CASE PRESENTATION: BREAST CANCER

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OUTLINE

- Case presentation
- Diagnosis
- Treatment
- Summary
- Future directions
- Discussion of literature

CASE

- 51F w/ no sig pmhx who initially presented six years ago (7/2014) with severe back pain
- Avid biker & runner who began experiencing back pain 10/2013 while training for 100 mile bike race
- Saw orthopedics 6/2014 and had MRI done which revealed burst fracture of T5, abnormal marrow signal throughout concerning for **metastasis** and liver lesions
- CTAP 6/2014 revealed 1.7 x 1.1 cm L breast mass concerning for neoplasm with prominent axillary LNs, lytic lesions in T3 and T4, two large liver masses, largest measuring 5.8 x 4.9 cm
- Pt urgently admitted to hospital for concern for suspected cord compression and breast biopsy was done

DIAGNOSIS

- Pathology revealed: infiltrating ductal carcinoma, intermediate grade, no lymphovascular invasion present
- Estrogen receptor – positive (greater than 90%, strong)
- Progesterone receptor – positive (70%, strong)
- Proliferation by Ki-67- 80%
- HER2 FISH: Amplified
- ER/PR+, HER-2 AMPLIFIED

TREATMENT

- Pt was determined to have spinal cord compression and underwent T4-T5 corpectomy and T2-T8 spinal fusion
- Pathology revealed infiltrating carcinoma consistent w/ breast primary
- Pt had bone scan done 7/2014 which revealed thoracic spine w/ multiple photophenic defects that correlate w/ hardware + areas of increased uptake 2/2 metastatic disease
- 7/2014 TTE – EF 60-65%
- 7/2014: CA 27-29= 515, CEA 58.7
- Pt began therapy, with **paclitaxel, pertuzumab, trastuzumab q21 days 7/2014**
- Pt started monthly denosumab 7/2014 for bone disease
- Pt began palliative radiation therapy to spine
- Pt underwent bilateral salpingo-oophorectomy 2/2015

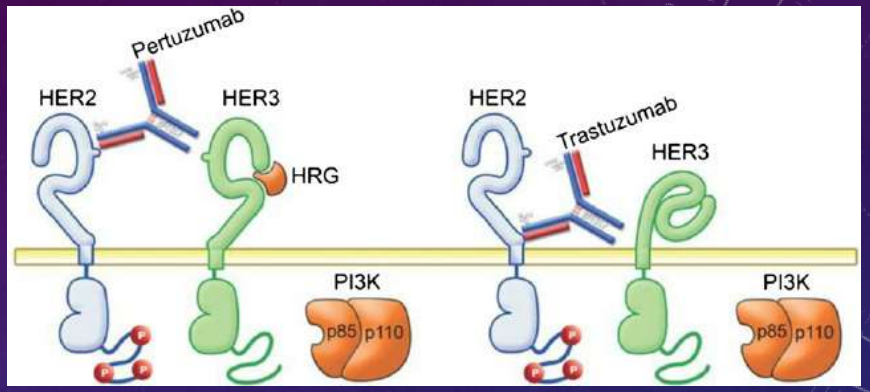
SUMMARY

- 7/2014- paclitaxel, pertuzumab, trastuzumab q21 days
- 9/2015- paclitaxel dropped, continued on pertuzumab and trastuzumab and anastrazole added
- 6/2016- taxane added back due to disease progression in liver
- 6/2017- switched to ado-trastuzumab
- 11/2017- capecitabine/lapatinib started, pt could not tolerate lapatinib

SUMMARY

- 1/2018- trastuzumab + capecitabine
- 7/2018- trastuzumab + vinorelbine
- 10/2018- everolimus added to vinorelbine + trastuzumab, pt self-discontinued
- 1/2019- trastuzumab + carboplatin
- 5/2019 – fulvestrant + palbociclib

