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Friday, 24 February

Advances in breast cancer management/diagnostics and treatment

- Routine use of Sienna+® and Sentimag® – the Swedish experience
- Sentimag® for Sentinel Lymph Node Detection
- Is total tumour load useful?
- Scalp cooling – a new way to improve cancer management
- On-slide-control for immunohistochemistry via Tissue Microarray (TMA) cores

How to reduce morbidity and mortality in colon cancer? From screening to therapy

- CRC Screening – Time for all countries to get FIT! Why and How?
- Molecular staging of colorectal cancer
- Improved patient management of CRC patients with liquid biopsy?
- Keynote lecture: Future directions of liquid biopsy in patient monitoring of melanoma patients

Saturday, 25 February

Perspectives in sentinel lymph node detection and analysis

- Magnetometer-guided SLN detection and perspectives of OSNA® for LN staging in prostate cancer
- SLN localisation in vulva cancer using SPIOs. Our small experience
- SLN ultrastaging in endometrial cancer
- SPIOs for SLN detection in melanoma. An alternative method
- Sentimag® and OSNA® to support SLN concept in Head and Neck cancer

New directions in axillary management – A session led by the EBC2 (European Multidisciplinary Breast Cancer Collaborative)

- Axilla in the neoadjuvant setting
- Axilla staging and molecular tumour biology
- Is it time to redefine a positive node?
- EBC2 projects and wrap-up
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Session:
Advances in breast cancer management/diagnostics and treatment

**Routine use of Sienna® and Sentimag® – the Swedish experience**
*Dr F. Wärnberg, University Hospital Uppsala, Sweden*

- Seven European studies have shown that using Super Paramagnetic Iron Oxide (SPIO) is as good as the former standard using Technetium and Blue ink for identifying sentinel nodes.
- To further facilitate the application and use of magnetic detection and to tackle the challenges of the technique such as pigmentation, various studies and injection modifications have been tested on-site in Sweden.
- Patient logistics was modified by avoiding radiotracer injection in the nuclear medicine department. A reduction of pigmentation was reached by deeper Sienna injection and a study was initiated to explore whether a sentinel node biopsy with the help of SPIO in patients with DCIS can be avoided.

**Sentimag® for Sentinel Lymph Node Detection**
*Dr R. Salmon, Clinique Saint Jean de Dieu, Paris, France*

- In a monocentric study with 79 breast cancer patients, Sienna-only and different tracer combinations (32 cases Sienna/Blue Dye and 3 cases Sienna/radiotracer) were applied to investigate detection performance in SLNB.
- Results provided two cases with detection failure of either tracer (former radiotherapy and high BMI). In the remaining cohort (98.5%) SLN were identified.
- In 1/3 of all patients a brown staining was detected.
- The results confirm the excellent results of the Sienna+/Sentimag® method from various publications.

**Is total tumour load useful?**
*Dr L. Bernet, Hospital Universitari de la Ribera, Alzira, Spain*

Dr Laia Bernet addressed the role of the axillary status for the surgeon, the medical oncologist and radio therapist nowadays. **Key messages from Dr Laia Bernet:**

- Axillary status information is important and Total Tumour Load (TTL) helps to define risk groups that may benefit from adjuvant or neo-adjuvant therapy.
- Without axillary information
  - 23.7% of patients with more than four positive lymph nodes may be infra-staged and will therefore not receive post-operative radiotherapy;
  - a loss of prognostic and predictive information leads to increasing residual disease risk from 14.7% to 27%. Medical oncologists have less information to individualise medical treatment and radiotherapists have less information to decide which fields to irradiate.
- TTL has a prognostic and predictive information and is needed by the surgeon, the medical oncologist and the radiotherapist.

**Scalp cooling – a new way to improve cancer management**
*Dr M. Thill, Agaplesion Markus Hospital Frankfurt, Germany*

- Report of psychological findings regarding hair loss in the practice of Dr Thill.
- Importance of chemotherapy induced alopecia with help of the publication: Development and Validation of Chemotherapy induced Alopecia Distress Scale (CADS) for breast cancer patients (Cho J et al., Ann Oncol 2014).
- How to measure the improved quality of life with DigniLife®? Schaffrin-Nabe et al. (2016): ‘All SC patients showed significantly better trichological hair results, an impressively higher quality of life and less psychological strain compared to the control group.’
- Presentation of own study results (Agaplesion Markus Hospital Frankfurt, Germany) regarding the parameters: age, chemotherapy, and hair preservation: 62% of the patients experienced alopecia less than 20%.

**Conclusion:** Scalp cooling with DigniLife® is an effective and valid method to prevent chemotherapy-induced alopecia.
**On-slide-control for immunohistochemistry via Tissue Microarray (TMA) cores**

*Dr. C. Geppert, University Clinics Erlangen, Germany*

The presentation by Dr. Carol Geppert (University of Erlangen, Germany) was focused on tissue microarray based applications in combination with digital image analysis. The presentation pinpointed exactly how TMA technique can be used for both on-slide controls for immunohistochemistry and for research projects thanks to the high-throughput digital TMA system from 3DHISTECH Ltd.

