

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Geyer CE, Forster J, Lindquist D, et al. Lapatinib plus capecitabine for HER2-positive advanced breast cancer. N Engl J Med 2006;355:2733-43.

Geyer Web Only Supplement 06-4320

Supplementary Table 1. Prohibited Medications Due to Inhibition or Induction of CYP3A4 by Lapatinib

Drug Class	Agent	Wash-out
CYP3A4 Inducers		
Antibiotics	All rifamycin class agents (eg, rifampicin, rifabutin, rifapentine)	14 days
Anticonvulsants	Phenytoin, carbamazepine, barbiturates (eg, phenobarbital)	
Antiretrovirals	Efavirenz, nevirapine	
Glucocorticoids (oral)	Cortisone (> 50 mg), hydrocortisone (> 40 mg), prednisone (>10 mg), methylprednisolone (>8 mg), dexamethasone (>1.5 mg)	
Other	St. John's Wort, modafinil	
CYP3A4 Inhibitors		
Antibiotics	Clarithromycin, erythromycin, troleandomycin	7 days
Antifungals	Itraconazole, ketoconazole, fluconazole (>150 mg daily), voriconazole	
Antiretrovirals, protease	Delaviridine, nelfinavir, amprenavir, ritonavir,	

inhibitors	indinavir, saquinavir, lopinivir	
Calcium channel blockers	Verapamil, diltiazem	
Antidepressants	Nefazodone, fluvoxamine	
GI Agents	Cimetidine, aprepitant	
Other	Grapefruit, grapefruit juice	
	Amiodarone	6 months
Miscellaneous		
Antacids	Eg, Calcium carbonate and magnesium hydroxide, calcium carbonate	1 hour before and after dosing

Supplementary Table 2. Comparison of Independent Review Committee and Investigator Assessments of Time-to-Progression Events

Independent time-to- progression events	Investigator time-to- progression events	
	Yes	No
Both Arms (N=324)		
Yes	87 (27%)	34 (10%)
No	46 (14%)	157 (48%)
Lapatinib + Capecitabine (N=163)		

	Yes	No
Yes	34 (21%)	15 (9%)
No	25 (15%)	89 (55%)
Capecitabine (N=161)	Yes	No
Yes	53 (33%)	19 (12%)
No	21 (13%)	68 (42%)

