containing regimes. Major concerns for lapatinib treatment are skin and gastro-intestinal toxicities (being an ErbB1 inhibitor) and cardiotoxicity (being an ErbB2 inhibitor). Cardiac events related to Lapatinib are rare and asymptomatic on meta-analyses. This review presents an analysis of lapatinib related skin (SE) and diarrhoea events (DE).
Methodology: 8 clinical trials of Lapatinib (1,126 pts) in MBC and other tumour types were analysed. Lapatinib (1000–1500 mg/day) was administered as mono-therapy (928 pts) or combination therapy (with tamoxifen 197 pts; with capecitabine 191 pts).
Results: SEs included dermatitis (commonest; 38% incidence), drug eruptions, dry skin, pruritus, urticaria, infection and nail/hair disorders. 54% pts experienced SEs and 50% DEs. Toxicities were usually CTC grade (G) 1 (55% SE; 54% DE) or 2 (35% SE and 30% DE). None had G4 SE while only 1% had G4 DE. Rashes and diarrhoea were early onset (45% SEs between days 1–14 and 44% DEs by day 6 from treatment). There was no necessity for dose reduction in 85% of patients and only 2% required discontinuation. 72% of SEs and 89% of DEs resolved. Diarrhoea was managed in 30% with standard medication (lomotil and loperamide). Severe cases required hydration, octreotide and antibiotics.
Conclusions: Laptinib induced skin and diarrhoeal events are mild and rarely require dose modification. Efficient clinical monitoring and standard medication is sufficient for more severe cases.

O-101 Effect of tamoxifen on serum lipid levels in women at increased risk of breast cancer

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Tamoxifen is well known for its beneficial effect in decreasing the development of breast cancer in women who are at high risk. Tamoxifen has also shown to decrease levels of total cholesterol and low-density lipids (LDL) and to increase levels of high-density lipids (HDL) and triglycerides.
In the International Breast cancer Intervention Study I (IBIS-I), 7,154 women at increased risk of breast cancer were randomised to either tamoxifen 20 mg/day or placebo for 5 years. Blood samples were taken at baseline, year 1, year 5, and year 6. Here, we investigate the effect of tamoxifen on lipid parameters in women at high risk of developing breast cancer.
After 60 months of follow-up, mean concentrations of total cholesterol and LDL were significantly decreased in tamoxifen users compared to baseline measurements (Both $P < 0.001$). In contrast, triglyceride levels were significantly increased in tamoxifen users ($P < 0.001$). After tamoxifen was ceased, all lipid parameters went back to baseline measurements. Compared to women on placebo, tamoxifen significantly decreased total cholesterol and LDL levels during active treatment. No clear effect of tamoxifen was seen for HDL levels.
Tamoxifen has clearly demonstrated a beneficial effect on reducing total cholesterol and LDL. In contrast, triglyceride levels in tamoxifen users were significantly increased compared to baseline measurements or placebo users. On the basis of our data, it appears that the beneficial effects of tamoxifen in women may not only reside in preventing breast cancer, but also reducing the risk of cardiovascular disease.

O-102 Results of a phase 2 study of the oral tyrosine kinase inhibitor (TKI): axitinib (AG-013736; AG) in combination with docetaxel (DOC) vs DOC plus placebo (PL) in first-line metastatic breast cancer (MBC)

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Background: AG is a potent TKI of VEGFR 1, 2&3. A phase 1 lead-in study identified 80 mg/m^2 q3wks of DOC in combination with 5 mg BID of AG as the recommended phase 2 dose. The primary objective was to determine whether the time to progression (TTP) of the AG+DOC arm is superior to that of the DOC+PL arm.
Methods: Pts with no prior chemotherapy for MBC and $\geqslant$12 mos from adjuvant chemotherapy (aCT), measurable disease, ECOG performance status (PS) of 0–2, and no uncontrolled brain metastases were randomly assigned (2:1) to receive treatment with either DOC+AG or DOC+PL, without prophylactic growth factor in cycle 1. Tumor measurements were performed q9wks. Pts were stratified according to estrogen receptor (ER) status, prior aCT and PS (0/1 or 2).
Results: A total of 168 pts were randomized. 92 pts had received prior aCT, 27 of whom received a prior taxane. Treatment arms were well balanced for prior adjuvant and taxane therapy. A median of 7 cycles of AG+DOC (range: 1–18) and 7 cycles of DOC+PL (range: 1–23) were administered. The most common non-hematologic all-grade adverse events observed in the AG+DOC arm included diarrhea (60%), nausea (53%), alopecia (51%), fatigue (49%), stomatitis (44%), and vomiting (40%). Grade 3/4 adverse events that were increased with AG+DOC vs DOC+PL included febrile neutropenia (16 vs 7%), fatigue (13 vs 5%), stomatitis (13 vs 2%), diarrhea (11 vs 0%), and hypertension (5 vs 2%). Other grade 3/4 hematologic toxicities were similar in both arms. The median TTP (by RECIST) was 8.2 mo with AG+DOC and 7.0 mo with DOC+PL, with a hazard ratio (AG:PL) of 0.73 (prespecified, one-sided $p = 0.052$). The overall response rate (ORR) was 40% in the AG+DOC arm and 23% in the DOC+PL arm ($p = 0.038$), with a duration of response of 6.9 and 5.3 mo respectively. In a hypothesis-generating subgroup analysis, the median TTP in patients receiving prior aCT was 9.0 mo with AG+DOC and 6.3 mo with DOC+PL, with a hazard ratio of 0.54 ($p = 0.012$). Within this stratum, ORR was 45% in the AG+DOC arm and 13% in the DOC+PL arm ($p = 0.003$).
Conclusions: The anti-angiogenic TKI AG combined with DOC (80 mg/m^2 q3wks) as first-line therapy for MBC has an acceptable safety profile and promising anti-tumor activity.

O-103 Validating response and toxicity predictions of the "virtual patient" in neoadjuvant and adjuvant breast cancer chemotherapy

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Introduction: Optimata Virtual Patient® (OVP) is a predictive biosimulation technology, comprising computer-implemented mathematical algorithms of physiological, pathological and pharmacological processes in a patient's body. Here we report validation of OVP accuracy in predicting chemotherapy efficacy and toxicity in breast cancer patients.
Materials & Methods: Clinical and pathological parameters were collected from 17 patients with locally-advanced breast cancer (neoadjuvant AC-Taxol therapy;