- TMA in combination with slide scanners enables high quality punching by digital TMA annotations. The workflow is economical & time-efficient and allows the creation of TMA clones.
- Large-scale projects can be realised very easily (e.g.: SAPE project: ngTMA for breast cancer, >5000 patients qualified; >10,000 patients planned).
- In diagnostics, there is increasing pressure in terms of time and cost –> For thousands of IHC stainings new solutions are needed to avoid explosion of cost & time (Erlangen: >70,000 IHCs/year in routine).
- Research: With GTMA & DIA huge numbers of tissue samples can be provided very quickly.
- Diagnostics: On-slide controls can be produced in an economical way, thereby saving tissue, time and resources.
- Especially interesting for certified & accredited institutes of pathology with a lot of IHC stainings (DAKKS).
- The ‘on-slide multi-block’ offers numerous combinations for control tissue in terms of high QM standards.
- Future aspects: QM pressure will increase and on-slide tools are needed!

**Session:**

**How to reduce morbidity and mortality in colon cancer? From screening to therapy**

*Dr. E. van Wieten, Erasmus Medical Centre, Rotterdam, The Netherlands*

Dr. E. Wieten is working closely on the well-known Dutch screening programme, a worldwide reference. She participated in LS Symposium on behalf of Prof. Manoon Spaander, an international KOL for CRC Screening and is directly involved in ongoing clinical trials for various FIT test comparisons.

Dr. E. Wieten shared with the Symposium attendants her opinion on why it is so important to implement FIT-based screening programmes and why it is currently a trend; she provided attendants with some critical aspects to consider before implementing a screening programme (pilot-phase) and addressed the importance of continuously assessing a screening programme to optimise programme cost-effectiveness and performance. **Key messages from Dr. E. Wieten:**

- In Europe, CRC is the second-most common malignancy and the second leading cause of cancer-related mortality.
- There are large variations among national CRC screening practices in Europe in terms of methodology (guaiac test, FIT test, colonoscopy) and in terms of scope – national, regional, opportunistic, pilot phase).
- The successful impact of FIT-based screening on CRC incidence and mortality rates on the (repeated) uptake of a screening test and the ability to detect CRC and advanced adenomas at all stages and locations.
- FIT tests are replacing the guaiac Tests as FITs is more sensitive for the detection of both CRCs and advanced adenomas than gFOBTs. FIT test also provide quantitative test results, which enables to adjust the cut-off to match available resources.
- In the Netherlands, the national screening programme for CRC, with biennial FITs, was initiated in 2014 after careful pilot studies and planning.
- In the Netherlands, a national information system for real-time monitoring was developed to allow for timely evaluation and conclude the importance of planning and monitoring for optimal screening programme performance.
- During the first year of the screening programme, the cut-off level for a positive FIT result was increased due to considerably higher than expected participation and positivity rates. This adjustment lowered the percentage of positive test results and increased the positive predictive value, which meant it was possible to reduce the burden of unnecessary colonoscopies and alleviate colonoscopy capacity.

**Conclusion:** After the panel session discussion led by Dr. Angel Lanas, Dr. E. Wieten highlighted the benefits of FIT test for screening, the importance of the close monitoring and adjustment needs of the FIT cut-off levels to optimise programme performance. Dr. E. Wieten also challenged the audience of their opinion on the possibility to have customised cut-offs levels in the future for genders and age gaps.
Friday, 24 February

**Molecular staging of colorectal cancer**  
*Dr M. Cuatrecasas, Hospital Clinic de Barcelona, Spain*

Dr Miriam Cuatrecasas highlighted the high potential of screening programmes for colorectal cancer patients and the economic impact. Once colorectal cancer was diagnosed, Dr Cuatrecasas highlighted the urgent need for a personalised staging system and the important role the lymph nodes play here. **Key messages from Dr Miriam Cuatrecasas:**

- 6–7% of patients with a positive colonoscopy are found in FIT-positive patients, leading to early detection and better diagnostic accuracy of early lesions.
- Up to 20% of pN0 (stage I and II) patients will recur from colorectal cancer within five years. Those patients may have positive lymph nodes, not detected with H&E.
- Molecular positivity in lymph nodes is placed with other classical high-risk factors of early-stage CRC.

The last two presentations on Friday afternoon given by Dr Sartore Bianchi (Oncologia Clinica Molecolare, Milano, Italy) and Dr Verena Haselmann (University of Mannheim, Germany) were dedicated to the advantage of liquid biopsies based on ctDNA from plasma for detecting RAS mutations in the blood of cancer patients that enable the selection of the most promising therapy.

