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Tentative title of the talk: Epigenetic regulation in breast cancer and combination therapy

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Traditional therapies do not kill cancer progenitor cells and drug-resistant cancer cells, causing cancer relapse. Interestingly, combination therapy, including epigenetic drugs, was effective against breast and ovarian cancers causing more than additive growth inhibition in various types of breast and ovarian cancer cells. Our recent analytical study suggests that breast and ovarian cancers possibly have similar epigenetic origin. Other studies have shown that combination therapy with epigenetic drugs reduced cancer relapse, sensitized drug resistant cancer cells, and killed cancer stem cells. These findings led us to hypothesize that initiation of cancer progenitor cell formation from predisposed cells requires an epigenetic switch. Further development of cancer involves mutations. This hypothesis contradicts current paradigm of carcinogenesis. CpG residue methylation in the upstream regions of genes is one of the epigenetic regulations involved in silencing of tumor suppressor genes in cancer cells. In addition, histone modifications, such as H3K4me, and H3K27me3, and other histone modifications regulate gene expression in concert with alterations in DNA methylation. Our system biology analysis revealed that DNA methyl transferase1 (DNMT1), the enzyme which maintains CpG residue methylation is allosterically activated in cancer cells. H3k9me3 recruits DNMT1 at the site of CpG methylation. It is possible that histone modification and CpG methylation work in a concert to regulate differential gene expression in carcinogenesis.

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First results of a pre-planned interim analysis of a national multicenter patient reported outcome study (PRO-Bra) in breast reconstruction following mastectomy with titaniferously coated polypropylene mesh (TiloopBra)

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Introduction: In the majority of interdisciplinary breast centers of Germany implant based, mesh-supported operations constitute a total of approximately 50-60% of reconstructive techniques. The BreastQ is the most valid and reliable measurement of quality of life aspects in important domains used in clinical routine.

Material & Method: Because the patient reported outcome is the most relevant factor reflecting the overall satisfaction from a patient perspective a prospective surveillance study with BreastQ-scales at 12 months as primary endpoint was conducted (2013) and ended 7/2016 with full recruitment (n=267). A pre-planned analysis of the first 60 pts with completion of the BreastQ after 6 months was done.

Results: Almost all surgeries were primary reconstructions (96.6%) and nipple-skin-sparing mastectomies (97.1%). The most frequent incision was inframammary (n=115), followed by T-shaped (n=45). The average of the pts was 50 y (19-77), BMI was 22 (17-33), 77.3% were non-smokers. Percentage of neoadjuvant chemotherapy was 23% of prior radiotherapy was 12%. Radiotherapy showed no significant influence of the BreastQ. Severe events occurred in 46 cases. The most frequent complications were necrosis (n=12), hematoma (n=12) and 9 pts were dropped out. The mean score of BreastQ was equal pre and postoperative after 6 months (67+/-16 to 65+/-15) satisfaction with breast from 67+/-22 to 61 +/-14; psycho-social well-being from 71+/-17 to 73+/-18, sexual well-being from 62+/-17 to 60+/-19, satisfaction with outcome was 75+/-18 and satisfaction with surgeon 90+/-15. 88.3% were very satisfied, 10.0% somewhat satisfied, only 1.7% somewhat dissatisfied and 0% very dissatisfied.

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