Bone marrow involvement was accompanied by suppression of red cell production ($p < 0,05$) while having no effect on granulocyte or platelet counts. Anemia was found in BMMM-positive patients two times more frequently than in the control. There was a significant increase in ESR in the group with BMMM ($p < 0.001$). Mean ESR level in patients free from BMMM was 23.5 mm/h (range 17.5 to 29.5) versus 51.7 mm/h (range 44.2 to 59.2) ($p < 0.001$) in micrometastasis-positive cases. There was a statistically significant increase in tumor markers: CA 15−3 ($p = 0.003$), MCA ($p = 0.005$) and CEA ($p = 0.011$) in the group of patients with BMMM. In spite of CA 19−9 increased more often in micrometastasis-positive patients (36.8% vs. 29.0%) the difference was not statistically significant.

Conclusion: Having no clinical signs, BMMM are likely to be suspected according to the following changes in hematological parameters: significant increase in ESR and decrease in Hb levels, tumor markers increase (CA 15−3, MCA, CEA, CA 19−9) and further bone marrow biopsy is required.

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Comparison of Inpatient and Out-patient Care Needs for Metastatic Breast Cancer Patients

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Background: Median survival in women with Metastatic Breast Cancer (MBC) is over 2 years, but many patients survive longer. MBC patients are now successfully managed with a range of systemic treatment interventions routinely in an Out Patient Clinic (OPC) setting. Knowledge of utilisation of resources is vital for the development of an efficient health system.

Materials and Methods: We reviewed the medical records of 76 MBC patients attending breast clinic at Wansbeck Hospital, UK, between August 2010 and February 2011. MBC patients represented 35% of total clinic attendances. During this period patient data collection included number of OPC and chemotherapy unit attendances along with number and frequency of chemotherapy cycles including biological agents. Hormonal treatments used since MBC diagnosis was also recorded.

Results: Median age of MBC patients attending the service was 61 years (range 39 -86 years). Their median disease free survival from time of diagnosis was 4 years (range 0−20 years). Twenty clinics were conducted during this period with a median of 4 (range 1−10) clinic attendances per patient. Out of 76 patients 28 (37%) had multiple sites of metastases, bone metastases were found in 41 (54%); lymph nodes metastases in 13 (17%); visceral metastases in 40 (53%) and brain metastases in 7 (9%) patients. During this period 35 (46%) patient were on chemotherapy. 106 one weekly chemotherapy sessions were delivered to 11 (14%) of patients, 15 two weekly sessions for 4 (5%) patients, 103 three weekly sessions for 24 (32%) patients and 3 four weekly sessions were delivered for 3 (4 %) patients. 53 (70%) patients were oestrogen receptor positive and received a median of 1 and maximum 3 endocrine treatments.

Conclusion: Our previous study from Wansbeck Hospital shows only 14% of MBC patients required inpatient care of average 4.2 days, for chemotherapy related toxicity. We demonstrate that OPC treatment comprises the bulk of MBC patient workload and a majority receive frequent systemic treatments not requiring hospital admission. Current data shows OPC and chemotherapy unit visits are important aspects of care and utilise major resources in the management of MBC patients.

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Meta Analysis to Compare Overall Survival Between Primary Metastatic Breast Cancer and Recurrent Metastatic Breast Cancer

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Background: The objective of this meta analysis was to determine whether differences in survival exist between women with primary metastatic and recurrent metastatic breast cancer, and also to explore the effect of other prognostic factors among survival of those patients.

Material and Methods: The data base for this meta analysis were collected from three studies, these three studies were located through search of PubMed and HINARI websites, all studies that were in English language and compared survival between primary metastatic(PMBC) and recurrent metastatic breast cancer(RMBC) were included in this meta analysis. The end point that I assessed was the survival, other factors that included in comparison were the rate of occurrence, age of patients, disease free interval (DFI), tumor size.

