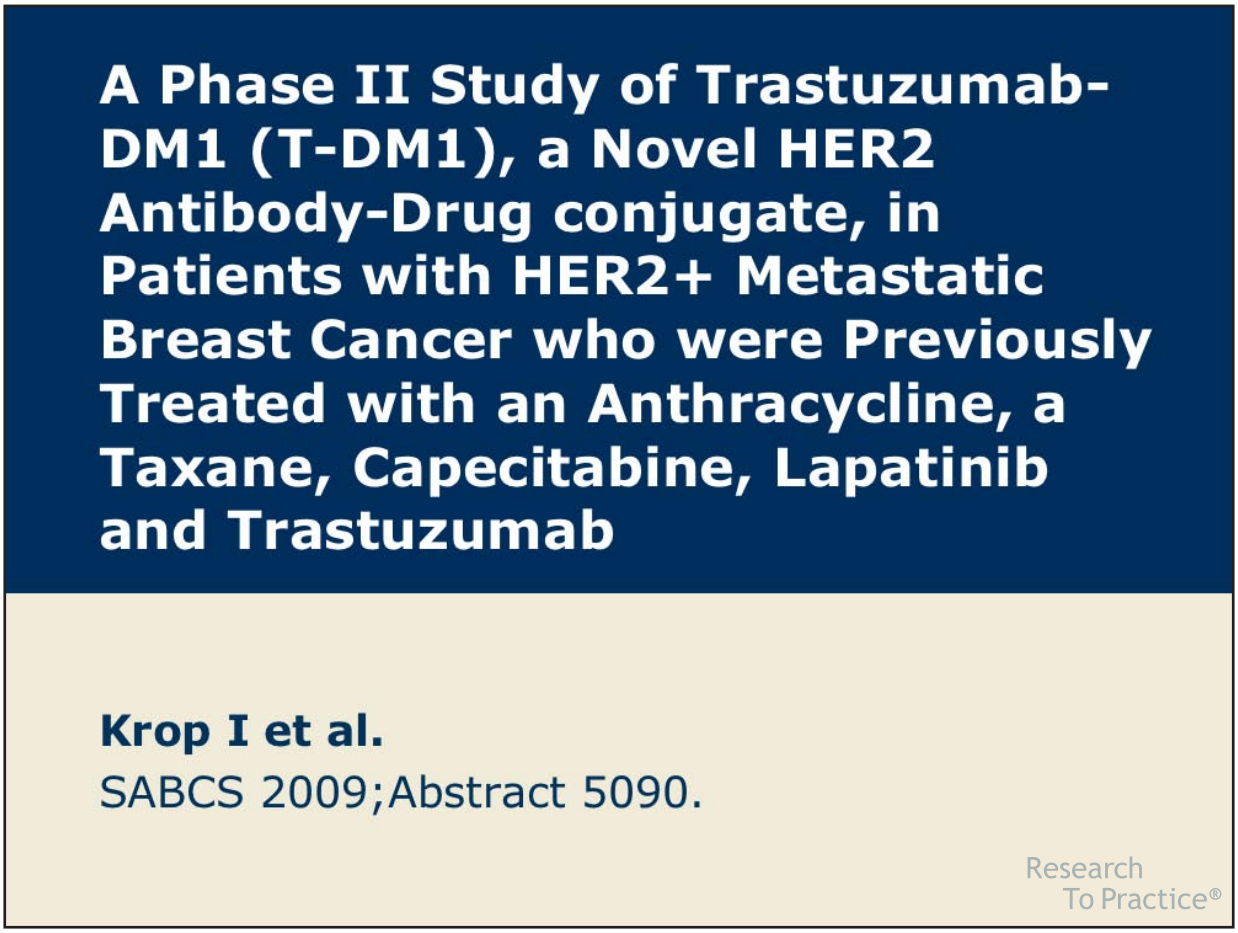
Phase II Study of Trastuzumab-DM1 (T-DM1) for Patients with Previously Treated HER2-Positive Metastatic Breast Cancer

Presentation discussed in this issue:

Krop I et al. **A Phase II study of trastuzumab-DM1 (T-DM1), a novel HER2 antibody-drug conjugate, in patients previously treated with lapatinib, trastuzumab, and chemotherapy.** SABCS 2009;**Abstract 5090**.

Slides from a poster at SABCS 2009



Introduction

- T-DM1 combines the HER2 targeting function of trastuzumab (T) with the DM1 anti-microtubule derivative.
- Proof-of-concept phase II study (4258g) examined single-agent T-DM1 in patients with previously treated, HER2+, metastatic breast cancer (*JCO* 2009;27;Abstract 1017).
  - In patients previously treated with lapatinib and T:
    - Objective response rate (ORR)=24.2%
  - In patients that were retrospectively, centrally confirmed HER2+:
    - ORR=33.8%
  - T-DM1 was well tolerated at the study dose and schedule (3.6 mg/kg IV q3wk).
- **Current study objectives:**
  - Confirm and extend findings of 4258g study in a homogenous population of patients with HER2+ metastatic breast cancer (mBC) that had been previously treated with chemotherapy, lapatinib and T.

Source: Krop I et al. SABCS 2009;Abstract 5090.