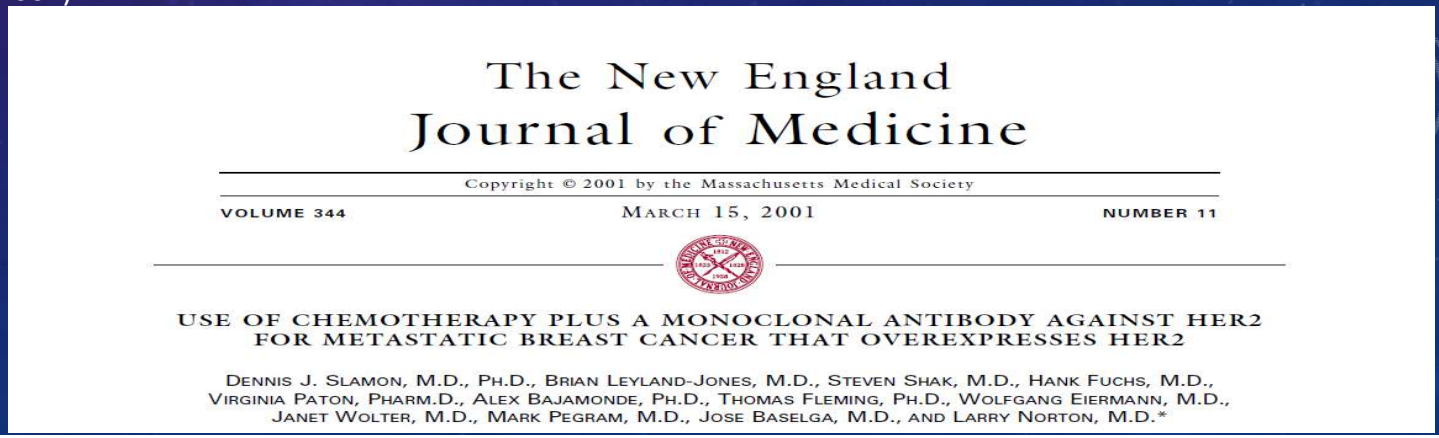
HER-2 BREAST CANCER



- Amplification or overexpression of the human epidermal growth factor receptor 2 (*HER2*) oncogene is present in approximately **15 percent** of primary invasive breast cancers
- Trastuzumab – monoclonal antibody that binds extracellular domain of HER2
- Pertuzumab – monoclonal antibody that binds the extracellular dimerization domain of HER2 and prevents it from binding to itself or to other members of the EGFR family

TRASTUZUMAB AND METASTATIC BREAST CANCER

- Randomized Phase III: First-line trastuzumab + various chemotherapy regimens compared with chemotherapy alone
- Significant improvement in survival benefit (25.1 v 20.3 months) and
- ORR (50% v 32%)
- Trastuzumab + Paclitaxel for the first-line treatment of HER2-overexpressing MBC
  - 62% reduction in the risk of disease progression (HR, 0.38;95%CI, 0.27 to 0.53)
  - Longer median PFS (6.9 v 3.0 months; P<.001)
  - Greater ORR (41% v 17%; P<.001)



