5084 POSTER

Pharmacokinetics and tolerability of lapatinib administered once daily in combination with tamoxifen

F. Cardoso[1], K.M. Koch[2], E. Brain[3], F. Lokiec[3], S. Marreaud[4], J. Bogaerts[4], P. Fumoleau[5]. *[1]Bordet Institute, Brussels, Belgium; [2]GlaxoSmithKline, USA; [3]Centre R. Huguenin, Saint Cloud, France; [4]EORTC, Brussels, Belgium; [5]Centre Georges-François Leclerc, Dijon, France*

Background: The pharmacokinetics (PK) and tolerability of daily oral dosing of lapatinib (LAP) and tamoxifen (TAM) in patients (pts) with advanced or metastatic breast cancer (MBC) were examined in this study. Optimal dose selection indeed requires characterization of PK to accommodate the potential for a bi-directional PK interaction involving LAP inhibition and TAM induction of CYP3A4 and P-glycoprotein (Pgp).
Methods: Previously treated pts with estrogen and/or progesterone positive MBC, whatever HER2 status, were randomly assigned to one of two groups, to separately assess each direction of the potential PK interaction at steady state during daily dosing of 1250 mg LAP and 20 mg TAM. In one group, the PK of LAP was assessed on the 14th day of dosing LAP alone, and again on the 28th day dosing of LAP and TAM together. In the other group, the PK of TAM was assessed on the 28th day of dosing TAM alone, and on the 7th day of dosing TAM and LAP together. LAP and TAM were dosed together throughout subsequent 28 day cycles.
Results: To date, 25 pts have been enrolled with a median age of 59 (39−83) and a median PS of 1. Preliminary PK data for LAP from six patients are summarized in the table below showing geometric median (95% confidence limits) parameters. They indicate that LAP plasma concentrations are decreased by TAM. Final PK analysis will be presented at the meeting. Most common adverse events for the combination were: fatigue grade (gr) 1/2 (76%), diarrhoea gr 1/2 (60%), pain gr 1/2 (60%), rash gr 1 (40%) and nausea gr 1/2 (32%). To date, best response observed was stable disease in 6/25 pts (24%). Ten pts progressed and 6 pts discontinued early.
Conclusions: These preliminary PK results are consistent with data indicating that TAM induces hepatic CYP3A, the primary route of LAP elimination. This key information may impact in ongoing adjuvant lapatinib studies.

Parameter (units)	LAP	LAP+TAM	Decrease in LAP+TAM vs LAP
LAP AUCtau (h × mg/L)	21.7 (13.8−51.3)	17.7 (10.3−29.6)	25% (18% to 46%)
LAP Cmax (mg/L)	1.42 (1.33−4.82)	1.19 (0.95−2.05)	32% (10 to 57%)
LAP Cmin (mg/L)	0.73 (0.23−1.23)	0.40 (0.22−0.61)	44% (3% to 58%)

5085 POSTER

HER-2 positive locally advanced breast cancer: one or two entities?

M. Rahal[1], A. Abdelwarith[1], E. Hassen[1], S. Deo[2], H. Ramadan[1], N. Al Naimy[3], N. Al Eissa[3], A. Al Garni[4], M. Al Idrissi[1], A. Al Faraj[1]. *[1]KFSH, Oncology, Dammam, Saudi Arabia; [2]KFSH, Surgery, Dammam, Saudi Arabia; [3]KFSH, Radiology, Dammam, Saudi Arabia; [4]KFSH, Pathology, Dammam, Saudi Arabia*

Background: Primary systemic chemotherapy is an established standard of care for LABC. Complete pathologic response (CpR) and minimal residual cancer burden (pT1a) are predictors for better disease free and overall survival.
This retrospective study evaluates the clinical activity of sequential AC followed by Docetaxel-Cisplatin (D-Cis) and Trastuzumab (T) in locally advanced HER-2 overexpressed breast cancer.
Methods: Non pretreated patients (pts), with invasive breast cancer, HER2 positive (IHC 3+), stage IIB-IIIB, with a baseline LVEF = 50% were eligible. The neo-adjuvant regimen consisted of 4 cycles of AC (60 mg/600 mg/m^2) followed by 4 cycles of D-Cis (75 mg/m^2 each) before surgery. T started with the first cycle of D-Cis at 8 mg/Kg loading dose then 6 mg/Kg for 1 year. Cycles were given every 3 weeks.
Results: Twenty four pts were reviewed. Median age: 49 years (28−64), premenopausal:14; median tumor size:7 cm (3−13) stage IIB: 3, IIIA: 8, IIIB: 13, ER/PR negative: 14. The toxicity related to AC was mild, with febrile neutropenia (FN) occurring in 3 pts and all pts completed the planned 4 cycles; while the second sequence with D-Cis was completed in 17 pts only. F.N, renal impairment, and hypersensitivity reaction were seen in 3, 1 and 1 pt respectively. An asymptomatic decline of 15 points in the LVEF occurred in 3 pts. Clinical evaluation of response by RECIST criteria pre surgery: OR: 23/24 (96%), CR (58%) and 1PD. The second sequence with D-Cis-T doubled the rate of clinical CR obtained with AC. All pts had surgery (except one with disease progression). Pathological assessment, (using NSABP criteria), revealed that 11 (47%) pts had no residual invasive carcinoma in the breast; 4 (17%) had residual occasional scattered tumor cells only (pT1a); 13 (56%) had negative nodes; 8 achieved CpR and 2 nCpR. 80% of the CpR/nCpR occurred in PR negative subset.
Conclusion: (1) The absence of progesterone receptor was associated with a high probability of CpR achievement suggesting 2 different entities within the all HER-2 positive breast cancer. (2) This high rate of CpR was obtained with a short exposure of 9 weeks to Trastuzumab raising the question of the optimal duration of anti her 2 therapy in the neoadjuvant setting.

