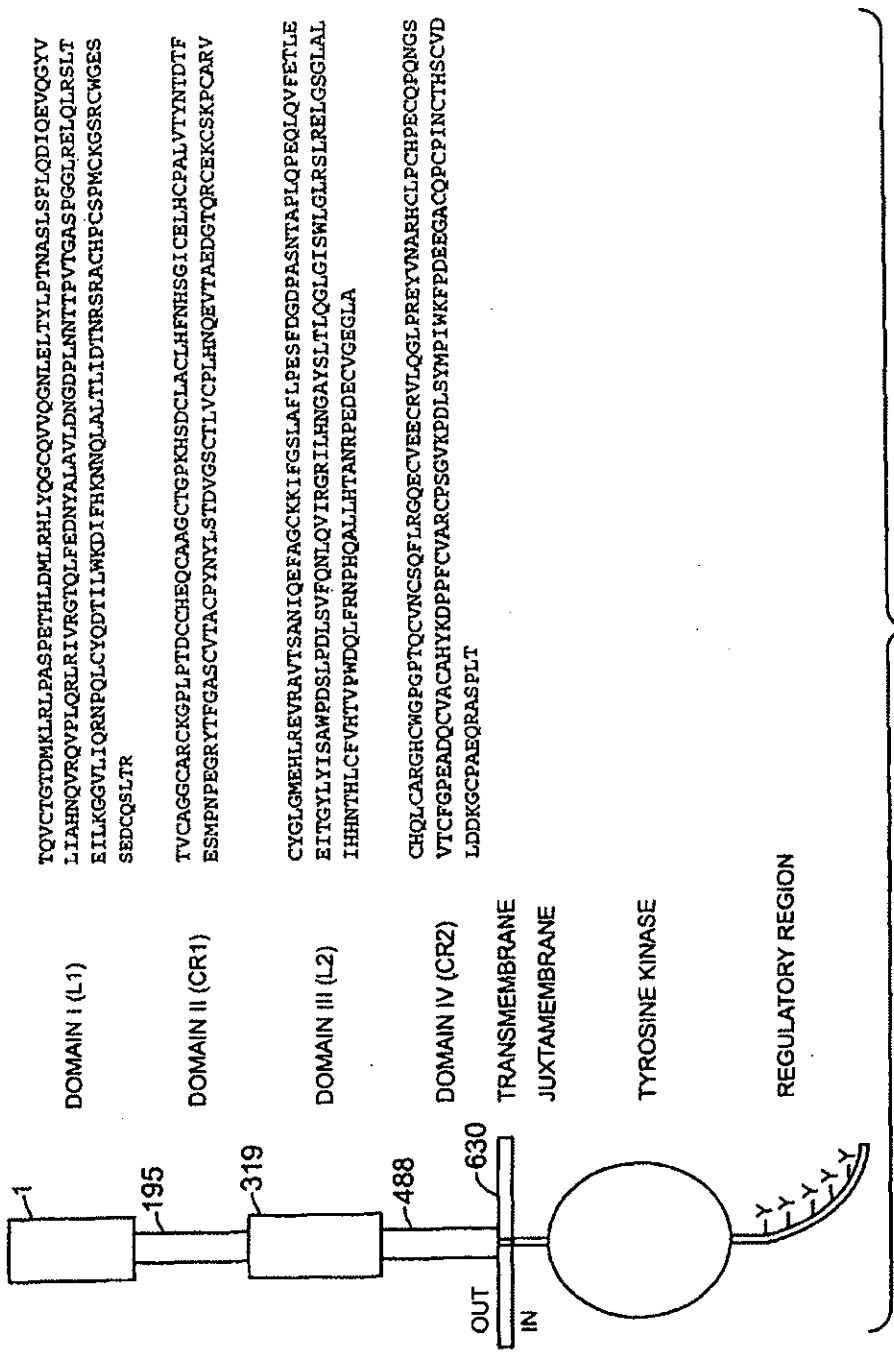

1
195
319
488
630
OUT
IN
DOMAIN I (L1)
TQVCTGTDMKLRLPASPETHLDMLRHLYQGCQVVQGNLELTYLPTNASLSFLQDIQEVQGYV
LIAHNQVRQVPLQRLRIVRGTQLFEDNYALAVLDNGDPLNNTTPVTGASPGGLRELQLRSLT
EILKGGVLIQRNPQLCYQDTILWKDIFHKNNQLALTLIDTNRSRACHPCSPMCKGSRCWGES
SEDCQSLTR
DOMAIN II (CR1)
TVCAGGCARCKGPLPTDCCHEQCAAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTF
ESMPNPEGRYTFGASCVTACPYNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARV
DOMAIN III (L2)
CYGLGMEHLREVRAVTSANIQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLE
EITGYLYISAWPDSLPDLSVFQNLQVIRGRILHNGAYSLTLQGLGISWLGLRSLRELGSGLAL
IHHNTHLCFVHTVPWDQLFRNPHQALLHTANRPEDECVGEGLA
DOMAIN IV (CR2)
CHQLCARGHCWGPGPTQCVNCSQFLRGQECVEECRVLQGLPREYVNARHCLPCHPECQPQNGS
VTCFGPEADQCVACAHYKDPPFCVARCPSGVKPDLSYMPIWKFPDEEGACQPCPINCTHSCVD
LDDKGCPAEQRASPLT
TRANSMEMBRANE
JUXTAMEMBRANE
TYROSINE KINASE
REGULATORY REGION
Y
Y
Y
Y
Y

FIG. 1

Variable Light

```
                10          20          30          40
2C4     DIVMTQSHKIMSTSVGDRVSITC [KASQDVSIGVA] WYQQRP
         **    **** *       *                     *
574     DIQMTQSPSSLSASVGDRVTITC [KASQDVSIGVA] WYQQKP
                                      *   ** ***
hum kI  DIQMTQSPSSLSASVGDRVTITC [RASQSISNYLA] WYQQKP

                50          60          70          80
2C4     GQSPKLLIY [SASYRYT] GVPDRFTGSGSGTDFTFTISSVQA
          **                  *  *        *    * *
574     GKAPKLLIY [SASYRYT] GVPSRFSGSGSGTDFTLTISSLQP
                   * *****
hum kI  GKAPKLLIY [AASSLES] GVPSRFSGSGSGTDFTLTISSLQP

                90          100
2C4     EDLAVYYC [QQYYIYPYT] FGGGTKLEIK (SEQ ID NO:1)
           * *                 *   *
574     EDFATYYC [QQYYIYPYT] FGQGTKVEIK (SEQ ID NO:3
                    *** *
hum kI  EDFATYYC [QQYNSLPWT] FGQGTKVEIK (SEQ ID NO:5)
```

FIG. 2A

Variable Heavy

```
                10          20          30          40
2C4     EVQLQQSGPELVKPGTSVKISCKAS [GFTFTDYTMD] WVKQS
            **  **  *  * ***  *                  * *
574     EVQLVESGGGLVQPGGSLRLSCAAS [GFTFTDYTMS] WVRQA
                                      ** * *
hum III EVQLVESGGGLVQPGGSLRLSCAAS [GFTFSSYAMS] WVRQA

                50 a        60          70          80
2C4     HGKSLEWIF [DVNPNSGGSIYNQRFKG] KASLTVDRSSRIVYM
        *  *   **                     *** *    **** *
574     PGKGLEWVA [DVNPNSGGSIYNQRFKG] RFTLSVDRSKNTLYL
                   ****** *** ****       * * *
hum III PGKGLEWVA [VISGDGGSTYYADSVKG] RFTISRDNSKNTLYL

                abc 90          100ab       110
2C4     ELRSLTFEDTAVYYCAR [NLGPSFYFDY] WGQGTTLTVSS (SEQ ID NO:2)
        ***  **                                **
574     QMNSLRAEDTAVYYCAR [NLGPSFYFDY] WGQGTLVTVSS (SEQ ID NO:4)
                           ********
hum III QMNSLRAEDTAVYYCAR [GRVGYSLYDY] WGQGTLVTVSS (SEQ ID NO:6)
```

FIG. 2B

Amino Acid Sequence for Pertuzumab Light Chain

```
1          10         20         30         40         50         60
|          |          |          |          |          |          |
DIQMTQSPSSLSASVGDRVTITCKASQDVSIGVAWYQQKPGKAPKLLIYSASYRYTGVPS

           70         80         90         100        110        120
           |          |          |          |          |          |
RFSGSGSGTDFTLTISSLQPEDFATYYCQQYYIYPYTFGQGTKVEIKRTVAAPSVFIFPP

           130        140        150        160        170        180
           |          |          |          |          |          |
SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT

           190        200        210
           |          |          |
LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
```

FIG. 3A

Amino Acid Sequence for Pertuzumab Heavy Chain

```
1          10         20         30         40         50         60
|          |          |          |          |          |          |
EVQLVESGGGLVQPGGSLRLSCAASGFTFTDYTMDWVRQAPGKGLEWVADVNPNSGGSIY

           70         80         90         100        110        120
           |          |          |          |          |          |
NQRFKGRFTLSVDRSKNTLYLQMNSLRAEDTAVYYCARNLGPSFYFDYWGQGTLVTVSSA

           130        140        150        160        170        180
           |          |          |          |          |          |
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG

           190        200        210        220        230        240
           |          |          |          |          |          |
LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP

           250        260        270        280        290        300
           |          |          |          |          |          *|
SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS

           310        320        330        340        350        360
           |          |          |          |          |          |
TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEM

           370        380        390        400        410        420
           |          |          |          |          |          |
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ

           430        440        448
           |          |          |
QGNVFSCSVMHEALHNHYTQKSLSLSPG
```

FIG. 3B

Ligand-activated EGFR Heterodimerizes with HER2 2C4 Binds at the Heterodimeric Binding Site

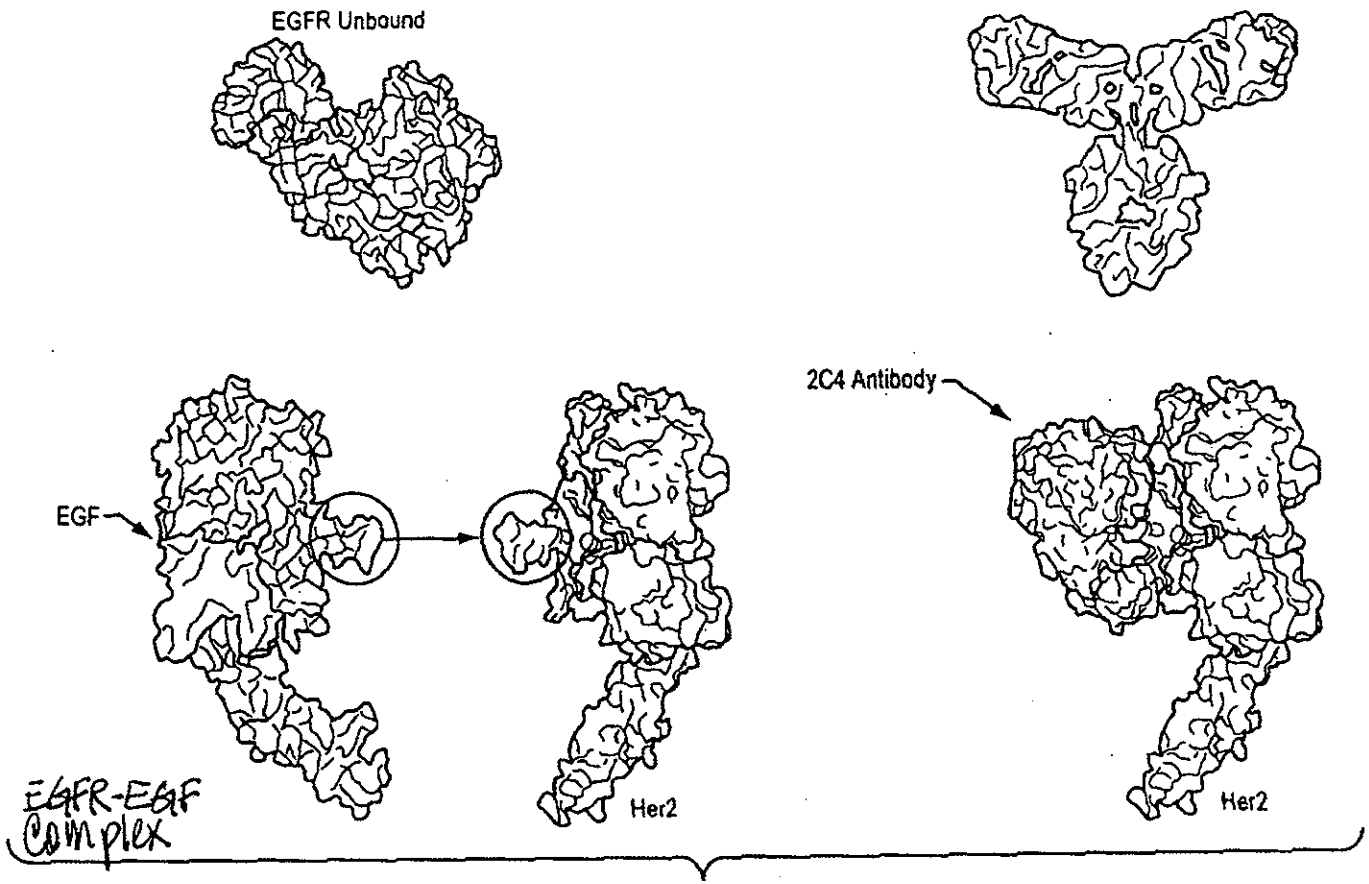


FIG. 4

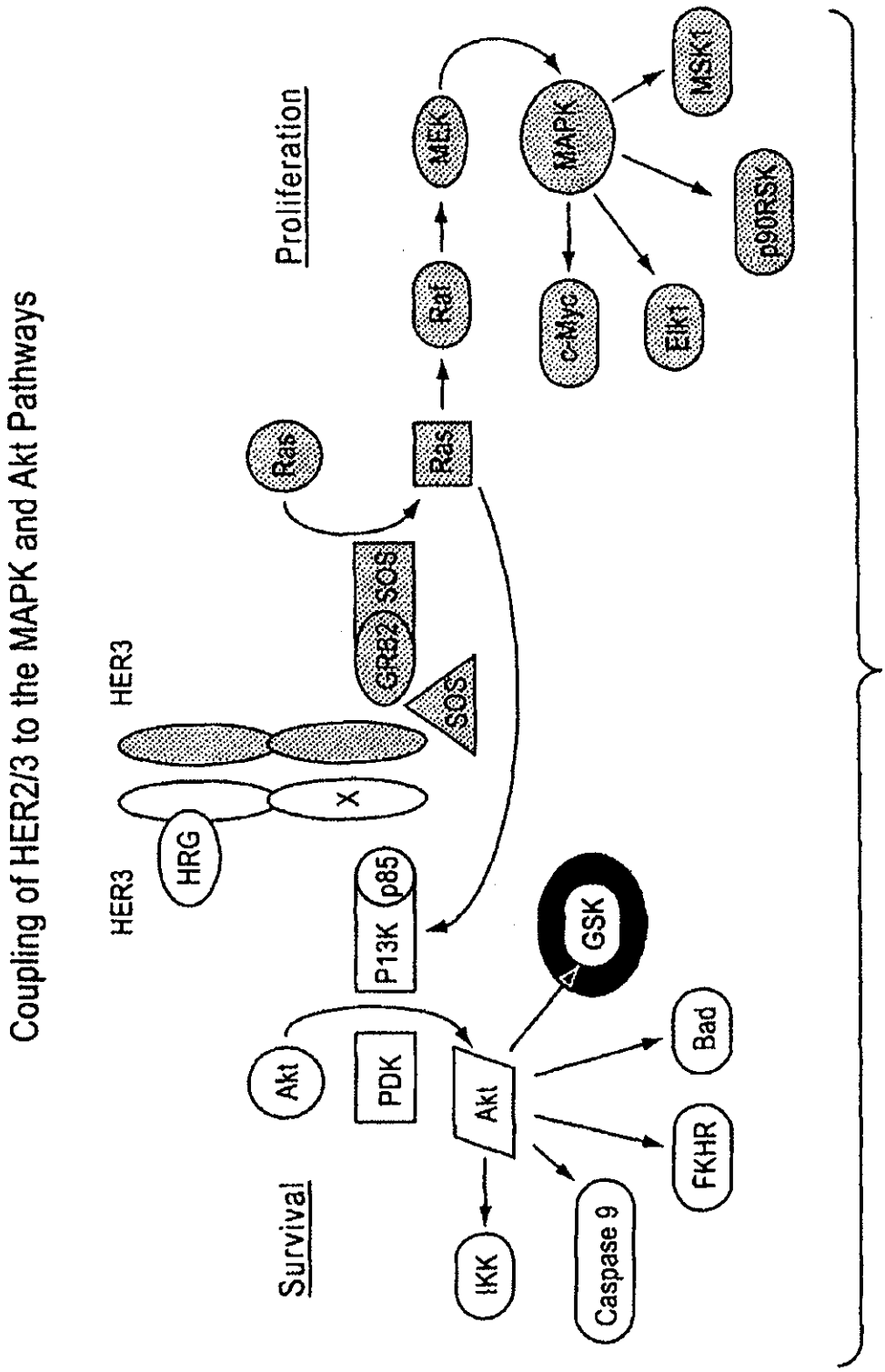

Coupling of HER2/3 to the MAPK and Akt Pathways
HER3
HER3
HRG
X
GRB2
SOS
SOS
Ras
Ras
Raf
MEK
MAPK
MSK1
p90RSK
c-Myc
Elk1
Proliferation
P13K
p85
GSK
Akt
PDK
Akt
Bad
FKHR
IKK
Caspase 9
Survival

FIG. 5

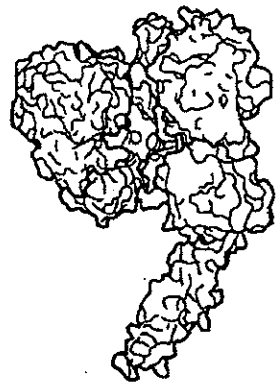
TRASTUZUMAB HERCEPTIN	PERTUZUMAB OMNITARG
	
• Binds in IV near JM • Protects against receptor shedding • Moderately affects receptor down-modulation • Slight effect on HER2's role as a coreceptor	• Binds in II at dimerization interface • Does not prevent receptor shedding • Moderately affects receptor down-modulation • Major effect on HER2's role as a coreceptor

FIG. 6

LIGHT CHAIN

```
1                               15                              30                              45
D I Q M T Q S P S S L S A S V G D R V T I T C R A S Q D V N T A V A W Y Q Q K P G K A P K

46                              60                              75                              90
L L I Y S A S F L Y S G V P S R F S G S R S G T D F T L T I S S L Q P E D F A T Y Y C Q Q

91                              105                             120                             135
H Y T T P P T F G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L

136                             150                             165                             180
L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K D S T Y S L S S T L T

181                             195                             210     214
L S K A D Y E K H K V Y A C E V T H Q G L S S P V T K S F N R G E C
```

FIG. 7A

HEAVY CHAIN

```
1                   15                  30                  45
E V Q L V E S G G G L V Q P G G S L R L S C A A S G F N I K D T Y I H W V R Q A P G K G L

46                  60                  75                  90
E W V A R I Y P T N G Y T R Y A D S V K G R F T I S A D T S K N T A Y L Q M N S L R A E D

91                  105                 120                 135
T A V Y Y C S R W G G D G F Y A M D Y W G Q G T L V T V S S A S T K G P S V F P L A P S S

136                 150                 165                 180
K S T S G G T A A L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S

181                 195                 210                 225
G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S C D K

226                 240                 255                 270
T H T C P P C P A P E L L G G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V S

271                 285                 300                 315
H E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D

316                 330                 345                 360
W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P S R E E

361                 375                 390                 405
M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q P E N N Y K T T P P V L D S D G

406                 420                 435                 449
S F F L Y S K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G
```

FIG. 7B

```
1                   15                  30                  45
VHSDIQMTQSPSSLSASVGDRVTITCKASQDVSIGVAWYQQKPGK

46                  60                  75                  90
APKLLIYSASYRYTGVPSRFSGSGSGTDFTLTISSLQPEDFATYY

91                  105                 120                 135
CQQYYIYPYTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV

136                 150                 165                 180
VCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSS

181                 195                 210         217
TLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
```

FIG. 8A

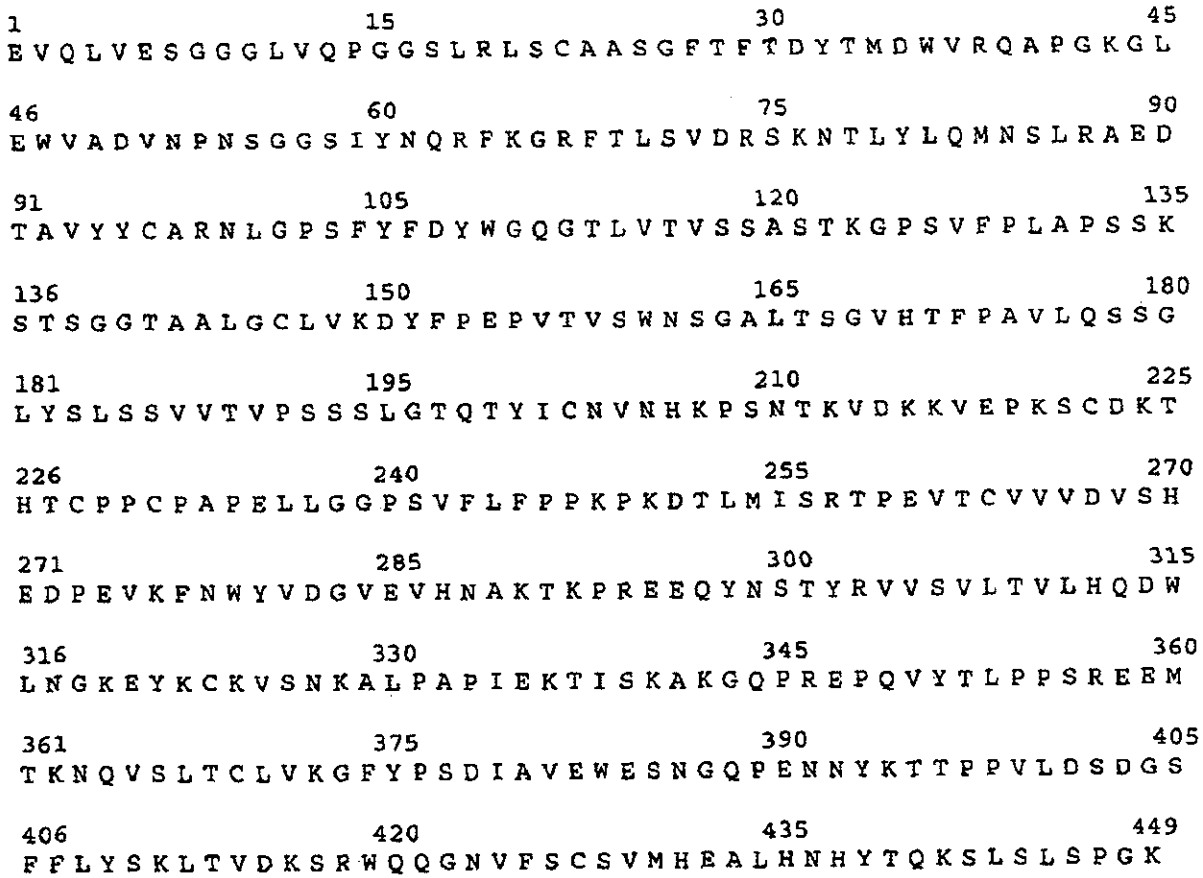

1 15 30 45
EVQLVESGGGLVQPGGSLRLSCAASGFTFTDYTMDWVRQAPGKGL
46 60 75 90
EWVADVNPNSGGSIYNQRFKGRFTLSVDRSKNTLYLQMNSLRAED
91 105 120 135
TAVYYCARNLGPSFYFDYWGQGTLVTVSSASTKGPSVFPLAPSSK
136 150 165 180
STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG
181 195 210 225
LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT
226 240 255 270
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
271 285 300 315
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
316 330 345 360
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEM
361 375 390 405
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGS
406 420 435 449
FFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 8B