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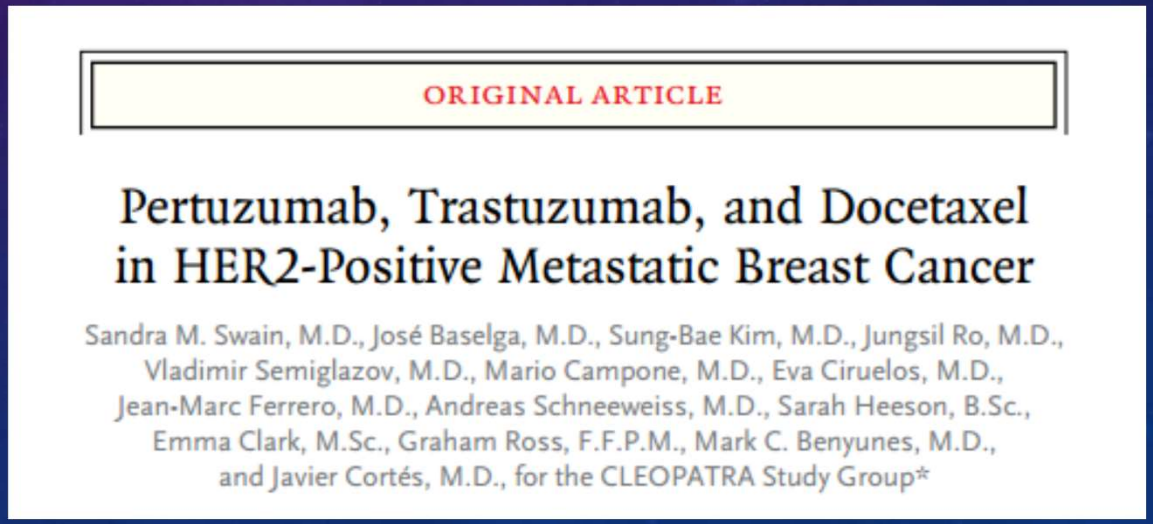
USE OF CHEMOTHERAPY PLUS A MONOCLONAL ANTIBODY AGAINST HER2 FOR METASTATIC BREAST CANCER THAT OVEREXPRESSES HER2

DENNIS J. SLAMON, M.D., PH.D., BRIAN LEYLAND-JONES, M.D., STEVEN SHAK, M.D., HANK FUCHS, M.D., VIRGINIA PATON, PHARM.D., ALEX BAJAMONDE, PH.D., THOMAS FLEMING, PH.D., WOLFGANG EIERMANN, M.D., JANET WOLTER, M.D., MARK PEGRAM, M.D., JOSE BASELGA, M.D., AND LARRY NORTON, M.D.*

TRASTUZUMAB AND PERTUZUMAB

- Patients with metastatic breast cancer with no previous therapies received trastuzumab, pertuzumab, docetaxel or placebo, trastuzumab, docetaxel
- Median overall survival 56.5 months in combo group vs 40.8 months in placebo combo
- Pertuzumab extended median duration of response by 7.7 months

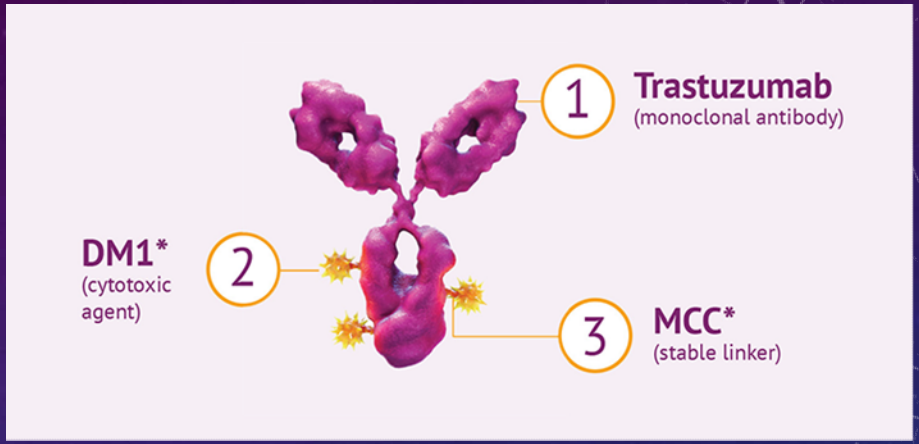


ORIGINAL ARTICLE

Pertuzumab, Trastuzumab, and Docetaxel in HER2-Positive Metastatic Breast Cancer

Sandra M. Swain, M.D., José Baselga, M.D., Sung-Bae Kim, M.D., Jungsil Ro, M.D., Vladimir Semiglazov, M.D., Mario Campone, M.D., Eva Ciruelos, M.D., Jean-Marc Ferrero, M.D., Andreas Schneeweiss, M.D., Sarah Heeson, B.Sc., Emma Clark, M.Sc., Graham Ross, F.F.P.M., Mark C. Benyunes, M.D., and Javier Cortés, M.D., for the CLEOPATRA Study Group*