Result: three studies with a total of 4145 patients were included in this meta analysis, 807 patients had primary metastatic breast cancer and 3338 patients had recurrent metastatic breast cancer. There were statically non significance difference in survival in two of these studies (25.1 vs 23.3 months, $p = 0.81$ and 39 vs 30 months, $p = 0.2$ in PMBC and RMBC respectively) and statically significance difference in survival in one of them (39.2 vs 27.2, $p < 0.0001$ in PMBC and RMBC respectively) in addition that patients with primary metastatic breast cancer were older and had larger tumor size than recurrent metastatic breast cancer patients.

Conclusion: the survival of patients with PMBC and RMBC was similar in both groups in spit of the difference in clinical and histological characteristic, also DFI play an important role in survival of patients with RMBC.

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PI3KCA Mutations in HER2-Positive Breast Carcinomas Treated with Trastuzumab

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Introduction: Aberrations of the components of the PI3K-AKT pathway are frequent in infiltrating breast carcinomas (IBC) and activating mutations of the *PI3KCA* gene mainly occur at hotspot in exons 9 and 20.

Material and Methods: We evaluated 123 Her2-positive IBC treated with trastuzumab at the S.Chiara Hospital of Trento, including 20 primary locally advanced IBC treated with neoadjuvant trastuzumab, 48 advanced metastatic IBC, and 55 early stage IBC treated with adjuvant trastuzumab. Genomic DNA was extracted from each paraffin-embedded tumor block using QIAamp DNA MiniKit (Qiagen Inc., Hilden, Germany). The samples were analyzed with Real-Time PCR and pyrosequencing reaction was performed according to the manufacturer's instructions PyroMark™ IDQ96 V2.0 kit (Qiagen). Pyrosequencing™ was performed using the PyroMark™ Gold Q96 reagent kit (Qiagen).

Results and Discussion: In our series *PI3KCA* gene mutations were observed in 11 % of locally advanced IBC, 10.4 % of metastatic IBC and 29% of early stage IBC. *PI3KCA* gene mutations were not associated with tumor size, grade, ER and PgR status and proliferative activity and were not predictive of response to trastuzumab treatment.

Conclusion: No statistically significant relations have been observed between status PI3K and pathological and biological parameters and response to treatment.

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Incorporating Epithelial Mesenchymal Plasticity (EMP) in the Detection and Isolation of Circulating and Disseminated Tumour Cells

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Background: Circulating tumour cells (CTC) in peripheral blood, and disseminated tumour cells (DTC) in bone marrow of cancer patients, represent 'seeds' that enable cancer recurrence or metastasis and are potential independent predictors of systemic relapse and death. However, current enrichment and detection methods rely on epithelial marker expression which may be lost by CTC/DTC undergoing epithelial-mesenchymal transition (EMT). This and other unresolved difficulties in detection due to low numbers prevent integration of this prognostic tool into routine clinical practice. Cells that share both epithelial and mesenchymal markers may have more aggressive properties and their detection will be an important factor in determining and monitoring treatment regimes.

Materials and Methods: To identify limitations of current widely used detection methods that rely on the expression of only epithelial markers, we undertook data-mining analysis which revealed that while mesenchymal breast cancer cell lines lose (epithelial) EpCAM expression, they gain expression of (mesenchymal) EGFR. We then developed and utilised anti-EGFR-coated immunomagnetic beads in parallel with anti-EpCAM beads to isolate CTC from peripheral blood and DTC from bone marrow of patients with advanced breast cancer and measured the expression of breast cancer markers in the isolated cells using RT-PCR.

Results: We observed CTC and DTC isolation using anti-EpCAM beads alone, or anti-EGFR beads alone. We were also able to isolate further CTC and DTC by using anti-EGRF beads after depletion with anti-EpCAM beads, demonstrating that by using this mesenchymal marker we are able to extract tumour cells that have lost or downgraded their epithelial marker expression and would be missed by current standard detection methods. RT-PCR analysis revealed that each population was positive for EPHB4,