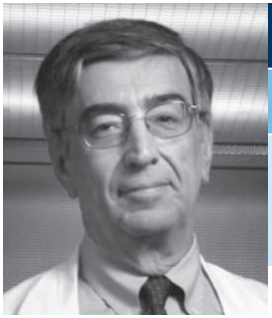


INTERVIEW

Luca Gianni, MD

Dr Gianni is Director of Medical Oncology 1 in the Department of Medical Oncology at the Istituto Nazionale Tumori di Milano in Milan, Italy.

Tracks 1-6

Track 1	Mechanisms of action of pertuzumab and trastuzumab
Track 2	NeoSphere: A randomized Phase II trial investigating anti-HER2 agents in the neoadjuvant setting
Track 3	Planned clinical trial evaluating adjuvant trastuzumab/pertuzumab for HER2-positive early BC
Track 4	Neoadjuvant therapy for HER2-positive BC
Track 5	Trastuzumab in HER2-normal early BC
Track 6	Approach to patients with metastatic BC after adjuvant chemotherapy/trastuzumab

Select Excerpts from the Interview

Track 1

DR LOVE: What is known about the mechanism of action of pertuzumab?

DR GIANNI: Pertuzumab is a monoclonal antibody that targets the external domain of the HER2 receptor at a different location than trastuzumab (4.1). Because no steric hindrance occurs, the two monoclonal antibodies — pertuzumab and trastuzumab — can be used together. According to animal models, laboratory models and patient models, the combined use of trastuzumab and pertuzumab yields at least additive if not synergistic effects (Baselga 2010; Gianni 2010). In women with breast cancer, a recent trial in metastatic disease showed that the introduction of pertuzumab soon after the failure of trastuzumab was associated with an unexpectedly high response rate (Baselga 2010; [4.2]).

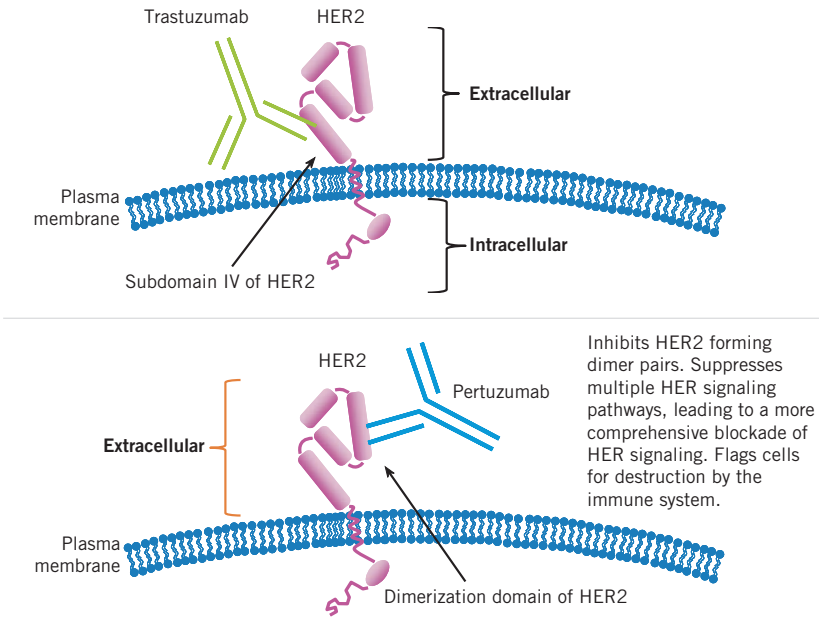
Track 2

DR LOVE: Would you discuss the NeoSphere trial findings that you presented in San Antonio?