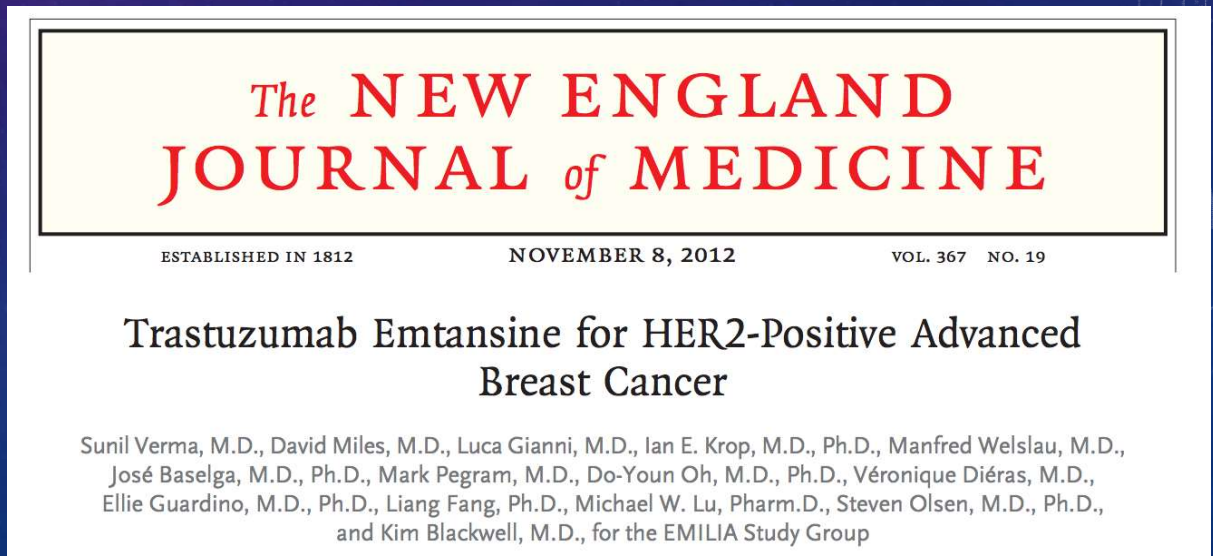
HER-2 BREAST CANCER



- Ado-trastuzumab emtansine (T-DM1)- an antibody drug conjugate composed of trastuzumab, a thioether linker, and the antimicrotubule agent, DM1
- Lapatinib - a tyrosine kinase inhibitor against EGFR1 and HER2 that results in inhibition of signaling pathways downstream of HER2

TRASTUZUMAB EMTANSINE (T-DM1)

- 991 patients previously treated with trastuzumab and a taxane were assigned to T-DM1 or lapatinib plus capecitabine
- Median PFS was 9.6 months with T-DM1 vs 6.4 months with lapatinib plus capecitabine
- Median overall survival 30.9 months vs 25.1 months
- Rates of adverse events of grade 3 or above were higher with capecitabine and lapatinib