FIG. 9

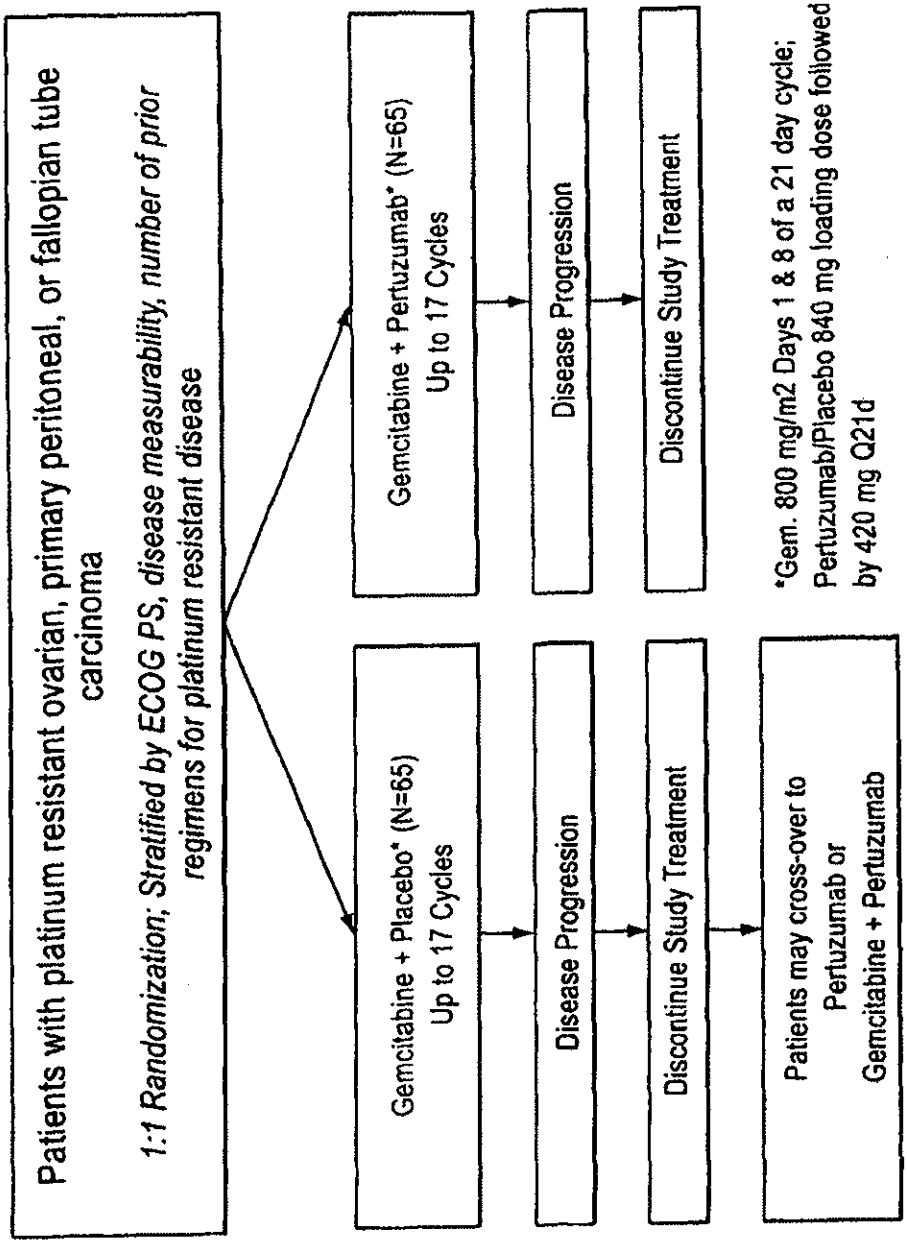

Patients with platinum resistant ovarian, primary peritoneal, or fallopian tube carcinoma
1:1 Randomization; Stratified by ECOG PS, disease measurability, number of prior regimens for platinum resistant disease
Gemcitabine + Placebo* (N=65)
Up to 17 Cycles
Gemcitabine + Pertuzumab* (N=65)
Up to 17 Cycles
Disease Progression
Disease Progression
Discontinue Study Treatment
Discontinue Study Treatment
Patients may cross-over to Pertuzumab or Gemcitabine + Pertuzumab
*Gem. 800 mg/m2 Days 1 & 8 of a 21 day cycle; Pertuzumab/Placebo 840 mg loading dose followed by 420 mg Q21d

FIG. 10A

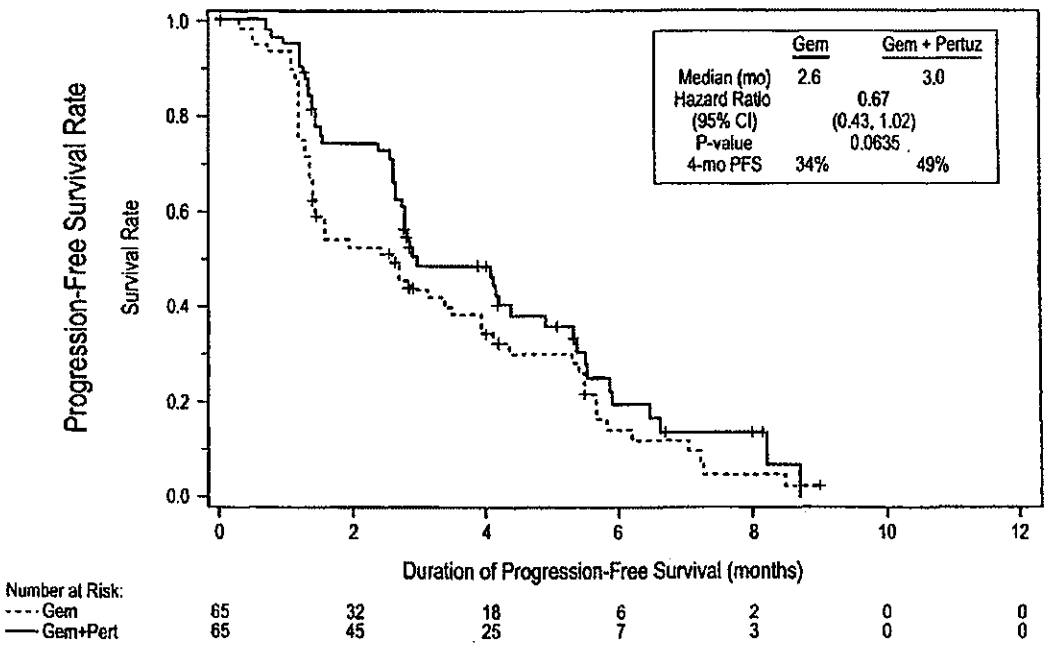

Progression-Free Survival Rate
Survival Rate
1.0
0.8
0.6
0.4
0.2
0.0
0
2
4
6
8
10
12
Duration of Progression-Free Survival (months)
Gem
Gem + Pertuz
Median (mo) 2.6 3.0
Hazard Ratio 0.67
(95% CI) (0.43, 1.02)
P-value 0.0635
4-mo PFS 34% 49%
Number at Risk:
Gem 65 32 18 6 2 0 0
Gem+Pert 65 45 25 7 3 0 0

FIG. 10B

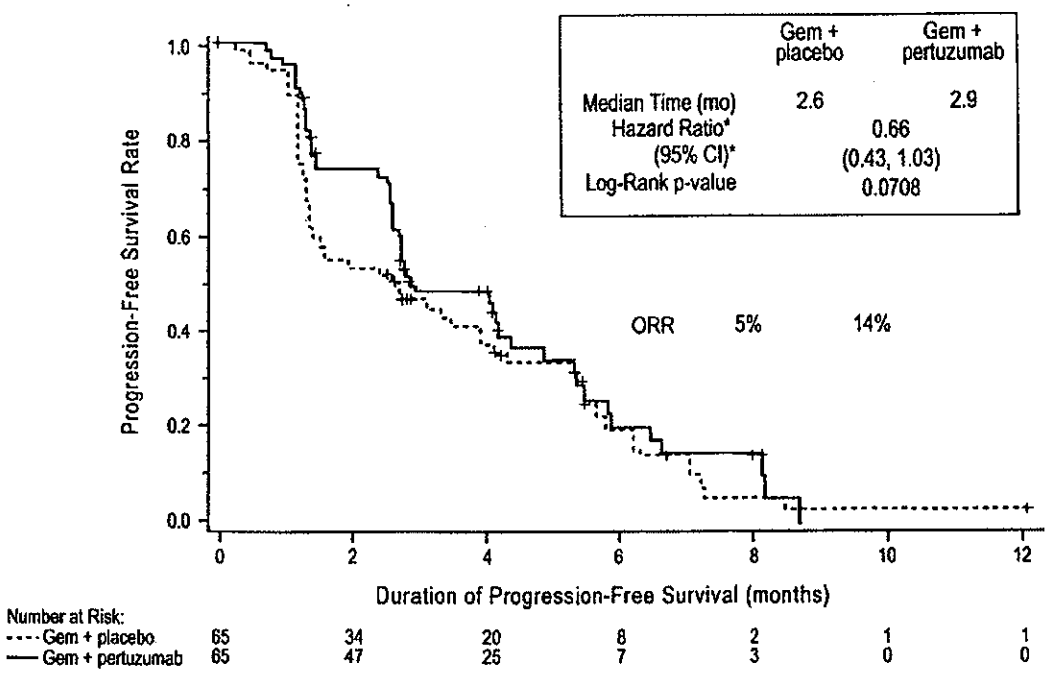
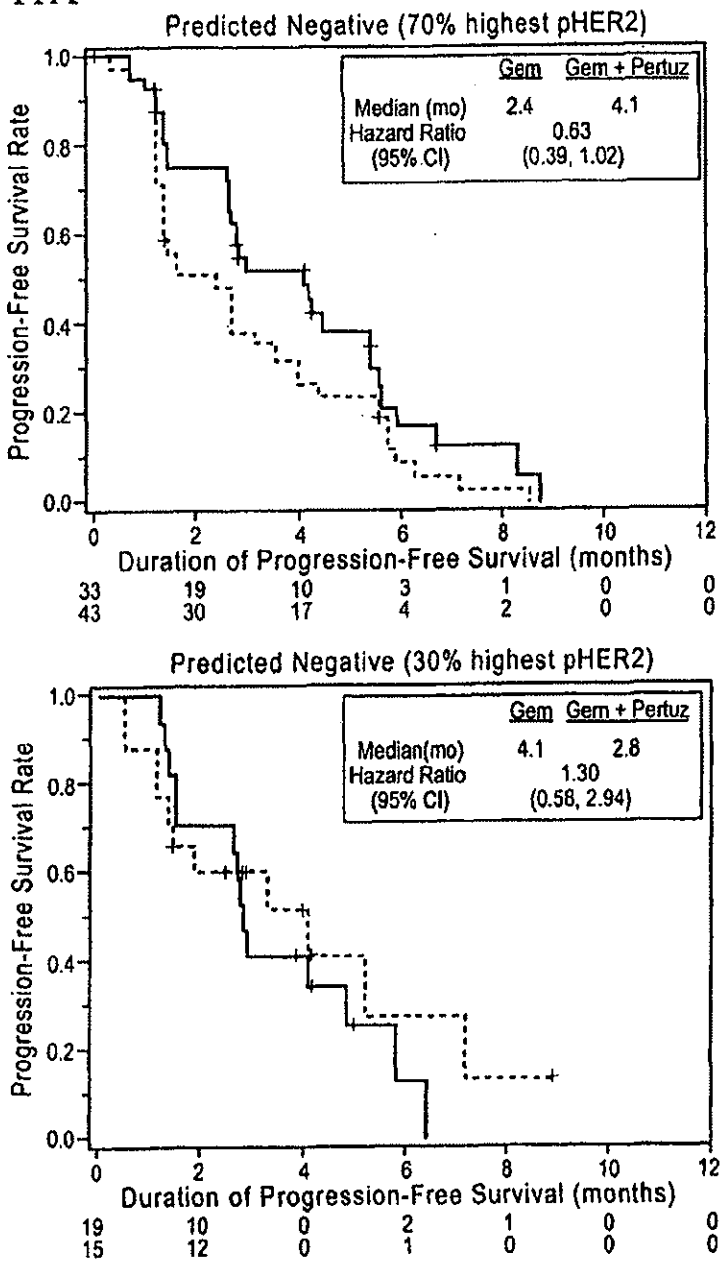
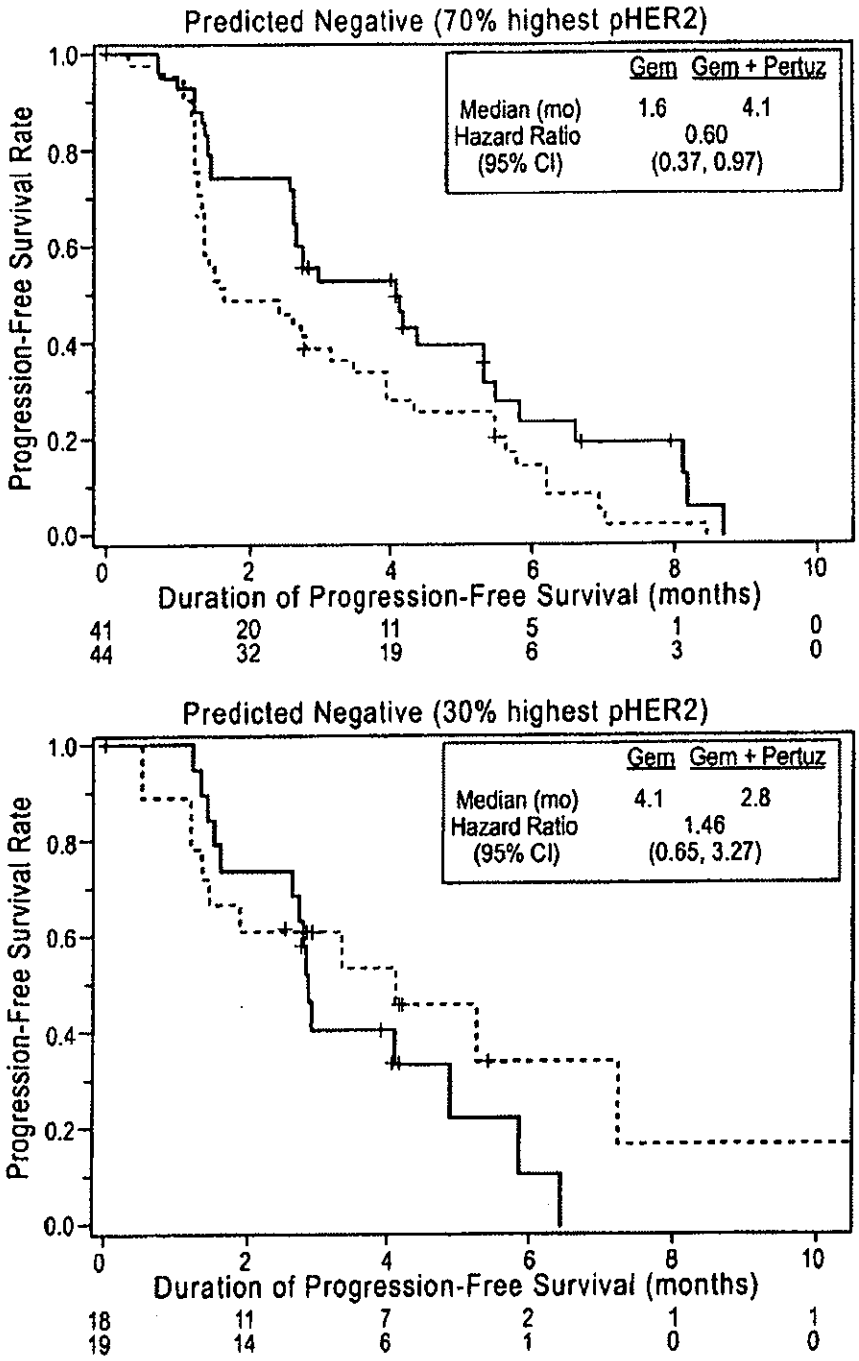

Gem + placebo
Gem + pertuzumab
Median Time (mo) 2.6 2.9
Hazard Ratio* 0.66
(95% CI)* (0.43, 1.03)
Log-Rank p-value 0.0708
ORR 5% 14%
Progression-Free Survival Rate
1.0
0.8
0.6
0.4
0.2
0.0
0
2
4
6
8
10
12
Duration of Progression-Free Survival (months)
Number at Risk:
---- Gem + placebo 65 34 20 8 2 1 1
—— Gem + pertuzumab 65 47 25 7 3 0 0

FIG. 11A



Note: Dx (+): the Amphi, Her2, Her3 sum score ≥ 70th percentile, Dx (-): Others

FIG. 11B



Note: Dx (+): the Amphi, Her2, Her3 sum score ≥ 70th percentile, Dx (-): Others

FIG. 12A

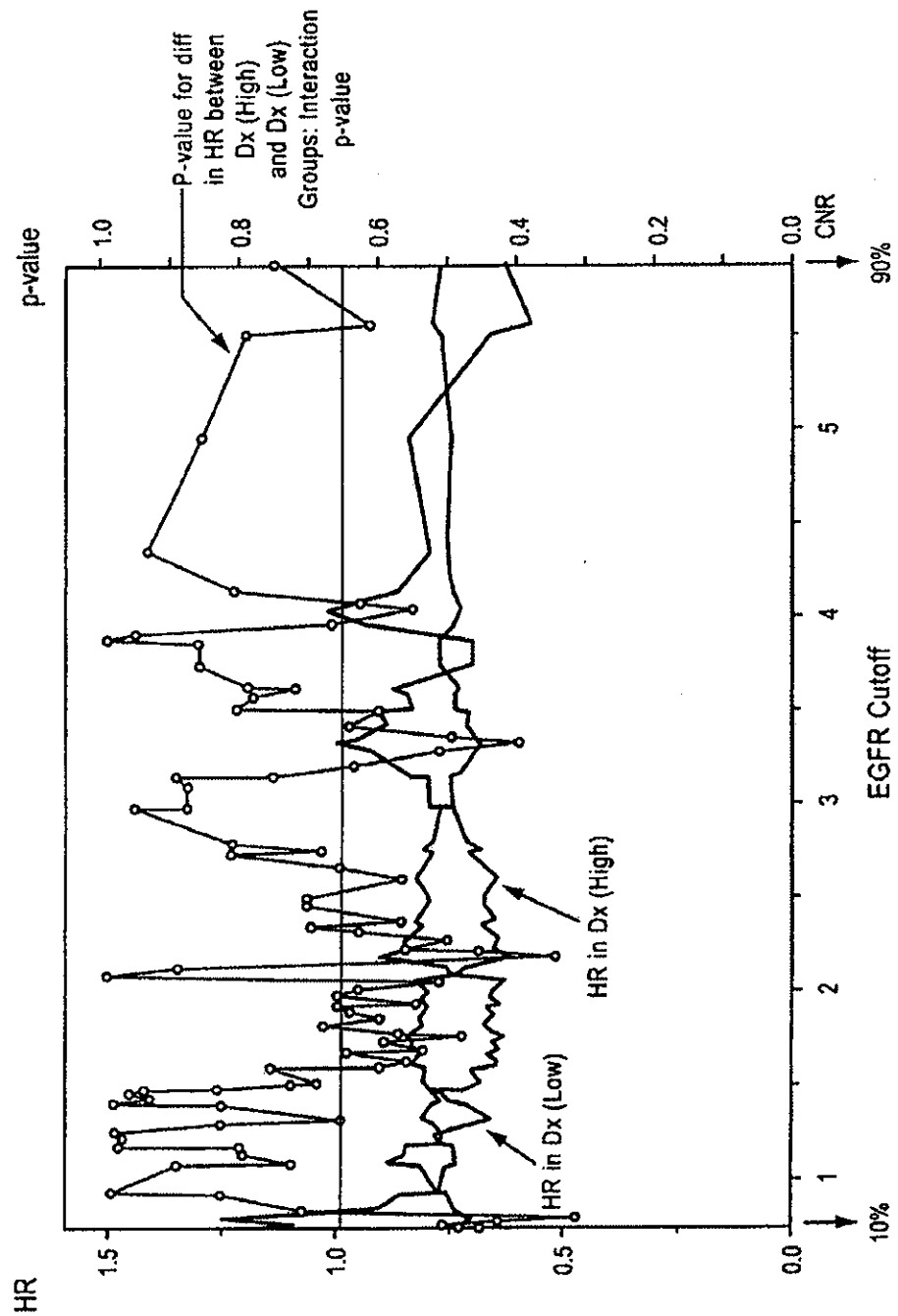

HR
p-value
1.5
1.0
0.5
0.0
1.0
0.8
0.6
0.4
0.2
0.0
P-value for diff in HR between Dx (High) and Dx (Low) Groups: Interaction p-value
HR in Dx (High)
HR in Dx (Low)
10%
1
2
3
4
5
90%
CNR
EGFR Cutoff
P-values were not adjusted for multiple comparisons

FIG. 12B

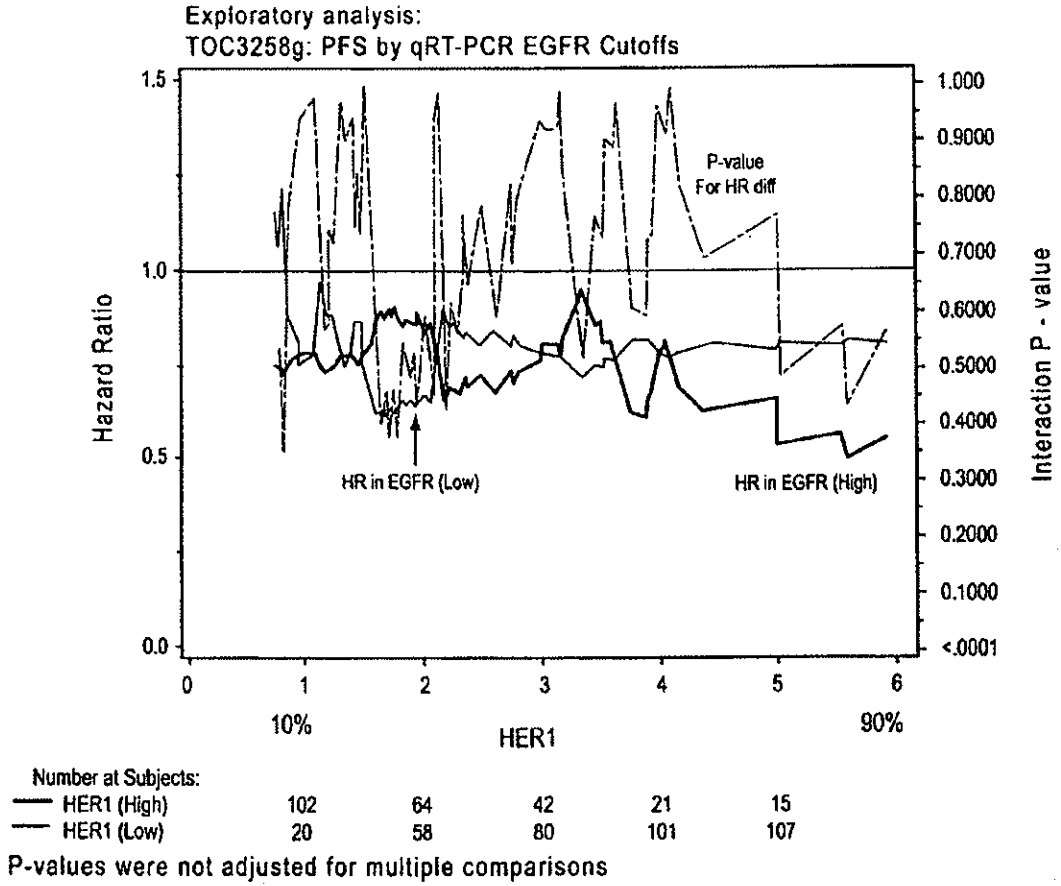

Exploratory analysis:
TOC3258g: PFS by qRT-PCR EGFR Cutoffs
Hazard Ratio
Interaction P - value
P-value
For HR diff
HR in EGFR (Low)
HR in EGFR (High)
1.5
1.0
0.5
0.0
1.000
0.9000
0.8000
0.7000
0.6000
0.5000
0.4000
0.3000
0.2000
0.1000
<.0001
0
1
2
3
4
5
6
10%
HER1
90%
Number at Subjects:
HER1 (High) 102 64 42 21 15
HER1 (Low) 20 58 80 101 107
P-values were not adjusted for multiple comparisons

