were sensory peripheral neuropathy (14%), fatigue (10%), myalgia (7%) and stomatitis (6%). Sensory neuropathy was cumulative and reversible; 6 pts discontinued due to neuropathy. Median time to resolution of G3 neuropathy (to G1 or baseline) was 5.4 wks. Sensory neuropathy in 23 pts (18%) was managed by dose reduction and of these pts, 20 (87%) had their neuropathy improve or not worsen. Promising activity and a manageable safety profile were achieved with I in this highly refractory population.

146PD RENAL INSUFFICIENCY IN BREAST CANCER PATIENTS: PREVALENCE AND IMPLICATIONS ON ANTICANCER DRUGS MANAGEMENT. SUBGROUP ANALYSIS OF THE 'IRMA' STUDY

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Background: The IRMA study reported the high prevalence of RI in 4684 cancer patients, with a glomerular filtration rate (GFR) <90 ml/min for near 60%. Furthermore, 80.1% were receiving nephrotoxic drugs and 79.9% drugs necessitating dosage adjustment. We present the results for IRMA patients with breast cancer.
Methods: Among IRMA patients for which type of tumour, sex, age, weight, serum creatinine (SCR), haemoglobinemia, and anticancer drugs were collected, those with breast cancer underwent subgroup analysis (no dialysis, no myeloma). The prevalence of SCR>110 µmol/L was assessed. GFR was estimated with the Cockcroft-Gault (CG) and the abbreviated MDRD (aMDRD) formulae. Patients were classified according to the K/DOQI stages of RI (see table below). Among anticancer drugs prescribed, those necessitating dosage adjustment and those potentially nephrotoxic were identified.
Results: 1898 patients with breast cancer were included: mean age 55.1, weight 64.2 kg, 20 men. The prevalence of SCR>110 µmol/L was 1.6%. That of GFR<90 ml/min was 51.9% with CG and 50.8% with aMDRD. Among patients with normal SCR, 57.1% and 56.0% had abnormal CG and aMDRD, respectively. 53.2% of the 3465 prescriptions were drugs needing dosage adjustment (or no data) and 90.4% of treated patients received at least one such drug. 41.6% of all prescriptions were potentially nephrotoxic and 76.7% of treated patients received at least one nephrotoxic drug. 44.1% and 20.6% had a serum haemoglobin lower than 12 and 11 g/dL, respectively.
Conclusions: RI is highly frequet in breast cancer patients and SCR dramatically underestimates this prevalence. Appropriate evaluation of renal function necessitates CG or aMDRD calculation. Nearly all those patients were treated with drugs that may necessitate dosage adjustment and half of them were receiving potentially nephrotoxic anticancer drugs. Furthermore, anemia was still highly frequent.

RI stages in IRMA patients with breast cancer according to K/DOQI classification

K/DOQI Stage of RI	GFR (mL/min or mL/min/1.73 m^2)	CG	aMDRD
1	≥90	36.6%	38.7%
2	60–89	37.6%	43%
3	30–59	13.8%	7.4%
4	15–29	0.4%	0.3%
5	<15	0.1%	0.1%
	NA	11.5%	10.5%

147PD SAFETY AND EFFECT ON TIME-TO-DISEASE PROGRESSION OF ADECATUMUMAB (MT201) IN PATIENTS WITH METASTATIC BREAST CANCER – INTERIM ANALYSIS OF A RANDOMISED, MULTICENTER PHASE II STUDY