**Improved patient management of CRC patients with liquid biopsy?**  
*Dr A. Sartore Bianchi, Oncologia Clinica Molecolare, Milan, Italy*

**Key messages from Dr Sartore Bianchi:**

- Future directions: monitoring during therapy due to the emergence of RAS mutation acquired during anti-EGFR treatment leading to therapy resistance.
- Circumvent the development of resistance by using an anti-EGFR antibody mixture instead of a monoclonal antibody is currently being investigated by several groups.
- There is an increasing interest in the concept of re-challenging patients with an anti-EGFR therapy after the mutant RAS clone has declined. For further evaluation, the CHRONOS study was initiated:

**CHRONOS study:** Phase II Trial of ReCHallenge With Panitumumab Driven by RAS CIONal-Mediated Dynamic Of ReSistance: evaluation of the efficacy of a third-line Panitumumab re-challenge in patients with metastatic colorectal cancer (mCRC), that have been originally responsive to anti EGFR therapy. Liquid biopsy will be used as a perfect tool to follow up these patients throughout the trial.

**Keynote lecture:**  
**Future directions of liquid biopsy in patient monitoring of melanoma patients**  
*Dr V. Haselmann, Medizinische Fakultät Universtitsklinikum Mannheim, Germany*

**Key messages from Dr Verena Haselmann:**

- BEAMing provides highest sensitivity for detecting the mutant DNA fraction.
- BRAF is a pharmacogenetic target in melanoma patients. These patients are rarely re-biopsied and the detection in blood might be advantageous and enable a real-time assessment of the tumour burden.
- Reliable biomarkers for monitoring metastasised melanoma patients are still missing.
- Two melanoma studies from Mannheim (prospective & retrospective): high degree of concordance (> 92%) between plasma (OncoBEAM™) and tissue testing.
- Assessing BRAF mutational status by liquid biopsy was superior to currently used generalised biomarkers like LDH or S-100 and reduced the lead time by about 110 days compared to imaging technologies.

**Conclusion:** Liquid biopsy for ctDNA detection delivers a dynamic and continued real-time picture of the tumour genomic landscape in CRC or melanoma patients so that one can detect and monitor disease from the early stages through disease evolution under treatment.
**Session: Perspectives in sentinel lymph node detection and analysis**

**Magnetometer-guided SLN detection and perspectives of OSNA® for LN staging in prostate cancer**

*Dr A Winter, University Hospital, Oldenburg, Germany*

- LN staging in PCa is a crucial prognostic factor, especially in patients with minimal lymphatic dissemination. The standard of care is Extended Pelvic Lymph Node Dissection (ePLND). Sentinel Plevic Lymph Node Dissection (sPLND) is under investigation.
- Imaging techniques such as CT, MRI or PSMA/PET are not accurate enough and lack performance particularly in detecting LN micrometastases or small metastases.
- Two studies comparing sPLND and magnetic detection with ePLND showed:
  - feasibility and safety of magnetometer-guided sentinel lymphadenectomy in PCa
  - high sensitivity for identifying LN metastases in intermediate and high-risk PCa
  - the reliability of intraoperative SLN detection by using the Sentimag® system has to be verified in further studies
- Besides the magnetic detection of SLN, Sienna+® is a suitable agent for accurately localising SLNs with MRI.
- A pilot study in 20 patients with intermediate or high risk PCa evaluated the feasibility of OSNA® in PCa. Result: In all PCa samples (20/20) a CK19 expression was detected with either ++ or +. The control with IHC detected 19/20 positive cases.
- The combination of sPLND and subsequent analysis of the nodes with OSNA® may provide rapid results and may reduce the high risk of missing LN metastases in clinical routine.

**SLN localisation in vulva cancer using SPIOs. Our small experience**

*Dr D. del Valle, Donostia University Hospital, San Sebastian, Spain*

- Vulva cancer (VCa) is the fourth most frequent type of gynaecological cancer. If the lymph nodes are affected, the five-year survival expectancy can go down from 70 %–90 % to 25 %–41 %.
- The standard of care is SLNB with the combined technique (radioisotope + blue dye). Detection rates are comparable with those in BCa between 96 %–98 %.
- A monocentric parallel observational study in ca. 13 patients with VCa and GROINSS-V criteria for SLNB (stage FIGO Ib – II) shall evaluate non-inferiority of the magnetic detection with Sienna+®/Sentimag® and the standard of care.
- So far 5 patients were treated within the learning curve for training and the first patient has been recruited and included for the study.

**SLN ultrastaging in endometrial cancer**

*Dr D. Hardisson, La Paz University Hospital, Madrid, Spain*

- The role of lymphadenectomy in endometrial cancer (ECa) is under discussion due to small evidence of benefit on overall or DFS.
- Aim of the presented monocentric study in Spain was to evaluate the efficacy of OSNA® for diagnosing SLN metastasis compared with histopathological examination in patients with ECa of stage I or II.
- 94 SLNs from 34 patients were staged by histology (H&E staining of 1mm central slice) and by OSNA® (on residual SLN material). Histologically negative slices underwent 200 µm serial sectioning for ultrastaging. For OSNA® staging, cut-off values of BCa were used.
- 11/94 nodes provided discordant staging results (histol.-; OSNA®+). The extent of possible tissue allocation bias is unquantified but regarded as major source of bia.
- It was concluded that OSNA® shows high sensitivity and specificity, which suggests its utility as a novel tool for the molecular detection of SLN metastasis in patients with endometrial carcinoma. A forthcoming multicentric OSNA® study in ECa will tackle the unsolved questions.