FIG. 13A

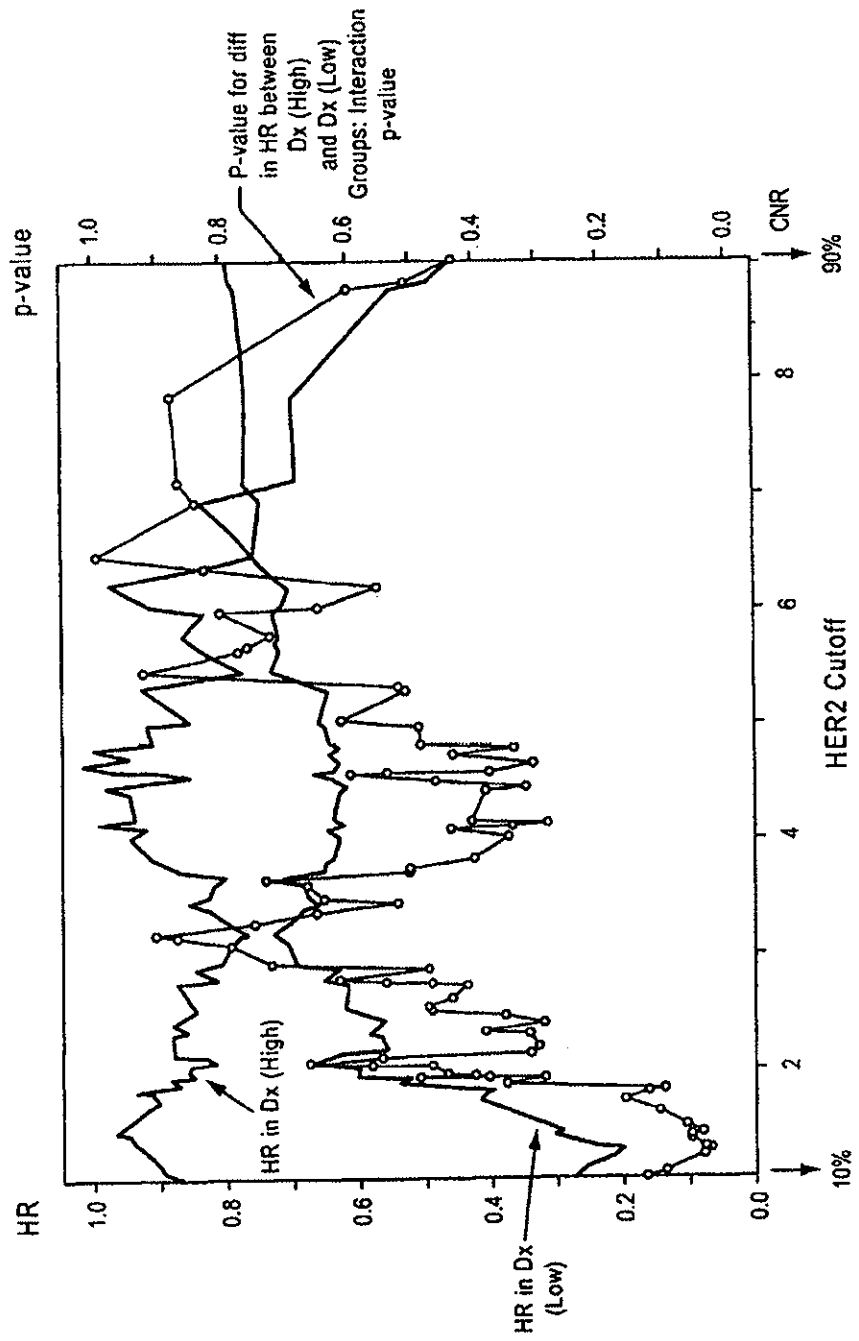
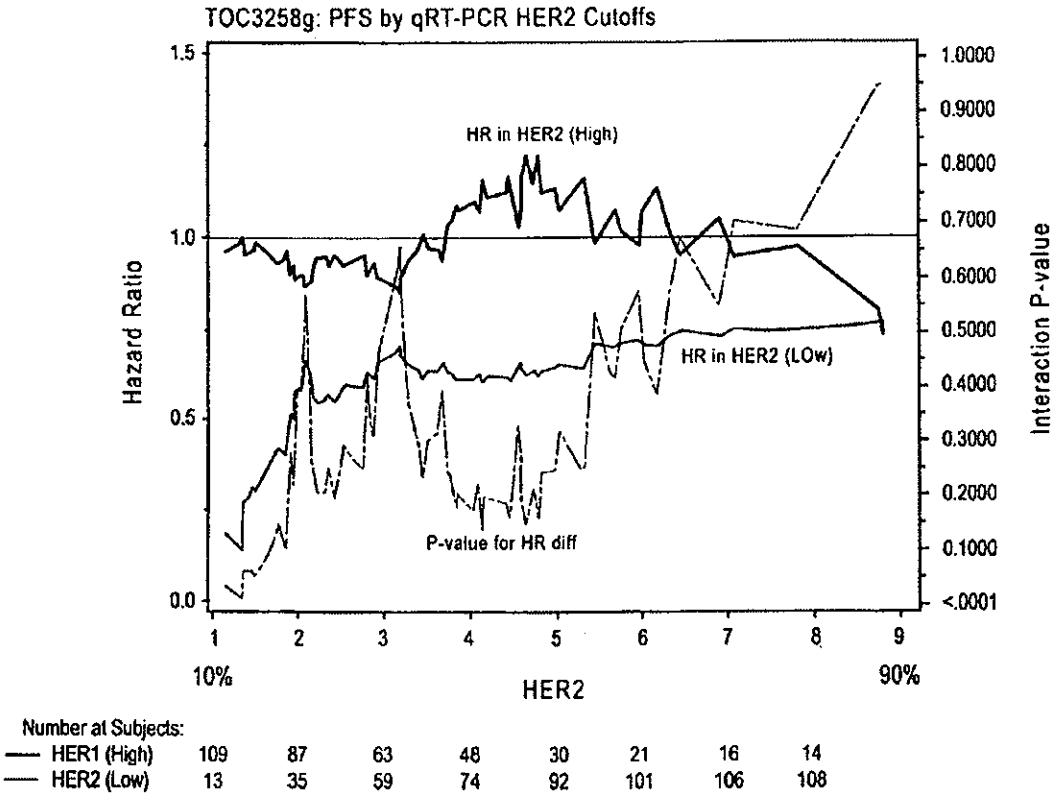
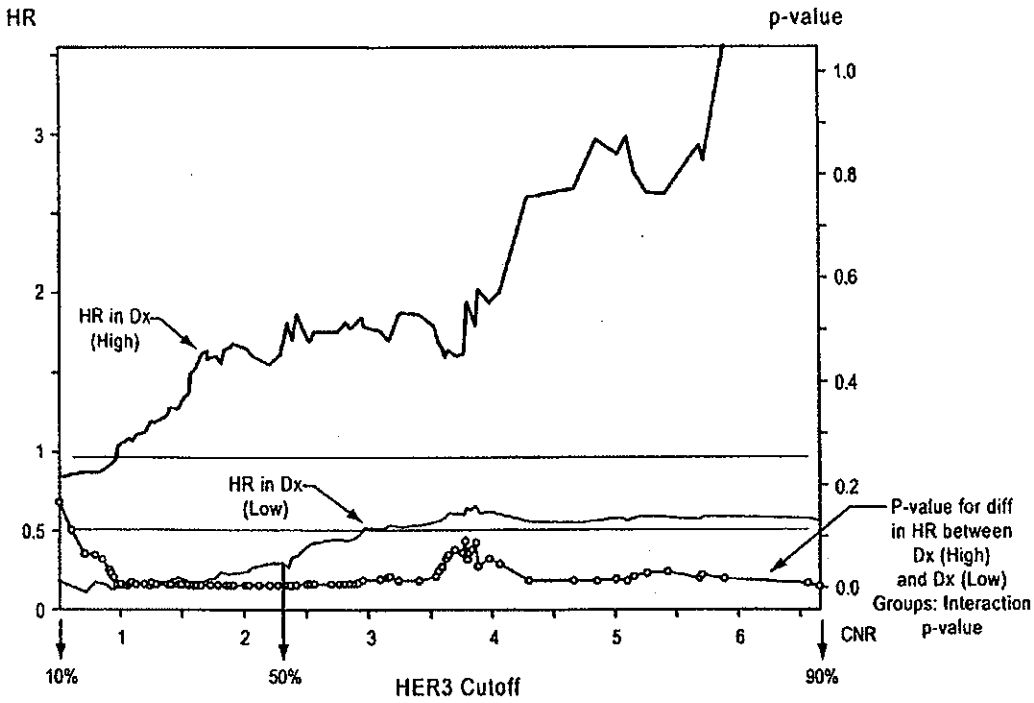

p-value
HR
1.0
0.8
0.6
0.4
0.2
0.0
P-value for diff in HR between Dx (High) and Dx (Low) Groups: Interaction p-value
HR in Dx (High)
HR in Dx (Low)
2
4
6
8
HER2 Cutoff
10%
90%
CNR
P-values were not adjusted for multiple comparisons

FIG. 13B



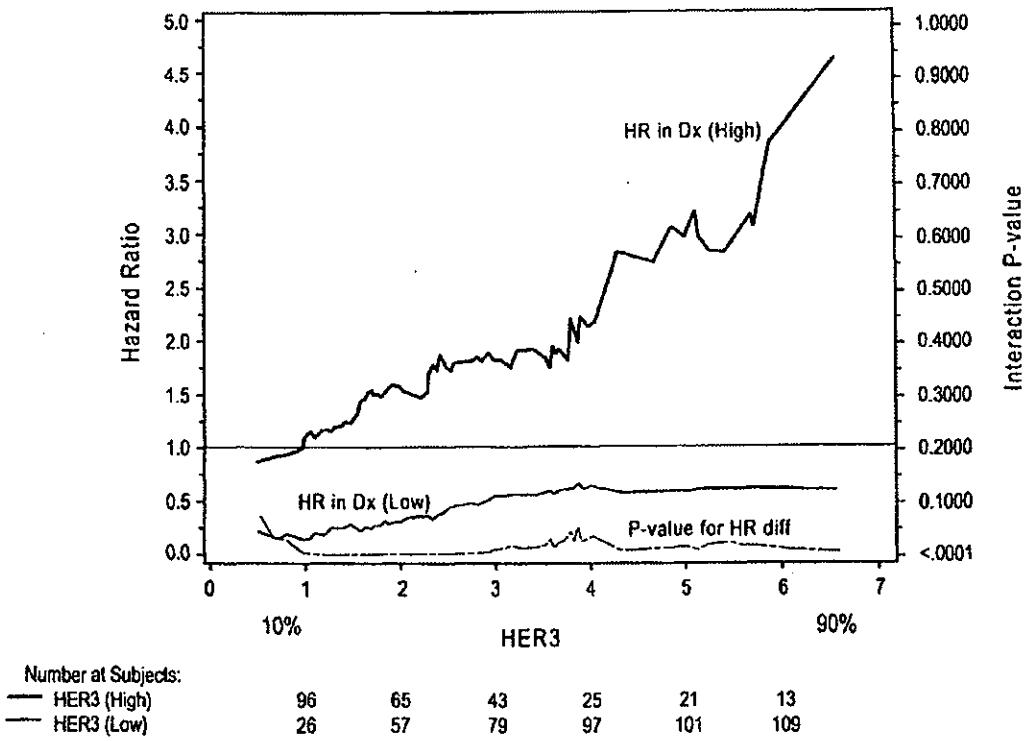
P-values were not adjusted for multiple comparisons

FIG. 14A



P-values were not adjusted for multiple comparisons

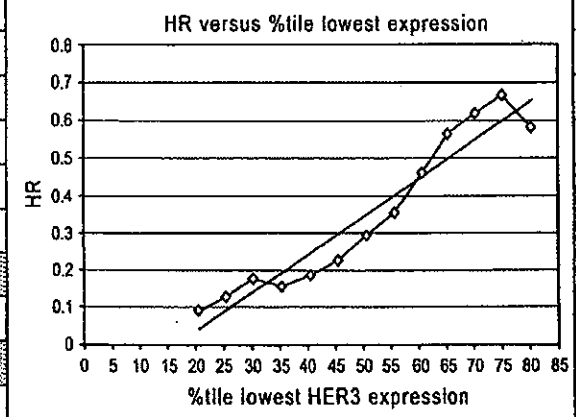
FIG. 14B



P-values were not adjusted for multiple comparisons

FIG. 15A

Cutoff		Low HER3 Expression			
%tile	Abs. Value	N	# Events	HR (96%CI)	Logrank P-value
20	0.99	20	16	0.09 (0.02, 0.42)	0.0002
25	1.19	28	21	0.13 (0.04, 0.45)	0.0002
30	1.4	35	28	0.18 (0.06, 0.52)	0.0004
35	1.57	41	32	0.16 (0.06, 0.43)	<.0001
40	1.71	47	36	0.19 (0.08, 0.47)	<.0001
45	1.88	53	40	0.23 (0.11, 0.50)	<.0001
50	2.28	59	46	0.30 (0.16, 0.58)	0.0002
55	2.41	65	52	0.36 (0.20, 0.65)	0.0005
60	2.6	71	57	0.47 (0.27, 0.81)	0.0063
65	3.14	77	63	0.57 (0.34 0.95)	0.0299
70	3.59	83	69	0.62 (0.38, 1.00)	0.0488
75	3.8	89	75	0.67 (0.42, 1.06)	0.0898
80	4.29	95	78	0.59 (0.37, 0.92)	0.0196



P-values were not adjusted for multiple comparisons

Cutoff Value		Low HER3 Expression			
%tile	Abs. Value	N	# Events	HR (96%CI)	Logrank P-value
25	1.19	30	23	0.13 (0.04, 0.41)	<.0001
30	1.39	36	29	0.22 (0.09, 0.56)	0.0005
35	1.56	42	33	0.20 (0.09, 0.48)	<.0001
40	1.70	48	38	0.22 (0.10, 0.50)	<.0001
45	1.87	54	42	0.29 (0.14, 0.58)	0.0002
50	2.24	61	48	0.34 (0.18, 0.63)	0.0004
55	2.38	66	53	0.36 (0.20, 0.65)	0.0005
60	2.75	73	59	0.48 (0.28, 0.84)	0.0080
65	3.08	79	65	0.56 (0.34, 0.94)	0.0255
70	3.56	85	71	0.62 (0.38, 1.00)	0.0459
75	3.77	91	76	0.65 (0.41, 1.03)	0.0650

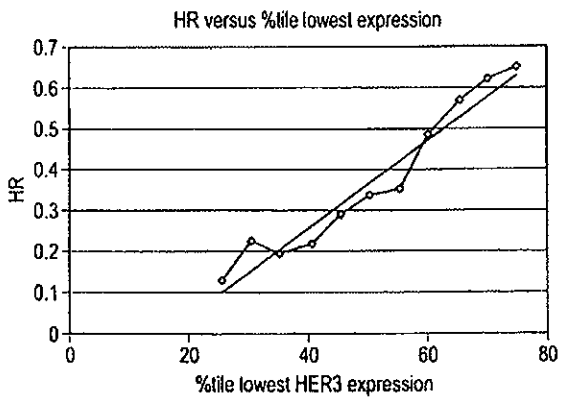


FIG. 15B

FIG. 16A

Cutoff		High HER3 Expression			
%tile	Abs. Value	N	# Events	HR (96%CI)	Logrank P-value
20	0.99	96	78	1.06 (0.67, 1.65)	0.8083
25	1.19	91	73	1.13 (0.71, 1.81)	0.5875
30	1.4	84	66	1.28 (0.77, 2.10)	0.3318
35	1.57	78	62	1.49 (0.89, 2.51)	0.1280
40	1.71	72	58	1.55 (0.90, 2.68)	0.1141
45	1.88	66	54	1.64 (0.94, 2.88)	0.0817
50	2.28	60	48	1.60 (0.89, 2.87)	0.1161
55	2.41	54	42	1.87 (0.97, 3.57)	0.0565
60	2.8	48	37	1.88 (0.92, 3.84)	0.0766
65	3.14	42	31	1.72 (0.78, 3.75)	0.1693
70	3.59	36	25	1.67 (0.72, 3.90)	0.2270
75	3.8	30	19	2.00 (0.71, 5.62)	0.1790
80	4.29	24	16	2.85 (0.89, 9.20)	0.0667

P-values were not adjusted for multiple comparisons

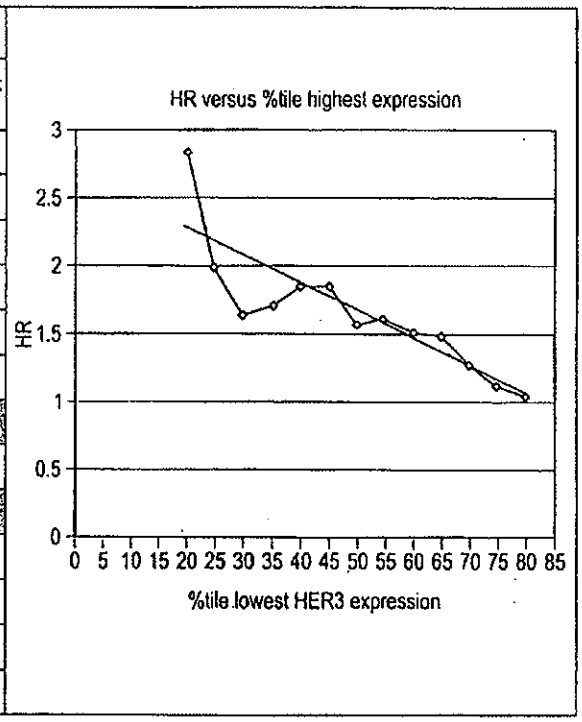


FIG. 16B

Cutoff Value		High HER3 Expression			
%tile	Abs. Value	N	# Events	HR (96%CI)	Logrank P-value
25	1.19	92	74	1.16 (0.73, 1.84)	0.5222
30	1.39	86	68	1.20 (0.74, 1.94)	0.4674
35	1.56	80	64	1.37 (0.83, 2.26)	0.2230
40	1.70	74	59	1.50 (0.88, 2.55)	0.1381
45	1.87	68	55	1.50 (0.87, 2.61)	0.1468
50	2.24	61	49	1.48 (0.83, 2.63)	0.1809
55	2.38	56	44	1.74 (0.93, 3.27)	0.0816
60	2.75	49	38	1.81 (0.90, 3.67)	0.0945
65	3.08	43	32	1.78 (0.82, 3.86)	0.1382
70	3.56	37	26	1.73 (0.75, 3.99)	0.1943
75	3.77	31	21	1.90 (0.73, 4.93)	0.1804

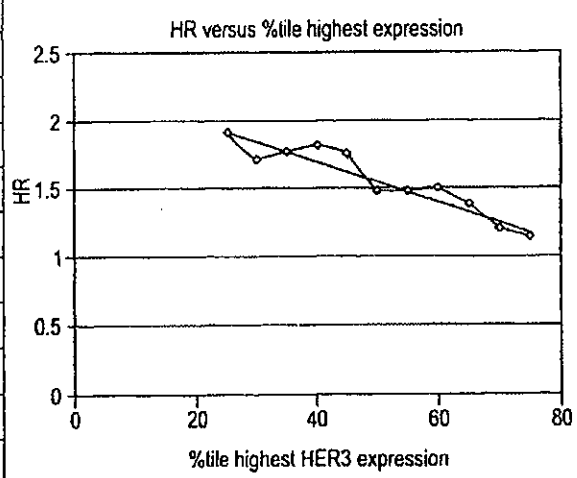


FIG. 17A

Cutoff		High HER3 Expression				Low HER3 Expression			
%tile	Abs. Value	N	# Events	HR (95%CI)	Logrank P-value	N	# Events	HR (95%CI)	Logrank P-value
20	0.99	96	78	1.06 (0.67, 1.65)	0.8083	23	16	0.09 (0.02, 0.42)	0.0002
KM	1.19	91	73	1.13 (0.71, 1.81)	0.5875	28	21	0.13 (0.04, 0.45)	0.0002
30	1.4	84	66	1.28 (0.77, 2.10)	0.3318	35	28	0.18 (0.06, 0.52)	0.0004
35	1.57	78	62	1.49 (0.89, 2.51)	0.1280	41	32	0.16 (0.06, 0.43)	<.0001
40	1.71	72	58	1.55 (0.90, 2.68)	0.1141	47	36	0.19 (0.08, 0.47)	<.0001
45	1.88	66	54	1.64 (0.94, 2.88)	0.0817	53	40	0.23 (0.11, 0.50)	<.0001
KM	2.28	60	48	1.60 (0.89, 2.87)	0.1161	59	46	0.30 (0.16, 0.58)	0.0002
55	2.41	54	42	1.87 (0.97, 3.57)	0.0565	65	52	0.36 (0.20, 0.65)	0.0005
60	2.8	48	37	1.88 (0.92, 3.84)	0.0766	71	57	0.47 (0.27,0.81)	0.0060
65	3.14	42	31	1.72 (0.78, 3.75)	0.1693	77	63	0.57 (0.34, 0.95)	0.0299
70	3.59	36	25	1.67 (0.72, 3.90)	0.2270	83	69	0.62 (0.38, 1.00)	0.0488
75	3.8	30	19	2.00 (0.71, 5.62)	0.1790	89	75	0.67 (0.42, 1.06)	0.0898
80	4.29	24	16	2.85 (0.89, 9.20)	0.0667	95	78	0.59 (0.37, 0.92)	0.0196

FIG. 17B

Cutoff Value		High HER3 Expression				Low HER3 Expression			
%tile	Abs. Value	N	# Events	HR (95%CI)	Logrank P-value	N	# Events	HR (95%CI)	Logrank P-value
KM	1.19	92	74	1.16 (0.73, 1.84)	0.5222	30	23	0.13 (0.04, 0.41)	<.0001
30	1.39	86	68	1.20 (0.74, 1.94)	0.4674	36	29	0.22 (0.09, 0.56)	0.0005
35	1.56	80	64	1.37 (0.83, 2.26)	0.2230	42	33	0.20 (0.09, 0.48)	<.0001
40	1.70	74	59	1.50 (0.88, 2.55)	0.1381	48	38	0.22 (0.10, 0.50)	<.0001
45	1.87	68	55	1.50 (0.87, 2.61)	0.1468	54	42	0.29 (0.14, 0.58)	0.0002
KM	2.24	61	49	1.48 (0.83, 2.63)	0.1809	61	48	0.34 (0.18, 0.63)	0.0004
55	2.38	56	44	1.74 (0.93, 3.27)	0.0816	66	53	0.36 (0.20, 0.65)	0.0005
60	2.75	49	38	1.81 (0.90, 3.67)	0.0945	73	59	0.48 (0.28, 0.84)	0.0080
65	3.08	43	32	1.78 (0.82, 3.86)	0.1382	79	65	0.56 (0.34, 0.94)	0.0255
70	3.56	37	26	1.73 (0.75, 3.99)	0.1943	85	71	0.62 (0.38, 1.00)	0.0459
75	3.77	31	21	1.90 (0.73, 4.93)	0.1804	91	76	0.65 (0.41, 1.03)	0.0650

FIG. 18A

qrt-PCR HER3	n	# of Events	Treatment HR (95% CI)	Log-rank P-value
0 - < 25th percentile	28	21	0.13 (0.04, 0.45)	0.0002
25 - < 50th percentile	31	25	0.42 (0.17, 1.00)	0.0465
50 - < 75th percentile	30	29	2.11 (0.94, 4.75)	0.0631
75 - 100th percentile	30	19	2.00 (0.71, 5.62)	0.1790

P-values were not adjusted for multiple comparisons

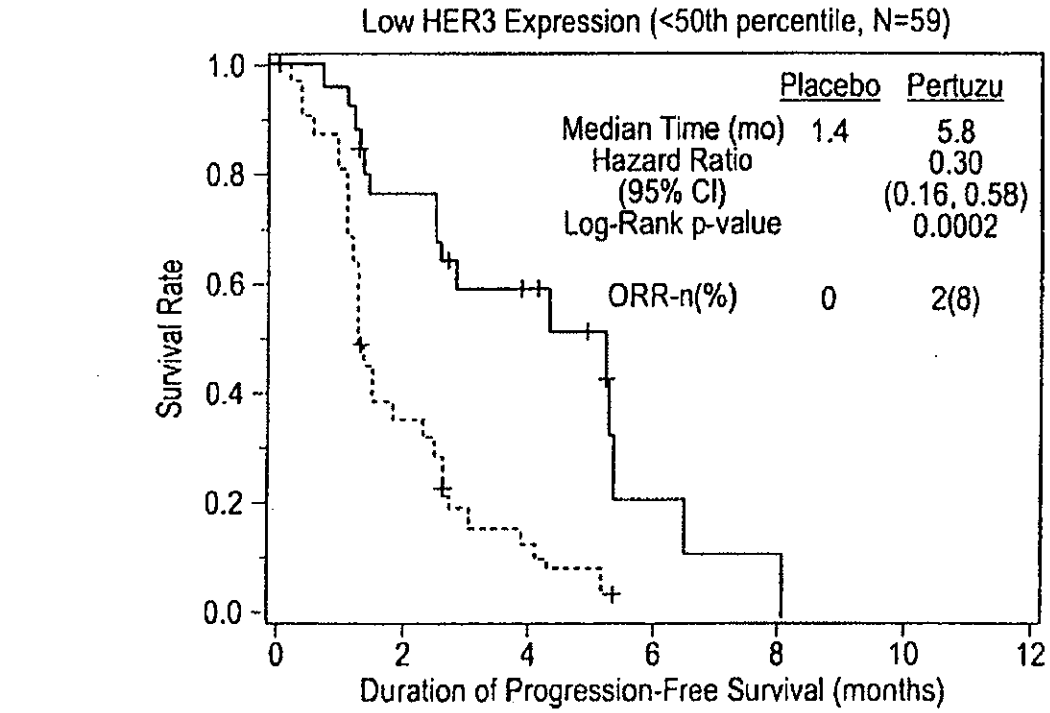
FIG. 18B

Progression-Free Survival (PFS) Analysis
by HER3 Expression Quartiles

qRT-PCR HER3	N	# of Events	Treatment HR (95% CI)	Log-rank P-value
0 - < 25th percentile	30	23	0.13 (0.04, 0.41)	<.0001
25 - < 50th percentile	31	25	0.66 (0.29, 1.48)	0.3181
50 - < 75th percentile	30	28	1.59 (0.73, 3.44)	0.2318
75 - 100th percentile	31	21	1.90 (0.73, 4.93)	0.1804

