

July 9 2014

Hong Kong Breast Cancer Foundation “Updates on Breast Cancer Management” Symposium

Summary of “Medical Oncology News in Breast Cancer 2014”, presented by Dr. Thomas Yau, Clinical Assistant Professor, Division of Medical Oncology, Department of Medicine, The University of Hong Kong

Recent studies have shown the significant clinical advances made in the treatment of breast cancer patients with human epidermal growth factor receptor-2-positive (HER2+) disease over the past 15 years. According to a meta-analysis conducted among HER2+ breast cancer patients who received the adjuvant trastuzumab therapy (including the HERA trial, the NCCTG N9831 trial, the NSABP B-31 trial, the PACS 04 trial and the FinHER trial), the therapy increased both the disease-free survival (DFS) and overall survival (OS) rates among patients with tumours ≤ 2 cm, while also contributed to favourable outcomes previously reported for patients with hormone receptor-positive (HR+) tumours ≤ 2 cm and 0-1 positive lymph node.

The ALTO trial that compared the sequential and concurrent uses of lapatinib and trastuzumab treatments for early stage HER2+ breast cancer patients indicated that lapatinib was associated with significant increase in adverse events (AEs) of special interest like diarrhea, hepatobiliary, and rash or erythema compared to trastuzumab alone but made no significant difference in 4-year DFS or OS. Meanwhile, the Text and Soft trial compared two types of hormonal therapy: tamoxifen with ovarian function suppression (OFS) and exemestane (EXE) with OFS. It found that EXE + OFS significantly improved DFS, breast cancer-free interval (BCFI) and distant recurrence-free interval (DRFI) and it could serve as another treatment option for postmenopausal women diagnosed with early HR+ breast cancer.

Another study, Bolero-2, looked at patients with estrogen-receptor-positive (ER+) and human epidermal growth factor receptor-2-negative (HER2-) locally advanced or metastatic breast cancer whose condition recurred or progressed after receiving nonsteroidal aromatase inhibitor (NSAI) treatment. The subjects were divided into two groups and treated with either everolimus (EVE) (10 mg/day) and EXE (25 mg/day), or placebo (PBO) + EXE (25 mg/day). The results showed that the period of progression-free survival (PFS) prolongation was clinically meaningful and statistically significant (median 4.6-month benefit; $P < .0001$) among the subjects, but the secondary endpoint of OS did not reach statistical significance ($P = .14$). In the Optimize-2 study, which aimed at examining the frequency of continued zoledronic acid for breast cancer patients with bone metastases after they received therapy with ≥ 9 doses of intravenous bisphosphonate (BP). Results showed that continuing zoledronic acid treatment at a reduced dosing frequency of every 12 weeks was noninferior to those with a dosing frequency of every 4 weeks (noninferiority margin: 10%).

Separately, a study conducted by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) concluded that obesity was independently

associated with breast-cancer-related mortality in premenopausal patients with ER+ breast cancer. However, obesity had no significant effect in premenopausal women with ER-negative disease or among postmenopausal women. Weight loss had a favourable effect on inflammatory and metabolic biomarkers.

All studies are propelling the development of medical oncology forward for the sake of patients' benefits. However, physicians should consider every individual factor when designing a treatment plan. The findings from various studies would be valuable references for the process of medical treatment.

END

References:

- Bardia, A., Modi, S., Gregor, M.C.M., Kittaneh, M., Marino, A.J., Matano, A., et al. (2014). Phase Ib/II study of LEE011, everolimus, and exemestane in postmenopausal women with ER+/HER2-metastatic breast cancer. *Journal of Clinical Oncology*, 32(Suppl. 5), abstract 535.
- Baselga, J., Campone, M., Piccart, M., Burris, H.A., Rugo, H.S., Sahmoud, T., et al. (2012). Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer. *The New England Journal of Medicine*, 366(6), 520-529.
- Baselga, J., Bradbury, I., Eidtmann, H., Di Cosimo, S., de Azambuja, E., Aura, C., et al. (2012). Lapatinib with trastuzumab for HER2-positive early breast cancer (NeoALTTO): A randomised, open-label, multicentre, phase 3 trial. *Lancet*, 379(9816), 633–640
- Goldhirsch, A., Gelber, R., Piccart-Gebhart, M.J., de Azambuja, E., Procter, M., Suter, T.M., et al. (2013). 2 years versus 1 year of adjuvant trastuzumab for HER2-positive breast cancer (HERA): An open-label, randomized controlled trial. *Lancet*, 382, 1021-1028.
- Hortobagyi, G.N., Lipton, A., Chew, H.K., Gradishar, W.J., Sauter, N.P., Mohanlal, R.W., et al. (2014). Efficacy and safety of continued zoledronic acid every 4 weeks versus every 12 weeks in women with bone metastases from breast cancer: Results of the OPTIMIZE-2 trial. *Journal of Clinical Oncology*, 32(Suppl. 5), abstract LBA9500.
- Lofffield, E., Harrigan, M., Li, F., Cartmel, B., Zhou, Y., Playdon, M., et al. (2014). Effect of weight loss intervention on inflammatory and metabolic markers in breast cancer survivors: The lifestyle, exercise, and nutrition (LEAN) study. *Journal of Clinical Oncology*, 32(Suppl. 5), abstract 1505.
- Joensuu, H., Bono, P., Kataja, V., Alanko, T., Kokko, R., Asola, R., et al. (2009). Fluorouracil, epirubicin, and cyclophosphamide with either docetaxel or vinorelbine, with or without trastuzumab, as adjuvant treatments of breast cancer: Final results of the FinHer trial. *Journal of Clinical Oncology*, 27(34), 5685-5692.
- Mayer, N.A., Abramson, V.G., Balko, J.M., Sanders, M, Juric, D., Li, Y., et al. (2014). SU2C phase Ib study of the PI3K α inhibitor BYL719 with letrozole in ER+/HER2- metastatic breast cancer (MBC). *Journal of Clinical Oncology*, 32(Suppl. 5), abstract 516.
- Munster, P.N., Hamilton, E.P., Franklin, C., Bhansali, S., Wan, K., Hewes, B., et al. (2014). Phase Ib study of LEE011 and BYL719 in combination with

