First Annual Review of Breast Cancer Highlights from 2020 International Oncology Meetings

HER-2 Positive Updates

Tracy S d’Entremont, MD
Clinical Assistant Professor of Medicine
Director of Oncology Services, Abramson Cancer Center at Valley Forge

July 16, 2020
Chemotherapy (CT) de-escalation using an FDG-PET/CT (F-PET) and pathological response-adapted strategy in HER2[+] early breast cancer (EBC): PHERGain Trial.

Study Design

- 376 Early Stage (I-III) Centrally Confirmed HER-2+ Br Ca pts randomized in 1:4 fashion to one of 2 cohorts

- **Cohort A**: Treated with Chemotherapy + dual HER2 blockade (TCHP) N = 71

- **Cohort B**: Treated with Endocrine therapy + dual HER2 blockade N = 285
  - Letrozole for post menopausal women
  - Tamoxifen for men and premenopausal women

- **Cohort C**: N=20; those pts identified as having possible sub-clinical metastases on initial imaging treated with TCHP x 6
PHERGain Trial

**AssignedTherapy x 2**

**Cohort A**

**Cohort B**

**PET SCAN**

**Randomize**

**4 Additional Cycles**

**Cohort A**

**Cohort B - Rx**

**Cohort B Non-Rx - TCHP x 6**

**Surgery**

**Dual HER 2 Blockade Total 1 year**

**Cohort A**

**Cohort A**

**Cohort A**

**Cohort A**

**No pCR**

**pCR**

**TCHP x 6**

**Surgery**

**Penn Medicine Abramson Cancer Center**
Primary Endpoint:
  - pCR

Secondary Endpoint:
  - 3 yr iDFS

Median Age 50 yrs
49% LN+
67% HR+
Conclusions

- pCR 57.7% in chemotherapy arm vs 35.4% in non-chemotherapy arm ($p < 0.01$)

- 79.6% of pts in non-chemotherapy arm were considered PET responders

- 37.9% of the PET responders went on to have pCR without any chemotherapy

- Among the PET non-responders, 25.9% went on to have pCR with addition of chemotherapy prior to surgery
Safety

- Grade 3 or higher adverse events was 58.8% for those in cohort A compared with 48.2% for PET non-responders and 3.1% in PET responders in cohort B.

- Grade 3/4 febrile neutropenia were 20.6%, 17.9%, and 0% in these 3 respective groups.
#500 KAITLIN Trial

A Study of Trastuzumab Emtansine (Kadcyla) Plus Pertuzumab (Perjeta) Following Anthracyclines in Comparison With Trastuzumab (Herceptin) Plus Pertuzumab and a Taxane Following Anthracyclines as Adjuvant Therapy in Participants With Operable HER2-Positive Primary Breast Cancer

Nadia Harbeck, Seock-Ah Im, Carlos H. Barrios, Herve R. Bonnefoi, Julie Gralow, Masakazu Toi, Paul Ellis, Luca Gianni, Sandra M. Swain, Young-Hyuck Im, Michelino De Laurentiis, Zbigniew Nowecki, Jigna Shah, Thomas Boulet, Haiying Liu, Harrison Macharia, Peter Trask, Chunyan Song, Eric P. Winer, Ian E. Krop.
Study Design

3-4 Cycles of Anthracycline Chemotherapy

Randomize

T-DM1 + Perjeta x 18

Taxane x 3-4 cycles + Herceptin and Perjeta x 18
Patient Population

- N = 1846
- 89% were LN +
- LN negative population had to be HR – and > 2cm
Endpoints

- **Primary:**
  - iDFS in Lymph Node + population
  - iDFS in ITT

- **Secondary:**
  - Overall Survival
  - Patient Reported Outcomes
  - Safety
Conclusions

▶ Primary Endpoints were not reached
▶ No difference in iDFS (92.8% vs 94%)
▶ Similar rates of grade 3 AE (51.8% vs 55.4%)
▶ and SAEs (21.4 % vs 23.3%)
▶ But higher discontinuation rate secondary to AE in the study arm (26.8% vs 4%)

Binghe Xu, Min Yan, Fei Ma, Xi-Chun Hu, Ji Feng Feng, Quchang Ouyang, Zhongsheng Tong, Huiping Li, Qingyuan Zhang, Tao Sun, Xian Wang, Yongmei Yin, Ying Cheng, Wei Li, Xiaoyu Zhu, Chunxia Chen, Jianjun Zou, The PHOEBE Group
Study Design

Stage 4 HER2 + BC Pts
Up to 2 prior lines of therapy
N = 267

- Pyrotinib 400 mg daily + Capecitabine 1000 mg/M2 bid days 1-14 q 21

- Lapatanib 1250 mg daily + Capecitabine 1000 mg/M2 bid days 1-14 q 21
Endpoints

- Primary Endpoint PFS

Patient Population

- Many patients had no prior treatment for MBC (42% and 35%)
- Only 15% of patients had 2 prior lines of therapy
Conclusions

- PFS 12.5 mos in study arm vs 6.8 mos in control (HR = 0.39) p <0.0001
- ORR 67.2% vs 51.5%
- CR 5.2% vs 0.8%
- Duration of response 11.1 months vs 7 months
- 1-year OS rates of 91.3% and 77.4% among pyrotinib- and lapatinib-treated participants, respectively.
## Safety

<table>
<thead>
<tr>
<th></th>
<th>Pyrotinib</th>
<th>Lapatinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRAE (at least grade 3)</td>
<td>57.5%</td>
<td>34.1%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td><strong>30.6%</strong></td>
<td>8.3%</td>
</tr>
<tr>
<td>Dose Modification</td>
<td>47%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Dose interruption</td>
<td>61.9%</td>
<td>48.5%</td>
</tr>
<tr>
<td>Treatment discontinuation</td>
<td>3%</td>
<td>2.3%</td>
</tr>
</tbody>
</table>