FIG. 19A (Part 1)

All patients	Gem	Gem + Pertuz
Median (mo)	2.6	3.0
Hazard Ratio*	0.67	
(95% CI)	(0.43, 1.02)	
P-value*	0.0635	
ORR-n(%)	3 (5)	5 (8)

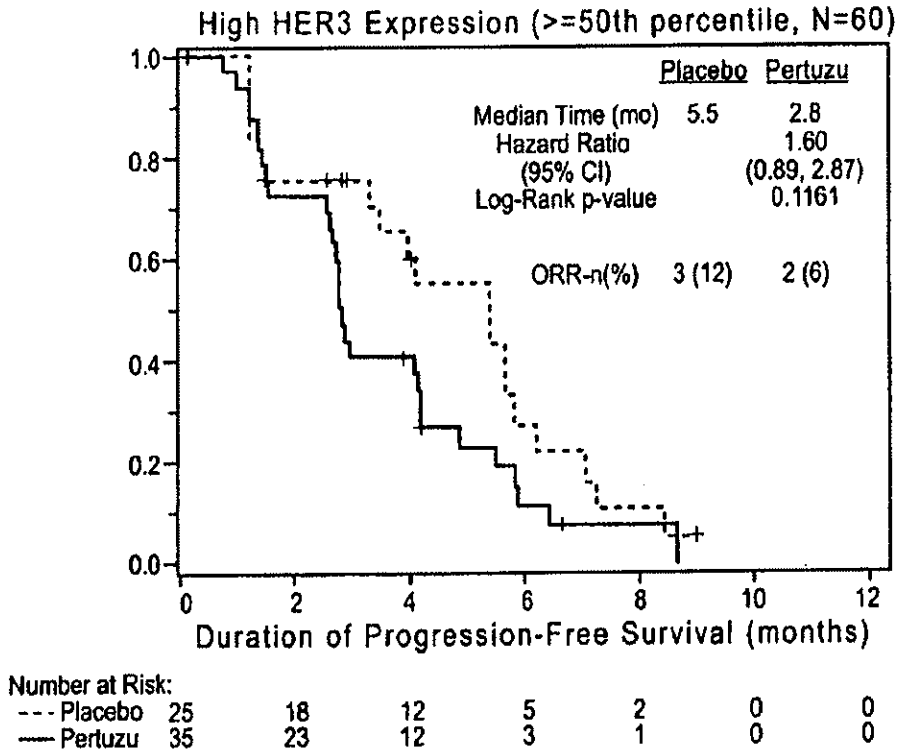


Number at Risk:

------ Placebo	33	11	4	0	0	0	0
—— Pertuzu	26	19	11	2	1	0	0

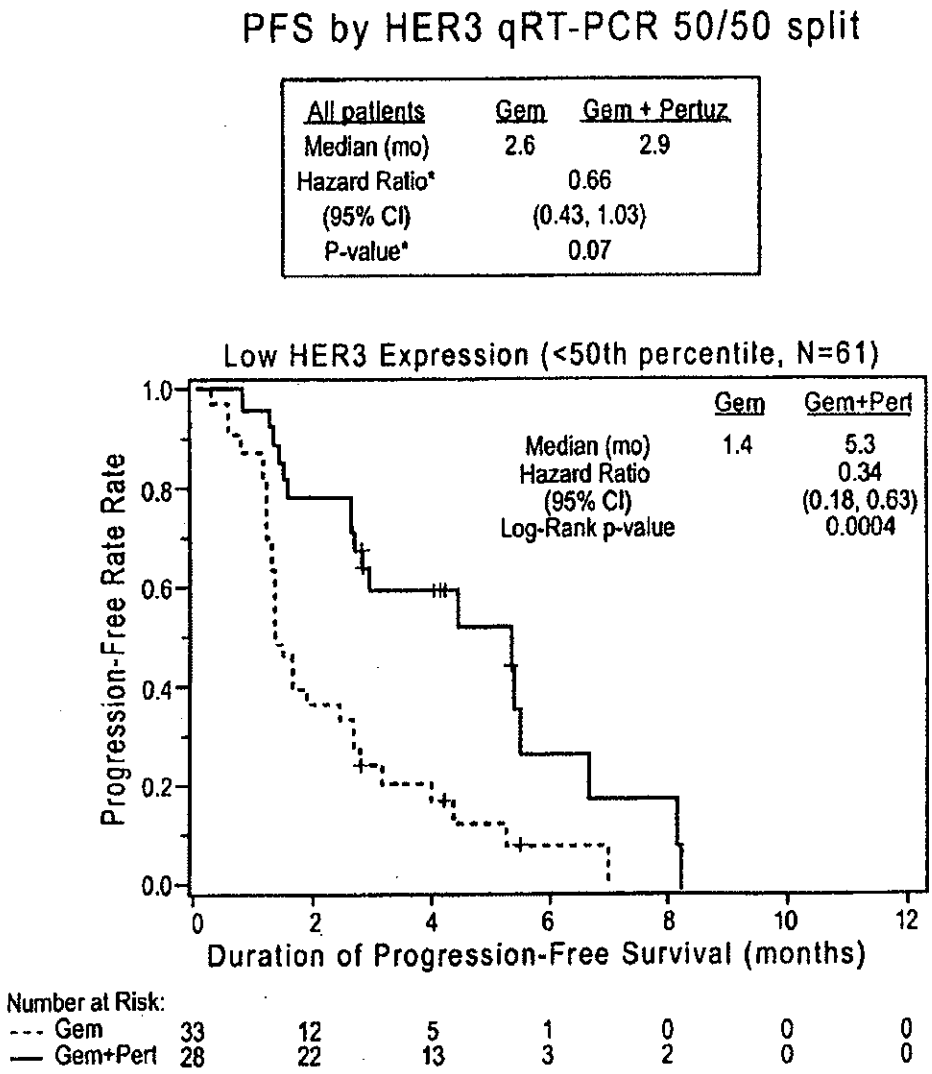
P-value for the difference.....

FIG. 19A (Part 2)



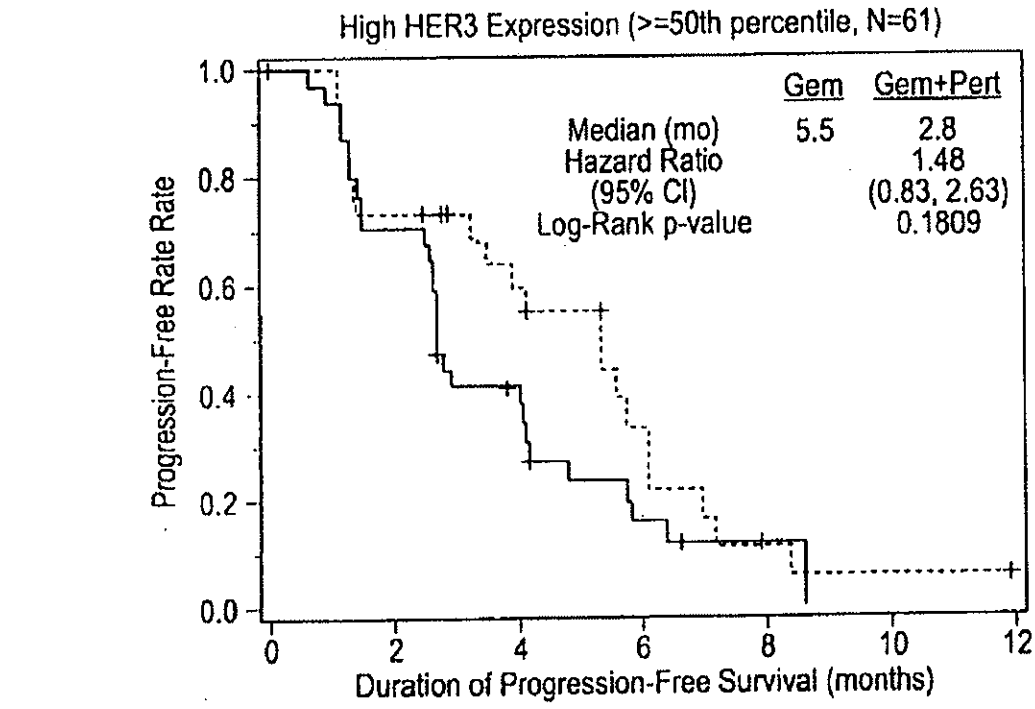
P-value for the difference in HR between two dx subgroups is 0.0001
Note: 50th percentile = 2.28 CNR

FIG. 19B (Part 1)



P-value for the difference in HR between two dx subgroups is 0.0005
Note: 50th percentile = 2.24 CNR

FIG. 19B (Part 2)



Number at Risk:

------ Gem	26	19	13	6	2	1	1
—— Gem+Pert	35	24	12	4	1	0	0

P-value for the difference.....

FIG. 20A

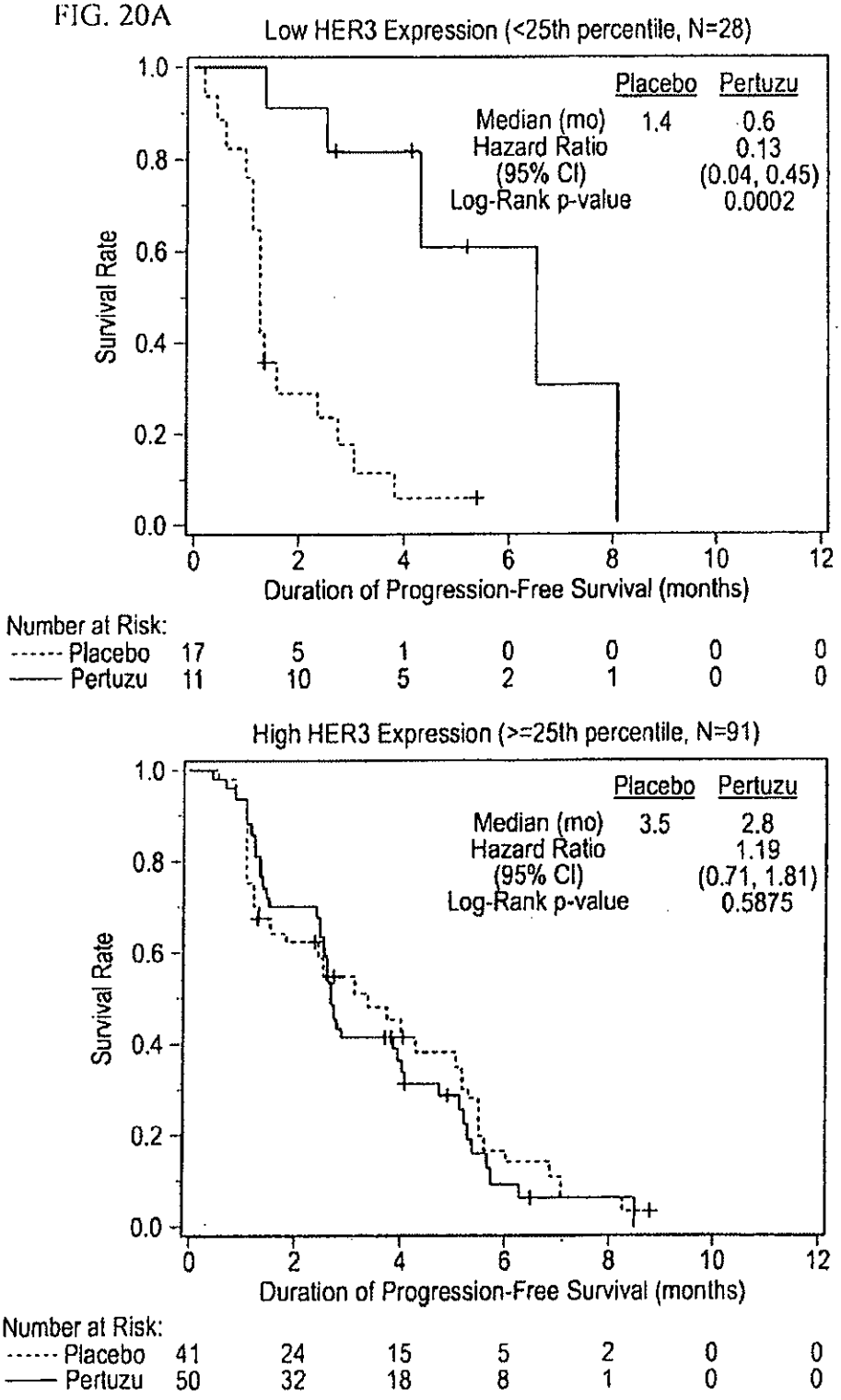
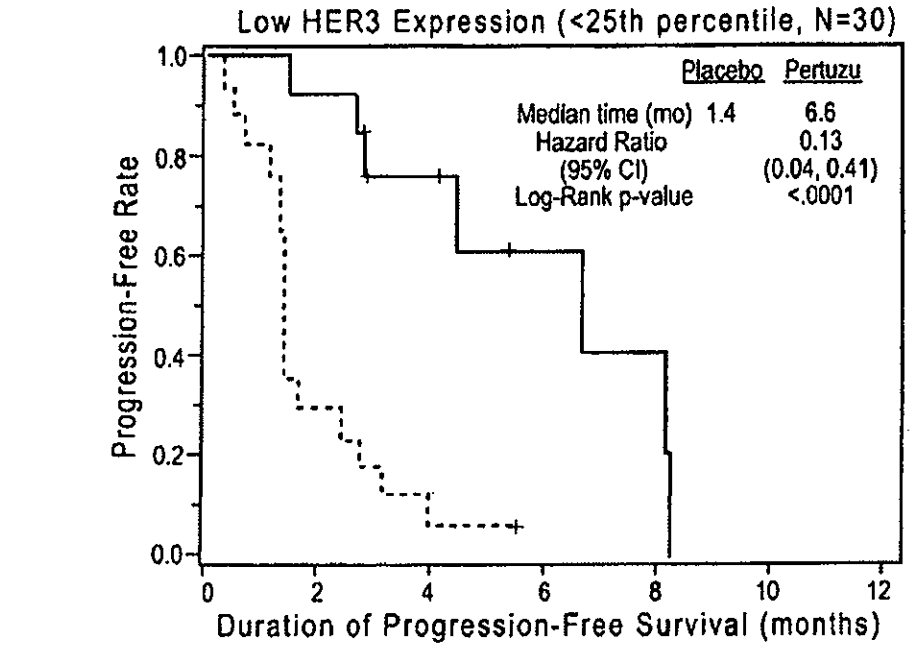

Low HER3 Expression (<25th percentile, N=28)
Placebo Pertuzu
Median (mo) 1.4 0.6
Hazard Ratio 0.13
(95% CI) (0.04, 0.45)
Log-Rank p-value 0.0002
Survival Rate
1.0
0.8
0.6
0.4
0.2
0.0
0 2 4 6 8 10 12
Duration of Progression-Free Survival (months)
Number at Risk:
------ Placebo 17 5 1 0 0 0 0
—— Pertuzu 11 10 5 2 1 0 0
High HER3 Expression (>=25th percentile, N=91)
Placebo Pertuzu
Median (mo) 3.5 2.8
Hazard Ratio 1.19
(95% CI) (0.71, 1.81)
Log-Rank p-value 0.5875
Survival Rate
1.0
0.8
0.6
0.4
0.2
0.0
0 2 4 6 8 10 12
Duration of Progression-Free Survival (months)
Number at Risk:
------ Placebo 41 24 15 5 2 0 0
—— Pertuzu 50 32 18 8 1 0 0

FIG. 20B (Part 1)

All patients	Gem	Gem + Pertuz
Median (mo)	2.6	2.9
Hazard Ratio*	0.66	
(95% CI)	(0.43, 1.03)	
P-value*	0.07	

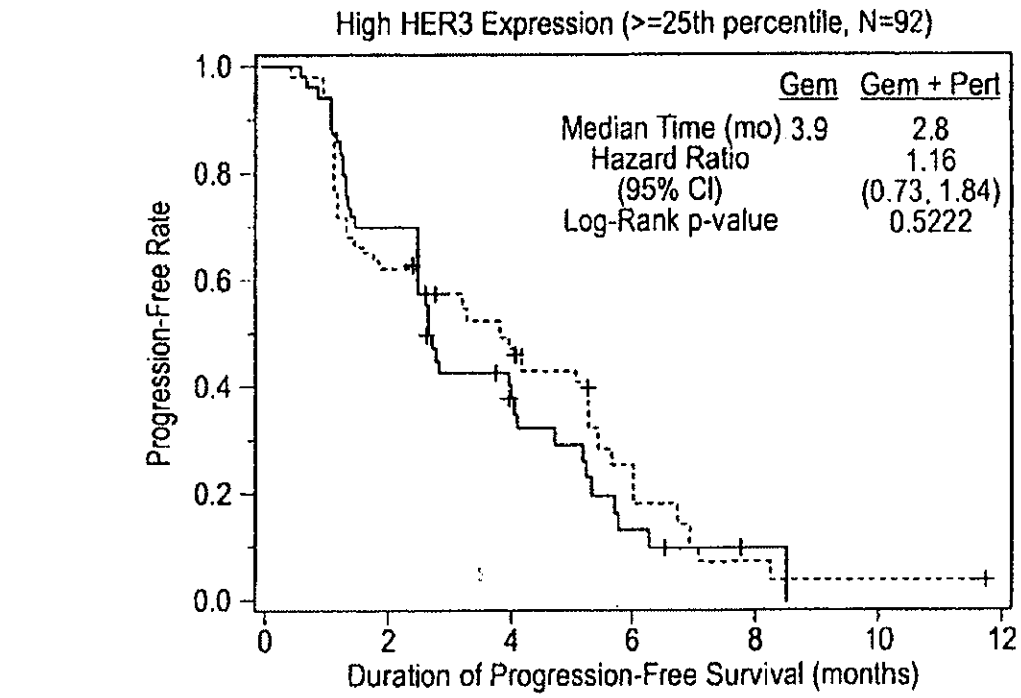


Number at Risk:

--- Gem	17	5	1	0	0	0	0
— Gem+ Pert	13	12	7	3	2	0	0

P-value for the difference in HR between two dx subgroups is 0.0003
Note: 25th percentile = 1.19 CNR

FIG. 20B (Part 2)



Number at Risk:

------ Gem	42	26	17	7	2	1	1
—— Gem + Pert	50	34	18	4	1	0	0

P-value for the difference.....

FIG. 21A

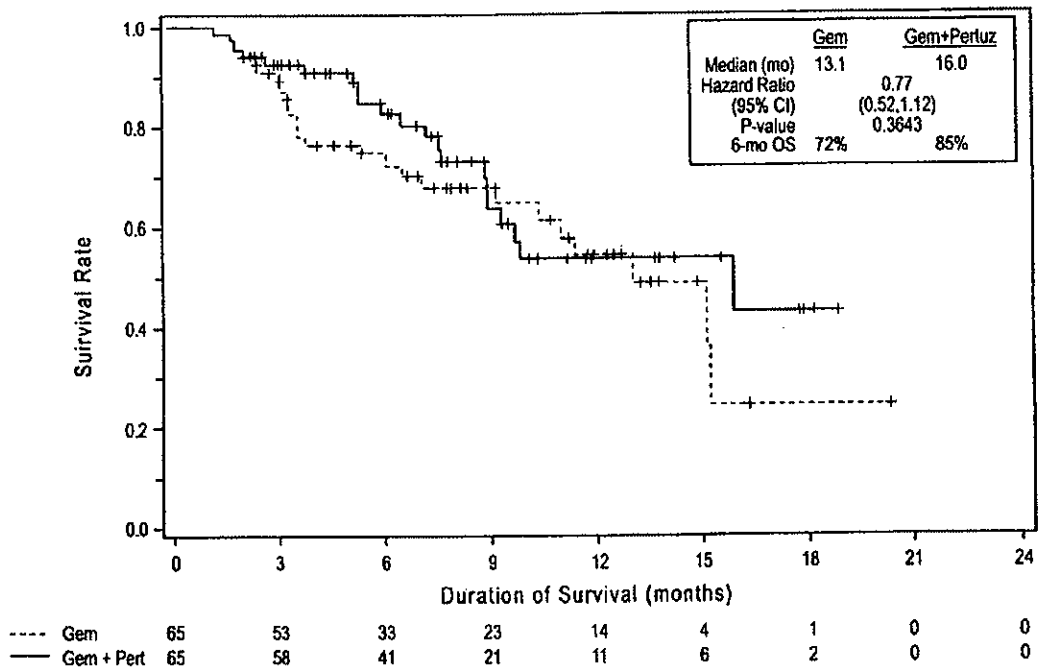
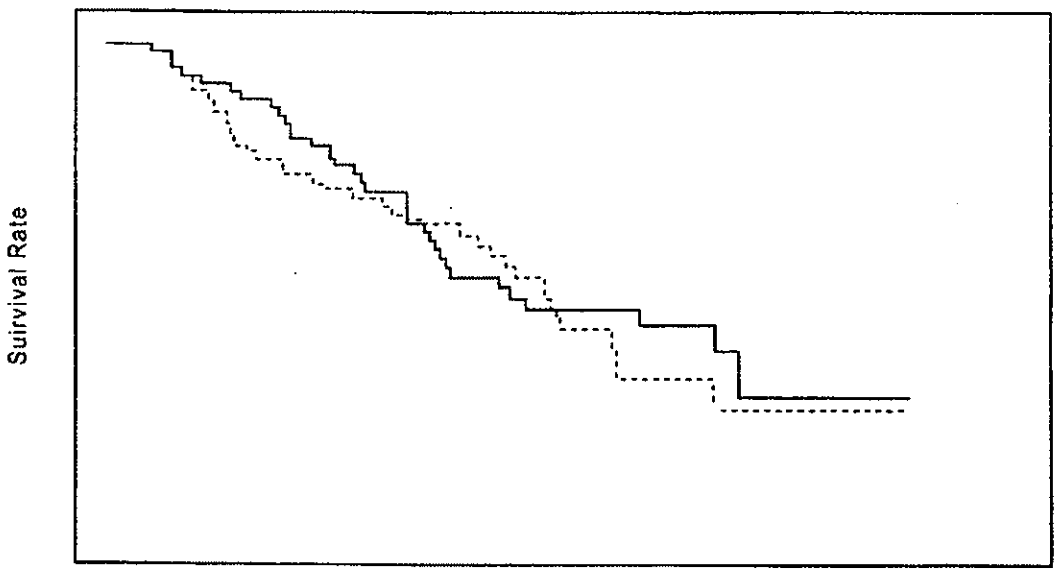

Gem
Gem+Pertuz
Median (mo) 13.1 16.0
Hazard Ratio 0.77
(95% CI) (0.52,1.12)
P-value 0.3643
6-mo OS 72% 85%
Survival Rate
1.0
0.8
0.6
0.4
0.2
0.0
0 3 6 9 12 15 18 21 24
Duration of Survival (months)
Gem 65 53 33 23 14 4 1 0 0
Gem + Pert 65 58 41 21 11 6 2 0 0