- letrozole in estrogen receptor-positive, HER2-negative breast cancer (ER+, HER2- BC). *Journal of Clinical Oncology*, 32(Suppl. 5), abstract 533.
- O'Sullivan, C.C.M., Bradbury, I., Azambuja, E.D., Perez, E.A., Rastogi, P., Spielmann, M., et al. (2014). Efficacy of adjuvant trastuzumab (T) compared with no T for patients (pts) with HER2-positive breast cancer and tumors \leq 2cm: A meta-analysis of the randomized trastuzumab trials. *Journal of Clinical Oncology*, 32(Suppl. 5), abstract 508.
- O'Sullivan, C.C., Holmes, E., Spielmann, M., Perez, E.A., Joensuu, H., Costantino, J.P., et al. (2013). The prognosis of small HER2+ breast cancers: A meta-analysis of the randomized trastuzumab trials. *Cancer Research*, 73(Suppl. 24), abstract nr S6-03.
- Pagani, O., Regan, M.M., Walley, B., Fleming, G.F., Colleoni, M., Lang, I., et al. (2014). Randomized comparison of adjuvant aromatase inhibitor (AI) exemestane (E) plus ovarian function suppression (OFS) vs tamoxifen (T) plus OFS in premenopausal women with hormone receptor-positive (HR+) early breast cancer (BC): Joint analysis of IBCSG TEXT and SOFT trials. *Journal of Clinical Oncology*, 32(Suppl. 5), abstract LBA1.
- Pan, H., & Gray, R. G. (2014). Effect of obesity in premenopausal ER+ early breast cancer: EBCTCG data on 80,000 patients in 70 trials. *Journal of Clinical Oncology*, 32(Suppl. 5), abstract 503.
- Patnaik, A., Rosen, L.S., Tolaney, S.M., Tolcher, A.W., Goldman, J.W., Gandhi, L., et al. (2014). LY2835219, a novel cell cycle inhibitor selective for CDK4/6, in combination with fulvestrant for patients with hormone receptor positive (HR+) metastatic breast cancer. *Journal of Clinical Oncology*, 32(Suppl.5), abstract 534.
- Perez, E.A., Romond, E.H., Suman, V.J., Jeong, J.H., Davidson, N.E., Charles, E. Geyer, C.E., et al. (2011). Four-year follow-Up of trastuzumab plus adjuvant chemotherapy for operable human epidermal growth factor receptor 2-positive breast cancer: Joint analysis of data from NCCTG N9831 and NSABP B-31. *Journal of Clinical Oncology*, 29(25), 3366-3373.
- Piccart-Gebhart, M.J., Holmes, A.P., Baselga, J., Azambuja, E.D., Dueck, A.C., Viale, G., et al. (2014). First results from the phase III ALTTO trial (BIG 2-06; NCCTG [Alliance] N063D) comparing one year of anti-HER2 therapy with lapatinib alone (L), trastuzumab alone (T), their sequence (T→L), or their combination (T+L) in the adjuvant treatment of HER2-positive early breast cancer (EBC). *Journal of Clinical Oncology*, 32(Suppl.5), abstract LBA4.
- Somlo, G., Frankel, P.H., Luu, T.H., Ma, C., Arun, B., Garcia, A., et al. (2014). Phase II trial of single agent PARP inhibitor ABT-888 (veliparib [vel]) followed by postprogression therapy of vel with carboplatin (carb) in patients (pts) with stage BRCA-associated metastatic breast cancer (MBC): California cancer consortium trial PHII-96. *Journal of Clinical Oncology*, 32(Suppl.5), abstract 1021.
- Spielmann, M., Roche, H., Delozier, T., Canon, J.L., Romieu, G., Bourgeois, H., et al. (2009). Trastuzumab for patients with axillary-node-positive breast cancer: Results of the FNCLCC-PACS 04 trial. *Journal of Clinical Oncology*, 27(36), 6129-6134.
- Tan, A.R., Wong, S.T.L., Warren, R.D., Wong, J.E., Liu, M.C., Zelnak, A.B., et al. (2014). Phase I/II study of letrozole and sorafenib as first-line therapy of

hormone-receptor positive (HR+) metastatic breast cancer (MBC). *Journal of Clinical Oncology*, 32(Suppl.5), abstract 531

Yardley, D.A., Noguchi, S., Pritchard, K.I., Burris, H.A., Baselga, J., Gnant, M., et al. (2013). Everolimus plus exemestane in postmenopausal patients with HR+ breast cancer: Bolero-2 final progression-free survival analysis. *Advances in Therapy*, 30(10), 870-884.