commencement of T respectively), 5 without disease relapse. Only 1 pt relapsed (with local in-breast recurrence) after T discontinuation. Eight pts are still alive and in CR (4 still on maintenance T). These pts are: ER negative 75%, liver only visceral disease 63%.
Conclusions: This is the largest series so far analysing long-term outcome of HER2+ MBC pts with DCR following T-containing CT. A small group of pts who show no further relapse at long-term FU can be identified. They are more frequently ER negative and have metastatic disease confined to liver. Our data suggests that in selected cases of CR lasting ⩾36 months maintenance T can be safely discontinued with very low risk of subsequent relapse. The molecular profile of this subset of pts should be specifically investigated to allow early identification of pts who are more likely to achieve DCR on T+CT.

5001 ORAL

Trastuzumab Emtansine (T-DM1) Vs Trastuzumab Plus Docetaxel (H+T) in Previously-untreated HER2-positive Metastatic Breast Cancer (MBC): Primary Results of a Randomized, Multicenter, Open-label Phase II Study (TDM4450 g/BO21976)

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Background: T-DM1 is a HER2-targeted antibody-drug conjugate in development for the treatment of HER2-positive cancer. It provides intracellular delivery of the cytotoxic agent DM1 while maintaining the antitumour activities of trastuzumab. We previously presented preliminary data from the first randomized phase II study of T-DM1 vs. H+T as first-line treatment in patients with HER2-positive MBC (Perez, et al. ESMO 2010, LBA3; TDM4450 g/BO21976; NCT00679341). Here we present the primary efficacy and updated safety results.
Methods: Patients (N = 137) were randomized 1:1 to T-DM1 3.6 mg/kg IV q3w, or H 6 mg/kg IV (8 mg/kg in cycle 1) + T 75 or 100 mg/m^2 IV q3w, until disease progression or unacceptable toxicity. Primary objectives were investigator-assessed progression-free survival (PFS) and safety. Results are based on a clinical data cutoff date of 15 November, 2010.
Results: Baseline characteristics were similar between groups. In the H+T arm, most patients (74.2%) initiated T at 75 mg/m^2. Median durations of follow-up were 13.5 mos (H+T) and 13.8 mos (T-DM1). Among safety evaluable patients, the most common adverse events (AEs) were alopecia (66.7%), neutropenia (63.6%), diarrhea (45.5%), and fatigue (45.5%) in the H+T arm; and fatigue (49.3%), nausea (47.8%), increased AST (39.1%), and pyrexia (39.1%) in the T-DM1 arm. Consistent with previously reported results, grade ⩾3 AEs were reported less frequently in the T-DM1 arm (46.4% vs 89.4%) as were treatment discontinuations due to AEs (7.2% vs 28.8%). Serious AEs occurred less frequently in the T-DM1 arm (18.8% vs 25.8%). One patient in each arm had an AE that resulted in death. At the data cut-off, 43.3% of patients were continuing T-DM1 vs 21.4% who were continuing H+T. Efficacy data, summarized in the table below, are notable for a significant improvement in PFS in the T-DM1 arm (14.2 vs 9.2 months, HR = 0.59, p = 0.035).
Conclusion: First-line treatment of HER2-positive MBC with T-DM1, compared to H+T, provided a significant improvement in PFS with a favorable safety profile. These results demonstrate the feasibility of T-DM1 in HER2-positive MBC.

	H+T	T-DM1
PFS	n = 70	n = 67
Median PFS (mos)	9.2	14.2
HR (95% CI), *P*-value	0.59 (0.36, 0.97), 0.035	
Objective Response	n = 69	n = 67
ORR, n (%), (95% CI)	40 (58.0), (45.5, 69.2)	43 (64.2), (51.8, 74.8)
Complete response, n (%)	3 (4.3)	7 (10.4)
Partial response, n (%)	37 (53.6)	36 (53.7)

5002 ORAL

Complications Associated With Chemotherapy in Patients With Metastatic Breast Cancer

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Background: Treatment with chemotherapy has been associated with significant rates of adverse events which may lead to expensive care or changes and delays in provided treatment. This study estimates the prevalence of chemotherapy-related complications in patients receiving chemotherapy for the treatment of metastatic breast cancer (mBC) in a real world setting.
Materials and Methods: The PharMetrics® Integrated Database (2004–2009) was used to select patients with mBC treated with chemotherapy and/or anti-HER2 targeted therapies. Episodes of mBC chemotherapy treatment with single-agent or combination of agents for a course of at least 30 days were identified. Complications were identified using medical claims with a diagnosis for one of the following events of interest: anemia, alopecia, arthralgia, bilirubin elevation, dehydration, dyspnea, infection, leukopenia, and neutropenia.
Results: A total of 1551 patients with 3157 eligible episodes of treatment met the inclusion criteria. The mean age of women was 57 years. The complication rates for the commonly used agents including anti-HER2 (i.e., trastuzumab and lapatinib), docetaxel, paclitaxel, gemcitabine, vinorelbine, and doxorubicin, are reported in the table.
Conclusions: Anemia, bilirubin elevation, and leukopenia were the most common complications during an episode of treatment, with substantial variations across types of regimen to treat mBC. Further research assessing the total impact (clinical, humanistic, and financial) of chemotherapy-related complications is required. There is a need for agents providing clinical efficacy without incurring significant toxicities.

	All episodes of treatment	Anti-HER2[1]	Trastuzumab + Vinorelbine[2]	Trastuzumab + Docetaxel[2]	Docetaxel[3,4]	Paclitaxel[3,4]	Gemcitabine[3,4]	Vinorelbine[3,4]	Doxorubicin[3,4]
Number of patients	1551	510	160	84	228	175	234	197	123
Number of episodes of treatment	3157	1157	172	90	264	188	240	207	133
Average by patient	2.0	2.3	1.1	1.1	1.2	1.1	1.0	1.1	1.1
Average duration (days)	131	158	169	141	118	115	94	107	95
Number of episodes with complications									
Anemia	51%	51%	70%	60%	55%	52%	70%	65%	50%
Arthralgia	12%	15%	18%	16%	9%	11%	9%	12%	10%
Bilirubin elevation	26%	29%	35%	31%	22%	31%	20%	21%	19%
Dehydration	10%	11%	14%	17%	11%	7%	10%	10%	13%
Dyspnea	19%	17%	24%	19%	21%	22%	24%	19%	20%
Infection	19%	20%	22%	22%	23%	14%	21%	16%	12%
Leukopenia	25%	18%	38%	20%	36%	23%	33%	46%	28%
Neutropenia	18%	13%	30%	14%	27%	15%	21%	30%	15%

[1]Based Regimen; Monotherapy or combination.
[2]Based Regimen; Including combination with anti-hormone therapy.
[3]Excluding anti-HER2-agents.
[4]Based regimen; Monotherapy or combination with anti-hormone therapy.

5003 ORAL

Inhibition of HER2 Positive Breast Cancer Cells by Drug Screening

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Background: About 20% of all breast cancers have an amplicon in 17q12−21 resulting in over-expression of the human epidermal growth factor receptor 2, *ERBB2*/*HER*-2. HER-2 is a receptor tyrosine kinase, belonging to the epidermal growth factor receptor (EGFR) family of proteins. Phosphorylation of the HER2 tyrosine domain activates downstream pathways like PI3K/Akt and MAPK that are involved in regulation of cell growth, survival, migration and proliferation. In the clinic, HER-2+ patients are treated with Trastuzumab (Herceptin), a monoclonal antibody targeted