FIG. 21B

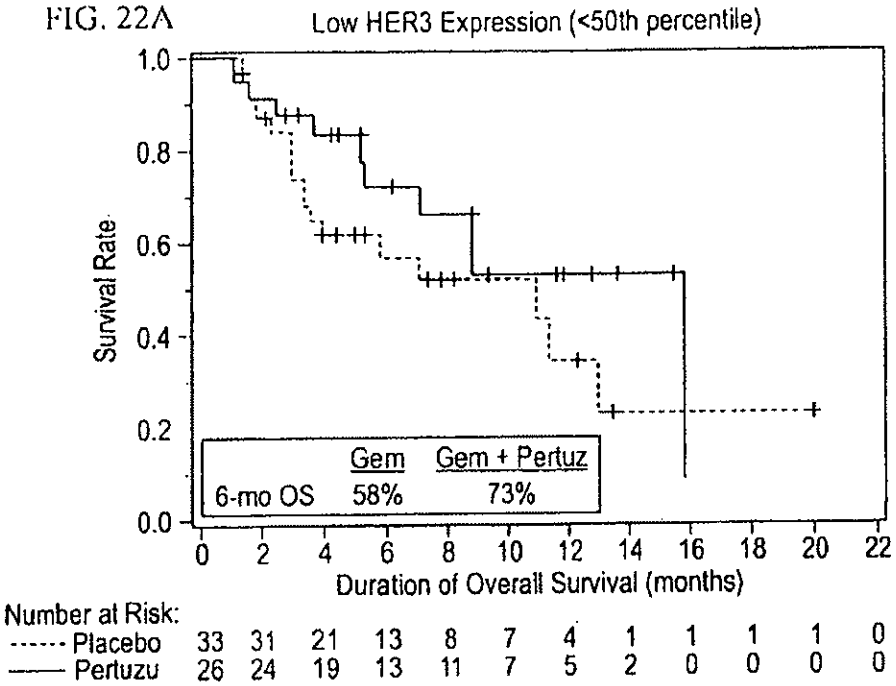
Preliminary Overall Survival

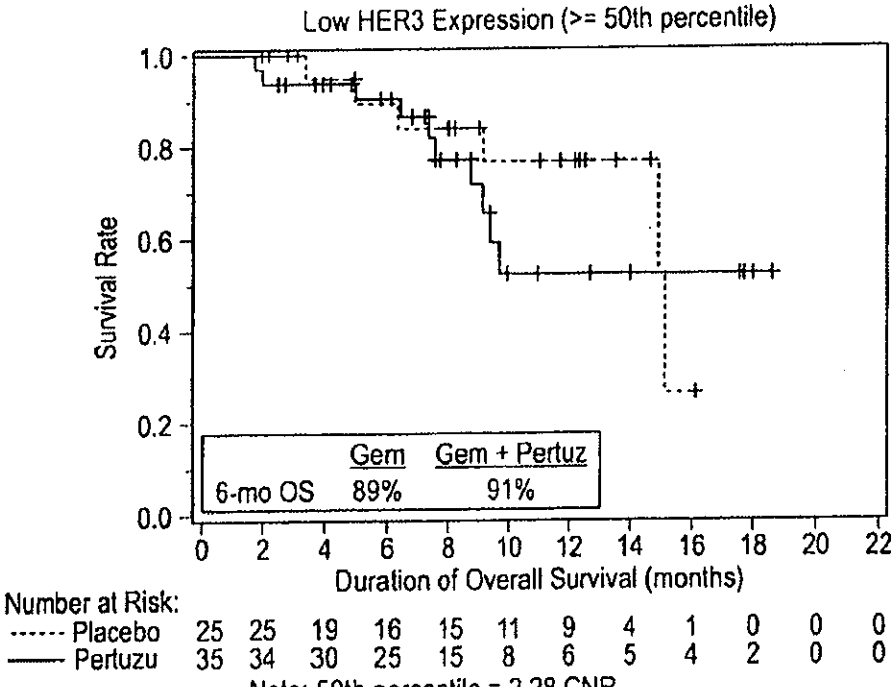
(71 deaths as of April 20, 2007



*Estimated using stratified Cox model and stratified log-rank test by randomization stratification factors (ECOG PS, number of prior regimens for platinum-resistant disease, and disease measurability)

FIG. 22A





Note: 50th percentile = 2.28 CNR

All 130 patients	Gem	Gem+Pertuz
6-mo OS	72%	85%

FIG. 22B

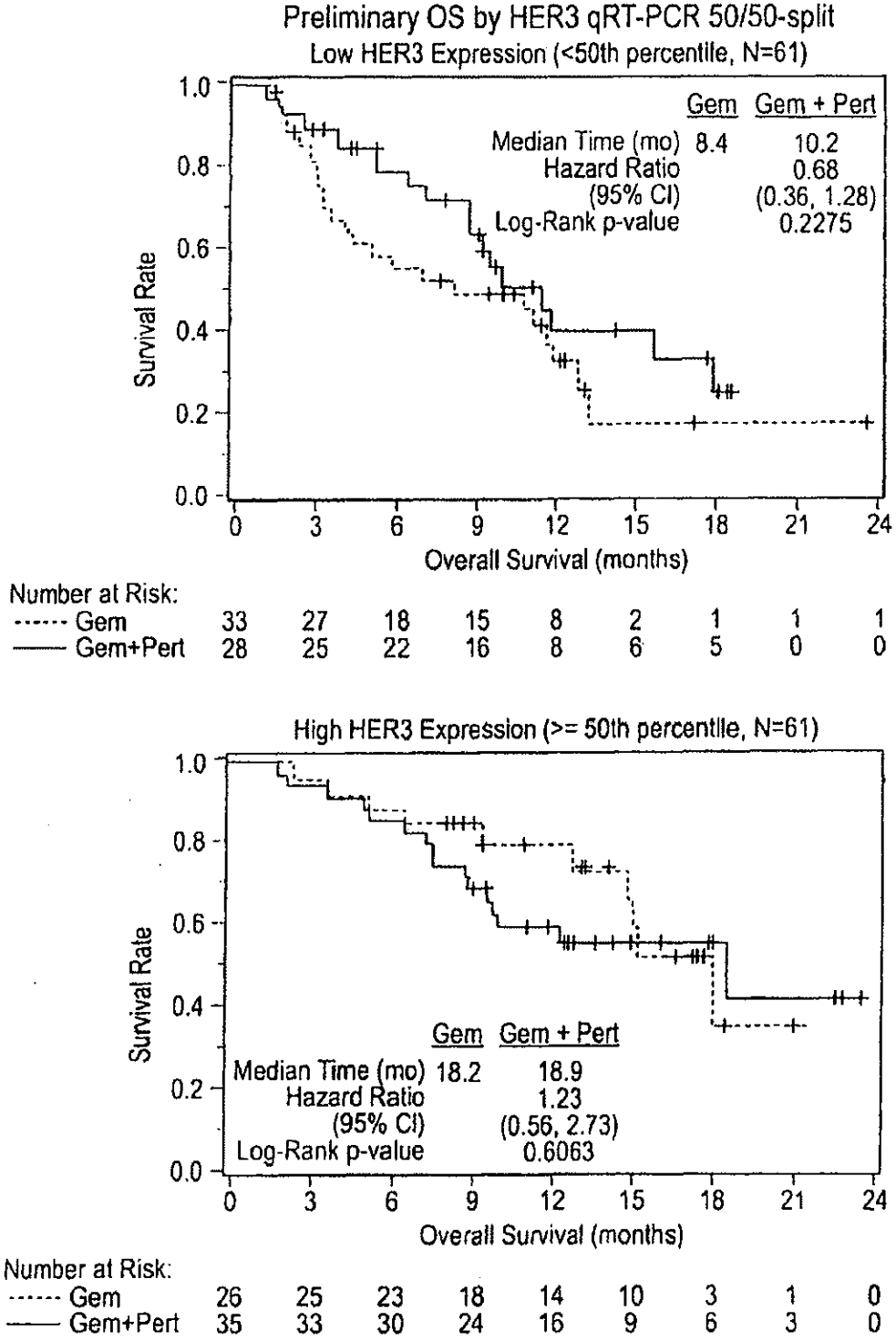

Preliminary OS by HER3 qRT-PCR 50/50-split
Low HER3 Expression (<50th percentile, N=61)
Gem
Gem + Pert
Median Time (mo) 8.4
10.2
Hazard Ratio
0.68
(95% CI)
(0.36, 1.28)
Log-Rank p-value
0.2275
Survival Rate
1.0
0.8
0.6
0.4
0.2
0.0
0
3
6
9
12
15
18
21
24
Overall Survival (months)
Number at Risk:
Gem 33 27 18 15 8 2 1 1 1
Gem+Pert 28 25 22 16 8 6 5 0 0
High HER3 Expression (>= 50th percentile, N=61)
Gem
Gem + Pert
Median Time (mo) 18.2
18.9
Hazard Ratio
1.23
(95% CI)
(0.56, 2.73)
Log-Rank p-value
0.6063
Survival Rate
Overall Survival (months)
Number at Risk:
Gem 26 25 23 18 14 10 3 1 0
Gem+Pert 35 33 30 24 16 9 6 3 0

FIG. 23A

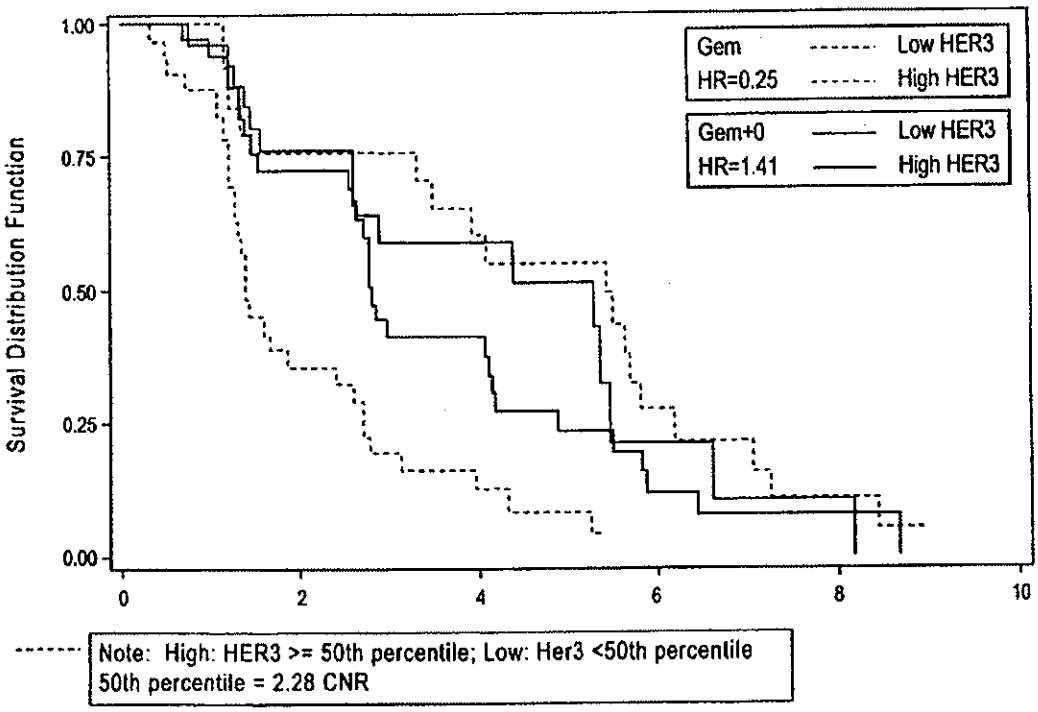

Survival Distribution Function
1.00
0.75
0.50
0.25
0.00
0
2
4
6
8
10
Gem
HR=0.25
Low HER3
High HER3
Gem+0
HR=1.41
Low HER3
High HER3
Note: High: HER3 >= 50th percentile; Low: Her3 <50th percentile
50th percentile = 2.28 CNR

FIG. 23B

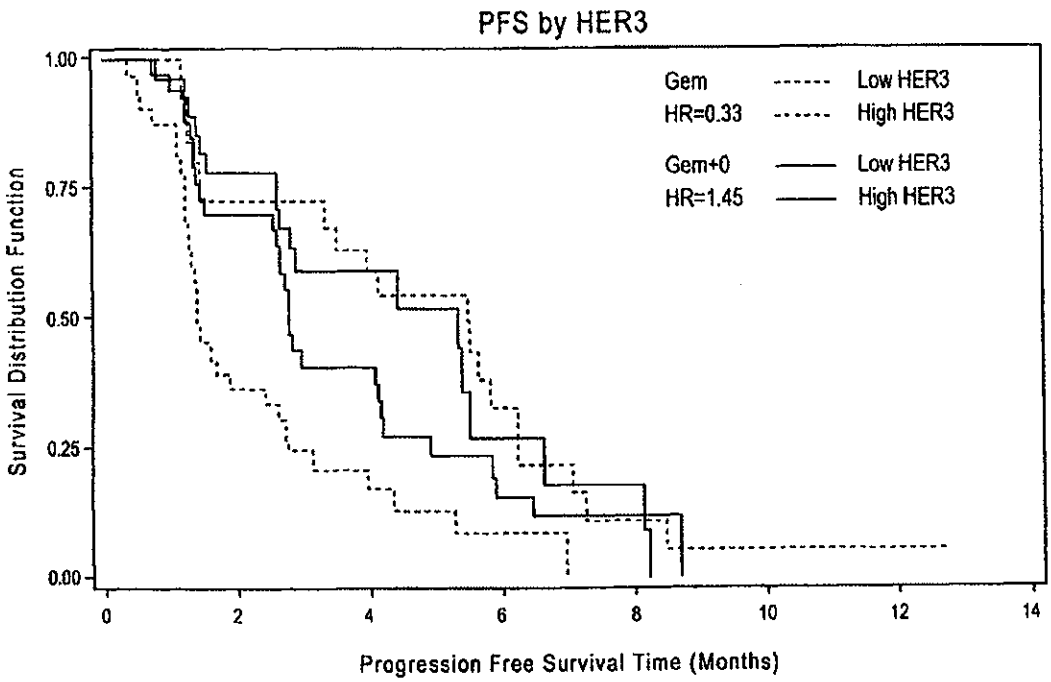

PFS by HER3
Survival Distribution Function
1.00
0.75
0.50
0.25
0.00
0
2
4
6
8
10
12
14
Progression Free Survival Time (Months)
Gem
HR=0.33
Low HER3
High HER3
Gem+0
HR=1.45
Low HER3
High HER3

FIG. 24A (Part 1)

Pertuzumab Platinum Resistant Ovarian Cancer: PFS by qRT-PCR HER3

Cutoff Value		HER3high Group				HER3low Group				
%tile	Abs. Value	N	# Events	HR (95%CI)	Logrank P-value	N	# Events	HR (95%CI)	Logrank P-value	# Events In Dx(+)
5	0.34	114	91	0.81 (0.53, 1.22)	0.3076	5	3	0.00 (0.00,.)	0.0389	44
10	0.48	108	87	0.84 (0.55, 1.28)	0.4076	11	7	0.15 (0.02, 1.29)	0.0497	44
15	0.91	102	83	0.92 (0.60, 1.42)	0.7155	17	11	0.14 (0.03, 0.66)	0.0048	43
20	0.99	96	78	1.06 (0.67, 1.65)	0.8083	23	16	0.09 (0.02, 0.42)	0.0002	41
25	1.19	91	73	1.13 (0.71, 1.81)	0.5875	28	21	0.13 (0.04, 0.45)	0.0002	40
30	1.4	84	66	1.28 (0.77, 2.10)	0.3318	35	28	0.18 (0.06, 0.52)	0.0004	39
35	1.57	78	62	1.49 (0.89, 2.51)	0.1280	41	32	0.16 (0.06, 0.43)	<.0001	38
40	1.71	72	58	1.55 (0.90, 2.68)	0.1141	47	36	0.19 (0.08, 0.47)	<.0001	37
45	1.88	66	54	1.64 (0.94, 2.88)	0.0817	53	40	0.23 (0.11, 0.50)	<.0001	34
50	2.28	60	48	1.60 (0.89, 2.87)	0.1161	59	46	0.30 (0.16, 0.58)	0.0002	29
55	2.41	54	42	1.87 (0.97, 3.57)	0.0565	65	52	0.36 (0.20, 0.65)	0.0005	28
60	2.8	48	37	1.88 (0.92, 3.84)	0.0766	71	57	0.47 (0.27, 0.81)	0.0060	26
65	3.14	42	31	1.72 (0.78, 3.75)	0.1693	77	63	0.57 (0.34, 0.95)	0.0299	22
70	3.59	36	25	1.67 (0.72, 3.90)	0.2270	83	69	0.62 (0.38, 1.00)	0.0488	17
75	3.8	30	19	2.00 (0.71, 5.62)	0.1790	89	75	0.67 (0.42,1.06)	0.0898	14
80	4.29	24	16	2.85 (0.89, 9.20)	0.0667	95	78	0.59 (0.37, 0.92)	0.0196	11
85	5.25	18	13	2.53 (0.67, 9.50)	0.1473	101	81	0.62 (0.40, 0.96)	0.0324	9
90	6.64	12	9	4.73 (0.93, 24.13)	0.0416	107	85	0.59 (0.38, 0.91)	0.0151	6
95	8.4	6	5	3.35 (0.34, 33.36)	0.2769	113	89	0.74 (0.49,1.13)	0.1582	3

Note: The HR and Log-rank p-values were not adjusted for multiple comparison

FIG. 24A (Part 2)

Gem+Omnitarg (n=61)			Gem Alone (n=58)				
# Events In Dx(-)	HR (95%CI)	Logrank P-value	# Events In Dx(+)	# Events In Dx(-)	HR (95%CI)	Logrank P-value	Interaction n P-value
1	1.55 (0.21, 11.48)	0.6559	47	2	0.32 (0.07, 1.38)	0.1073	0.1195
1	2.54 (0.35, 18.64)	0.3357	43	6	0.73 (0.30, 1.74)	0.4723	0.2021
2	2.80 (0.67, 11.68)	0.1377	40	9	0.54 (0.26, 1.14)	0.1001	0.0296
4	3.28 (1.16, 9.25)	0.0174	37	12	0.49 (0.25, 0.98)	0.0385	0.0017
5	2.62 (1.02, 6.69)	0.0369	33	16	0.40 (0.21, 0.76)	0.0035	0.0007
6	2.17 (0.91, 5.16)	0.0737	27	22	0.35 (0.19, 0.65)	0.0006	0.0004
7	2.33 (1.03, 5.25)	0.0355	24	25	0.27 (0.14, 0.52)	<.0001	<.0001
8	2.55 (1.04, 4.86)	0.0339	21	28	0.30 (0.16, 0.59)	0.0002	<.0001
11	1.96 (0.99, 3.89)	0.0508	20	29	0.27 (0.14, 0.54)	<.0001	<.0001
16	1.41 (0.76, 2.62)	0.2700	19	30	0.25 (0.13, 1.51)	<.0001	0.0001
17	1.33 (0.72, 2.44)	0.3610	14	35	0.25 (0.12, 0.49)	<.0001	0.0002
19	1.38 (0.76, 2.50)	0.2943	11	38	0.36 (0.18, 0.71)	0.0023	0.0020
23	1.06 (0.59, 1.93)	0.8337	9	40	0.36 (0.17, 0.76)	0.0050	0.0158
28	0.82 (0.44, 1.53)	0.5400	8	41	0.33 (0.15, 0.71)	0.0029	0.0384
31	0.77 (0.40, 1.49)	0.4392	5	44	0.29 (0.11, 0.73)	0.0054	0.0528
34	1.40 (0.70, 2.80)	0.3428	5	44	0.33 (0.13, 0.84)	0.0146	0.0119
36	1.25 (0.60, 2.62)	0.5534	4	45	0.32 (0.11, 0.92)	0.0264	0.0262
39	2.58 (1.06, 6.23)	0.0290	3	46	0.26 (0.08, 0.86)	0.0185	0.0020
42	2.57 (0.77, 8.56)	0.1052	2	47	0.95 (0.23, 3.94)	0.9478	0.3840

FIG. 24B (Part 1)

Pertuzumab Platinum Resistant Ovarian Cancer: PFS by qRT-PCR HER3

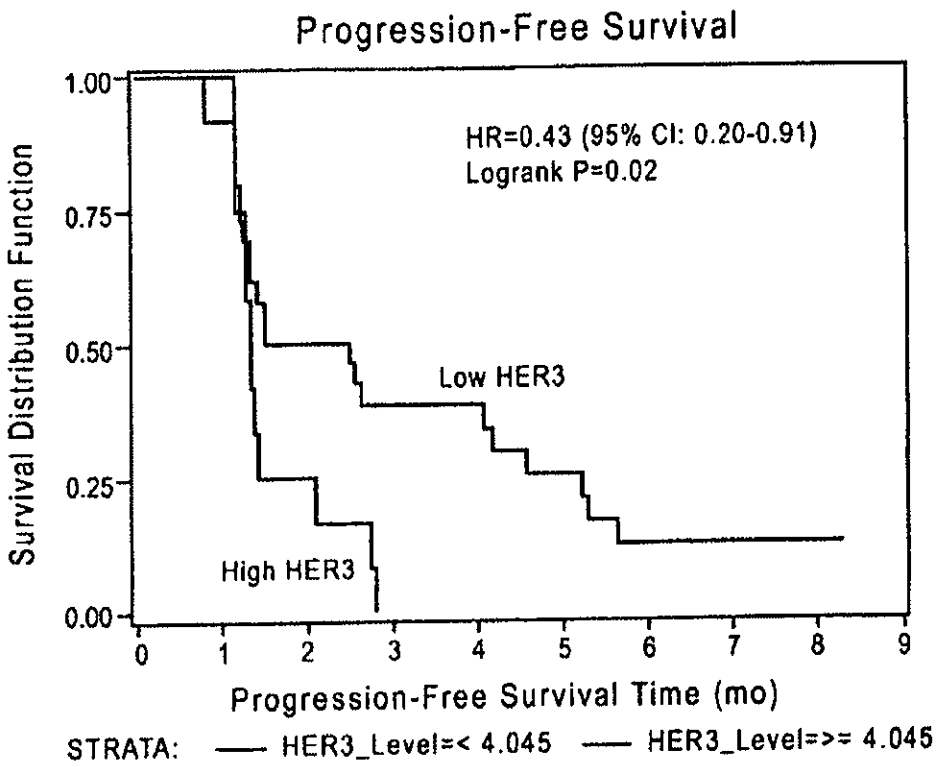
Cutoff Value		Dx(High) Group				Dx(Low) Group				
%tile	Abs. Value	N	# Events	HR (95%CI)	Logrank P-value	N	# Events	HR (95%CI)	Logrank P-value	# Events In Dx(High)
20	0.99	98	80	1.09 (0.70, 1.70)	0.6973	24	17	0.08 (0.02, 0.37)	<.0001	42
25	1.19	92	74	1.16 (0.73, 1.84)	0.5222	30	23	0.13 (0.04, 0.41)	<.0001	40
30	1.39	86	68	1.20 (0.74, 1.94)	0.4674	36	29	0.22 (0.09, 0.56)	0.0005	39
35	1.56	80	64	1.37 (0.83, 2.26)	0.2230	42	33	0.20 (0.09, 0.48)	<.0001	38
40	1.70	74	59	1.50 (0.88, 2.55)	0.1381	48	38	0.22 (0.10, 0.50)	<.0001	37
45	1.87	68	55	1.50 (0.87, 2.61)	0.1468	54	42	0.29 (0.14, 0.58)	0.0002	34
50	2.24	61	49	1.48 (0.83, 2.63)	0.1809	61	48	0.34 (0.18, 0.63)	0.0004	29
55	2.38	56	44	1.74 (0.93, 3.27)	0.0816	66	53	0.36 (0.20, 0.65)	0.0005	29
60	2.75	49	38	1.81 (0.90, 3.67)	0.0945	73	59	0.48 (0.28, 0.84)	0.0080	27
65	3.08	43	32	1.78 (0.82, 3.86)	0.1382	79	65	0.56 (0.34, 0.94)	0.0255	23
70	3.56	37	26	1.73 (0.75, 3.99)	0.1943	85	71	0.62 (0.38, 1.00)	0.0459	18
75	3.77	31	21	1.90 (0.73, 4.93)	0.1804	91	76	0.65 (0.41, 1.03)	0.0650	15
80	4.05	25	18	2.33 (0.82, 6.64)	0.1053	97	79	0.64 (0.41, 1.00)	0.0493	13

Note: The HR and Log-rank p-values were not adjusted for multiple comparison

FIG. 24B (Part 2)

Gem + Pertuzumab (n=63)			Gem Alone (n=59)				
# Events In Dx(Low)	HR (95%CI)	Logrank P-value	# Events In Dx(High)	# Events In Dx(Low)	HR (95%CI)	Logrank P-value	Interaction n P-value
5	3.20 (1.25, 8.23)	0.0109	38	12	0.47 (0.24, 0.93)	0.0272	0.0007
7	2.34 (1.03, 5.30)	0.0360	34	16	0.38 (0.20, 0.72)	0.0020	0.0003
8	2.03 (0.93, 4.39)	0.0683	29	21	0.44 (0.24, 0.79)	0.0046	0.0014
9	2.19 (1.05, 4.56)	0.0330	26	24	0.37 (0.21, 0.67)	0.0007	0.0001
10	2.14 (1.06, 4.34)	0.0312	22	28	0.35 (0.19, 0.63)	0.0004	<.0001
13	1.84 (0.97, 3.51)	0.0617	21	29	0.35 (0.19, 0.65)	0.0005	0.0002
18	1.45 (0.80, 2.62)	0.2230	20	30	0.33 (0.18, 0.62)	0.0003	0.0005
18	1.45 (0.80, 2.62)	0.2230	15	35	0.31 (0.16, 0.60)	0.0002	0.0004
20	1.33 (0.74, 2.38)	0.3459	11	39	0.37 (0.19, 0.73)	0.0030	0.0030
24	1.14 (0.64, 2.04)	0.6516	9	41	0.36 (0.18, 0.76)	0.0050	0.0112
29	0.89 (0.49, 1.62)	0.6916	8	42	0.33 (0.15, 0.71)	0.0028	0.0295
32	0.89 (0.47, 1.66)	0.6992	6	44	0.33 (0.14, 0.79)	0.0086	0.0427
34	1.04 (0.54, 2.03)	0.9069	5	45	0.32 (0.13, 0.83)	0.0136	0.0291

FIG. 25 (Part 1)



High HER3: HER3 >= 75th percentile
Low HER3: HER3 < 75th percentile
75th percentile = 4.045

FIG. 25 (Part 2)

