Disease Progression as a Predictor of Overall Survival in Metastatic Breast Cancer: A Meta-analysis

Sherrill B[1], Amonkar MM[2], Wu Yun[1], Hirst C[3], Stein SH[2], Walker M[4], Cuzick J[5]

[1]RTI Health Solutions, Research Triangle Park, NC, United States
[2]GlaxoSmithKline, Collegeville, PA, United States
[3]RTI Health Solutions, Barcelona, Spain
[4]GlaxoSmithKline, Manchester Park, United Kingdom
[5]Wolfson Institute of Preventive Medicine, London, United Kingdom

Presented April 18, 2008
6th European Breast Cancer Conference
(EBCC-6) Berlin, Germany

B. Sherrill

Disease Progression as a Predictor of Overall Survival in Metastatic Breast Cancer: A Meta-analysis

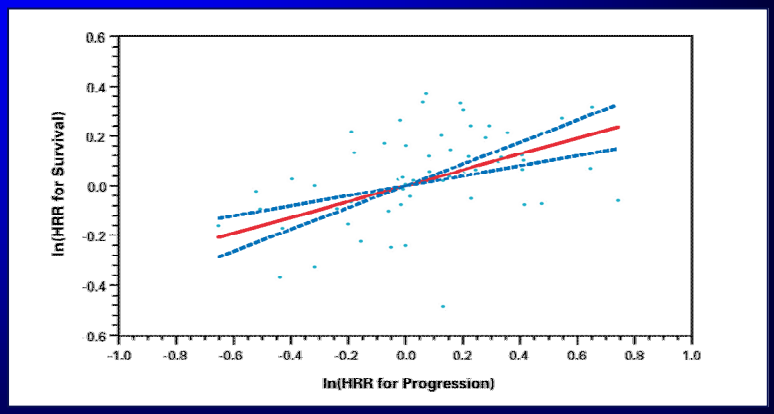
OBJECTIVE: Assess the relationship between disease progression endpoints and overall survival (OS) in metastatic breast cancer (MBC) using published data.

METHODS:

- A literature search retrieved RCTs since 1994 in which both progression endpoints and OS were reported.
- A wide range of treatment types was represented in 67 studies covering 17,081 MBC patients (first-line and refractory).
- Logarithm of the hazard rate ratio (HRR) for survival was regressed on the HRR for progression without an intercept and weighted by sample size. The resulting equation was exponentiated, yielding predictions for a range of progression effects.

B. Sherrill

Regression of
ln (HRR for Survival) vs. ln (HRR for Progression
with 95% CI of Mean, Weighted by Number of Patients



Regression equation: ln(OS1/OS2) = 0.32 * ln(TTP1/TTP2)
N = 67 studies; R2(adj) = 0.29

Subset analyses of studies using hormonal agents (n=12) and studies in HER2+ patients (n=4) yielded similar results.

B. Sherrill

RESULTS: Treatment effects on progression are expected to coincide with treatment effects on survival

$$HRR_{Survival} = (HRR_{Progression})^{0.32}$$

Observed Treatment Effect on Progression	Predicted Treatment Effect on Survival
0.5	0.80
0.6	0.85
0.7	0.89
0.8	0.93

B. Sherrill

CONCLUSIONS:

- Findings indicate that increases in time to progression ultimately correspond to survival benefits for MBC patients as previously established in other tumor types.
- Survival differences may be underestimated due to patient switching after progression in some studies.
- Findings are important given the difficulty of demonstrating overall survival in late-stage cancer trials.

B. Sherrill