improvements in this area will certainly be major contributions to the fight against BC.

9 Invited

Modulation of Resistance to Biological Agents

Abstract not received.

10 Invited

Modulation of Resistance to Hormonal Agents

Abstract not received.

11 Proffered paper oral

Everolimus (Rad001) as Treatment in Breast Cancer Patients with Bone Metastases Only – First Results of the Multi-centre, Placebo-controlled, Randomized Discontinuation Phase II RADAR Study

N. Harbeck[1], N. Maass[2], C. Mundhenke[3], C. Lerchenmüller[4], J. Barinoff[5], J. Ettl[6], B. Aktas[7], V. Nekljudova[8], G. von Minckwitz[9], S. Loibl[9]. *[1]Unifrauenklinik Köln, Brustzentrum, Köln, Germany; [2]Universitätsfrauenklinik Aachen, Gynäkologie und Geburtshilfe, Aachen, Germany; [3]Universitätsklinikum Kiel, Gynäkologie und Geburtshilfe, Kiel, Germany; [4]Gemeinschaftspraxis, Onkologie, Münster, Germany; [5]Dr.-Horst-Schmidt-Kliniken, Gynekologie und Onkologie, Wiesbaden, Germany; [6]Klinikum rechts der Isar, Frauenklinik, München, Germany; [7]Universitätsklinikum Essen, Klinik für Frauenheilkunde und Geburtshilfe, Essen, Germany; [8]German Breasts Group, Statistic Department, Neu-Isenburg, Germany; [9]German Breasts Group, Medicine and Research, Neu-Isenburg, Germany*

Background: RAD001 is an orally bioavailable rapamycin ester analogue, which acts by selectively inhibiting mTOR (mammalian target of rapamycin). mTor is a key player in down stream signaling of different pathways In vitro, RAD001 stops formation and activity of osteoclasts. Therefore, treating advanced breast cancer with progressive bone metastases with RAD001 seems to be reasonable.

Patients and Methods: We evaluated RAD001 in a placebo-controlled, phase II, randomized discontinuation study in breast cancer patients (pts) with bone metastases only. Pts were eligible if they had HER2-negative, hormone-receptor (HR)-positive or -negative disease, with a maximum of 2 previous lines of endocrine therapy (ET) and 1 previous line of chemotherapy (CT). All pts received zoledronate and pts with HR-positive disease could receive (ET). All pts started with RAD001 during a run-in phase of 8 weeks. Pts with stable disease were randomized to RAD001 or placebo; pts with response continued with RAD001 and pts with progression went off study. Primary outcome was time to progression (TTP) in pts being stable on 8 weeks of RAD001. Main secondary objectives were response rate after 8 weeks, TTP in pts with a response after 8 weeks of RAD001, overall clinical benefit, safety and toxicity of RAD001. It was assumed that placebo would obtain a median TTP of 8 weeks which would then be increased by to 16 weeks (hazard rate of 2), thus requiring 76 randomized pts. It was expected that 70% of all pts would have stable disease after the run-in phase. Overall, 110 pts were planned for enrollment. Due to slow recruitment and a dysbalance between pts randomized and discontinued, study recruitment stopped in December 2012.

Results: From 11/06 until 12/10, 89 pts were enrolled. Median age was 59.5 years. All were HER2-negative, 93% had HR-positive disease. 15% had prior chemotherapy; 58% had prior ET for metastases. 1/3 received concomitant ET. Three pts did not start therapy, 41 discontinued during run-in phase, 32 due to progression. Six continued as responder, of whom three are still on treatment. 39 pts. with SD after the run in phase were randomized to RAD001 or placebo. Twenty-seven stopped due to progression; 9 discontinued due to AE, 4 are still on treatment.

Conclusion: This is the first trial recruiting pts with bone metastases only for treatment with RAD001. Overall 7/89 showed a sustained response on RAD001 + zoledronate ± ET. Final analysis will be presented at the meeting.