**SPIOs for SLN detection in melanoma. An alternative method**

*Dr A. Piñero, Virgen de la Arrixaca University Hospital, Murcia, Spain*

- SLN involvement is a crucial prognostic factor in cutaneous melanoma.
- The gold standard is the combined technique (radiotracer + ink) including lymphoscintigraphy.
- The IMINEM study aims to assess the equivalence of the Sienna+®/Sentimag® system in parallel with the standard used in routine for detecting SLNs in 186 patients with cutaneous melanoma.
- Eight Spanish centres participating.
Sentimag® and OSNA® to support SLN concept in Head and Neck cancer
Dr F. Godey, Centre Eugène Marquis, Rennes, France

- Involvement in cervical SLNs is a crucial prognostic factor in Head and Neck Squamous Cell Carcinoma (HNSCC). Until recently, a neck dissection was advocated routinely. A more recent approach consists of limiting lymph node surgery to a staging procedure by taking only the sentinel lymph nodes (SLN) that are representative of the whole neck node system.

- Challenges for the SLNB concept in HNSCC are:
  - The detection of SLNs is limited to HNSCC accessible for tracer injection (oral cavity) under local anaesthesia, but could be extended to other localisations if possible intraoperatively (Sienna+®/Sentimag® could be a ready-to-use solution);
  - Classical histopathological intraoperative SLN examination is not sufficiently sensitive for metastasis detection.
  - The application of OSNA® during surgery could be a solution;
  - In case of a positive lymph node, a second surgery is necessary. This and the serial examination of SLNs delay the adjuvant therapy and create additional patient distress.

- Initial results of an OSNA® study in HNSCC (26 patients/158 nodes) provided 87.9% of concordant cases. Discordant cases are mainly micrometastases and probably due to tissue allocation bias.

- Study results will be ready in 2017 and an evaluation of Sentimag in HNSCC will follow.

Key messages:
- Magnetic detection of sentinel lymph nodes (SLN) with the Sienna+®/Sentimag® system has been proven to be as effective as the standard of care in an increasing number of cancer entities, such as breast cancer, prostate cancer, endometrial cancer, vulvar cancer and head and neck squamous-cell cancer.
- First results suggest that Sienna+® may solve the problematic LN localisation with imaging methods (LN mapping) in cancer entities, where LN dissection is still standard of care.
- In all entities, but particularly in those in which the SLN concept is still under debate, the combined application of magnetic LN detection and LN analysis and LN staging with OSNA® provides promising progress in workflow and performance due to faster LN analysis and more accurate staging.

Session:
New directions in axillary management – A session led by the EBC2 (European Multidisciplinary Breast Cancer Collaborative)

The session started with a short presentation of the EBC2 members to explain who they are and the goals of the collaborative. The group consists of members of the scientific board that developed last year’s symposium programme. As scientific collaboration is a central focus, presentations looked at clinical scenarios that are a matter of debate and where further clinical evidence is required. At the end of the session, attendees were invited to participate in planned/future projects.

Axilla in the neoadjuvant setting
Dr Tracey Irvine, Royal Surrey County Hospital, Guildford

Key messages from Dr Tracey Irvine:
- There is controversy about the right management of the axilla in patients having received pre-operative systemic treatment.
- There is concern regarding the higher false negative rate of the SLNB (results from different studies have been shown, e.g. SENTINA).
- Guidelines do not give clear recommendations (only NCCN recommend excising min three nodes or usage of clips).
- In cN+ (clinical node positive) patients, about 40% have cPR (complete pathological response) and negative SLN after neoadjuvant chemotherapy. Consequently, ALND can be considered as overtreatment.
- Results of several studies have shown the feasibility of the OSNA® application in this setting.
- Clinical practice in Guildford and results have been reported indicating that not all patients might require axillary clearance in both scenarios cN-/+ and depending on the grade of cPR.

Conclusion:
- SLNB post chemo can be accurate (accuracy can be improved by clips).
- OSNA® is feasible post NACT but larger studies are required to increase evidence for the meaning of the obtained results in terms of appropriate surgical procedure and further therapy steps.
Axilla staging and molecular tumour biology
Dr Florence Godey, Centre Eugene Marquis, Rennes

Key messages from Dr Florence Godey:

- Tumour biology and nodal status are known to be strong prognostic factors.
- Currently used multigene platforms look at different target genes (very small overlap) and provide different result classifications. Nodal status is directly included in the risk assessment or not.
- Comparability is difficult and there is only limited concordance when several platforms are applied to the same patient (about 55% in tests with categorization in three risk groups, about 80% in tests with two risk groups).
- Nodal status impacts the result but might vary per the grade of histopathological analysis. In case no ALND is performed, staging information is limited anyhow.
- OSNA® is a standardised test that provides accurate results of the SLN tumour burden. The CK19 copy number has proven its ability to predict further non-SLN involvement, providing staging information that is not available when ALND is omitted. Furthermore, recent results indicate that SLN-TTL (Total Tumour Load) enables classification of patients in a low/high-risk group.
- Multi gene risk classification is a risk assessment but does not predict response to adjuvant therapy. Therefore, a more precise determination of prognosis helps to decide treatment.

