CLINICAL EFFICACY OF PERTUZUMAB, TRASTUZUMAB, TAXANE THERAPY FOR METASTATIC BREAST CANCER AFTER FIRST PROGRESSION

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BACKGROUND

- HER2 is overexpressed in approximately 20% of breast cancers and is connected with higher proliferation rates and poor patient prognosis[1]
- Pertuzumab is an anti-HER2 monoclonal antibody that prevents dimerization with other HER receptors[2]
- Pertuzumab, trastuzumab, and docetaxel vs trastuzumab + docetaxel improves progression-free survival by 6.1 months as first-line treatment[2]
- Pertuzumab is currently FDA approved for use in combination of trastuzumab and docetaxel:
  1. First line therapy for HER2-positive metastatic breast cancer (MBC)
  2. Neoadjuvant treatment of locally advanced, or early stage HER2-positive, breast cancer
- The PFS benefit of pertuzumab, trastuzumab, and taxane (PHT) therapy is currently unknown beyond first-line therapy for metastatic breast cancer
- NCCN Recommended Chemotherapy Regimens for HER2-positive recurrent or MBC Preferred First-line Agents:[1]
  1. Pertuzumab + trastuzumab + docetaxel (category 1)
  2. Pertuzumab + trastuzumab + paclitaxel (category 2A)

PURPOSE

- To determine the progression free survival of patients receiving pertuzumab, trastuzumab, and taxane therapy for metastatic breast cancer after first line therapy compared to trastuzumab based therapy.

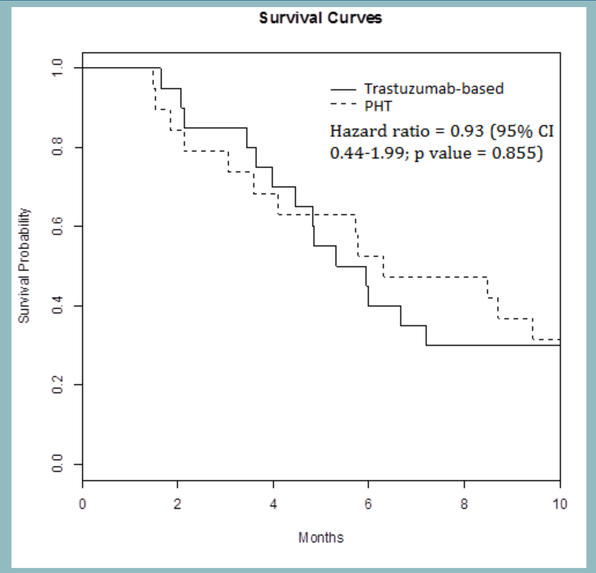
METHODS

- Retrospective cohort analysis of HER2 metastatic breast cancer patients at the Helen Diller Comprehensive Cancer Center from July 2011 to November 2013
- Two cohorts were established to assess progression free survival of chemotherapy regimens administered beyond first line therapy:
  1. Pertuzumab + Trastuzumab + Taxane (PHT)
  2. Trastuzumab-based therapy (standard of care)
- Standard of care was defined as trastuzumab in combination with any single chemotherapy or hormone therapy approved for breast cancer
- Inclusion criteria: 18 years old or greater, HER2-positive breast cancer, administration of PHT or trastuzumab based therapy as chemotherapy after first progression
- Exclusion criteria: Enrollment in clinical trial for metastatic breast cancer, surgery as primary treatment
- Elements of data collection included: Age, hormone receptor status, HER2 expression, date of breast cancer diagnosis, date of metastatic breast cancer diagnosis, previous chemotherapy for non-metastatic and metastatic breast cancer, dose and schedule of pertuzumab, dose and schedule of trastuzumab-based therapy, date of progression or death

BASELINE CHARACTERISTICS

	Pertuzumab, Trastuzumab, and Taxane (N = 19)	Trastuzumab based therapy (N = 20)	p-value
Female Sex	19 (100%)	20 (100%)	1.00
Age			
Median	47.5	45.6	0.556
Range	27.1 – 64.4	26.4 – 66.4	
Height (cm)	161.8	160.6	0.621
Weight (kg)	64.8	67.8	0.551
Hormone-receptor status			
ER-positive, PR-positive, or both	12 (63%)	15 (75%)	
ER-negative and PR-negative	10 (53%)	6 (30%)	
HER2 status			1.00
Assessed by FISH	13 (68%)	3 (15%)	
Assessed by IHC	11 (58%)	15 (75%)	
Prior adjuvant or neoadjuvant chemotherapy			
No	6 (32%)	5 (25%)	
Yes	13 (68%)	15 (75%)	0.731
Anthracycline	11 (58%)	12 (60%)	1.00
Hormone	8 (42%)	9 (45%)	1.00
Taxane	10 (53%)	10 (50%)	0.751
Trastuzumab	6 (32%)	5 (25%)	0.731
Prior chemotherapy for metastatic disease			
Number of therapies (Median, Range)	3 (1 – 13)	2 (1 – 11)	0.171
Gemcitabine	3 (16%)	2 (10%)	0.661
Capecitabine	5 (26%)	4 (20%)	0.716
Taxane	13 (68%)	10 (50%)	0.333
Trastuzumab	17 (89%)	16 (80%)	0.661
Lapatinib	9 (47%)	6 (30%)	0.333

RESULTS



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RESULTS

	Pertuzumab, Trastuzumab, and Taxane (N = 19)	Trastuzumab based therapy (N = 20)	p-value
Mean Time Progression Free (SD)	4.4 (1.7)	4.8 (2.8)	0.713
Number Without Progression	6	6	
Mean baseline LVEF	62.6%	69.7%	--
Mean LVEF change	-1%	-5%	--
Febrile Neutropenia events	0	0	--
LVEF Dysfunction	0	0	--
Asymptomatic LVEF decrease	2 (11%)	1 (5%)	--
Median cycles received	4	5	--

DISCUSSION/CONCLUSION

- PHT did not confer additional benefit in PFS over standard of care
- PHT had similar efficacy benefit in patients receiving only pertuzumab and trastuzumab for MBC that progressed on prior trastuzumab therapy (PFS of 5.5 months) [3]
- PHT arm had 7 patients discontinuing taxane due to adverse events
- No left ventricular systolic dysfunction was seen with PHT therapy
- No febrile neutropenia events were documented during treatment
- Addition of pertuzumab confers similar benefit as trastuzumab-based therapy without detrimental effects on LVEF

FUTURE DIRECTION

- Pertuzumab stewardship
  - Present data to breast oncologists to discuss results
  - Contacting providers for utilizing pertuzumab after first progression of metastatic breast cancer
- Further exploration of the usage of pertuzumab
  - Review utilization of pertuzumab in neoadjuvant setting
  - Emerging data of pertuzumab combined with different chemotherapy agents
  - Increase utilization of pertuzumab

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