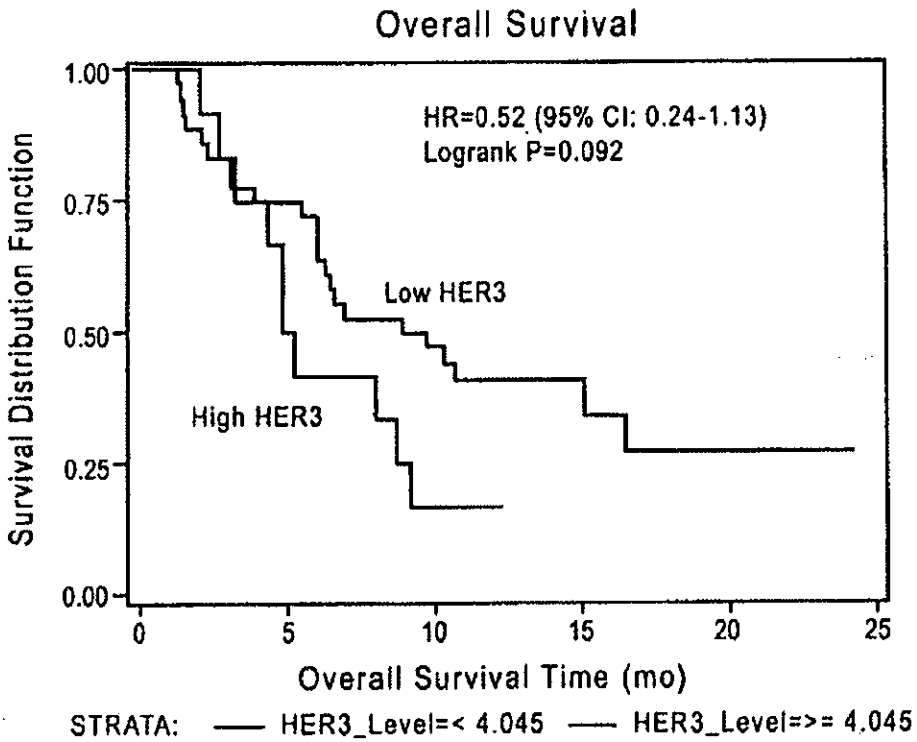

Overall Survival
HR=0.52 (95% CI: 0.24-1.13)
Logrank P=0.092
Low HER3
High HER3
Survival Distribution Function
1.00
0.75
0.50
0.25
0.00
0
5
10
15
20
25
Overall Survival Time (mo)
STRATA: HER3_Level=< 4.045 HER3_Level=>= 4.045

FIG. 26A

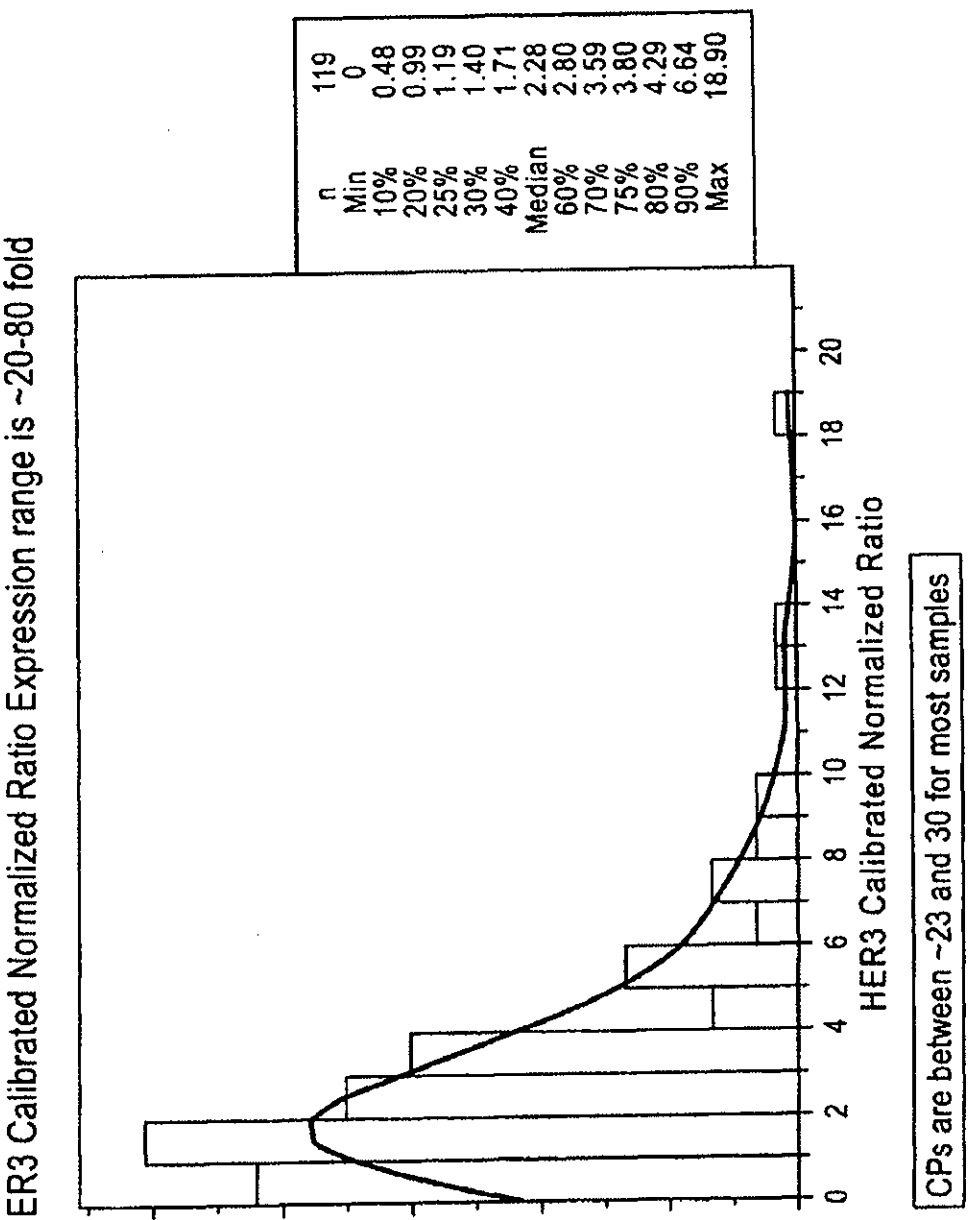

HER3 Calibrated Normalized Ratio Expression range is ~20-80 fold
n 119
Min 0
10% 0.48
20% 0.99
25% 1.19
30% 1.40
40% 1.71
Median 2.28
60% 2.80
70% 3.59
75% 3.80
80% 4.29
90% 6.64
Max 18.90
0.25
0.20
0.15
0.10
0.05
0.00
0
2
4
6
8
10
12
14
16
18
20
HER3 Calibrated Normalized Ratio
CPs are between ~23 and 30 for most samples

FIG. 26B

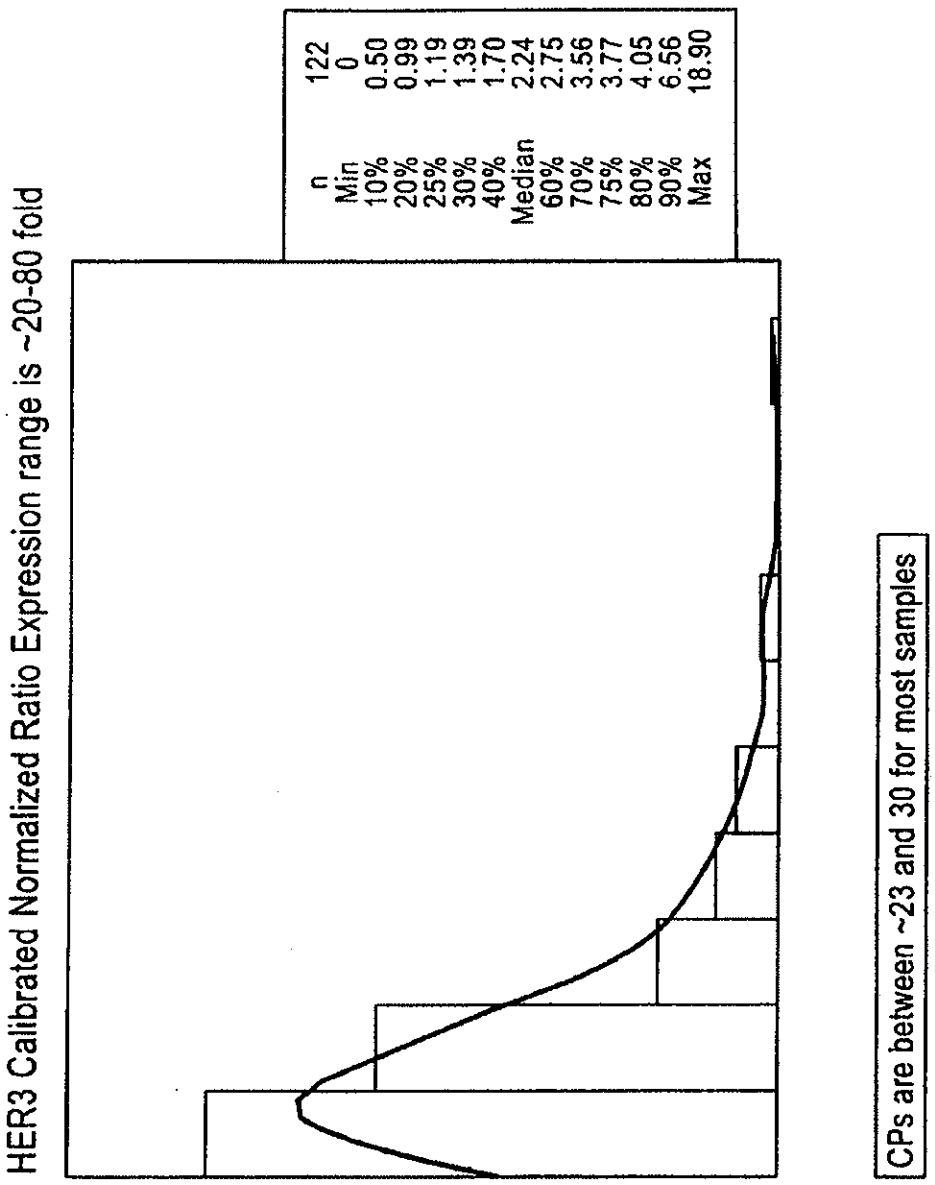

HER3 Calibrated Normalized Ratio Expression range is ~20-80 fold
n 122
Min 0
10% 0.50
20% 0.99
25% 1.19
30% 1.39
40% 1.70
Median 2.24
60% 2.75
70% 3.56
75% 3.77
80% 4.05
90% 6.56
Max 18.90
CPs are between ~23 and 30 for most samples

FIG. 27

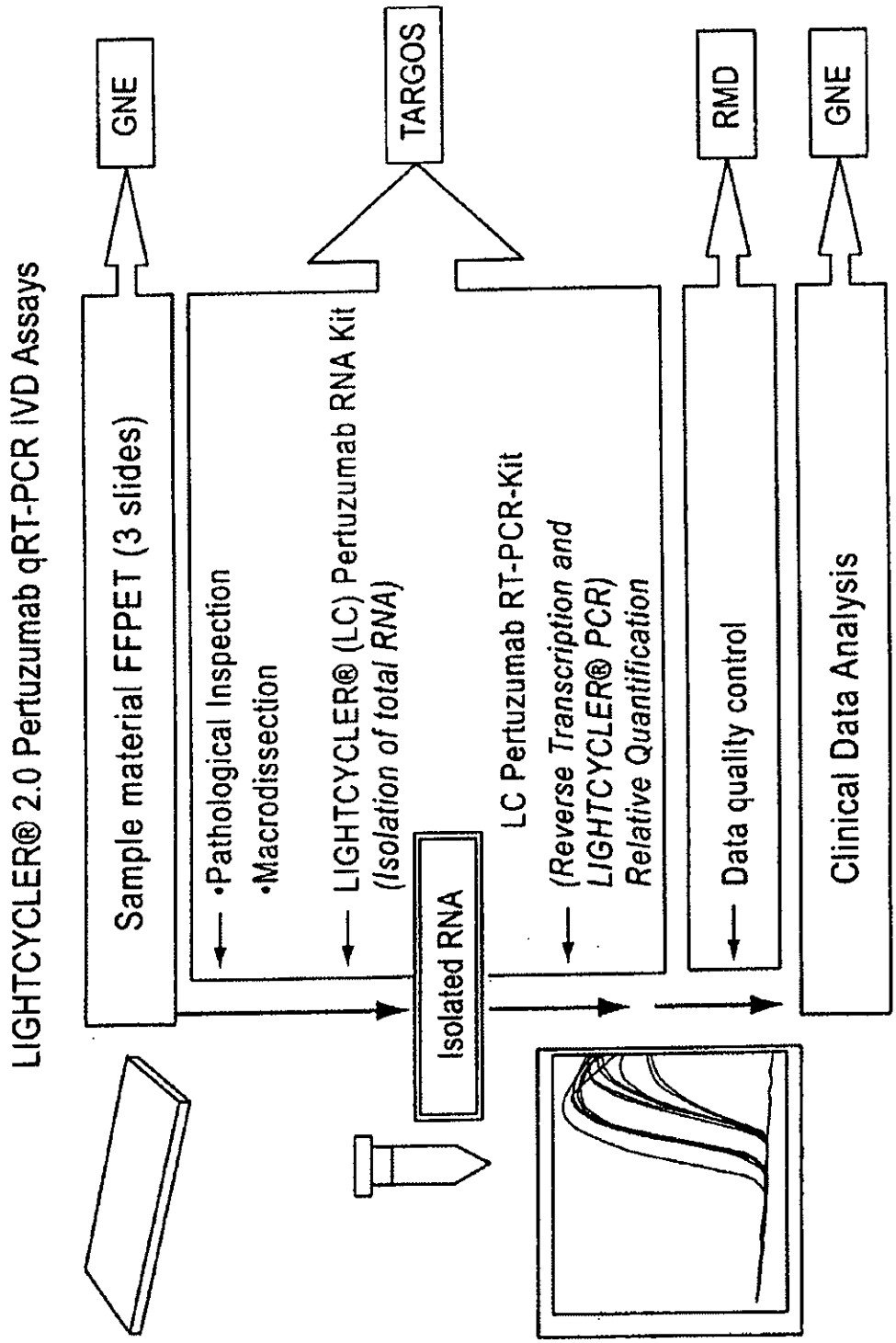

LIGHTCYCLER® 2.0 Pertuzumab qRT-PCR IVD Assays
GNE
TARGOS
RMD
GNE
Sample material FFPET (3 slides)
•Pathological Inspection
•Macrodissection
LIGHTCYCLER® (LC) Pertuzumab RNA Kit
(Isolation of total RNA)
Isolated RNA
LC Pertuzumab RT-PCR-Kit
(Reverse Transcription and
LIGHTCYCLER® PCR)
Relative Quantification
Data quality control
Clinical Data Analysis

FIG. 28

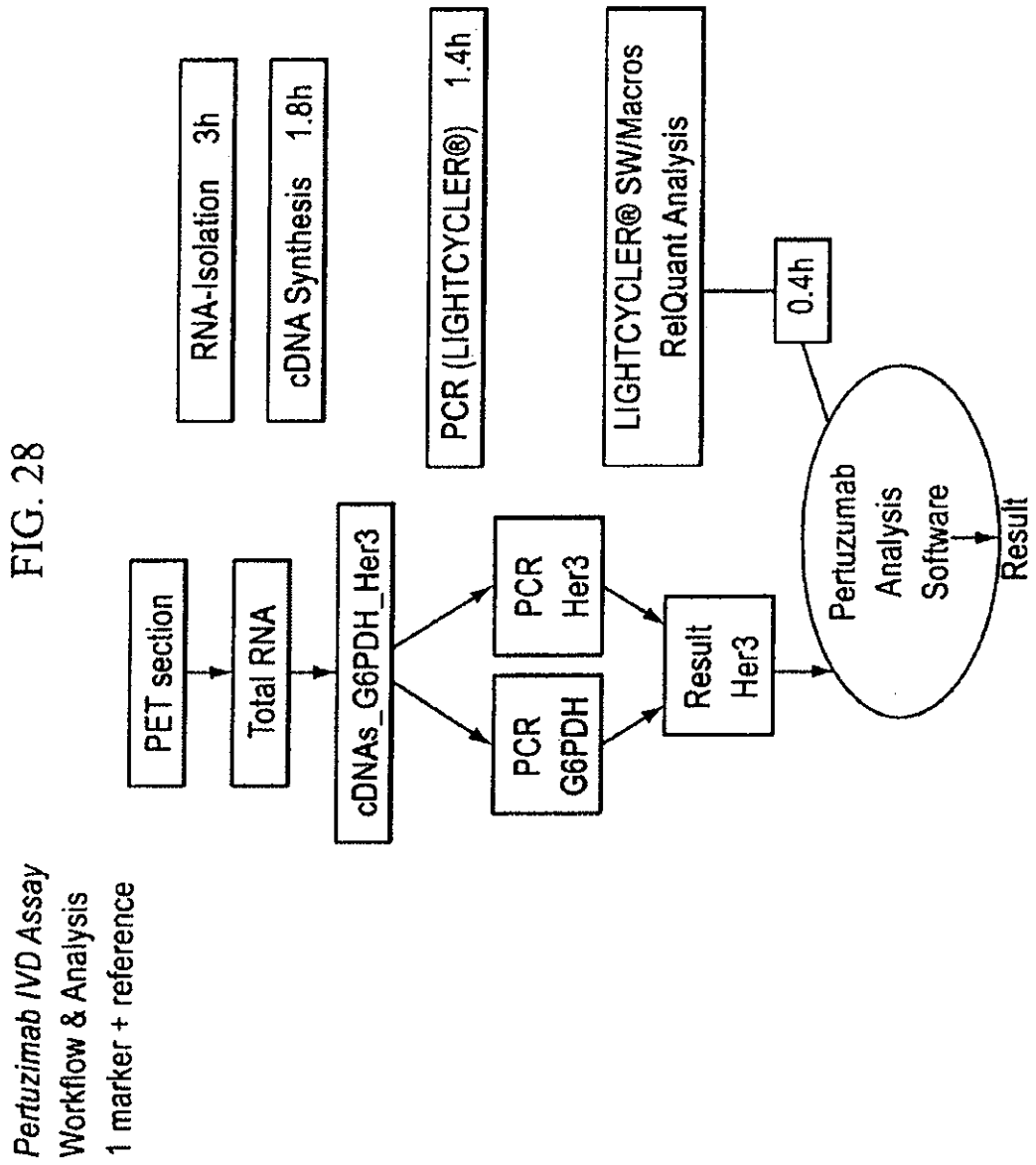

Pertuzimab IVD Assay
Workflow & Analysis
1 marker + reference
PET section
Total RNA
cDNAs_G6PDH_Her3
RNA-Isolation 3h
cDNA Synthesis 1.8h
PCR Her3
PCR G6PDH
PCR (LIGHTCYCLER®) 1.4h
Result Her3
LIGHTCYCLER® SW/Macros RelQuant Analysis
0.4h
Pertuzumab Analysis Software
Result

FIG. 29A (Part 1)

PFS by qRT-PCR HER2/HER3 (percentiles)

Cutoff Value		Dx (High) Group				Dx (Low) Group				
%tile	Abs. Value	N	# Events	HR (95%CI)	Logrank P-value	N	# Events	HR (95%CI)	Logrank P-value	# Events In Dx(High)
20	0.74	95	72	0.63 (0.39, 1.02)	0.0616	23	21	2.04 (0.58, 7.13)	0.2475	26
25	0.82	89	67	0.46 (0.27, 0.76)	0.0021	29	26	2.85 (1.10, 7.37)	0.0249	24
30	0.90	83	62	0.41 (0.24, 0.69)	0.0007	35	31	2.52 (1.13, 5.62)	0.0197	22
35	1.06	77	60	0.39 (0.22, 0.68)	0.0005	41	33	2.51 (1.14, 5.54)	0.0189	20
40	1.13	71	55	0.39 (0.22, 0.69)	0.0009	47	38	1.91 (0.95, 3.83)	0.0640	18
45	1.26	65	50	0.31 (0.16, 0.61)	0.0003	53	43	1.93 (0.99, 3.77)	0.0492	14
50	1.53	59	47	0.31 (0.15, 0.61)	0.0004	59	46	1.71 (0.91, 3.21)	0.0937	13
55	1.70	54	45	0.34 (0.17, 0.68)	0.0015	64	48	1.44 (0.78, 2.65)	0.2293	13
60	1.86	48	40	0.27 (0.12, 0.57)	0.0003	70	53	1.35 (0.77, 2.37)	0.2885	12
65	2.15	42	34	0.27 (0.12, 0.62)	0.0010	76	59	1.10 (0.65, 1.86)	0.7119	11
70	2.49	36	29	0.21 (0.08, 0.54)	0.0004	82	64	1.13 (0.69, 1.87)	0.6280	8
75	2.62	30	24	0.13 (0.04, 0.46)	0.0003	88	69	1.08 (0.67, 1.75)	0.7534	6
80	2.92	24	20	0.10 (0.02, 0.43)	0.0002	94	73	1.06 (0.67, 1.70)	0.7886	4

FIG. 29A (Part 2)

Gem+Omnitarg (n=60)			Gem Alone (n=58)				
# Events In Dx(Low)	HR (95%CI)	Logrank P-value	# Events In Dx(High)	# Events In Dx(Low)	HR (95%CI)	Logrank P-value	Interaction n P-value
17	0.57 (0.31, 1.06)	0.0734	46	3	1.39 (0.43, 4.55)	0.5881	0.1823
20	0.53 (0.29, 0.97)	0.0370	43	6	4.07 (1.41, 11.74)	0.0055	0.0005
22	0.46 (0.25, 0.84)	0.0104	40	9	3.04 (1.33, 6.94)	0.0056	0.0002
24	0.49 (0.26, 0.90)	0.0192	40	9	3.41 (1.50, 7.73)	0.0019	0.0001
26	0.52 (0.28, 0.96)	0.0340	37	12	2.76 (1.36, 5.59)	0.0034	0.0004
30	0.54 (0.28, 1.03)	0.0584	36	13	3.21 (1.57, 6.56)	0.0007	0.0001
31	0.57 (0.30, 1.10)	0.0926	34	15	2.94 (1.50, 5.77)	0.0010	0.0003
31	0.66 (0.34, 1.28)	0.2161	32	17	2.55 (1.34, 4.83)	0.0028	0.0022
32	0.60 (0.31, 1.18)	0.1348	28	21	2.60 (1.41, 4.81)	0.0015	0.0009
33	0.56 (0.28, 1.12)	0.0974	23	26	1.81 (1.00, 3.27)	0.0447	0.0084
36	0.52 (0.24, 1.12)	0.0895	21	28	2.07 (1.14, 3.76)	0.0145	0.0032
38	0.46 (0.19, 1.10)	0.0766	18	31	2.11 (1.12, 3.96)	0.0167	0.0035
40	0.42 (0.15, 1.19)	0.0949	16	33	2.60 (1.36, 4.97)	0.0026	0.0022

FIG. 29B (Part 1)

Platinum Resistant Ovarian Canver:
PFS by qRT-PCR HER2/HER3 Ratio

Cutoff Value		Dx (High) Group				Dx (Low) Group				
%tile	Abs. Value	N	# Events	HR (95%CI)	Logrank P-value	N	# Events	HR (95%CI)	Logrank P-value	# Events In Dx(High)
20	0.76	97	75	0.67 (0.42, 1.06)	0.0884	24	21	1.70 (0.56, 5.19)	0.3418	29
25	0.83	91	71	0.50 (0.31, 0.82)	0.0050	30	25	2.53 (0.99, 6.49)	0.0452	27
30	0.91	85	66	0.48 (0.29, 0.80)	0.0042	36	30	1.98 (0.89, 4.40)	0.0876	25
35	1.06	79	63	0.45 (0.26, 0.77)	0.0026	42	33	1.99 (0.94, 4.24)	0.0691	23
40	1.13	73	58	0.40 (0.23, 0.71)	0.0011	48	38	1.76 (0.89, 3.47)	0.0979	21
45	1.26	67	53	0.35 (0.19, 0.65)	0.0006	54	43	1.78 (0.93, 3.41)	0.0780	17
50	1.54	61	49	0.32 (0.17, 0.63)	0.0005	60	47	1.63 (0.88, 3.02)	0.1154	15
55	1.73	55	46	0.36 (0.18, 0.70)	0.0018	66	50	1.37 (0.77, 2.45)	0.2828	15
60	2.04	49	41	0.29 (0.14, 0.60)	0.0005	72	55	1.35 (0.78, 2.34)	0.2830	13
65	2.17	43	35	0.28 (0.12, 0.61)	0.0007	78	61	1.13 (0.68, 1.88)	0.6512	13
70	2.50	37	30	0.19 (0.07, 0.48)	0.0001	84	66	1.16 (0.71, 1.90)	0.5512	10
75	2.65	31	25	0.10 (0.03, 0.37)	<.0001	90	71	1.12 (0.70, 1.80)	0.6370	7
80	2.99	25	21	0.11 (0.03, 0.40)	<.0001	96	75	1.06 (0.67, 1.67)	0.8088	6