Conclusion:

- Combining the OSNA® result/TTL with multi gene assays might improve prognosis and decision-making for patient-tailored therapy.
- A study project (MOTTO) has been set up to investigate the relation between TTL and molecular subtypes and the role of TTL as parameter to determine ROR score.
- As multi gene assays are still expensive, the OSNA® result could give an indication which patient might be eligible for such a test.

Is it time to redefine a positive node?
Dr V. Peg, Hospital Universitari Vall d’Hebron, Barcelona

Key messages from Dr V. Peg:

- Lymph node positivity is defined as metastatic spread to lymph nodes in the armpit. The more lymph nodes contain cancer cells the more serious the cancer might be (prognosis).
- SLNB in BC is established in cN0: SN -> in 90%–95% no further involvement of non-SLN; SN+ > in 40%–60% no further involvement of non-SLN (prediction).
- Study results show (Z0011, IBCSG 23-01) that a positive SLN does not have the same meaning and that there are patients with positive SLNs whom can be spared ALND.
- OSNA has demonstrated its reliability to more accurately determine the SLN tumour burden.
- The SOLO1113 trial has demonstrated that TTL (Total Tumour Load) better predicts non-SLN involvement than the number of positive SLNs whom can be spared ALND.
- The PLUTTO trial has shown that TTL is also of prognostic value in term of DFS, LRDFS and OS enabling differentiation of patients in a low risk and high risk group.

Conclusion:

- Molecular analysis of SLN (TTL) predicts better axillary involvement and survival.
- Total tumour burden in the SLN defines two groups of risk in terms of survival.
- Micrometastasis definition could be reviewed (up to 25,000 copies CK19 mRNA/μL?).
EBC2 projects and wrap-up

- Need a NACT OSNA® study.
  - Does TTL predict NSLN involvement?
  - Do we need to clear in all patients?
- Investigate the role of CK19 copy number/TTL as parameter to redefine EPclin score.
- Validation of the prognostic value of OSNA® in further studies.

Who we are and how to get in contact:

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Saturday, 25 February, Room Elbe 1

Session: Providing innovative therapies – Part I: Funding and financing opportunities

The first part of the DigniLife® section focused on the topic of funding and new financing opportunities to support DigniLife® and to guarantee that each patient can in the near future benefit from a scalp cooling treatment to improve the quality of life and better manage one of the worst collateral effects of chemotherapy.

The voice of patients during chemo (Kemioamiche activities) – how DigniLife® is perceived

Prof R. Masetti, Fondazione Policlinico Gemelli, Rome, Italy

- Policlinico Gemelli in Roma, Italy has created a new department completely dedicated to Women’s Cancer. With the cooperation of Komen Italia, several initiatives have been developed to increase patient quality of life, to promote research against cancer and an educational programme. Since October 2015, DigniLife® has also been part of that programme with 60 patients already treated with promising results.

- Policlinico Gemelli and Komen Italia underlined the importance of increasing and promoting AWARENESS OF DIGNILIFE®. Kemioamiche is a ‘docu-fiction’ that tells the stories of nine patients from the time of diagnosis to the completion of treatment (broadcast on two national channels – TV2000 and Real time). It is also the name of a WhatsApp chat created by a group of chemotherapy friends to exchange advice, post photos with new wigs and meet virtually to not feel alone. Part of the story is DigniLife® and its benefit for patients with a diagnosis of breast cancer to prevent hair loss during chemotherapy.

- ‘Scalp cooling to prevent alopecia is not only a cosmetic issue and should be covered by health public system as for breast reconstruction following mastectomy.’ (Prof R. Masetti, Rome, Italy)

Financing concept DigniLife® at the Mammazentrum Hamburg – an example of social responsibility in the care of breast cancer patients

Prof F. Hilpert, Mammazentrum Hamburg, Germany

- The Mammazentrum Hamburg has an integrative oncology department. It offers DigniLife® as well as supportive medicine such as traditional Chinese therapy and complementary medicine. This could be financed by a foundation.

- The donations come from active tournaments (galas, sports events) from private members, from the fundraising group and from other sources.

- Mammazentrum continuously promotes scalp cooling with DigniLife® on public TV, in the press, in their own internet portal ‘senolog.de’. With activities, the foundation helps to collect money and it benefits for the awareness of breast cancer.

- An example of social responsibility in the care of breast cancer. Not easy, but with several positive results.
Patients associations and multidisciplinary teams moving forward together

Dr S. Migliuolo, Europa Donna Italia responsible for medical and scientific communication

- Europa Donna is a European Breast Cancer Coalition representing the interests of European women regarding breast cancer to local and national authorities as well as to European Union institutions. One of their goals is to support the creation of Breast Unit as a model of patient care for a better quality of life. Europa Donna Italia has 95 affiliated member associations in 13 regions: representative of thousands of women throughout the country.

- Quality is diagnosis, is treatment, is support. Caregivers associations are highly committed in fundraising to ensure a range of services, equipment and support for patients to improve their quality of life.

