# Early-stage breast cancer Poster discussion

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# Disclosure slide

- I have received honoria and research support from Roche, GlaxoSmithKline, Merck, Pfizer and Boehringer Ingelheim

# Unifying theme of posters to be discussed


Familiar questions

- Will I respond to this treatment?
- How much treatment will I need?
- How will I look and feel after treatment?

# Prognostic vs predictive

- Prognostic: predict outcome irrespective of treatment
  - Does she need treatment?
- Predictive: predict outcome with a specific treatment
  - Which treatment will be best for her?

# Circulating tumour cells (CTCs)

- Prognostic in early and metastatic settings[1–3]
- No evidence of predictive role for pCR with chemotherapy in REMAGUS 02 or GeparQuattro neoadjuvant trials[3,4]
- In HER2-positive BC:
  - Dramatic reduction in CTC count in patients receiving anti-HER2 therapy for mBC[5]
  - No correlation with pCR in patients receiving neoadjuvant trastuzumab + bevacizumab + chemotherapy[6]
  - Limited information in patients receiving lapatinib

1. Bidard et al. Ann Oncol 2010; 2. Zhao et al. Breast Cancer Res Treat 2011
3. Pierga et al. Clin Cancer Res 2008; 4. Riethdorf et al. Clin Cancer Res 2010
5. Pierga et al. Ann Oncol 2012; 6. Pierga et al. Lancet Oncol 2012

# NeoALTTO biomarker substudy

- No correlation between number of CTCs and pCR or PET/CT response at any timepoint tested
- Or was a predictive effect simply not detected?
  - Well-conducted study, independent double review of scoring
  - BUT evaluable samples from only 46 patients (10%) in this optional substudy
  - Only 33 patients (7%) had corresponding FDG-PET/CT



1. Muller et al. Breast Cancer Res 2012; 2. Nadal et al. Breast Cancer Res 2012

# What now?

- Optional biomarker substudies are invariably underpowered
  - Researchers must insist on mandatory, appropriately powered biomarker research within trials
  - Can we do better with new anti-HER2 agents?
- NeoALTTO translational research includes:
  - Ki67, p27, Cyclin-D1, ErbB1, ErbB2, ErbB3, pErbB1, pErbB2, Akt and pAkt, S6 and pS6, MAPK and pMAPK, c-myc, IGFR1, p95HER2, PTEN, ER (alpha, beta), PgR, CD34, terminal deoxyneucleotidyl transferase biotin-dUTP nick and labelling technique [TUNEL] and topoisomerase II
  - Can we expect anything from this effort?

# HannaH: subcutaneous vs 3-weekly i.v. neoadjuvant trastuzumab

- Fixed dose
  - No loading dose required
  - Potentially improves convenience, compliance and medical resource use
- Similar treatment effect and pCR rate irrespective of:
  - Body weight
  - Serum trough trastuzumab

  $\Rightarrow$ Change in nursing practice, education will be important

# Additional posters on trastuzumab subcutaneous

| | |
|---|---|
| 272P (Pivot et al) | Injection of trastuzumab SC was generally well tolerated with a low incidence of injection site reactions (grades 1 and 2). These findings support the potential of trastuzumab SC to provide improved convenience for patients compared to the existing IV formulation |
| 273P (Hegg et al) | Using a highly sensitive assay, anti-drug antibodies against both trastuzumab (IV/SC) and rHuPH20 (SC only) were observed transiently and were of no relevance in terms of efficacy or safety |
| 315TiP (Gligorov et al) | SAFEHER: A study of assisted- and self-administered SC trastuzumab as adjuvant therapy in patients with early HER2-positive breast cancer |
| 470P (Wynne et al) | This study demonstrated comparability of two modes of administration for trastuzumab SC based on standard PK parameters, with comparable safety for trastuzumab SC administered manually and using the single-use injection device, which demonstrated consistent performance and tolerability |

# Impact of treatment on QoL and appearance

- SECRAB randomised phase III trial (n=2296) showed improved efficacy with synchronous vs sequential radiotherapy[1]:
  - Reduced risk of local recurrence (HR 0.65, p=0.03)
  - Improved 5-year local recurrence rates (5.1% vs 2.8%)
- Despite increased acute skin toxicity, there was:
  - No difference in quality of life
  - No difference in cosmesis or telangiectasia between arms
  - No difference in patient perception of breast appearance (EORTC BR23 QoL questionnaire, Q39–42)