The NEW ENGLAND JOURNAL of MEDICINE

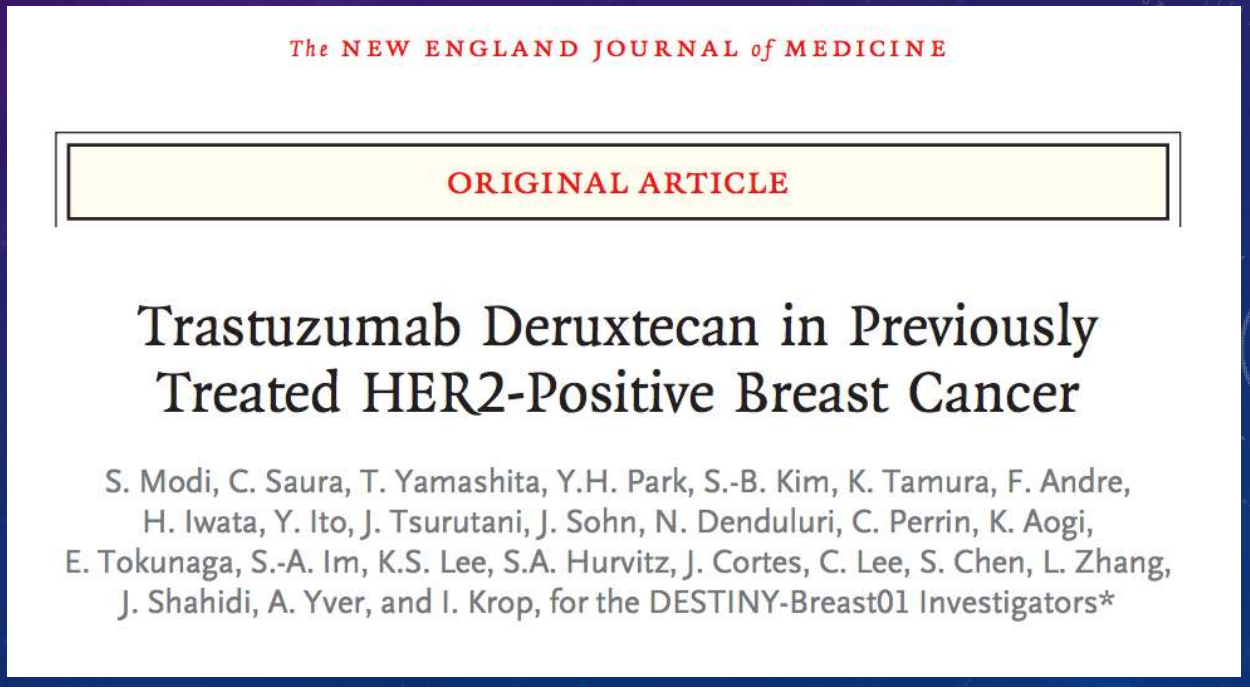
ESTABLISHED IN 1812 NOVEMBER 8, 2012 VOL. 367 NO. 19

Trastuzumab Emtansine for HER2-Positive Advanced Breast Cancer

Sunil Verma, M.D., David Miles, M.D., Luca Gianni, M.D., Ian E. Krop, M.D., Ph.D., Manfred Welslau, M.D., José Baselga, M.D., Ph.D., Mark Pegram, M.D., Do-Youn Oh, M.D., Ph.D., Véronique Diéras, M.D., Ellie Guardino, M.D., Ph.D., Liang Fang, Ph.D., Michael W. Lu, Pharm.D., Steven Olsen, M.D., Ph.D., and Kim Blackwell, M.D., for the EMILIA Study Group

FUTURE DIRECTIONS

- December 20, 2019- FDA grants accelerated approval to fam-trastuzumab deruxtecan-nxki for the treatment of unresectable or metastatic HER2-positive breast cancer who have received **two or more** prior anti-HER2-based regimens in metastatic setting



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trastuzumab Deruxtecan in Previously Treated HER2-Positive Breast Cancer