Scalp cooling awareness campaign in the Netherlands

Dr C. van den Hurk, Comprehensive Cancer Center (IKNL), The Netherlands

Although scalp cooling has been used in most Dutch hospitals for the last decade, it is known that it is still not offered to all eligible patients. To increase the use of scalp cooling, the focus is not only on sharing knowledge with oncology professionals, but also on raising awareness amongst the public. When patients ask for scalp cooling in the hospital they are likely to get it and professionals are becoming increasingly aware of the added value of scalp cooling for their patient’s quality of life.

- The ‘Give hair a chance’ foundation found some professionals with backgrounds in communication, marketing, social media and design who participated in the awareness campaign free of charge.

- Besides this campaign IKNL and the foundation have invested a great deal of effort in implementing scalp cooling in the Netherlands. We have initiated research on many topics, launched websites and a decision tool, circulated newsletters, given clinical lessons to oncology nurses and MDS in their own hospitals and at their professional associations.

- There have also been two other public campaigns in the past and we ensured the information about hair loss and scalp cooling was included in the patient website of the Dutch cancer society and in the national online patient information about the side effects of chemotherapy.

Session:
Providing innovative therapies – Part II: Current and future progress in scalp cooling.

Tolerability and effectiveness of sensor controlled scalp cooling

Prof T.W. Park-Simon, Medical School, Hannover, Germany

Hair loss during chemotherapy means a reduction in the quality of life for patients and is one of the most distressing side effects. In contrast to previous scalp cooling devices, DigniCap® uses flexible silicone caps of different sizes controlled by various temperature sensors within the cap. In our prospective study named 'coolHAIR' we focused on the effectiveness with regards to hair loss and tolerability by patients’ contentment with the system. As the final study has not been published yet, please wait a little for more details.

Scalp cooling: results of a prospective cohort study

PD Dr Mathias Fehr, Frauenklinik Kantons-spital Frauenfeld, Germany

The aim was to assess the effectiveness of a sensor-controlled scalp cooling system (DigniCap®) to prevent chemotherapy-induced alopecia in breast- or gynaecological cancer patients receiving one of seven regimens. For the present prospective study, 55 women receiving neo-adjuvant, adjuvant, or palliative chemotherapy were enrolled. Clinical assessments, satisfaction questionnaires, and alopecia evaluations [World Health Organization (WHO) grading for toxicity] were completed at baseline, at each cycle, and at completion of chemotherapy.

- Of the 55 patients, 78% underwent scalp cooling until completion of chemotherapy.

- In multivariate analysis, younger women and those receiving paclitaxel weekly or paclitaxel – carboplatin experienced less alopecia.

- The compound successful outcome (‘no head covering’ plus ‘who grade 0/1’) was observed in all patients 50 years of age and younger receiving four cycles of docetaxel–cyclophosphamide or six cycles of paclitaxel–carboplatin.

- Conversely, alopecia was experienced by all women receiving triplet polychemotherapy (six cycles of docetaxel – doxorubicin – cyclophosphamide).

- For women receiving sequential polychemotherapy regimens (three cycles of fluorouracil – epirubicin – cyclophosphamide followed by three cycles of docetaxel or four cycles of doxorubicin – cyclophosphamide followed by four cycles of docetaxel), the subgroup 50 years of age and younger experienced a 43% success rate compared with a 10% rate for the subgroup of older women receiving the same regimens.

Conclusion: The ability of scalp cooling to prevent chemotherapy-induced alopecia varies with the chemotherapy regimen and the age of the patient. Use of a compound endpoint with subjective and objective measures provides insightful and practical information when counselling patients.
Preventing chemotherapy-induced alopecia by scalp cooling: Preliminary data from a study on the efficacy and safety of DigniCap® System in breast cancer patients
Dr E. Munzone, European Institute of Oncology, Milan, Italy

- IEO in Milano recently completed a study (to be published soon) with the aim of evaluating the efficacy and safety of the DigniLife® concept in women with early breast cancer undergoing adjuvant chemotherapy regimens. Primary endpoint was the reduction of hair loss in at least 55% of patients with a maximum of ≤ grade 2 hair loss (corresponding to 25%-50% HL); secondary end points included assessment of side-effects in terms of head/scalp pain, feeling chilled, rash and QoL (EORTC BR-23 and EORTC QLQ-30 questionnaires).

- A good cooperation among nurses and clinician is important for ensuring routine implementation of scalp cooling treatment with DigniLife®

The results are very promising and they registered a success (within the grade 2 of DEAN Scale) in 77% of patients with breast cancer who received adjuvant chemotherapy regimens (especially EC protocol) – Poster published XVIII AIOM congress – Rome Italy.

Conclusions:

- Hair has always been a social symbol and over time is related to perceptions of age, social status, beliefs, and even more individuality and a sense of attractiveness. Further research is needed to determine the presence and the extent of the adverse effect of alopecia induced by chemotherapy on various aspects of QoL.

- The speakers agreed that a new multicentric study could be a solution to align the results now available. In fact, the selection criteria of the patients and the different end points in the studies currently available do not permit combining them in a unique line. This could be very important, in the near future, to start the procedure for reimbursement and for the guidelines.