1. Fernando et al. EMCC 2011

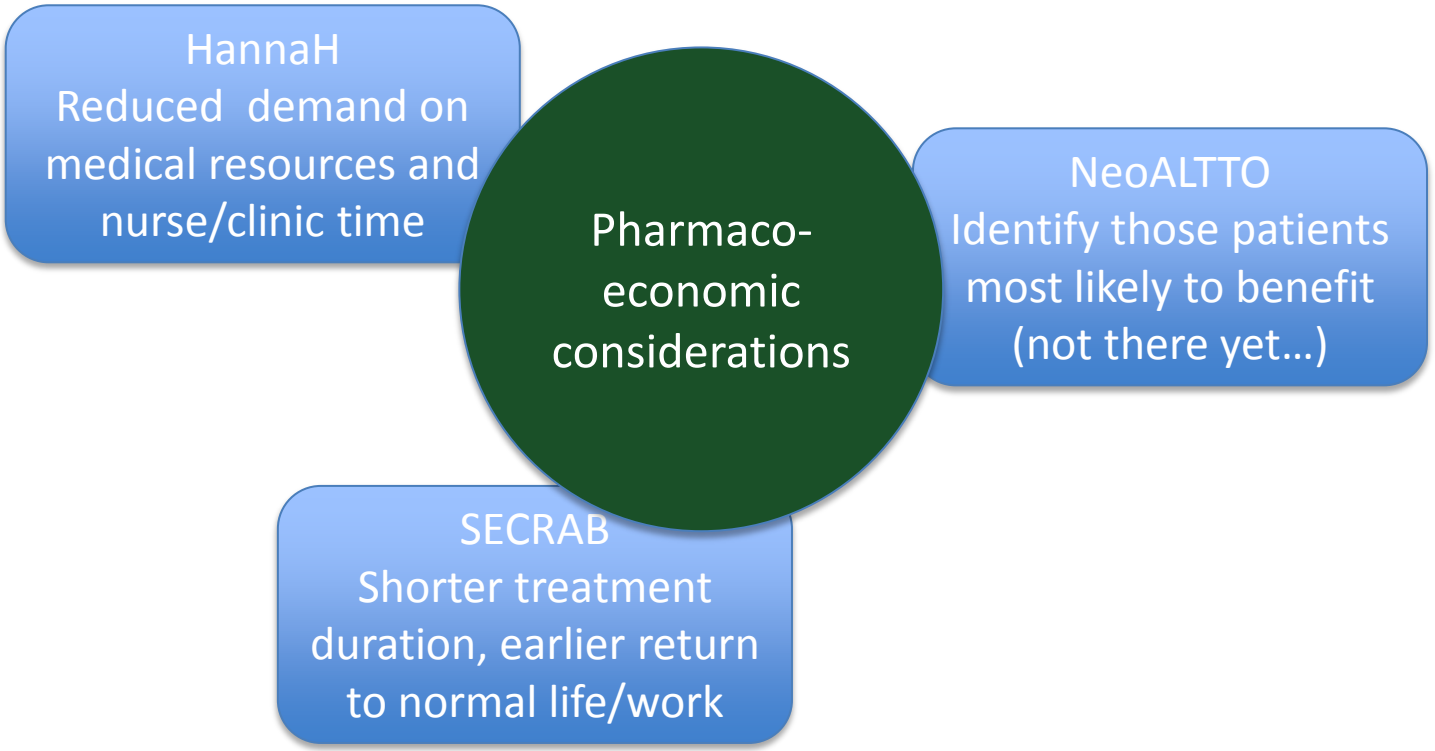
# Some caveats

- Cosmesis study population balanced between treatment arms but perhaps not representative of the entire study population
  - Axillary clearance: 46% (substudy) vs 76% overall
  - >3 weeks radiotherapy: 18% vs 32%
- Were there no differences … or were they just not detected?
  - Odds ratio for cosmesis: 1.87 (95% CI: 0.82–4.27)
- How do patients balance risk of local recurrence vs cosmesis?

# Familiar questions

- Will I respond to this treatment?
  - NeoALTTO: We don't know
- How much treatment will I need?
  - HannaH: One fixed dose suits all
- How will I look and feel after treatment?
  - SECRAB: No difference in appearance vs control

# Pharmacoeconomic and practical implications of findings



# Unanswered questions

- Was it the small sample size of NeoALLTO that prevented demonstration of a predictive effect of CTCs?
- Should we switch from IV to subcutaneous trastuzumab in patients already under treatment when the subcutaneous formulation becomes available?
- Do we ask the right questions when evaluating the impact of treatment on patients? And do we understand the answers?