Note: The HR and Log-rank p-values were not adjusted for multiple comparison

FIG. 29B (Part 2)

Gem+Pertuzimab (n=63)				Gem Alone (n=59)			
# Events In Dx(Low)	HR (95%CI)	Logrank P-value	# Events In Dx(High)	# Events In Dx(Low)	HR (95%CI)	Logrank P-value	Interaction P-value
17	0.74 (0.40, 1.37)	0.3323	46	4	1.73 (0.62, 4.87)	0.2958	0.1685
19	0.68 (0.37, 1.24)	0.2026	44	6	4.34 (1.51, 12.43)	0.0033	0.0022
21	0.65 (0.36, 1.17)	0.1529	41	9	2.92 (1.28, 6.66)	0.0075	0.0030
23	0.63 (0.35, 1.13)	0.1204	40	10	2.96 (1.37, 6.42)	0.0039	0.0015
25	0.65 (0.36, 1.17)	0.1512	37	13	2.87 (1.44, 5.71)	0.0017	0.0011
29	0.66 (0.36, 1.21)	0.1782	36	14	3.49 (1.70, 7.14)	0.0003	0.0004
31	0.64 (0.34, 1.19)	0.1566	34	16	3.15 (1.60, 6.19)	0.0005	0.0005
31	0.72 (0.39, 1.35)	0.3116	31	19	2.64 (1.41, 4.94)	0.0016	0.0033
33	0.62 (0.33, 1.20)	0.1585	28	22	2.69 (1.47, 4.93)	0.0009	0.0010
33	0.62 (0.33, 1.20)	0.1585	22	28	2.16 (1.18, 3.96)	0.0104	0.0053
36	0.58 (0.28, 1.18)	0.1290	20	30	2.64 (1.40, 4.96)	0.0018	0.0010
39	0.42 (0.18, 0.94)	0.0314	18	32	2.23 (1.19, 4.21)	0.0100	0.0010
40	0.45 (0.19, 1.08)	0.0694	15	35	2.46 (1.28, 4.74)	0.0055	0.0015

FIG. 30A-1

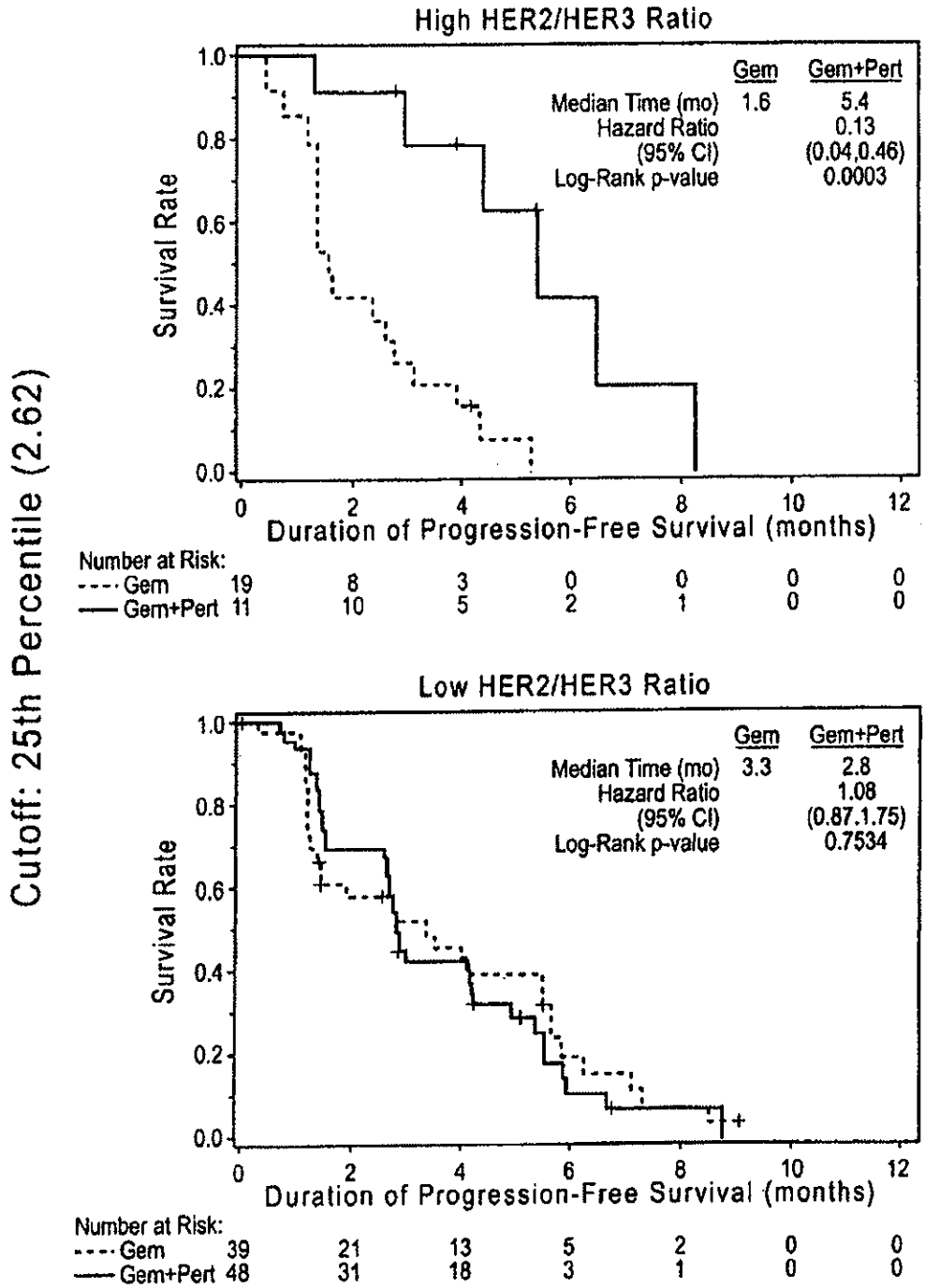

Cutoff: 25th Percentile (2.62)
High HER2/HER3 Ratio
Gem
Gem+Pert
Median Time (mo) 1.6 5.4
Hazard Ratio 0.13
(95% CI) (0.04,0.46)
Log-Rank p-value 0.0003
Survival Rate
1.0
0.8
0.6
0.4
0.2
0.0
0 2 4 6 8 10 12
Duration of Progression-Free Survival (months)
Number at Risk:
Gem 19 8 3 0 0 0 0
Gem+Pert 11 10 5 2 1 0 0
Low HER2/HER3 Ratio
Gem
Gem+Pert
Median Time (mo) 3.3 2.8
Hazard Ratio 1.08
(95% CI) (0.87,1.75)
Log-Rank p-value 0.7534
Survival Rate
1.0
0.8
0.6
0.4
0.2
0.0
0 2 4 6 8 10 12
Duration of Progression-Free Survival (months)
Number at Risk:
Gem 39 21 13 5 2 0 0
Gem+Pert 48 31 18 3 1 0 0

FIG. 30A-2

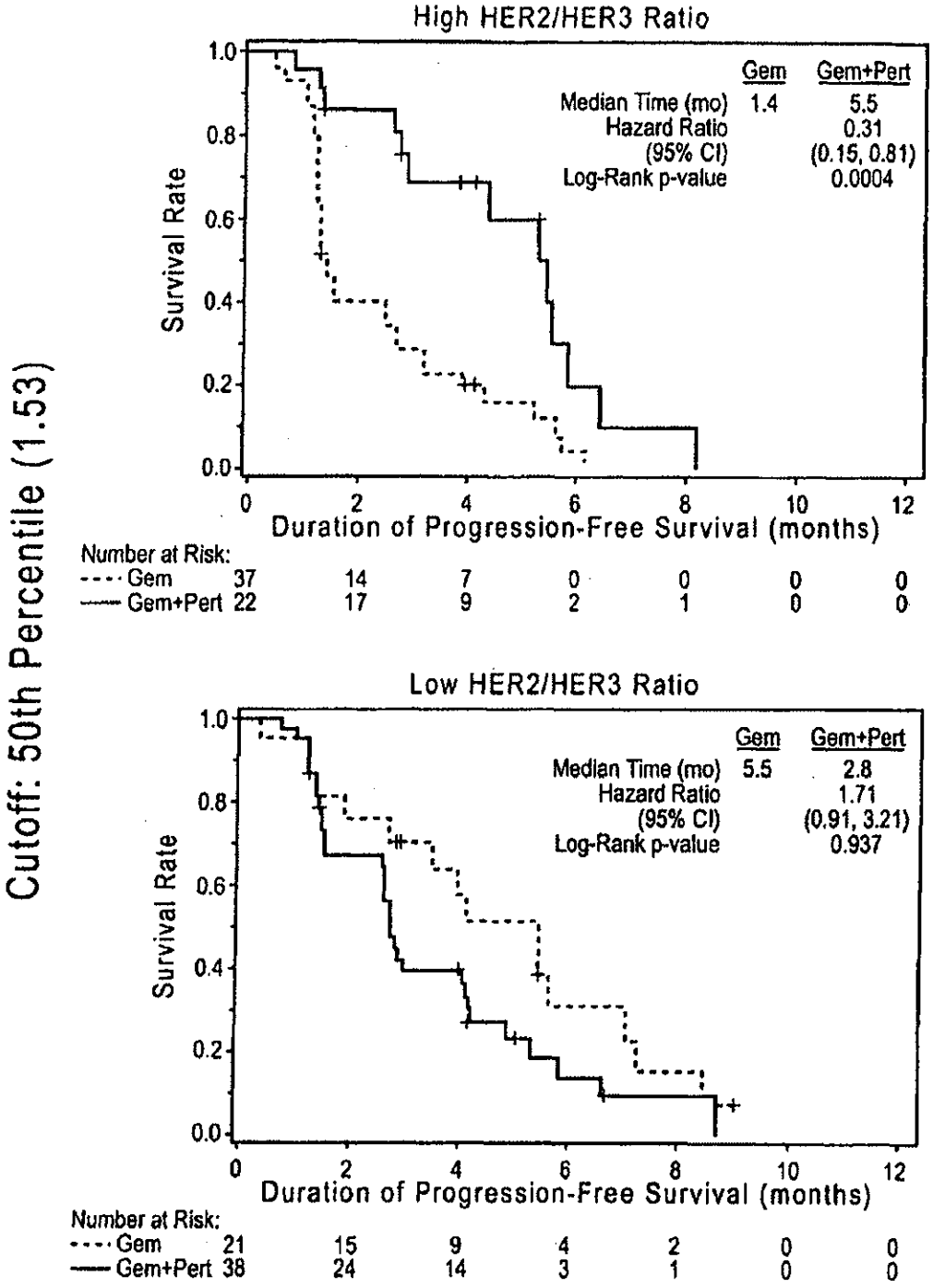

Cutoff: 50th Percentile (1.53)
High HER2/HER3 Ratio
Survival Rate
1.0
0.8
0.6
0.4
0.2
0.0
Gem
Gem+Pert
Median Time (mo) 1.4 5.5
Hazard Ratio 0.31
(95% CI) (0.15, 0.81)
Log-Rank p-value 0.0004
0 2 4 6 8 10 12
Duration of Progression-Free Survival (months)
Number at Risk:
Gem 37 14 7 0 0 0 0
Gem+Pert 22 17 9 2 1 0 0
Low HER2/HER3 Ratio
Survival Rate
1.0
0.8
0.6
0.4
0.2
0.0
Gem
Gem+Pert
Median Time (mo) 5.5 2.8
Hazard Ratio 1.71
(95% CI) (0.91, 3.21)
Log-Rank p-value 0.937
0 2 4 6 8 10 12
Duration of Progression-Free Survival (months)
Number at Risk:
Gem 21 15 9 4 2 0 0
Gem+Pert 38 24 14 3 1 0 0

FIG. 30B-1

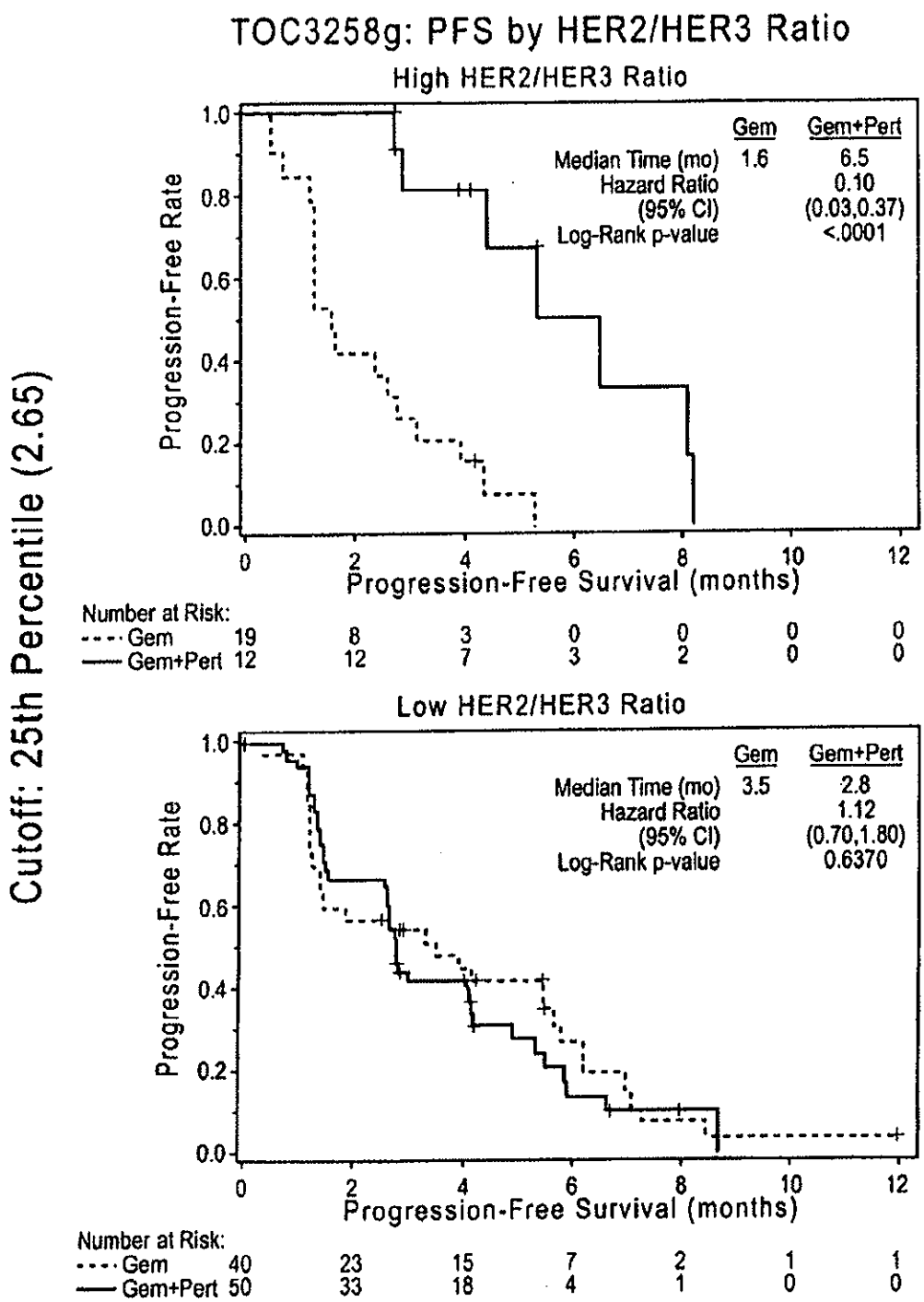

TOC3258g: PFS by HER2/HER3 Ratio
Cutoff: 25th Percentile (2.65)
High HER2/HER3 Ratio
Progression-Free Rate
Gem
Gem+Pert
Median Time (mo) 1.6 6.5
Hazard Ratio 0.10
(95% CI) (0.03,0.37)
Log-Rank p-value <.0001
Progression-Free Survival (months)
Number at Risk:
Gem 19 8 3 0 0 0 0
Gem+Pert 12 12 7 3 2 0 0
Low HER2/HER3 Ratio
Progression-Free Rate
Gem
Gem+Pert
Median Time (mo) 3.5 2.8
Hazard Ratio 1.12
(95% CI) (0.70,1.80)
Log-Rank p-value 0.6370
Progression-Free Survival (months)
Number at Risk:
Gem 40 23 15 7 2 1 1
Gem+Pert 50 33 18 4 1 0 0

FIG. 30B-2

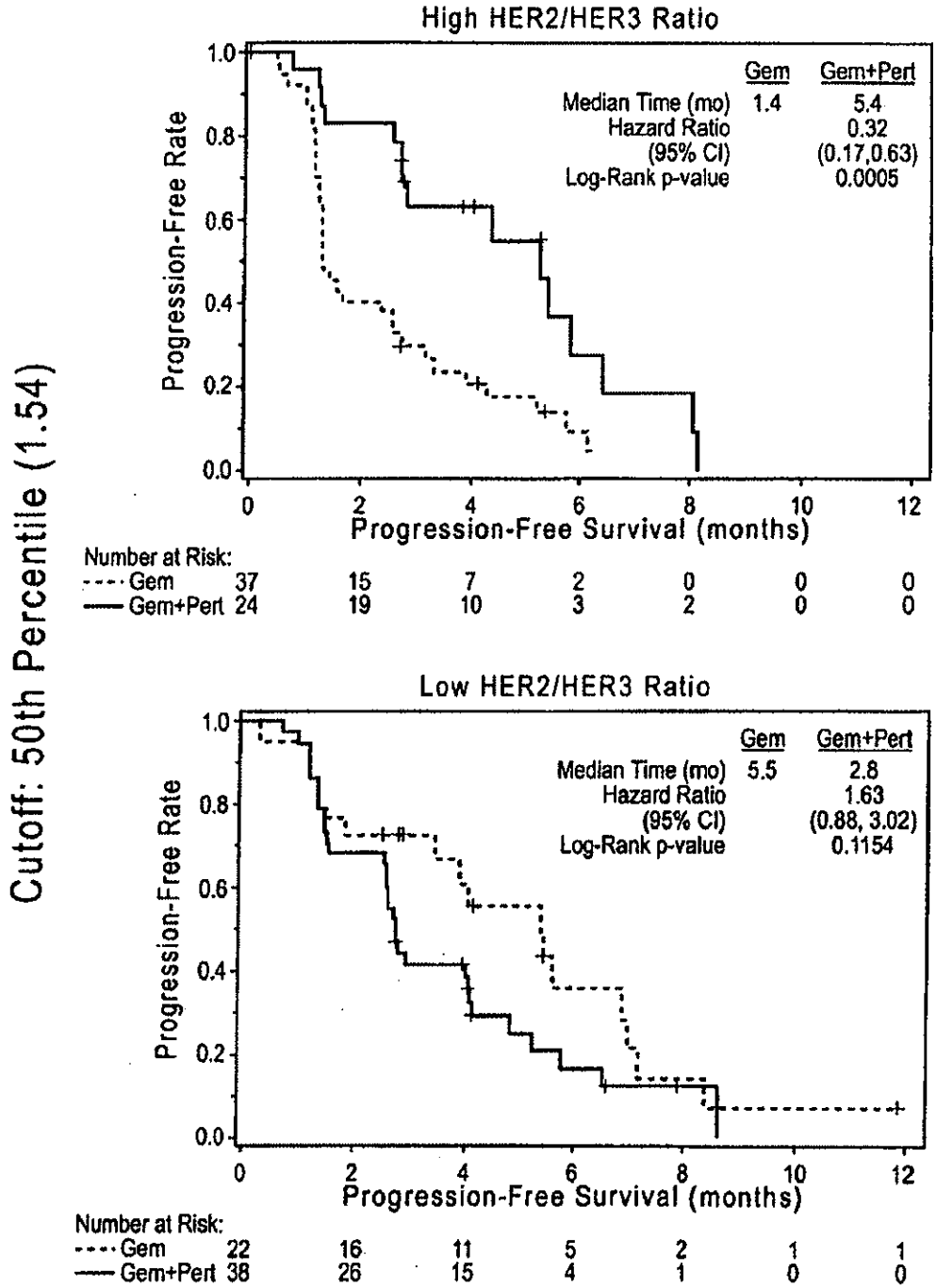

Cutoff: 50th Percentile (1.54)
High HER2/HER3 Ratio
Progression-Free Rate
1.0
0.8
0.6
0.4
0.2
0.0
Gem
Gem+Pert
Median Time (mo) 1.4 5.4
Hazard Ratio 0.32
(95% CI) (0.17,0.63)
Log-Rank p-value 0.0005
0 2 4 6 8 10 12
Progression-Free Survival (months)
Number at Risk:
Gem 37 15 7 2 0 0 0
Gem+Pert 24 19 10 3 2 0 0
Low HER2/HER3 Ratio
Progression-Free Rate
1.0
0.8
0.6
0.4
0.2
0.0
Gem
Gem+Pert
Median Time (mo) 5.5 2.8
Hazard Ratio 1.63
(95% CI) (0.88, 3.02)
Log-Rank p-value 0.1154
0 2 4 6 8 10 12
Progression-Free Survival (months)
Number at Risk:
Gem 22 16 11 5 2 1 1
Gem+Pert 38 26 15 4 1 0 0

FIG. 31A

		Total	Gem Alone			Gem + Omnitarg				
qRT-PCR HER2/HER3 Ratio	N	# Events	N	# Events	Medium (mo)	N	# Events	Medium (mo)	HR (95%CI)	Logrank P-value
0 - < 25th percentile	29	26	7	6	5.5	22	20	2.6	2.85 (1.10, 7.37)	0.0249
25 - < 50th percentile	30	20	14	9	3.7	16	11	4.2	1.02 (0.41, 2.54)	0.9649
50 - < 75th percentile	29	23	18	16	1.3	11	7	5.5	0.61 (0.25, 1.52)	0.2978
75 - 100th percentile	30	24	19	18	1.6	11	6	5.4	0.13 (0.04, 0.46)	0.0003

FIG. 31B

Progression-Free Survival (PFS) Analysis by HER2/HER3 Quartiles

qRT-PCR HER2/HER3	N	# Events	HR (95%CI)	Logrank P-value
0 - < 25th percentile	30	25	2.53 (0.99, 6.49)	0.0452
25 - <50th percentile	30	22	1.28 (0.52, 3.15)	0.5952
50 - < 75th percentile	30	24	0.76 (0.32, 1.83)	0.5618
75 - 100th percentile	31	25	0.10 (0.03, 0.37)	<.0001

