Poster discussion presentations
(Wed, 23 Sep, 17:00–18:00)

Breast cancer

5016 POSTER DISCUSSION

Efficacy in patient subgroups in RIBBON-1, a randomized, double-blind, Phase III trial of chemotherapy with or without bevacizumab (B) for first-line treatment of HER2-negative locally recurrent or metastatic breast cancer (MBC)

V. Dieras[1], J. Glaspy[2], A. Brufsky[3], I. Bondarenko[4], O. Lipatov[5], E.A. Perez[6], S. Chan[7], X. Zhou[8], S.C. Phan[9], N. Robert[10]. *[1]Institut Curie, Department of Medical Oncology, Paris, France; [2]UCLA TORI, Department of Medical Oncology, Los Angeles, USA; [3]University of Pittsburgh, Department of Medical Oncology, Pittsburgh, USA; [4]State Medical Academy, Department of Medical Oncology, Dnipropetrovsk, Ukraine; [5]Bashkirian Republican Clinical Oncology, Department of Medical Oncology, Ufa, Russian Federation; [6]Mayo Clinic, Department of Medical Oncology, Jacksonville, USA; [7]Nottingham University Hospital (City Campus), Department of Medical Oncology, Nottingham, United Kingdom; [8]Genentech Inc., Biostatistics, South San Francisco, USA; [9]Genentech Inc., Clinical Science, South San Francisco, USA; [10]Fairfax-Northern Virginia Hematology-Oncology, Department of Medical Oncology, Fairfax, USA*

Background: In 2 prior Phase III trials (E2100 and AVADO), B in combination with taxanes (T) as first-line therapy for MBC improved progression-free survival (PFS) compared with T alone. In RIBBON-1, the addition of B to standard first-line chemotherapy regimens also improved PFS in MBC patients (pts).
Methods: Pts were randomized 2:1 to B+chemotherapy vs. placebo (pl)+chemotherapy. Prior to randomization, investigators chose capecitabine (Cap) (2000 mg/m^2 x 14 d), taxane (nab-paclitaxel 260 mg/m^2, or docetaxel (D) 75 or 100 mg/m^2), or anthracycline (Ant) (doxorubicin [A] or epirubicin [E] combinations-AC, EC, FAC, FEC)-based chemotherapy given q3 wk. B or pl was administered at 15 mg/kg q3 wk.
Key eligibility criteria: MBC or locally recurrent disease, no prior cytotoxic treatment for MBC, ECOG PS 0–1, HER2-negative disease, no CNS mets. The 1º endpoint was investigator-assessed PFS. The Cap cohort and pooled T or Ant (T+Ant) cohorts were independently powered and analyzed using 2-sided stratified log-rank test (Cap: 80% power to detect HR = 0.75; T+Ant: 90% power to detect HR = 0.7).
Results: 1237 pts (Cap = 615; T = 307; Ant = 315) were enrolled. Addition of B improved PFS (Cap: pl 5.7 mo, B 8.6 mo, p = 0.0002; T+Ant: pl 8.0 mo, B 9.2 mo, p < 0.0001). In prespecified subgroups, HRs favored B arms of the respective chemotherapies.

	Cap n = 615	T+Ant n = 622
All patients	0.67 (0.55, 0.82)	0.66 (0.54, 0.81)
Age, yr		
<65	0.67 (0.53–0.84)	0.63 (0.50–0.78)
⩾65	0.69 (0.47–1.02)	0.83 (0.52–1.34)
Triple negative		
Yes	0.72 (0.49–1.06)	0.78 (0.53–1.15)
No	0.68 (0.54–0.86)	0.61 (0.48–0.77)
No. of metastatic sites		
<3	0.63 (0.49–0.83)	0.65 (0.49–0.86)
⩾3	0.74 (0.55–0.98)	0.64 (0.48–0.85)
Bone-only disease		
Yes	0.47 (0.26–0.87)	0.39 (0.18–0.88)
No	0.70 (0.57–0.86)	0.72 (0.59–0.89)
Visceral involvement		
Yes	0.72 (0.57–0.90)	0.68 (0.54–0.86)
No	0.58 (0.40–0.83)	0.63 (0.42–0.94)
Disease-free interval		
<12 mo	0.81 (0.54–1.21)	0.62 (0.45–0.85)
⩾12 mo	0.63 (0.51–0.79)	0.69 (0.53–0.89)
Prior adjuvant chemotherapy		
Yes	0.64 (0.51–0.80)	0.67 (0.50–0.90)
No	0.80 (0.54–1.18)	0.64 (0.49–0.85)
Prior adjuvant taxane		
Yes	0.62 (0.45–0.84)	0.65 (0.39–1.07)
No	0.72 (0.56–0.92)	0.66 (0.53–0.83)

Conclusions: The overall treatment effect of combining B with capecitabine, taxanes, or anthracyclines in RIBBON-1 is seen across the prespecified clinically relevant subgroups. These results are consistent with the findings of E2100 and AVADO and suggest that B with standard chemotherapies provides benefit to HER2-negative MBC pts with differing clinical characteristics and disease history.

