VeriStrat® Overview

VeriStrat®

- VeriStrat is a serum proteomic test that identifies 2nd and 3rd line NSCLC patients who are likely to have good or poor outcomes (OS) following erlotinib therapy
- VeriStrat is processed in Biodesix' CLIA-accredited laboratory and test results provided within 72 hours

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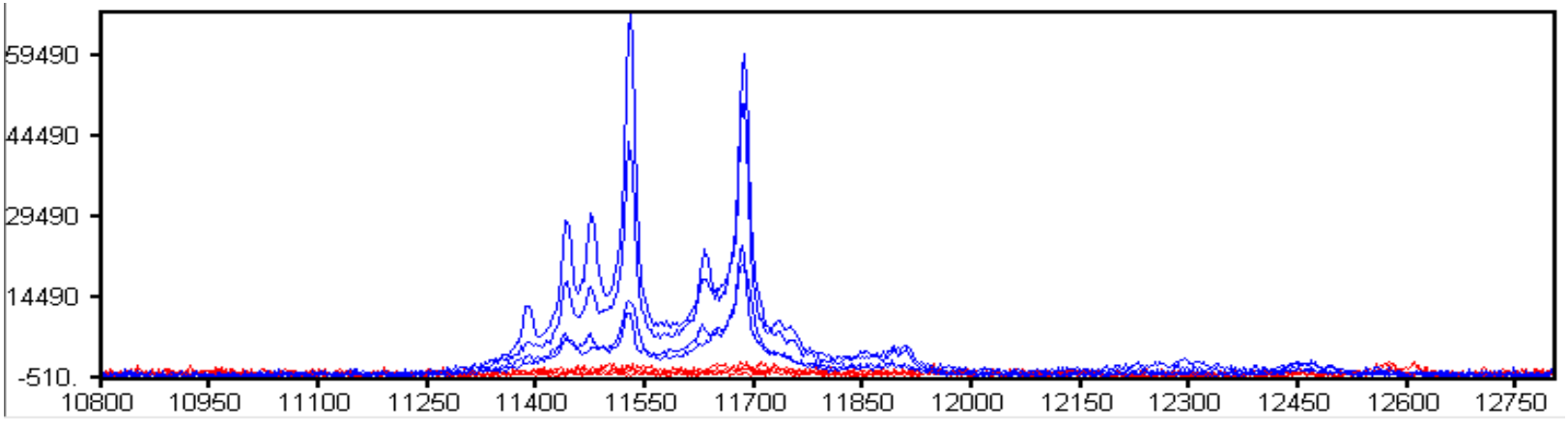
What is VeriStrat?

- The VeriStrat classifier uses 8 peaks (selected during VeriStrat development)
- VeriStrat assigns a result of either Good or Poor according to an algorithm using the mass spectral intensity of these peaks.
- These peaks are predominantly present in the VeriStrat Poor group



4 Good (red) and 4 Poor (blue) spectra. Only a sub-range of the spectra is shown.

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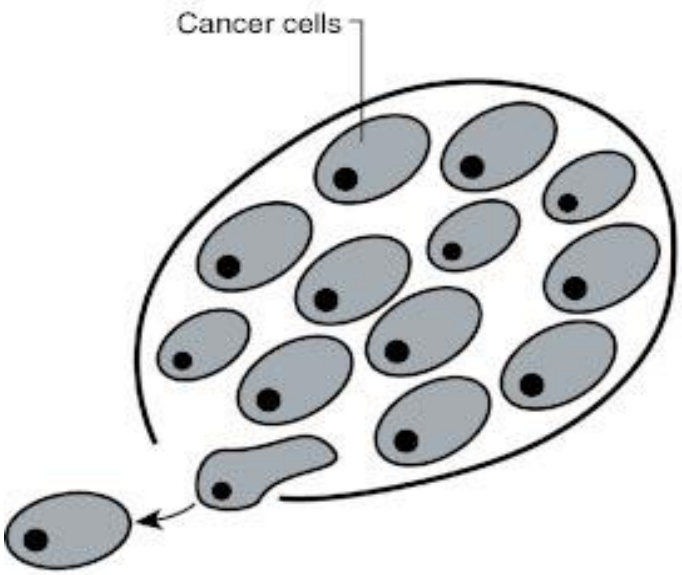
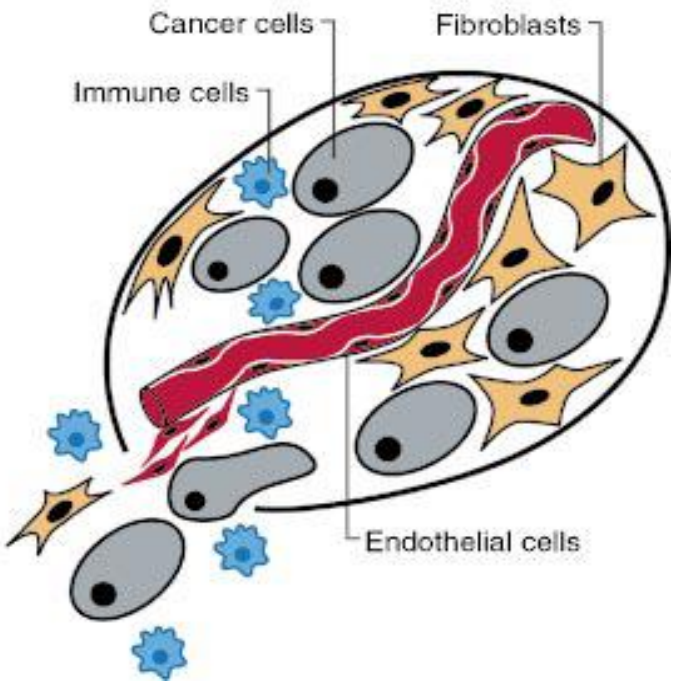
Cancer is more than the tumor