FIG. 32-1

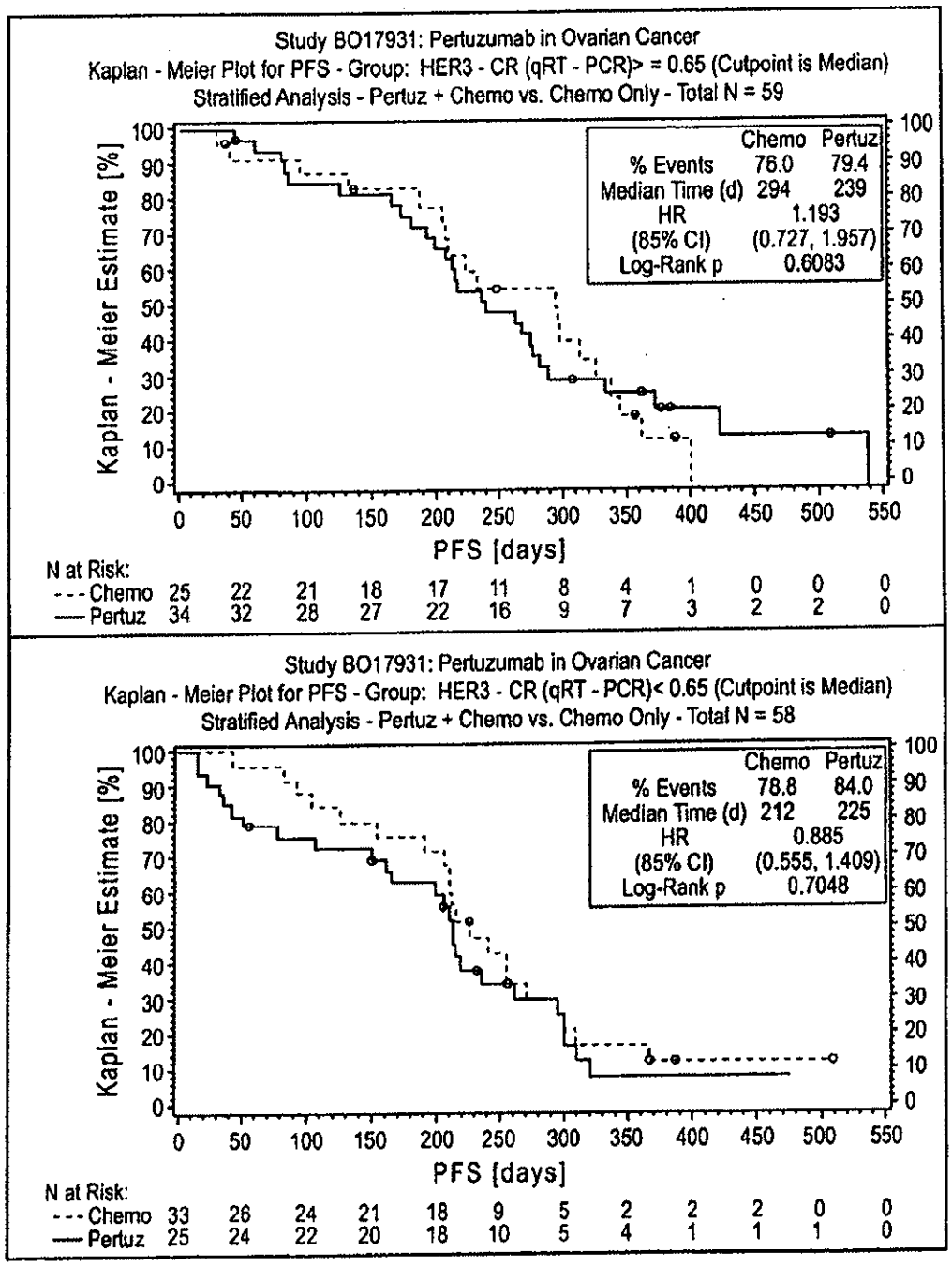

Study BO17931: Pertuzumab in Ovarian Cancer
Kaplan - Meier Plot for PFS - Group: HER3 - CR (qRT - PCR)> = 0.65 (Cutpoint is Median)
Stratified Analysis - Pertuz + Chemo vs. Chemo Only - Total N = 59
Kaplan - Meier Estimate [%]
PFS [days]
Chemo Pertuz
% Events 76.0 79.4
Median Time (d) 294 239
HR 1.193
(85% CI) (0.727, 1.957)
Log-Rank p 0.6083
N at Risk:
Chemo 25 22 21 18 17 11 8 4 1 0 0 0
Pertuz 34 32 28 27 22 16 9 7 3 2 2 0
Study BO17931: Pertuzumab in Ovarian Cancer
Kaplan - Meier Plot for PFS - Group: HER3 - CR (qRT - PCR)< 0.65 (Cutpoint is Median)
Stratified Analysis - Pertuz + Chemo vs. Chemo Only - Total N = 58
Kaplan - Meier Estimate [%]
PFS [days]
Chemo Pertuz
% Events 78.8 84.0
Median Time (d) 212 225
HR 0.885
(85% CI) (0.555, 1.409)
Log-Rank p 0.7048
N at Risk:
Chemo 33 26 24 21 18 9 5 2 2 2 0 0
Pertuz 25 24 22 20 18 10 5 4 1 1 1 0

FIG. 32-2

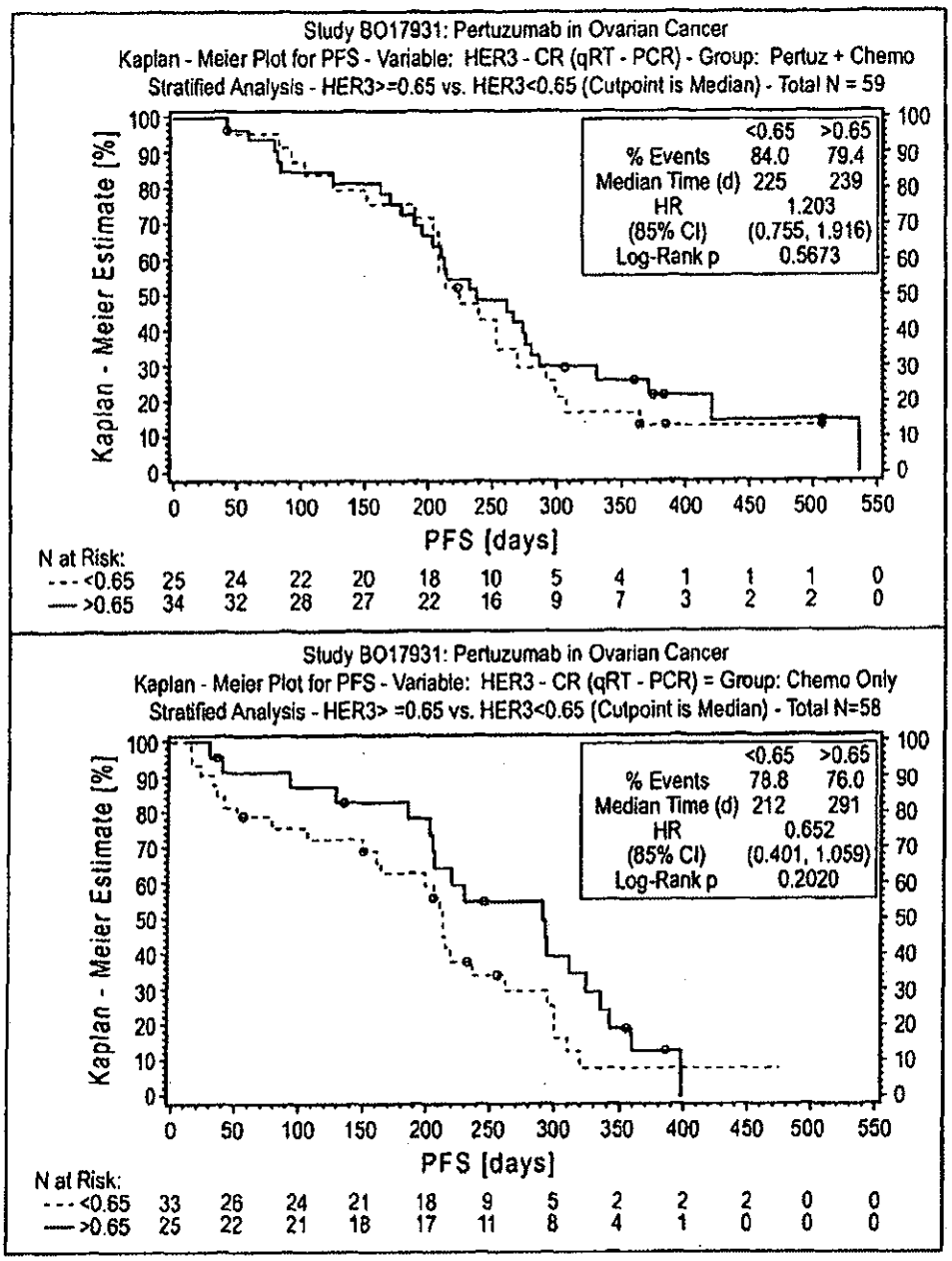

Study BO17931: Pertuzumab in Ovarian Cancer
Kaplan - Meier Plot for PFS - Variable: HER3 - CR (qRT - PCR) - Group: Pertuz + Chemo
Stratified Analysis - HER3>=0.65 vs. HER3<0.65 (Cutpoint is Median) - Total N = 59
Kaplan - Meier Estimate [%]
PFS [days]
<0.65 >0.65
% Events 84.0 79.4
Median Time (d) 225 239
HR 1.203
(85% CI) (0.755, 1.916)
Log-Rank p 0.5673
N at Risk:
---<0.65 25 24 22 20 18 10 5 4 1 1 1 0
——>0.65 34 32 28 27 22 16 9 7 3 2 2 0
Study BO17931: Pertuzumab in Ovarian Cancer
Kaplan - Meier Plot for PFS - Variable: HER3 - CR (qRT - PCR) = Group: Chemo Only
Stratified Analysis - HER3> =0.65 vs. HER3<0.65 (Cutpoint is Median) - Total N=58
Kaplan - Meier Estimate [%]
PFS [days]
<0.65 >0.65
% Events 78.8 76.0
Median Time (d) 212 291
HR 0.652
(85% CI) (0.401, 1.059)
Log-Rank p 0.2020
N at Risk:
---<0.65 33 26 24 21 18 9 5 2 2 2 0 0
——>0.65 25 22 21 18 17 11 8 4 1 0 0 0

FIG. 33

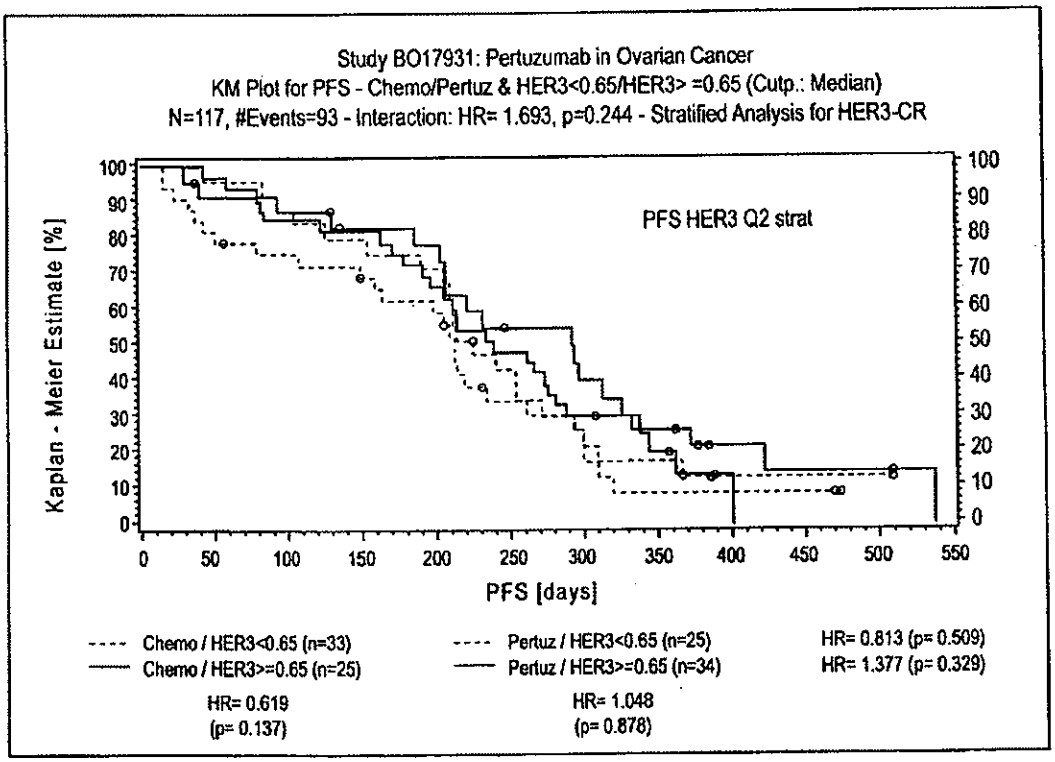

Study BO17931: Pertuzumab in Ovarian Cancer
KM Plot for PFS - Chemo/Pertuz & HER3<0.65/HER3> =0.65 (Cutp.: Median)
N=117, #Events=93 - Interaction: HR= 1.693, p=0.244 - Stratified Analysis for HER3-CR
PFS HER3 Q2 strat
Kaplan - Meier Estimate [%]
PFS [days]
Chemo / HER3<0.65 (n=33)
Chemo / HER3>=0.65 (n=25)
HR= 0.619
(p= 0.137)
Pertuz / HER3<0.65 (n=25)
Pertuz / HER3>=0.65 (n=34)
HR= 1.048
(p= 0.878)
HR= 0.813 (p= 0.509)
HR= 1.377 (p= 0.329)

FIG. 34-1

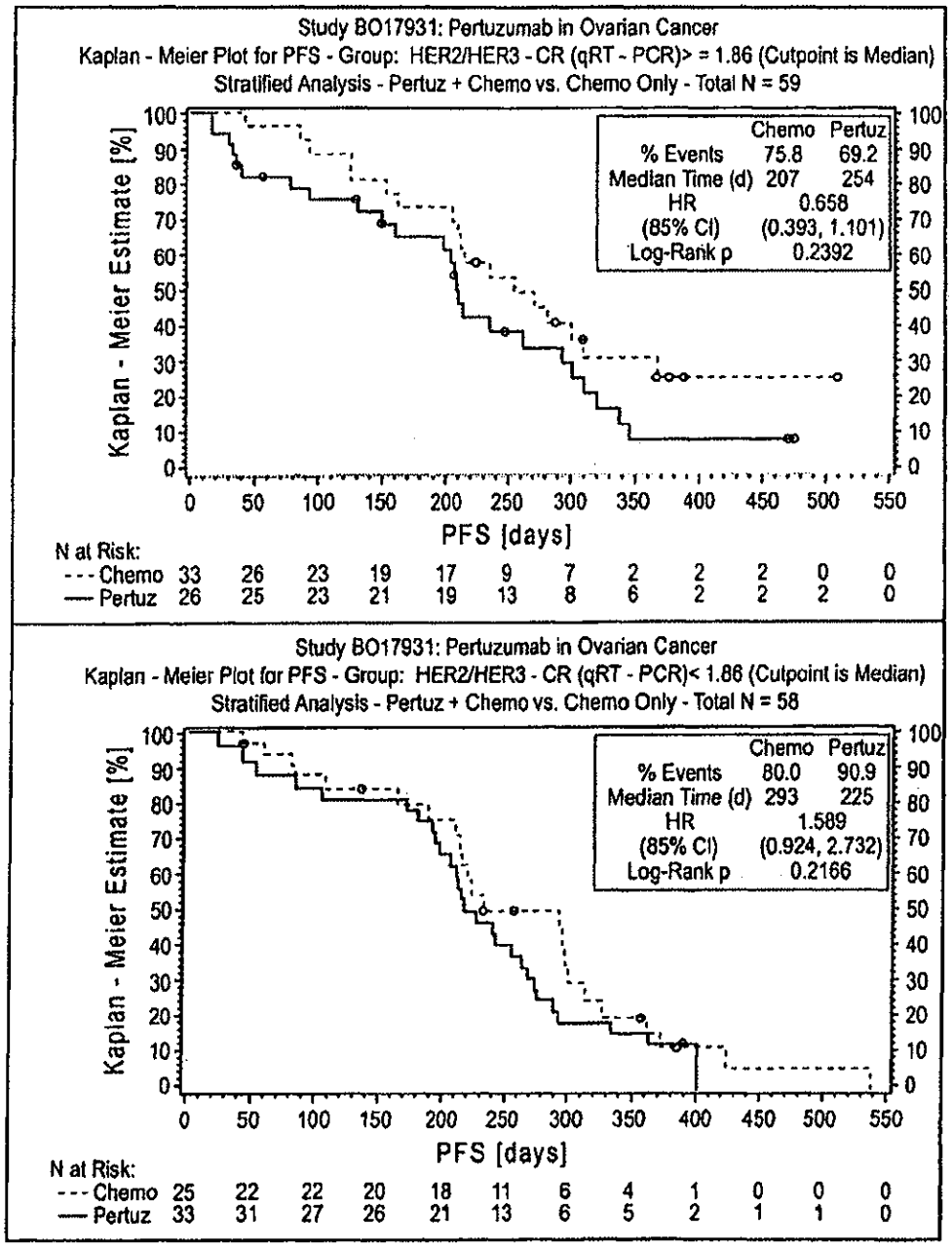

Study BO17931: Pertuzumab in Ovarian Cancer
Kaplan - Meier Plot for PFS - Group: HER2/HER3 - CR (qRT - PCR)> = 1.86 (Cutpoint is Median)
Stratified Analysis - Pertuz + Chemo vs. Chemo Only - Total N = 59
Kaplan - Meier Estimate [%]
PFS [days]
Chemo Pertuz
% Events 75.8 69.2
Median Time (d) 207 254
HR 0.658
(85% CI) (0.393, 1.101)
Log-Rank p 0.2392
N at Risk:
--- Chemo 33 26 23 19 17 9 7 2 2 2 0 0
— Pertuz 26 25 23 21 19 13 8 6 2 2 2 0
Study BO17931: Pertuzumab in Ovarian Cancer
Kaplan - Meier Plot for PFS - Group: HER2/HER3 - CR (qRT - PCR)< 1.86 (Cutpoint is Median)
Stratified Analysis - Pertuz + Chemo vs. Chemo Only - Total N = 58
Kaplan - Meier Estimate [%]
PFS [days]
Chemo Pertuz
% Events 80.0 90.9
Median Time (d) 293 225
HR 1.589
(85% CI) (0.924, 2.732)
Log-Rank p 0.2166
N at Risk:
--- Chemo 25 22 22 20 18 11 6 4 1 0 0 0
— Pertuz 33 31 27 26 21 13 6 5 2 1 1 0

FIG. 34-2

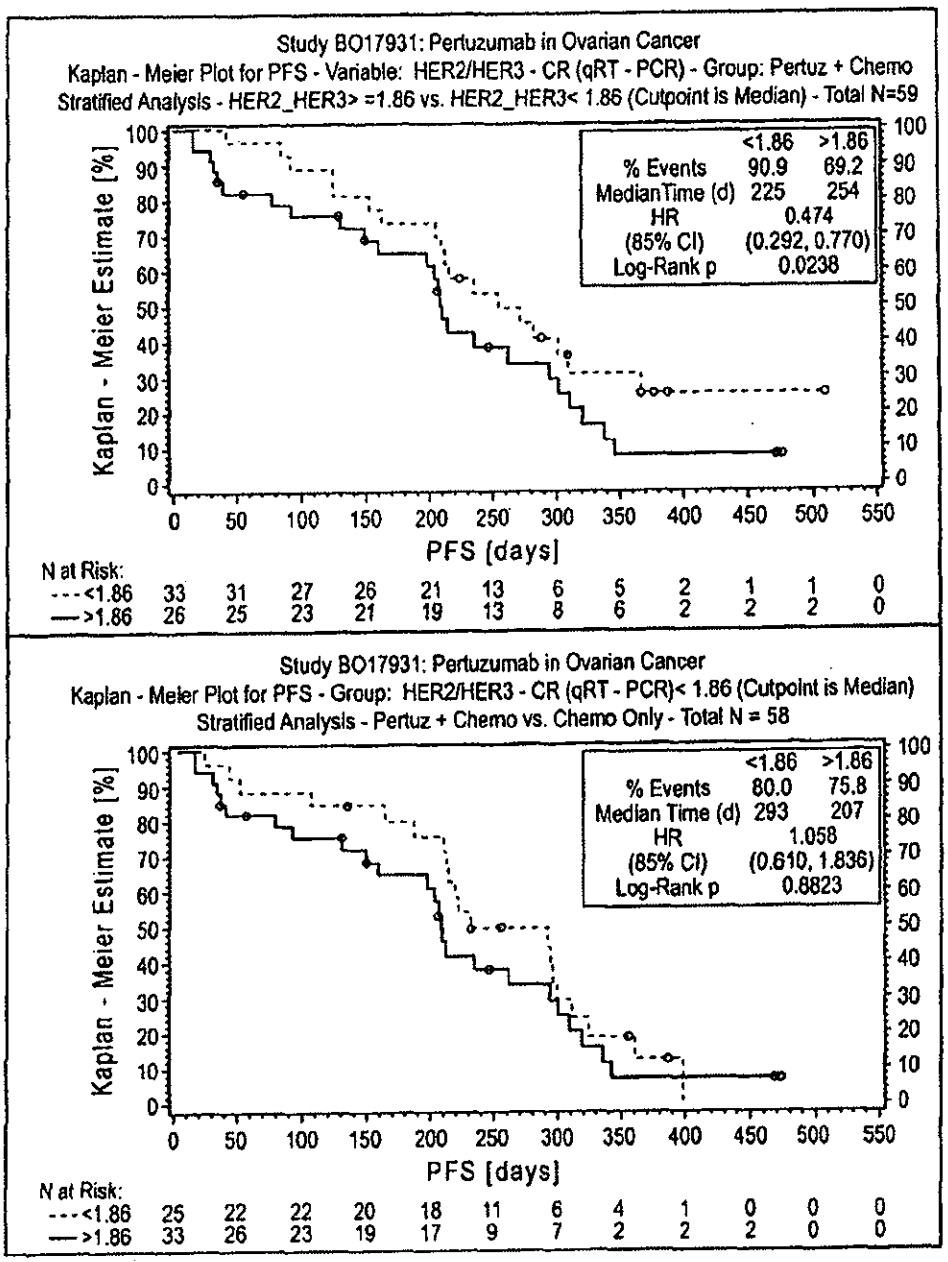
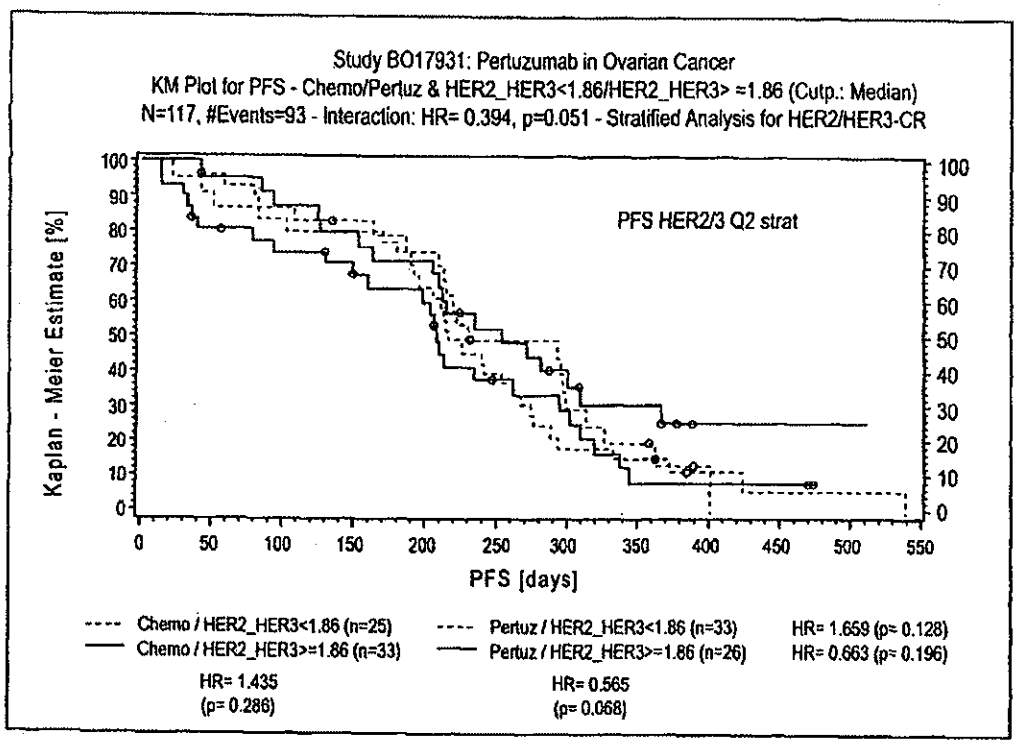

Study BO17931: Pertuzumab in Ovarian Cancer
Kaplan - Meier Plot for PFS - Variable: HER2/HER3 - CR (qRT - PCR) - Group: Pertuz + Chemo
Stratified Analysis - HER2_HER3> =1.86 vs. HER2_HER3< 1.86 (Cutpoint is Median) - Total N=59
Kaplan - Meier Estimate [%]
PFS [days]
<1.86 >1.86
% Events 90.9 69.2
Median Time (d) 225 254
HR 0.474
(85% CI) (0.292, 0.770)
Log-Rank p 0.0238
N at Risk:
---<1.86 33 31 27 26 21 13 6 5 2 1 1 0
—>1.86 26 25 23 21 19 13 8 6 2 2 2 0
Study BO17931: Pertuzumab in Ovarian Cancer
Kaplan - Meier Plot for PFS - Group: HER2/HER3 - CR (qRT - PCR)< 1.86 (Cutpoint is Median)
Stratified Analysis - Pertuz + Chemo vs. Chemo Only - Total N = 58
Kaplan - Meier Estimate [%]
PFS [days]
<1.86 >1.86
% Events 80.0 75.8
Median Time (d) 293 207
HR 1.058
(85% CI) (0.610, 1.836)
Log-Rank p 0.8823
N at Risk:
---<1.86 25 22 22 20 18 11 6 4 1 0 0 0
—>1.86 33 26 23 19 17 9 7 2 2 2 0 0

FIG. 35


Study BO17931: Pertuzumab in Ovarian Cancer
KM Plot for PFS - Chemo/Pertuz & HER2_HER3<1.86/HER2_HER3> =1.86 (Cutp.: Median)
N=117, #Events=93 - Interaction: HR= 0.394, p=0.051 - Stratified Analysis for HER2/HER3-CR
PFS HER2/3 Q2 strat
Kaplan - Meier Estimate [%]
PFS [days]
Chemo / HER2_HER3<1.86 (n=25)
Chemo / HER2_HER3>=1.86 (n=33)
HR= 1.435
(p= 0.286)
Pertuz / HER2_HER3<1.86 (n=33)
Pertuz / HER2_HER3>=1.86 (n=26)
HR= 0.565
(p= 0.068)
HR= 1.659 (p= 0.128)
HR= 0.663 (p= 0.196)