SDSCH and **DBCG**

**Invite you to a joint meeting**

**Bridging Oncology and Pathology**

with

International Guest Speaker
**Prof. Giuseppe Viale,**
European Institute of Oncology and University of Milan School of Medicine, Milan, Italy.

**Date:** 26th November 2009  
**Time:** 15.30 – 19.00  
**Venue:** Dako, Produktionsvej 42, 2600 Glostrup  
Building C, Auditorium C-1.4

<table>
<thead>
<tr>
<th>Moderator</th>
<th>Henning Mouridsen, <em>Department of Oncology, Rigshospitalet</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>15.30 – 15.40</td>
<td>Welcome</td>
</tr>
</tbody>
</table>

**Diagnostic and Markers**

<table>
<thead>
<tr>
<th>Time</th>
<th>Topic</th>
</tr>
</thead>
</table>
| 15.40 – 16.05 | Recent efforts to standardize ER and PgR assays in breast cancer: The ASCO/CAP recommendations and the FDA approval of immunohistochemical markers (see abstract)  
by Prof. Giuseppe Viale, European Institute of Oncology and University of Milan School of Medicine, Milan, Italy |
| 16.05 – 16.15 | Discussion |
| 16.15 – 16.45 | Integrating molecular profiling, histologic type and other variables: Defining the fingerprint of responsiveness to treatment (see abstract)  
by Prof. Giuseppe Viale, European Institute of Oncology and University of Milan School of Medicine, Milan, Italy |
| 16.45 – 16.55 | Discussion |

**Clinical Studies**

<table>
<thead>
<tr>
<th>Time</th>
<th>Topic</th>
</tr>
</thead>
</table>
by Bent Ejlertsen, *Department of Oncology, Rigshospitalet* |
| 17.20 – 17.45 | Neoadjuvant treatment protocols  
by Bent Ejlertsen and Birgitte Bruun Rasmussen *Department of Oncology, Rigshospitalet and Department of Pathology, Herlev Hospital.* |
| 17.45 – 18.05 | Latest results of the Danish sentinel node registration  
by Tove Tvedskov, *Department of Surgery, Rigshospitalet* |
| 18.05 – 18.20 | Discussion |
| 18.20 – 19.00 | Networking. Wine and sandwich will be served. |

Please R.S.V.P no later than **November 19, 2009** to Ulla Evald, Patologisk Institut, BBH,  
u01@bbh.regionh.dk
Prof. Viale was born in Torino, June 23, 1952, and graduated from University of Milan in 1976. He became a specialist in pathology in 1979, and is now full professor of pathology at the University of Milan School of Medicine. He has been director of the Division of Pathology and Laboratory Medicine at the IEO since 1994. Previously, he was assistant pathologist at S. Raffaele Hospital, Milan (1978-1981), and vice director of Department of Pathology S. Paolo Hospital, Milan (1981-1994). A member from 1987, he was elected Fellow of the Royal College of Pathologists in 1997. Scientific interests include abnormal expression of oncogenes and tumour-suppressor genes in human malignancies, derangements in cell-cycle control and apoptotic pathways, and the role of angiogenesis in tumour progression and response to therapy.

He is an active member of many international societies, organizations and committees such as the AJCC working group for the TNM classification of breast cancer, Pathology Sub-Study Group of the Intergroup Exemestane Study (PathIES), Executive and Steering Committees of the ALTTO trial, co-chair of the International Pathology Committee and responsible for the Central Pathology Laboratory for non-US Centers, member of the FFPE Working Group of the Breast International (BIG) and National Cancer Institute (NCI)-sponsored breast cancer Cooperative Groups. Chairman of the Biological Protocol Working Group of the IBCSG, Early Breast Cancer Trialists’ Collaborative Group Steering Committee, founding Member of the International Sentinel Node Society, co-chair of the Translational Research Committee of the BIG2-98 Trial (Trans-TAX), member of the Executive and Steering Committees of the Breast International Group (BIG) and of the MINDACT trial, Vice-President for Europe of the Senologic International Society, Translational Research Committee of the HERA trial, Scientific/Translational Research Committee of the Breast International Group (BIG), Scientific Committee of the Italian National Institute of Health, co-chairman of the Central Pathology Office of the International Breast Cancer Study Group (IBCSG) and the Scientific Committee of the International Breast Cancer Study Group (IBCSG).

Prof. Viale is the author of 260 articles in indexed international Journals and of 36 book chapters.
With the emergence of target therapeutics based on biomarker assessment, so-called pharmacodiagnostics, companion diagnostics or theranostics, the pathologist’s job transcends beyond the traditional task of diagnosing a cancer patient to actively contributing to the oncologist’s choice of treatment for the said patient, by identifying patients eligible for a certain treatment. Furthermore, pathologists are increasingly playing an active role in clinical trials for target therapies.

It is a shared objective between the pathologists and oncologists to provide the right treatment for the right patient. The ability to do so is strictly dependent on the accuracy with which the pathologist can predict what treatment will be efficacious for the individual patient. Pharmacodiagnostic tests form the basis for the pathologist stratification of patients. Hence, the accuracy and clinical utility of a given pharmacodiagnostic test will be a main determinant in the treatment recommendation being provided by the oncologist to a patient.