- ‘Scalp cooling to prevent alopecia is not only a cosmetic issue and should be covered by the public health system as for breast reconstruction following mastectomy.’ (Prof R. Masetti, Rome, Italy)

- In addition, another important aspect will be the necessary increased patient awareness, following the example of the Netherlands and other countries. This will contribute to increasing the demand from patients and will help also for the important topics mentioned previously. All patients should be able to benefit from sensor-controlled scalp cooling treatments to prevent alopecia during chemotherapy and to improve their quality of live.

Creating a prospective registry for scalp cooling
Prof R. Felberbaum, Medical Centre Kempten-Oberallgäu, Kempten, Germany

Only the reliable evaluation of results obtained by scalp cooling and its public discussion can facilitate an increase in its acceptance as a safe and successful form of treatment, while at the same time avoiding misunderstandings. This is of utmost importance as the fate of controlled scalp cooling – despite encouraging study results – will be decided in daily clinical practice. In addition, such an analysis is a valuable tool for the reliable advice of the affected patients. To fulfil this task, a national or international registry should be created for data collection and data evaluation. Such a registry, based on a prospective data collection should allow a very precise statement on the current situation within gynaecological oncology, focused on chemotherapy regimens applied and the results obtained by controlled scalp cooling.

- The fate of controlled scalp cooling – despite encouraging study results – will be decided in daily clinical practice.

Conclusion: CoolCapData database should be an institution of a scientific society with its own rules of procedure independent of industrial influence and interest. It would be a voluntary association of all centres using controlled scalp-cooling for preventing CIA (chemotherapy-induced alopecia). Each medical group should produce a computer – aided documentation in accordance with the catalogue of the CoolCapData base, designed by its steering committee. The demand of a prospective data input would be a significant qualitative advance for this registry to act as a tool for quality control within oncology.
Session:
Molecular diagnostics of gastrointestinal cancers

Dr F. Crafa and Dr S. Noviello (AO Moscati Hospital, Avellino, Italy) demonstrated the potential of their technique for in-vivo node mapping in colorectal cancer. An initial experience with the parallel implementation of OSNA® for molecular detection of lymph node metastasis in colorectal cancer and gastric cancer was presented by Dr Bruno Märkl (Klinikum Augsburg, Germany). Dr Iban Aldeacoa (Hospital Clinic Barcelona, Spain) showed how lymph node analysis can be optimised by tattooing for better localisation and pooling to reduce the workload. The presentations given by Dr Annarosa Arcangeli (Department of Experimental and Clinical Medicine of the University of Florence, Italy) and Dr Clara Montagut (University Hospital Del Mar, Barcelona, Spain) were dedicated to the benefit of liquid biopsy for monitoring CRC patients during anti-EGFR therapy.

Sentinel node in colorectal and gastric cancer

Dr F. Crafa, AO Moscati Hospital, Avellino, Italy; Dr S. Noviello, AO Moscati Hospital, Avellino, Italy

- Additional analysis of serial sections allows the identification in up to 20% of lymph nodes that were determined as negative by standard technique.
- Sentinel node navigation surgery in colorectal cancer can be useful for organ-sparing surgery, tailored and successful lymphadenectomy and aberrant and skip metastases.
- Indocyanine-green and OSNA® are the route to tailor-made surgery.

Implementation of OSNA® for colon cancer and gastric cancer – experience from two parallel applications

Dr B. Märkl, Klinikum Augsburg, Germany

- The technical part of OSNA® was easy to establish and a one-day training course was sufficient to train technicians without prior experience in molecular techniques.
- Methylene Blue Technique helps to identify lymph nodes.
- The application is fast enough for intra-operative evaluation of SLN.

Molecular lymph node analysis in colorectal cancer

Dr I. Aldeacoa, Hospital Clinic Barcelona, Spain

- Coloniscopic tattooing is highly efficient for LN identification. It leads to a higher number of LN that are harvested and might help identify the LN’s that might shelter the tumour.
- Pooling permits the analysis of a high number of LNs with few molecular determinations per patient.
- Pooling warrants a more accurate LN pathological staging.

Blood-based RAS detection in colorectal cancer: an Italian pilot study

Prof A. R. Arcangeli, University of Florence, Italy

- Major challenge for treating stage IV CRC patients is the occurrence of primary or secondary therapy resistance.
- Clinical study imminent: Determining the time course of ‘molecular relapse’ compared with the actual appearance of the ‘clinical relapse’.
  - Metastasised CRC patients will be differentiated according to their RAS mutational status and will receive either chemotherapy and anti-EGFR (RAS WT cohort) or chemotherapy and/or anti-VEGF therapy (RAS mut cohort).

Why is sensitivity so important for detecting RAS mutations with liquid biopsy?