5017 POSTER DISCUSSION

Multinational study (n = 2041) of first-line bevacizumab (Bev) plus taxane-based chemotherapy (CT) for locally recurrent or metastatic breast cancer (LR/mBC): updated results of MO19391

H. Cortes-Funes[1], K.I. Pritchard[2], L. Biganzoli[3], C. Thomssen[4], J. Pierga[5], I. Koza[6], A. Kwong[7], P. Kellokumpu-Lehtinen[8], A. Chlistalla[9], I. Smith[10]. *[1]University Hospital 12 de Octubre Madrid, Division of Medical Oncology, Madrid, Spain; [2]Sunnybrook Odette Cancer Centre Faculty of Medicine University of Toronto, Department of Medicine, Toronto, Canada; [3]Hospital of Prato Istituto Toscano Tumori, Medical Oncology Unit, Prato, Italy; [4]Martin-Luther-University Halle-Wittenberg, Universitaetsklinik und Poliklinik fuer Gynaekologie, Halle (Saale), Germany; [5]Institut Curie Université Paris Descartes, Medical Oncology, Paris, France; [6]National Cancer Institute, Oncology, Bratislava, Slovak Republic; [7]Queen Mary and Tung Wah Hospital The University of Hong Kong, Division of Breast Surgery, Hong Kong, Hong Kong; [8]Tampere University Hospital, Oncology, Tampere, Finland; [9]F. Hoffmann-La Roche, Basel, Switzerland; [10]Royal Marsden Hospital and Institute of Cancer Research, Breast Unit, London, United Kingdom*

Background: Three randomised phase III trials (E2100, AVADO, RIBBON-1) have shown that Bev combined with first-line CT significantly improves PFS versus CT alone. The open-label, multicentre MO19391 trial further assessed safety and efficacy of first-line Bev combined with taxane-based therapy in a broader patient (pt) population, representative of general oncology practice.
Materials and Methods: Eligible pts had HER2-negative LR/mBC (or trastuzumab-pretreated HER2-positive LR/mBC), ECOG PS 0–2, no prior CT for LR/mBC and no evidence of CNS metastases. Pts received Bev 10 mg/kg q2w or 15 mg/kg q3w combined with a taxane (alone or with another CT) or non-anthracycline CT according to the physician's decision, until disease progression, unacceptable toxicity or withdrawal. The primary endpoint was safety (CTCAE v3.0); secondary endpoints included TTP and OS.
Results: Between Sept 2006 and data cut-off for this analysis (March 2009), 2041 pts were treated. Median age was 54 years (range 21–93). Most pts (76%) received taxane-based therapy with Bev, predominantly paclitaxel or docetaxel monotherapy. Mean duration of therapy was 7.0±4.7 months for Bev and 4.7±3.1 months for CT. Grade (G) 3–5 adverse events (AEs) occurring at any G in >15% of pts (related or unrelated to Bev) are shown below. The incidences of ⩾G3 predefined Bev-related AEs of special interest were: DVT in 0.3% (all G3); thrombosis in <0.1% (G3); GI perforation in 0.2% (<0.1% G3, <0.1% G4, 0.1% G5); CHF in 0.1% (G3); impaired healing in 0.2% (0.1% G3, 0.1% G4); cerebral haemorrhage in <0.1% (G5), pulmonary embolism in 0.4% (0.1% G3, 0.2% G4, <0.1% G5); hypertension in 3.0% (3.0% G3, <0.1% G4). Median TTP is 9.5 months (95% CI: 9.1–10.0). OS data are still immature (78% of pts alive at data cut-off).

	AE (%)		
	G3	G4	G5
Pts with ⩾1 AE	48.4	15.4	3.4
Neutrophil count decreased	9.9	5.2	0
WBC count decreased	7.2	1.6	0
Fatigue	4.9	0	0
Hypertension	4.0	0.1	0
Alopecia	2.9	0	0
Stomatitis	2.0	0	0
Hb decreased	1.6	0.1	0
Diarrhoea	1.6	<0.1	0
Neuropathy	1.6	0	<0.1
Proteinuria	1.0	<0.1	0
Anorexia	0.9	0	0
Nausea	0.7	<0.1	0
Constipation	0.5	<0.1	0
Headache	0.4	0	0
Epistaxis	0.2	<0.1	0

*Related or unrelated to Bev.