Likewise, the clinical practitioners jointly pursue as accurate and conclusive data arising out of clinical trials for target therapeutics, employing biomarkers for patient stratification. Again, the quality of the outcome data is dependent on the quality, i.e. the consistency and reliability of the biomarker test being applied in the clinical study.

Inaccurate results from a pharmacodiagnostic tests are likely to lead to false negative or false positive diagnoses, which in turn will lead to inaccurate treatment recommendations with a deleterious effect on the patient’s life. The patient will receive a non-efficacious or unnecessary treatment, while at the same time suffering often severe side-effects and experiencing disease progression.

Similarly, non-quality biomarker results from clinical trials will lead to erroneous conclusions regarding the efficacy of the experimental drug, likely preventing the compound to proceed in the clinical trial, or sub-optimal treatment decisions in relation to the drug will be made once the drug is on the market. It is well known that numerous parameters affect the reliability of test results, including those assessing biomarkers used in a pharmacodiagnostic setting, i.e. to determine a patient’s eligibility for a certain treatment. In order to arrive at consistent, reliable diagnostic results, it is pivotal to control as many of these parameters as possible. For the biomarker assessment, the control of these parameters should translate into the use of standardized, validated biomarker kits, often assisted by automated processing, i.e. automated stainers. Furthermore, the interpretation of the stained slides may be assisted by image analysis algorithms for improved interobserver variability.

ER/PR pharmDx from Dako is a validated and FDA cleared test to aid in the selection of the right patients for hormone treatment. The ER antibody cocktail and PR antibody demonstrate high sensitivity and specificity are clinically validated using the Allred scoring method. Such parameters gives confidence in the test sensitivity and specificity and lessens the burden of extensive validation of homebrew test by laboratory staff.

ASCO/CAP have established an expert panel to formulate new guidelines on hormone receptor testing.

Upcoming law suits in Canada (Newfoundland/Labrador) have made it clear that standardization and focus on using validated and approved diagnostic kits is needed. In the Newfoundland/Labrador case 2000 original negative cases were retested with the result that 40% came back positive. A total of 383 patients were affected by this. Also the UK NEQAS have evaluated the results from 150 laboratories in 26 countries worldwide and identified error rates in some laboratories rivaling those in Newfoundland and Labrador.
One of the most important aims of the multidisciplinary approach to patients with breast carcinoma is tailoring systemic treatments. To achieve this goal several questions remain to be addressed, including who are the patients that could be spared chemotherapy, who are those getting the greatest benefit from aromatase inhibitors, and who is benefitting most from the different anti-HER2 interventions? Much has been done in the past to select the candidate patients to different treatments, but it is now necessary to identify, among the candidate patients, those who actually are responsive to a given treatment. Undoubtedly, responsiveness to different treatments is determined by multifactorial processes, and it is very unlikely that it will ever be possible to predict tumor response to a given treatment by the analysis of a single (or a few) parameters. On the other side, it is also unrealistic – at least for the time being – to conclude that gene expression profiling (by whole genome screening or by targeting a finite number of genes) is the only viable and reliable approach to predict tumor responsiveness. A more feasible and cost-effective way of addressing this issue is to adopt a hierarchical approach, starting from the traditional morphological examination of the tumor samples, then performing a complete and accurate immunohistochemical assay for the relevant predictive parameters, and eventually adding the more sophisticated molecular assays to address additional questions or to refine the predictive model.

The actual benefit of systemic chemotherapy, given alone or with endocrine therapy, may indeed be predicted by the morphological typing of breast cancer. Invasive lobular carcinomas of the classic type are very poorly responsive to chemotherapy (as it has been repeatedly shown in studies of neoadjuvant chemotherapy), whereas high-grade invasive ductal carcinomas with medullary-like features or with large central or geographic necrosis are exquisitely sensitive to chemotherapy. Unfortunately, the vast majority of breast carcinomas do not belong to the above tumor types, and the morphological characterization is much less contributory to predict their responsiveness to chemotherapy. In the hierarchical approach, additional predictive information is sought with immunohistochemical assays for the expression of powerful predictive markers, i.e. estrogen and progesterone receptors, HER2 and Ki-67. The lower the expression of hormone receptors, the higher is the likelihood for the tumor to benefit from chemotherapy, and the opposite is true for the tumor proliferative fraction (as defined by Ki-67 labeling index). HER2 over-expression may also be predictive of a different benefit of different chemotherapeutic options. The combined assessment of these predictive parameters, in addition to tumor type and grade, may results in predictive models that allow better tailoring of systemic therapies. On top of all these morphological and immunophenotypical analyses, assays for gene expression are now become available. It has been already shown that these assays not only have a prognostic value, but they may also have predictive implications. Defined gene expression profiles may indeed predict the response to neoadjuvant chemotherapy and the benefit of chemotherapy given in association with endocrine therapy in the adjuvant setting. It remains to be assessed, however, how much the molecular assays contribute to the prediction of responsiveness beyond what is already provided by clinical, morphological and immunohistochemical investigations. The randomized clinical trials currently ongoing will eventually allow to address this question.