	PR−	PR+
CpR/nCpR	8/15 (53%)	2/8 (25%)

5086 POSTER

Brain metastasis from triple negative breast cancer

R. Venkitaraman[1], T. Joseph[1], S. Upadhyay[1], A. Dhadda[1], A. Chaturvedi[1], E. Long[2]. *[1]Queen's Centre for Oncology and Hematology, Clinical Oncology, Hull, United Kingdom; [2]Pathology Queen's Centre for Oncology and Hematology, Clinical Oncology, Hull, United Kingdom*

Background: Brain metastasis in patients with breast cancer is a clinical dilemma with few effective therapeutic options. There is a compelling clinical need to identify patients who are at high risk of developing this disastrous event, so that early detection and early treatment could be considered.
Aims of the study: To characterize the receptor profile (ER, PR and HER2) of patients with brain metastasis from breast cancer. To assess the prognosis of patients with brain metastasis with respect to receptor status, focussing on patients with triple negative breast cancer.
Materials and Methods: 62 consecutive patients with brain metastasis from 2003 to 2008 were included in this retrospective study. The receptor status was assessed and compared to that of a control population of 631 breast cancer patients diagnosed during the same period. The survival of patients with triple negative disease was compared to other subsets of patients with brain metastasis.
Results: 17 (27.4%) of the 62 patients with brain metastasis had triple negative breast cancer, compared to 104 (16.48%) of the 631 control patients (p = 0.047). The proportion of patients who were ER negative (48.4% Vs 24.2%; p = 0.001) and HER2 positive (40% Vs 14%; p = 0.001) was also higher in the study population. Patients with triple negative tumors had a shorter overall survival (3.0 years Vs 4.4 years; p = 0.041) compared to other patients. These patients had a shorter time to development of brain metastasis after diagnosis, though not statistically significant (2.3 years Vs 3.9 years; p = 0.107). Patients with triple negative breast cancer had shorter survival after the development of brain metastasis, compared to patients with receptor positive cancer (2.4 months Vs 6.2 months; p = 0.0086).
Conclusion: Patients with triple negative breast cancer are at a high risk of developing brain metastasis and have a poor survival. There may be case for screening for brain metastasis and even prophylactic treatment in this subset of patients.

5087 POSTER

New isolated mediastinal lymph node or pulmonary nodule during surveillance of breast cancer: clinical factors to differentiate metastasis from benign lesion

T.Y. Kim[1], H.Y. Yhim[1], S.W. Han[1], D.Y. Oh[1], S.A. Im[1], Y.T. Kim[2], D.Y. Noh[3], S.W. Ha[4], Y.J. Bang[1]. *[1]seoul National University Hospital, Department of Internal Medicine, Seoul, South Korea; [2]seoul National University Hospital, Department of Thoracic Surgery, Seoul, South Korea; [3]seoul National University Hospital, Department of Surgery, Seoul, South Korea; [4]seoul National University Hospital, Department of Radiation Oncology, Seoul, South Korea*

Background: New isolated mediastinal lymph node (LN) or pulmonary nodule during surveillance of breast cancer is not always possible to be pathologically diagnosed. We conducted this study to reveal clinical factors which are useful to differentiate metastasis from benign lesion in this situation.
Material and Methods: We consecutively enrolled breast cancer patients who presented new isolated mediastinal LN or pulmonary nodule during surveillance, and whose lesions were pathologically confirmed, between 1995 and 2008 at Seoul National University Hospital. Tissue diagnosis was made by mediastinoscopy, video-assisted thoracic surgery (VATS) or thoracotomy. Clinical factors including initial TMN stage, biologic subtype, lesion size, total number of lesions and maximal standardized uptake value (SUV) of positron-emission tomography (PET) were retrospectively analyzed between malignant and benign group.