Dr C. Montagut, Hospital del Mar, Barcelona, Spain

- Prerequisite for monitoring patients during therapy: highly sensitive liquid biopsy assay.
- Correlation between circulating RAS mutations frequency and clinical characteristics:
  - mCRC patients with hepatic metastases have higher mut RAS ctDNA levels and patients with peritoneum or lung involvement.
- Need to re-evaluate tumour molecular profile during the course of the disease; monitoring enables the follow-up of mutations of resistance in patients’ blood.
- A new paradigm in the treatment of mCRC: Treating clonal evolution constitutes.
- What is the clinically relevant cut-off for mutant RAS level for predicting early relapse?
- Does RAS testing in ctDNA help identify candidates for Cetuximab rechallenge?
- Liquid biopsy-driven clinical trials like the Fire-IV study are going to answer these questions and will optimise treatment strategies to improve patient outcome.

Conclusion: Both speakers agreed that Sysmex OncoBEAM™ represents the cutting edge technology due to its unparalleled sensitivity in detecting and monitoring the RAS mutational status in the plasma of CRC patients.
Applications of next-generation Tissue Microarray (ngTMA) to study the tumour microenvironment in colorectal cancer
Prof I. Zlobec, University of Bern, Switzerland

Tissue microarray (TMA) technology revolutionised the investigation of potential biomarkers from paraffin-embedded tissues. However, conventional TMA construction is laborious, time-consuming and imprecise. Next-generation tissue microarrays (ngTMA) combine histological expertise with digital pathology and automated tissue microarraying. The aim of this study was to test the feasibility of ngTMA for investigating biomarkers within the tumour microenvironment (tumour centre and invasion front) of six tumour types using CD3, CD8 and CD45RO as an example.

CDX1 and CDX2 are possibly predictive biomarkers in colorectal cancer. The group combined digitally-guided (next generation) TMA construction (ngTMA) and the utility of digital image analysis (DIA) to assess accuracy, tumour heterogeneity and the selective impact of different combined intensity-percentage levels on prognosis. CDX1 and CDX2 immunohistochemistry was performed on ngTMAs covering normal tissue, tumour centre and invasive front. The percentages of all epithelial cells per staining intensity per core were analysed digitally.

Beyond classical prognosis analysis following REMARK guidelines, the group investigated pre-analytical conditions, three different types of heterogeneity (mosaic-like, targeted and haphazard) and influences on cohort segregation and patient selection. The ngTMA-DIA approach produced robust biomarker data with infrequent core loss and excellent on-target punching. The detailed assessment of tumour heterogeneity could – except for a certain diffuse mosaic-like heterogeneity – exclude differences between the invasive front and tumour centre, as well as detect haphazard clonal heterogeneous elements. Moreover, lower CDX1 and CDX2 counts correlated with mucinous histology, higher TNM stage, higher tumour grade and worse survival (p < 0.01, all). Different protein expression intensity levels shared comparable prognostic power and a great overlap in patient selection. The combination of ngTMA with DIA enhances accuracy and controls for biomarker analysis.

Beyond the confirmation of CDX1 and CDX2 as prognostically relevant markers in CRC, this study highlights the greater robustness of CDX2 in comparison to CDX1. For the assessment of CDX2 protein loss, cut-points as percentage data of complete protein loss can be deduced as a recommendation.

The Power of Digital Pathology for Improving Intraoperative Patient Management
Prof C. Guettier, Hospital Paul Brousse/Kremlin Bicêtre, France

Intraoperative diagnosis by frozen sections is used to guide the surgeon during oncological surgery. The ongoing restructuration of pathology structures in France and the shortage of pathologists make essential an alternative solution to the presence of a pathologist at every surgical site.

Telediagnosis for frozen sections was set up in July 2013 in the ‘Hôpitaux Universitaires Paris Sud’ between Paul Brousse and Bicêtre Hospitals. The hospitals are 2.5 km apart and share the same pathology lab located in Bicêtre since 2008.

This first experience with telediagnosis for frozen sections in France was included in the 18-month pilot project of a regional Telepathology Network (June 2014 to December 2015) supported by the Health Agency for Ile de France.

Within the network, telediagnosis for frozen sections was tried by three binomials including Paul Brousse/Bicétre Hospitals. 747 intraoperative telediagnosis on frozen sections were performed from June 2014 to December 2015.

The presentation described workflows and provide quantitative and qualitative results of the project as well as possible approaches for improving the procedure.

Conclusions
Based on manual selection criteria, ngTMA can precisely capture histological zones or cell types of interest in a precise and accurate way, aiding the pathological study of the tumour microenvironment. This approach would be advantageous for visualising proteins, DNA, mRNA and microRNAs in specific cell types using in situ hybridisation techniques.

In conclusion, the group attributes a role as tumour suppressors to both biomarkers. Several investigated parameters indicate that CDX2 performs more robustly than CDX1 in terms of applicability. The projected results show that (1) ngTMA is highly accurate and leads to a low frequency of tissue core loss, (2) different types of tumour heterogeneity can be investigated using the combined ngTMA-DIA workflow and (3) low percentages of CDX1 and CDX2 positive cells are associated with more aggressive tumour biology and the influence of different staining intensities on patient selection is much less in CDX2 than in CDX1. Combining all data from this analysis, we recommend that CDX2 ‘loss’ be scored as percentage of cells with complete absence of immunoreactivity.