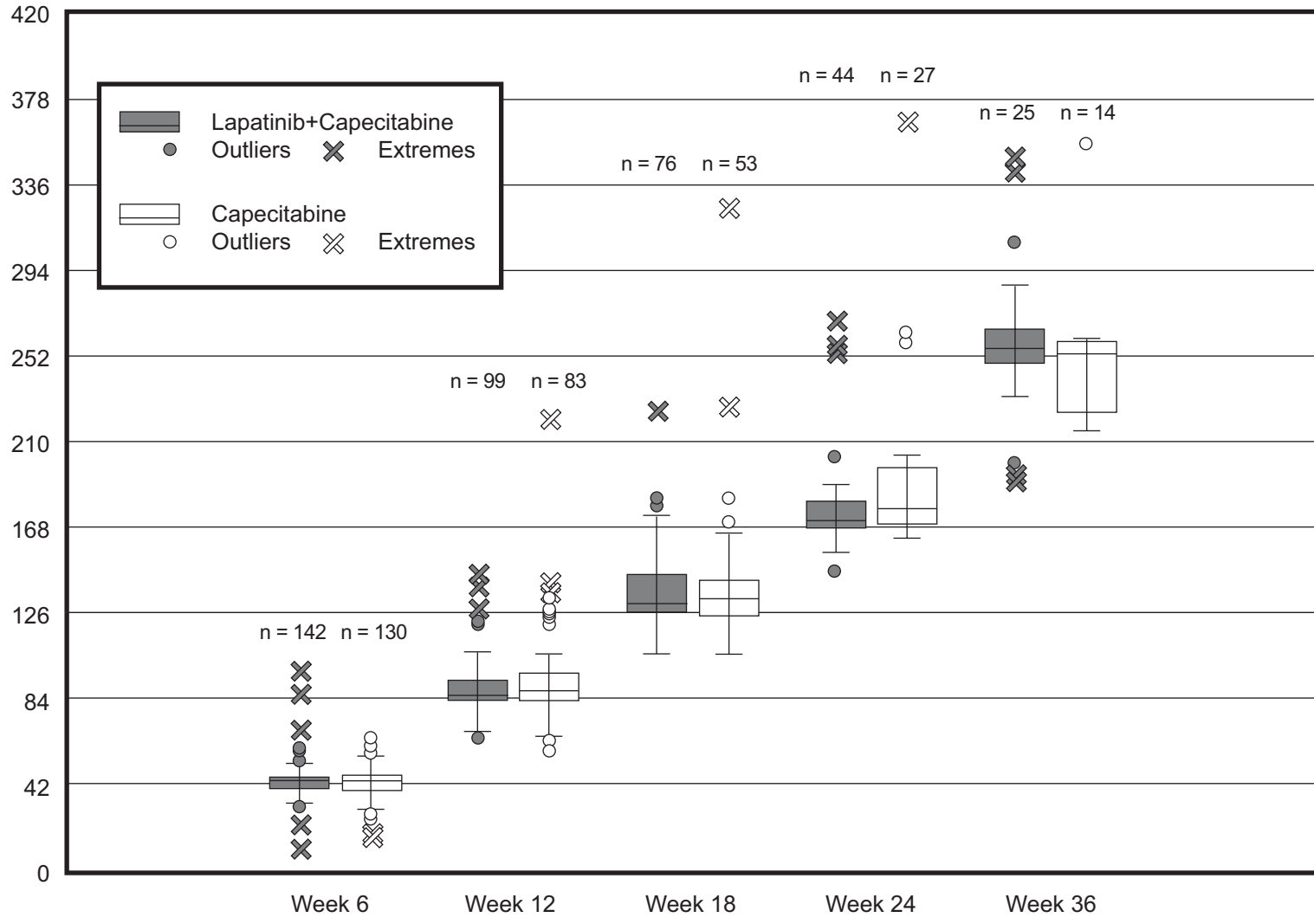
Supplementary Figure Legends

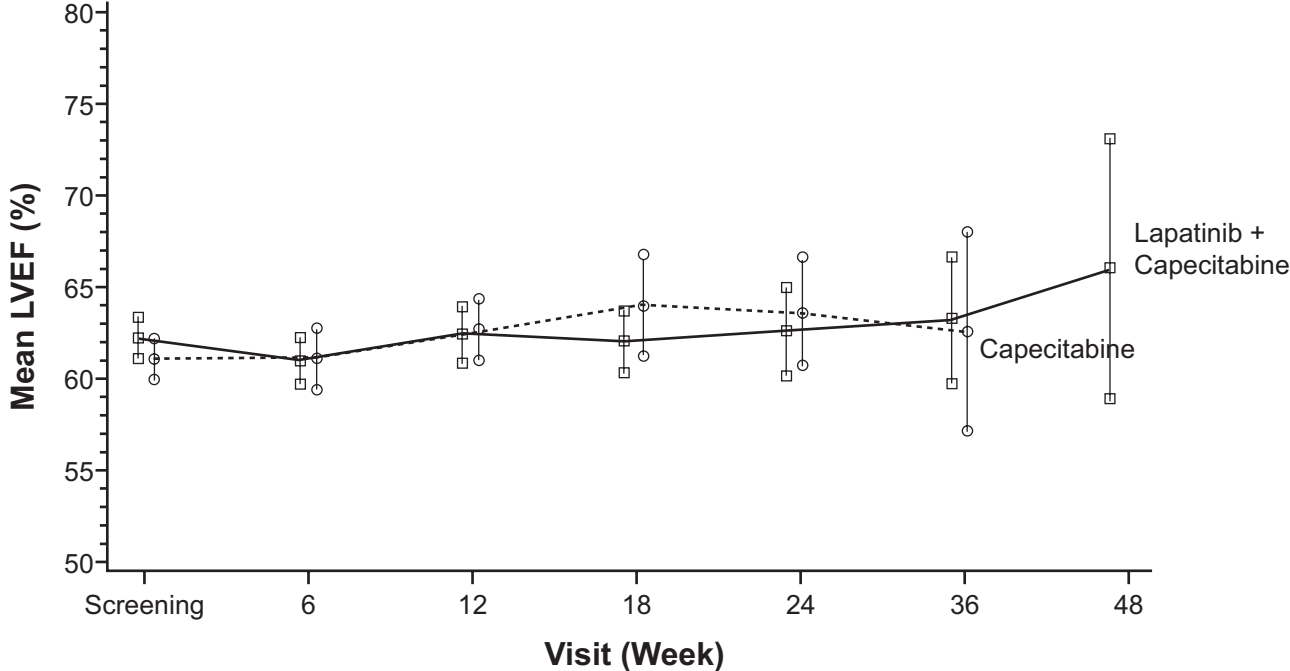
Supplementary Figure 1. Compliance with Timing of Disease Status Assessments. Box plots with median, 25th and 75th percentiles and outliers

Supplementary Figure 2. Mean (95% CI) LVEF at Scheduled Assessments

Compliance with Disease Status Assessment Times

Time to Assessment D





No. at Risk

Lapatinib+Cape	162	112	85	65	40	18	8
Capecitabine	151	88	66	35	23	6	0