DR GIANNI: The design of the trial was simple. We decided to evaluate the use of neoadjuvant drugs for HER2-positive breast cancer and to rank the efficacy of the treatments we tested. Because the laboratory and clinical data associ-

4.1

Targets of Trastuzumab and Pertuzumab on the Human Epidermal Growth Factor Receptor



Park Y et al. *World J Clin Oncol* 2011;2(2):125-34. With permission, © 2011 Baishideng Publishing Group.

ated with pertuzumab/trastuzumab were favorable, we also designed an arm on which women received only the two monoclonal antibodies for four cycles. We used conventional treatment, consisting of trastuzumab with docetaxel, as a comparator, and we also studied a triple combination of pertuzumab/trastuzumab/docetaxel. We found that the triple combination of docetaxel/trastuzumab/pertuzumab was associated with a high rate — 45.8 percent — of pCR in the breast, which was significantly higher than that of the conventional treatment with docetaxel and trastuzumab — 29 percent (4.3).

DR LOVE: Does anyone have plans to evaluate the combination of trastuzumab/pertuzumab in the adjuvant setting?

DR GIANNI: A trial has already been designed by the Breast International Group as a joint effort and is planned to launch by the end of 2011.

DR LOVE: Is there interest in studying the antibody combination in women who are not candidates for chemotherapy?

DR GIANNI: That is an important question. In the NeoSphere study, the two monoclonal antibodies were administered for only four cycles because the trial was designed to rank therapies, not to fully explore therapeutic potential. Because the NeoSphere study demonstrated that you can eradicate disease in

a subset of women with HER2-positive breast cancer without the addition of chemotherapy, the challenge is to further explore and identify a priori which women will benefit from this combination because the tolerability of this monoclonal regimen is so high. ■

4.2

Efficacy of Pertuzumab Combined with Trastuzumab During a Phase II Study for Women with Metastatic Cancer Whose Disease Progressed on Prior Treatment* with Trastuzumab-Containing Regimens

Best response	N = 66 (80% CI)
Complete response	7.6% (3.7-13.6)
Partial response	16.7% (10.9-24.1)
Stable disease ≥6 months	25.8% (18.8-33.9)
Progressive disease	50% (41.5-58.5)

* Patients received prior trastuzumab-based therapy for a mean of 16.2 months.

Baselga J et al. *J Clin Oncol* 2010;28(7):1138-44.

4.3

Efficacy of Neoadjuvant Trastuzumab and Pertuzumab by Breast and Lymph Node Status During the NeoSphere Study

	TH (n = 107)	THP* (n = 107)	HP (n = 107)	TP (n = 96)
pCR in breast	29.0%	45.8%	16.8%	24.0%
pCR in breast and node-negative at surgery	21.5%	39.3%	11.2%	17.7%
pCR in breast and node-positive at surgery	7.5%	6.5%	5.6%	6.3%

T = docetaxel; H = trastuzumab; P = pertuzumab; pCR = pathologic complete response

* *p*-value was significant for THP versus all other arms for each outcome shown.

Gianni L et al. San Antonio Breast Cancer Symposium 2010;**Abstract S3-2**.

SELECT PUBLICATIONS

Baselga J et al. **Phase II trial of pertuzumab and trastuzumab in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer that progressed during prior trastuzumab therapy.** *J Clin Oncol* 2010;28(7):1138-44.

Gianni L et al. **Neoadjuvant pertuzumab (P) and trastuzumab (H): Antitumor and safety analysis of a randomized Phase II study ('NeoSphere').** San Antonio Breast Cancer Symposium 2010;**Abstract S3-2**.

Gianni L et al. **Open-label, phase II, multicenter, randomized study of the efficacy and safety of two dose levels of pertuzumab, a human epidermal growth factor receptor 2 dimerization inhibitor, in patients with human epidermal growth factor receptor 2-negative metastatic breast cancer.** *J Clin Oncol* 2010;28(7):1131-7.

Scheuer W et al. **Strongly enhanced antitumor activity of trastuzumab and pertuzumab combination treatment on HER2-positive human xenograft tumor models.** *Cancer Res* 2009;69(24):9330-6.