12 Proffered paper oral

Everolimus Added to Exemestane Reduced Bone Markers in Postmenopausal Women with Advanced Breast Cancer (ABC): the BOLERO-2 Trial

M. Gnant[1], G.N. Hortobagyi[2], H. Rugo[3], H.A. Burris[4], S. Noguchi[5], K.I. Pritchard[6], J. Baselga[7], T. Sahmoud[8], H. Bauly[9], M. Piccart[10]. *[1]Medical University of Vienna, Department of Surgery, Vienna, Austria; [2]University of Texas MD Anderson Cancer Center, Department of Breast Medical Oncology, Houston, USA; [3]University of California San Francisco, Helen Diller Family Comprehensive Cancer, San Francisco, USA; [4]Sarah Cannon Research Institute, Drug Development Program, Nashville, USA; [5]Osaka University, Department of Breast and Endocrine Surgery, Osaka, Japan; [6]Sunnybrook Odette Cancer Center and the University of Toronto, Department of Medicine, Toronto, Canada; [7]Massachusetts General Hospital Cancer Center, Division of Hematology/Oncology, Boston, USA; [8]Novartis Pharmaceuticals Corporation, Global Oncology Department, Florham Park, USA; [9]Novartis Pharma AG, Biostatistics, Basel, Switzerland; [10]Jules Bordet Institute, Department of Medicine, Brussels, Belgium*

Background: The BOLERO-2 study, a multinational, double-blind, placebo-controlled, phase III study comparing everolimus (EVE) in combination with exemestane (EXE) with EXE alone in postmenopausal women with estrogen receptor-positive (ER+) ABC refractory to letrozole or anastrozole, demonstrated improved response and progression-free survival (PFS) with the addition of EVE to EXE. Non-steroidal aromatase inhibitors (NSAIs) are associated with decrease in bone mineral density and increased risk of fractures. Therefore, it is important to evaluate whether new therapies in combination with NSAIs affect bone turnover. This sub-analysis evaluated the effect of EVE in combination with EXE compared with EXE alone on markers associated with bone formation and reabsorption from the BOLERO-2 study.

Methods: Eligible patients were treated with EXE 25 mg/d and randomized (2:1) to EVE 10 mg/d or placebo (PBO). Primary endpoint was PFS based on 457 events and median follow-up of 12.5 months. Bone turnover markers were exploratory endpoints analyzed at 6 and 12 weeks after treatment initiation. They included bone-specific alkaline phosphatase (BSAP), amino-terminal propeptide (PINP) of type I collagen, and C-terminal cross-linking telopeptide of type I collagen (CTX).

Results: 724 patients were randomized to receive EVE+EXE (n = 485) or EXE (n = 239). Median age was 62 years, 56% had visceral involvement, and 84% were sensitive to prior hormone therapy. At study entry, bone metastases were present in 76% of patients on EVE+EXE and 75% on EXE; 45% and 55%, respectively, used bisphosphonates at baseline. PFS per investigator assessment showed a hazard ratio (HR) of 0.44 ($P < 1 \times 10^{-16}$) with a median duration of 7.4 vs 3.2 months (for EVE+EXE vs EXE alone). PFS by central assessment showed an HR of 0.36 ($P < 1 \times 10^{-16}$) and a median duration of 11.0 vs 4.1 months, respectively. At 6 weeks, EVE+EXE resulted in a 24%, 56%, and 36% decrease in BSAP, PINP, and CTX compared with EXE alone during the same time interval. At 12 weeks, EVE+EXE resulted in a 19%, 68%, and 42% reduction in the presence of BSAP, PINP, and CTX compared with EXE alone. Updated results based on an additional 5 months of data (cutoff date: 08-Jul-2011) will be presented.

Conclusion: The combination of EVE+EXE reduced bone turnover markers compared with EXE alone during the first 12 weeks of therapy, suggesting favorable bone health clinical benefits.

Wednesday, 21 March 2012 15:45–17:15

CLINICAL SCIENCE SYMPOSIUM

The Axilla – A "No Go" Zone?

13 Invited

No Axillary Surgery in Breast Cancer?

S. Alran[1], C. Ngô[1], F. Reyal[1], V. Fourchotte[1], A. Tardivon[2], J.Y. Pierga[3], A. Salomon-Vincent[4], A. Fourquet[4]. *[1]Institut Curie, Surgery, Paris, France; [2]Institut Curie, Radiology, Paris, France; [3]Institut Curie, Medical Oncology, Paris, France; [4]Institut Curie, Pathology, Paris, France*

Sentinel lymph node dissection (SLND) is the standard axillary surgery for T1-T2 (*3 cm) breast cancer (BC) patients. SLND is negative in 60 to 75% of the cases, so how can we select breast cancer patients for 'No Axillary