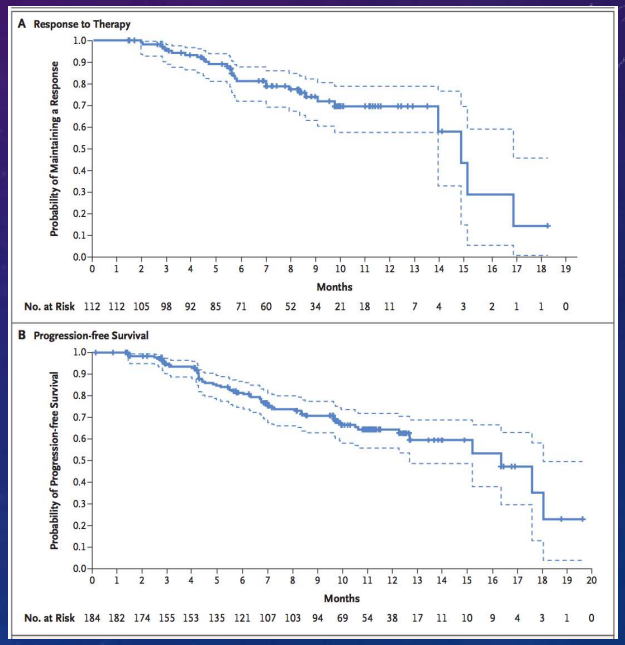
S. Modi, C. Saura, T. Yamashita, Y.H. Park, S.-B. Kim, K. Tamura, F. Andre, H. Iwata, Y. Ito, J. Tsurutani, J. Sohn, N. Denduluri, C. Perrin, K. Aogi, E. Tokunaga, S.-A. Im, K.S. Lee, S.A. Hurvitz, J. Cortes, C. Lee, S. Chen, L. Zhang, J. Shahidi, A. Yver, and I. Krop, for the DESTINY-Breast01 Investigators*

DISCUSSION OF LITERATURE

- Dec 2019 NEJM article revealed Phase 2 study with 184 patients who had undergone a median of **six** previous treatments
- Trastuzumab deruxtecan is an antibody-drug conjugate composed of anti-HER2 antibody and a topoisomerase I inhibitor
- A response to therapy was reported in 112 patients (60.9%)
- Median duration of follow-up was 11.1 months (range 0.7 to 19.9)

DISCUSSION OF LITERATURE

- Median duration of response was 14.8 months
- Median duration of progression free survival was 16.4 months



DISCUSSION OF LITERATURE

- Most common adverse events were nausea, fatigue, decreased neutrophil count, anemia
- Interstitial lung disease was observed in subgroup of patients (13.6%).

Table 2. Adverse Events in the Overall Population of 184 Patients.*

Adverse Events	Any Grade	Grade 3	Grade 4
	number of patients (percent)		
Any adverse event†	183 (99.5)	89 (48.4)	7 (3.8)
Nausea	143 (77.7)	14 (7.6)	0
Fatigue	91 (49.5)	11 (6.0)	0
Alopecia	89 (48.4)	1 (0.5)	0
Vomiting	84 (45.7)	8 (4.3)	0
Constipation	66 (35.9)	1 (0.5)	0
Decreased neutrophil count‡	64 (34.8)	36 (19.6)	2 (1.1)
Decreased appetite	57 (31.0)	3 (1.6)	0
Anemia§	55 (29.9)	15 (8.2)	1 (0.5)
Diarrhea	54 (29.3)	5 (2.7)	0
Decreased white-cell count¶	39 (21.2)	11 (6.0)	1 (0.5)
Decreased platelet count‖	39 (21.2)	7 (3.8)	1 (0.5)
Headache	36 (19.6)	0	0
Cough	35 (19.0)	0	0
Abdominal pain**	31 (16.8)	2 (1.1)	0
Decreased lymphocyte count††	26 (14.1)	11 (6.0)	1 (0.5)
Adverse events of special interest			
Interstitial lung disease‡‡	25 (13.6)	1 (0.5)	0
Prolonged QT interval	9 (4.9)	2 (1.1)	0
Infusion-related reaction	4 (2.2)	0	0
Decreased left ventricular ejection fraction§§	3 (1.6)	1 (0.5)¶¶	0

CONCLUSION

- Special thanks to Dr Collins-Burow and Dr Barata!