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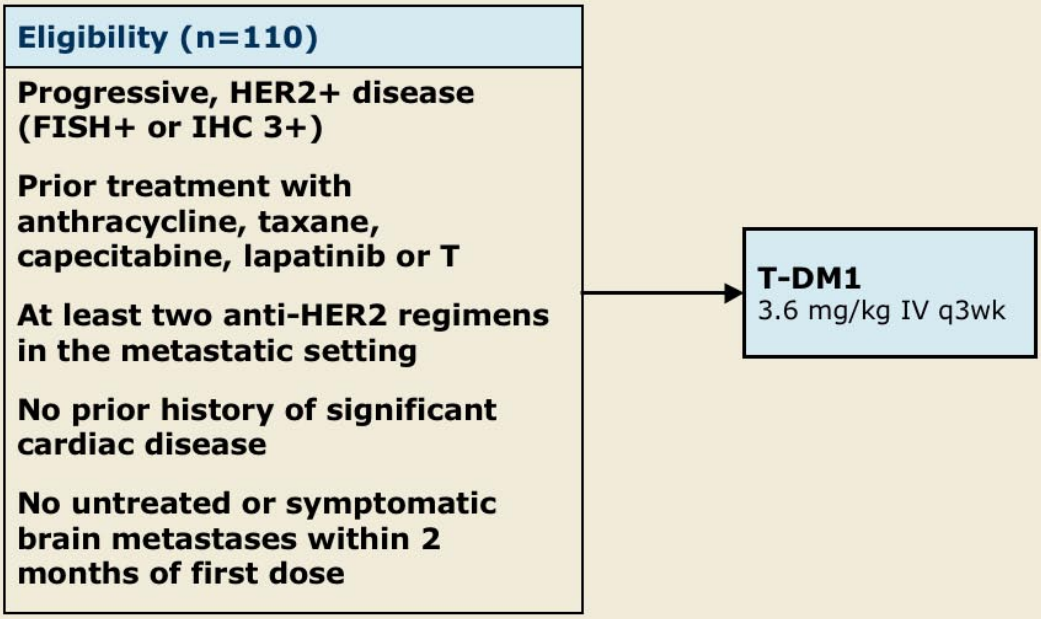
4374g: Phase II, Open-Label, Multicenter Trial of T-DM1 in Previously Treated Patients with mBC



Source: Krop I et al. SABCS 2009;Abstract 5090.

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Prior Chemotherapy and Anti-HER2 Therapy

	n=110
Median number of agents for metastatic disease (range)*	7.0 (1 - 15)
Median number of agents in all therapy settings (range)*	8.0 (1 - 19)
Number of patients with 5 prior agents (%)**	109 (99.1)
Median duration of prior T in metastatic setting (range)	19.4 mos (2 - 116)
Median duration of prior lapatinib in metastatic setting (range)	6.9 mos (0 - 23)

**Includes all agents intended for the treatment of breast cancer except hormonal therapy.*

***One patient did not receive a taxane.*

Source: Krop I et al. SABCS 2009;Abstract 5090.

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T-DM1 Exposure

	n=110
Number of doses administered, median (range)	7.0 (1 - 19)
Exposure duration, median (range)	19.3 weeks (0 - 56)
Average T-DM1 dose, median (range)	3.57 mg/kg (2.5 - 3.9)
Dose reductions* Patients with dose reductions to 3.0 mg/kg Patients with dose reductions to 2.4 mg/kg	 11 6

**Values reported are from an independent review facility assessment.*

Source: Krop I et al. SABCS 2009;Abstract 5090.

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Efficacy Results (median follow-up 8.3 mos)

Clinical Response*	All Treated Patients (n=110)	HER2+ Patients[1] (n=76)	HER2 Normal Patients[1] (n=15)
ORR	32.7%	39.5%	20.0%
Complete response	0%	—	—
Partial response	32.7%	—	—
Clinical benefit rate (CBR)	44.5%	52.6%	26.7%

**Values reported are from an independent review facility assessment.*
[1]HER2 status was retrospectively centrally confirmed.

Source: Krop I et al. SABCS 2009;Abstract 5090.

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Serious Adverse Events Occurring in ≥2 Patients

Adverse Event (All Grades)	n=110
Pyrexia	2.7%
Cellulitis	2.7%
Pneumonia	2.7%
Nausea	1.8%
Axillary pain	1.8%
Convulsion	1.8%
LVEF*	
Post-baseline < 45%	0%
Maximum decrease from baseline ≥ 25%	0%

**n=107*

Source: Krop I et al. SABCS 2009;Abstract 5090.

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Conclusions

- T-DM1 demonstrated anti-tumor activity in an extensively pretreated population of patients with mBC.
  - ORR=32.7% and CBR=44.5%
- Clinical benefit was observed in a prespecified patient population not previously studied.
  - Patients having received prior treatment with an anthracycline, a taxane, capecitabine, lapatinib and T
  - Patients having received two HER2-directed regimens in the metastatic setting
  - Patients with progressive disease on last regimen received
- T-DM1 was well tolerated with no observed dose-limiting cardiotoxicity or new safety signals.

Source: Krop I et al. SABCS 2009;Abstract 5090.