

tumor response. However, assessment of tumor response following CRT and prior to radical surgery may identify patients with complete clinical response that could be managed by organ preserving strategies. These strategies may include transanal local excision (by endoscopic microsurgery platforms - TEMs) or even no immediate surgery (known as the Watch & Wait strategy). Local excision in this setting (in a complete clinical response) has the advantages of providing histological confirmation of complete primary tumor regression and still provide an organ-preservation alternative. However, the morbidity of local excision may be quite significant due to the risk of wound dehiscences and subsequent functional detrimental consequences. Even in patients with (unexpected) residual cancer, the need for completion TME may result in worse outcomes when compared to TME alone. On the other hand non-operative management requires a very strict follow-up (Watch & Wait Strategy). It avoids unnecessary postoperative morbidity, including long-term urinary, sexual, and fecal continence dysfunctions and the frequent need for temporary or definitive stomas associated with TME and TEMs. Critical aspects in this treatment strategy include timing and studies (clinical, endoscopic and radiological) for the assessment of tumor response. Many studies have suggested that longer intervals between RT completion and assessment of tumor response were associated with increased rates of complete response even though one recent randomized study has challenged this assumption. Clinical and endoscopic assessment using strict criteria have been used for the selection of patients based on the presence of whitening of the mucosa, teleangiectasia and minimal loss of pliability of the rectal wall in the absence of any ulceration, stenosis or mass. Radiological studies with high-resolution magnetic resonance (MR) with or without diffusion-weighted series has been the preferred method of assessment of response and the presence of low-signal intensity areas are usually consistent with a complete response. With the use of these studies, selection of patients for a non-immediate surgical approach (without TME or TEMs) may provide good oncological outcomes and excellent functional results. Local recurrences may develop in nearly 25-30% after 3 years from initial tumor response assessment. Most local recurrences have an endoluminal component (90%) and are amenable to simple clinical and endoscopic detection. Even patients that do develop local recurrences may undergo salvage surgery with apparent no oncological compromise. In this setting, after a complete clinical response in selected patients and expert centers, the preferred initial approach should be non-immediate surgical resection and strict follow-up.

#### SP-0230 Targeted imaging in rectal cancer

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##### Abstract text

Tumor-targeted fluorescence imaging has the potential to revolutionize current practice of oncologic surgery by selectively highlighting malignant tissue during surgery and other minimal invasive procedures. Various targets were explored for real-time tumor visualization by different research groups. Carcinoembryonic antigen (CEA) is overexpressed in the majority of colorectal cancers (CRC) and is a promising target for CRC imaging. Therefore, a dose-escalating study was performed by our group to determine pharmacokinetics (PK) and tolerability of SGM-101, a novel fluorescent anti-CEA monoclonal antibody, and to investigate the feasibility to detect rectal cancer with fluorescence imaging in real-time. Nine patients with primary and 17 (expansion cohort) with recurrent or with peritoneal metastases (scheduled for HIPEC) were included in this study. SGM-

101 did not cause any treatment-related adverse events and a dose of 10 mg, administered four days before the surgical procedure, showed the highest tumor-to-background ratio. In the expansion cohort, 19 (43% of all lesions) additional malignant lesions were detected using fluorescent imaging, which changed the treatment strategy in 6/17 patients (32%). This study presents the first clinical experience of CEA-targeted detection of CRC and demonstrates that SGM-101 can influence pre-operative clinical decision-making in a substantial number of patients. In our opinion, CEA-targeted fluorescence imaging might also be very useful for locally advanced rectal cancers where fibrosis and tumor tissue are difficult to differentiate intraoperatively after neo-adjuvant chemo-radiotherapy and pre-operative MRI imaging is neither sufficiently sensitive, this newly developed modality can hopefully be of added value. In addition, following the absence of fluorescence in two resected specimens of primary rectal cancer patients with a pCR, a promising future application of SGM-101 could be screening for tumor (re)growth during Watch and Wait treatment strategies. Latter organ sparing strategies will be addressed during the lecture as well as the application of other tumor targeting agents (e.g. Avastin-800CW, Cetuximab-800CW) for this application.

#### SP-0231 The optimal radiotherapy approach for organ preservation

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##### Abstract text

The watch-and-wait strategy (w&w) for patients with rectal cancer achieving clinical complete response (cCR) after preoperative radiotherapy is gaining momentum, even though it is still considered as experimental treatment. Such a strategy may use an "accidental" or "intentional" approach. The former confers routine indications and schedules of radio(chemo)therapy; the latter consists of extended indications and/or higher doses of radio(chemo)therapy. The first approach seems to be currently more accepted by the medical community. After routine preoperative chemoradiation of an average patient population, about 10% cCRs can be expected. This rate increases to about 30% for tumours up to 5 cm and involving less than 50% of the bowel circumference. Thus far, w&w has been possible only after chemoradiation. For short-course radiotherapy (5 x 5 Gy) and immediate surgery, the interval between radiation and operation is too short for tumours to disappear. The Stockholm III randomised trial comparing short with long interval after 5 x 5 Gy has shown oncological safety for the long interval. Additionally, this trial has demonstrated 12% of pathological complete responses after the long interval; another study has also shown a clinically relevant rate of cCR. Thus, short-course radiation with a long interval can be used for the "accidental" approach of w&w.