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Introduction: High level expression of the epithelial cell adhesion molecule (EpCAM) identifies a subgroup of breast cancer patients with unfavourable prognosis (Gastl et al., 2000). Adecatumumab (MT201) was developed as a low-affinity human IgG1 antibody mediating antibody-dependent cellular cytotoxicity (ADCC) and complement-mediated cytotoxicity (CDC) against EpCAM-positive cancer cells (Naundorf et al., 2002).
Methods: This open label phase II study enrolled a total of 109 EpCAM-positive breast cancer patients. An initial restriction to allow for a maximum of one previous chemotherapy for metastatic disease was subsequently removed during the study. Patients were stratified into low/medium and high-level EpCAM expression according to their primary tumours IHC estimated staining intensity (Spizzo et al., 2004), and subsequently randomised to receive either high-dose (6 mg/kg) or low-dose (2 mg/kg) adecatumumab i.v. every other week until disease progression.
Results: This report summarizes the results of a pre-specified interim analysis on the first 67 evaluable patients. Patients receiving high-dose adecatumumab (n= 35) showed a higher rate of AE as compared to patients (n= 32) in the low-dose group (97 vs. 92% of patients), with no significant increases in serious AE (33 vs. 26 SAE). Gastrointestinal (nausea, vomiting, diarrhoea, constipation) and constitutional symptoms (chills, fatigue, headache) were reported as the most common toxicities and were mostly mild to moderate. A longer time-to-disease progression (TTP) was observed in patients receiving high-dose adecatumumab as compared to the low-dose group (median TTP: 78 vs. 43 days; p = 0.0348), with the longest TTP seen in patients expressing high levels of EpCAM and receiving high-dose adecatumumab (n=21; median TTP: 90 days; p = 0.0238).
Summary: This interim analysis demonstrates the safety and feasibility of adecatumumab treatment in patients with metastatic breast cancer. Moreover, there is suggestive evidence for clinical efficacy of the high-dose adecatumumab regimen, which appears to be more pronounced in patients with high EpCAM expression.

148PD BCIRG 007: RANDOMIZED PHASE III TRIAL OF TRASTUZUMAB PLUS DOCETAXEL WITH OR WITHOUT CARBOPLATIN AS FIRST LINE THERAPY IN HER2 AMPLIFIED METASTATIC BREAST CANCER (MBC)

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Background: Based on preclinical synergism between docetaxel (T), carboplatin (C) and trastuzumab (H), BCIRG conducted a phase III trial with HER2 + MBC to evaluate efficacy and safety of H in combination with T or TC.
Methods: 263 patients (pts) with HER2 FISH+ MBC were randomized to TH, (H with T 100mg/m^2) or TCH, (H with T 75mg/m^2 and C AUC=6). Chemo was given q3 wks for 8 cycles with wkly H at 2mg/kg (loading dose of 4 mg/kg), followed by H q3 wks at 6 mg/kg until progression. Pts were stratified by centre and prior (neo) adjuvant taxane chemo. Primary endpoint was TTP. Secondary endpoints include overall survival, response rate, duration of response (DR), clinical benefit (CB) and safety.
Results: 131 pts were treated in each arm. Pt characteristics were well balanced in both groups. Importantly, only 52% of pts received C at the protocol specified dose (RDI>0.9). Efficacy analysis was conducted at 204 events. There was no significant difference between TH and TCH in median TTP (11.1 vs 10.4 mos, p=0.57), ORR (73% in both arms), DR (10.7 vs 9.4 mos) and CB (67% in both arms). Serum HER2 ECD and biochemical marker results (BNP and Troponin I) will be presented to determine if they are predictive of tumor response and cardiac events respectively. Grade 3/4 toxicities were: infection (44% vs 30%), neutropenic infection (22% vs 12%), thrombocytopenia (2% vs 15%), febrile neutropenia (12% vs 13%) asthenia (5% vs 12%) and anemia (5% vs 11%). Two pts died (1.5%) due to sepsis in TCH. Absolute LVEF decline > 15% were seen in 5.5% vs 6.7% of pts. One pt (0.8%) had a symptomatic CHF in TH arm.
Conclusion: The already effective TH regimen does not benefit from the addition of C in women with HER2+ MBC.

149PD OVEREXPRESSION OF BMI-1 ONCOPROTEIN CORRELATES WITH IMPROVED SURVIVAL IN BREAST CARCINOMA

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