemotherapy (IPCT). The combination of paclitaxel/carboplatin (TC) is the generally agreed standard for first-line treatment since 2003 and the control arm of all recent randomized trials. So far, no other regimen has shown to outperform the TC regimen. The addition of a third drug has no impact. The two approaches presently of interest are (1) a dose-dense TC regimen as presented by *Isohishi et al* at ASCO 2008 (abstract #5506) and (2) the use of IPCT in women with optimally debulked epithelial ovarian cancer. It is clear that further studies with IPCT are needed with the purpose to further enhance efficacy (heating, biological agents) and to reduce toxicity (other taxane, other platinum, or reduced dosages). IPCT after NACT will be studied in a new *GCIG trial*. Also the benefit of IPCT in the consolidation setting needs to be assessed. Interestingly, in a substudy of *GOG #172* it was found that the C8092A polymorphism in ERCC1 was an independent predictor of progression-free and overall survival when treated with IPCT.

There are several positive randomized trials in second-line with impact on clinical management (*Vermorken JB, Int J Gynecol Cancer 2008; 18 (Suppl. 1): 59-66*). At the present meeting, data on *OVA-301* (pegylated liposomal doxorubicin [PLD] vs PLD plus trabectidin) were presented showing for the first time an improvement in progression-free survival with a non-platinum-containing combination over a single agent. Ongoing randomized phase III registration trials in ovarian cancer include (1) bevacizumab (*GOG 218, ICON 7, GOG 213, OCEANS*), (2) paclitaxel poliglumex /CTI-2103 (*GOG 212*), (3) paupilone, (4) phenoxodiol, (5) abagovomab, (6) cediranib / AZD 2171 (*ICON 6*) and (7) karenitecin.

Correspondence address

Authors: J.B. Vermorken, MD, PhD [1] and A. Poveda, MD [2]

[1]Antwerp University Hospital, Department of Oncology, Edegem, Belgium; [2]Instituto Valenciano de Oncologia, Department of Medical Oncology, Valencia, Spain

Please send all correspondence to:
Prof. Dr. J.B. Vermorken
Department of oncology
Antwerp university hospital
Wilrijkstraat 10
2650 Edegem
Tel: 0032 (0)3 821 33 75
Fax: 0032 (0)3 825 05 64
Jan.B.Vermorken@uza.be

Conflicts of interest: the authors have nothing to disclose and indicate no potential conflicts of interest.