#### SP-0232 Dose escalation for non-surgical management

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##### Abstract text

Recent years have seen increased focus on organ preservation and non-surgical management strategies for rectal cancer, and this has resulted in considerable interest in radiotherapy dose-escalation approaches. There are reasonably good data to suggest that there may exist a dose response relationship for pathological tumour regression after preoperative (chemo-)radiotherapy (see e.g. Appelt et al, IJROBP 2013). A number of patient and

tumour specific factors may influence this relationship; such as tumour volume, lymph node involvement, and distance from anal verge. However, it is still unclear whether such a dose-response relationship also exists for clinical complete response (cCR) to treatment - and importantly, whether increase in cCR rates by dose-escalation will translate into improved long term local control without surgery. Existing studies using dose escalation for non-surgical management will be briefly reviewed, and an analysis of the relationship between tumour dose and 2-year local control in published studies will be presented. If dose escalation is to be attempted, several potential radiotherapy modalities exist. They include external beam boost, endorectal brachytherapy and contact X-ray therapy (Papillon technique). The technical challenges of treatment optimization and delivery will be summarised for each technique, including (lack of) organ at risk definitions and dose constraints. Tumour doses achievable with the three techniques will also be mentioned. An additional issue concerns patient selection: patients most benefitting from dose escalation may be those with small, early cancers who we would not usually be irradiated at all; and there may be a subset of patients with high risk of surgical morbidity and mortality who will have a better risk/benefit ratio with dose escalation. These challenges will be discussed. Finally, ongoing and planned trials of dose escalation in this setting will be covered. They include the OPERA trial (NCT02505750), the Canadian MORPHEUS study (NCT03051464), the Danish Watchful Waiting II study (NCT02438839), and the Dutch RECTAL-BOOST (NCT01951521) and HERBERT II studies.

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#### Symposium: Cosmetic appearance after brachytherapy

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##### SP-0233 How to measure brachytherapy-related cosmetic changes?

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##### Abstract text

The long-term success of Interventional Radiotherapy (brachytherapy) can be evaluated in terms of disease free survival and rate of toxicities. In the past, local control was in focus of the analyses and reporting adverse effects was usually reduced to functional disorders. With the introduction of new technologies in this field such as image guided and intensity modulated interventional radiotherapy (I-RT), more attention is dedicated for preventing toxicity also in terms to achieve not only functional but also cosmetic well being of the patients. Nowadays, I-RT represent the highest level of technology and interdisciplinarity. In some anatomic sites, such as breast, H&N and skin, the measurement of the treatment related cosmetic changes is usually one of the main study end points. Furthermore, published experiences showed that the cosmetic outcome has a significant influence on quality of life (QoL). Nevertheless, the cosmetic assessment in I-RT remains a complex issue since non-standardized evaluation systems usually work with very different methods. Moreover, especially in the past, cosmesis was not accurately measured and often underestimated with a confusion/overlap with late toxicity. There are many ways to evaluate this topic. Some systems use qualitative, others quantitative methods. Additionally, a cosmetic evaluation system could be subjective or objective. Some groups published their experiences using specific scoring systems (SS) for radiotherapy, others, considering the nature of this procedure, preferred a system used in the post-surgery

assessment. The most frequently applied systems are: EORTC-RTOG, LENT-SOMA, CTCAE, Harvard NSABP, Breast Retraction Assessment (BRA), Facelift Outcomes Evaluation, the Rhinoplasty Outcomes Evaluation (ROE), the Blepharoplasty Outcomes Evaluation (BOE), and the Skin Rejuvenation Outcomes Evaluation (SROE). Recently, new technologies are involved for evaluation of cosmetic results, which can provide an objective estimation of the treatment effects through the use of high definition images, 3D scanners or photogrammetric methods. All of these are very useful tools for absolute but also for relative evaluation, especially for the comparison with a benchmark or other treatment. Moreover, methods using dedicated software solutions are spreading in the clinical practice. In conclusion, the attention to psychological and social aspects in modern oncology is an important factor to be considered in the choice of an optimal treatment. The standardized objective cosmetic assessment could play a central role for analyzing the results of interventional radiation therapy, especially for the comparison with those of other treatments such as external beam radiotherapy or surgery.

##### SP-0234 Cosmetic outcome after APBI

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##### Abstract text

Multiple phase 2 and two phase 3 randomized trials proved the non-inferiority of APBI with interstitial HDR/PDR brachytherapy (BT) in terms of local control and overall survival compared with whole-breast irradiation (WBI). Cosmetic outcome was reported good to excellent in the majority multicatheter BT-based APBI trials. However cosmetic results based on direct comparison between APBI and WBI were only reported from the Hungarian and GEC-ESTRO phase 3 trials. In the Hungarian APBI trial (n=258), 10-year cosmetic results were significantly better after HDR BT alone compared to WBI: the rate of excellent-good cosmetic result was 81% in the APBI arm and 63% in the WBI arm (p<0.01). The rate of excellent-good cosmesis in the APBI group was 85% after HDR BT and 72.5% after external beam electrons (p=0.97), whereas in the WBI group it was 67% using 6-9 MV photons and only 48% using telecobalt (p=0.08). In the GEC-ESTRO APBI trial (n=1184), 5-year cosmetic results were similar in patients treated with HDR/PDR BT or WBI: according to patients' view, 92% in the APBI group versus 91% in the WBI group had excellent to good cosmetic results (p=0.62); when judged by the physicians, 93% and 90%, respectively, had excellent to good cosmetic results (p=0.12). Furthermore, neither APBI nor WBI deteriorated the cosmesis during the years of follow-up, as represented by the stability of cosmetic outcomes over time. Findings from prospective randomized trials confirm that multicatheter BT-based APBI is not only as effective as WBI but also provides at least equivalent cosmetic outcome compared with conventional WBI.

##### SP-0235 Facial growth and developmental outcomes following pediatric head and neck brachytherapy

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##### Abstract text

Survival in head and neck rhabdomyosarcoma (HNRMS) patients is improving, with current overall survival rates around 66-97%. However, the majority of patients needs radiotherapy potentially combined with surgery to achieve and maintain local control. HNRMS patients are