The Reductionist View



A Heterotypic Cell Biology



Cancer is the tumor + tumor environment

1.Hanahan D, Weinberg RA. The hallmarks of cancer. Cell 2000;100:57-70.

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VeriStrat MOA Hypothesis

- VeriStrat is unique
  - Novel biomarker, unlike other biomarkers (unrelated to other tests like EGFR mutations, KRAS, FISH)
  - Not specific to a tumor type or histology.
  - Independent of the mode of action: TKI and AB based EGFRIs.
  - Independent of clinical features (smoking history, gender, race).
- VeriStrat is related to circulating markers involved in the host's inflammatory response
  - Various isoforms of SAA may be part of the VeriStrat Poor signature.
- Hypothesis: VeriStrat Poor indicates a non-standard activation of downstream pathways (e.g. MAPk) resulting in resistance to therapies targeting upstream receptors and transduction pathways.

Development of VeriStrat®

Assay developed and optimized
Training Set (n=139)

↓

All parameters frozen (2005)
No subsequent changes to assay or classification algorithm

↓

Assay validated in two
independent patient sets (Validation Sets, n=67 and n=96)
and
Reproducibility of assay demonstrated

↓

Control Sets evaluated (n=32, n=61, and n=65)
Prognostic or Predictive?

Taguchi F et al. *J Natl Cancer Inst.* 2007;99:838-46.

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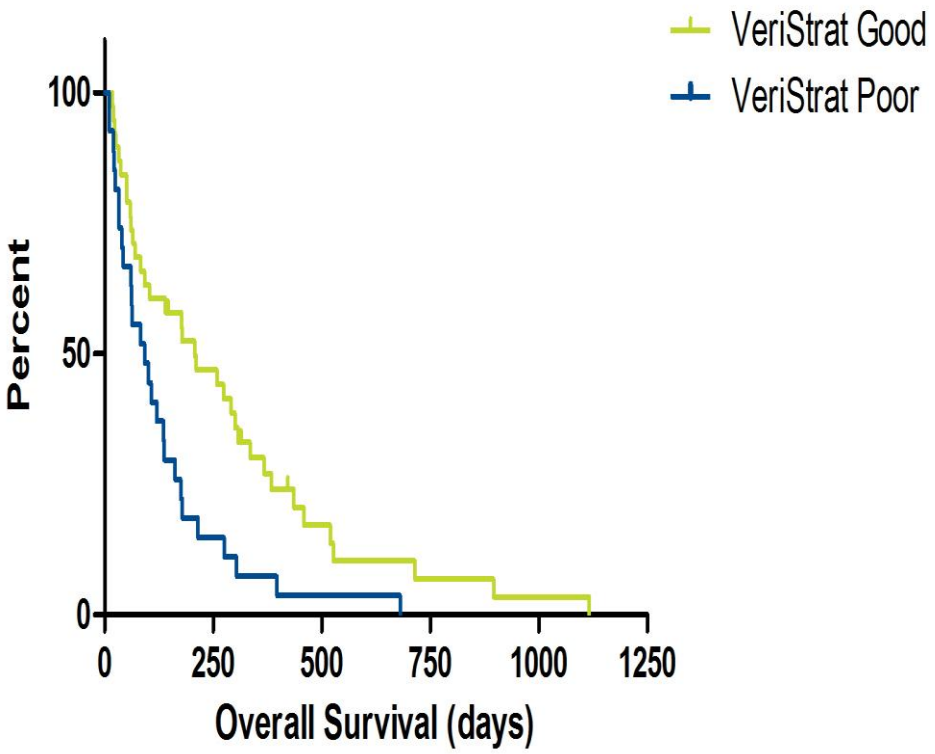
VeriStrat® Validation 1: Italian B
2nd line + NSCLC Patients Treated with Gefitinib

Italian B (N=67)		
Median Survival = 128 days		
1 year survival = 19%		
VeriStrat Applied to Italian B		
	VeriStrat Good 39	**VeriStrat Poor 27**
Events	35	27
Median Survival (days)	207	92
1 year survival (%)	26	8
	***p*=0.0062, HR=0.45**	



- In the VeriStrat Poor patient group, the risk of death was 2x that of the VeriStrat Good group after treatment with EGFR-TKIs.

Taguchi F et al. *J Natl Cancer Inst.* 2007;99:838-46.

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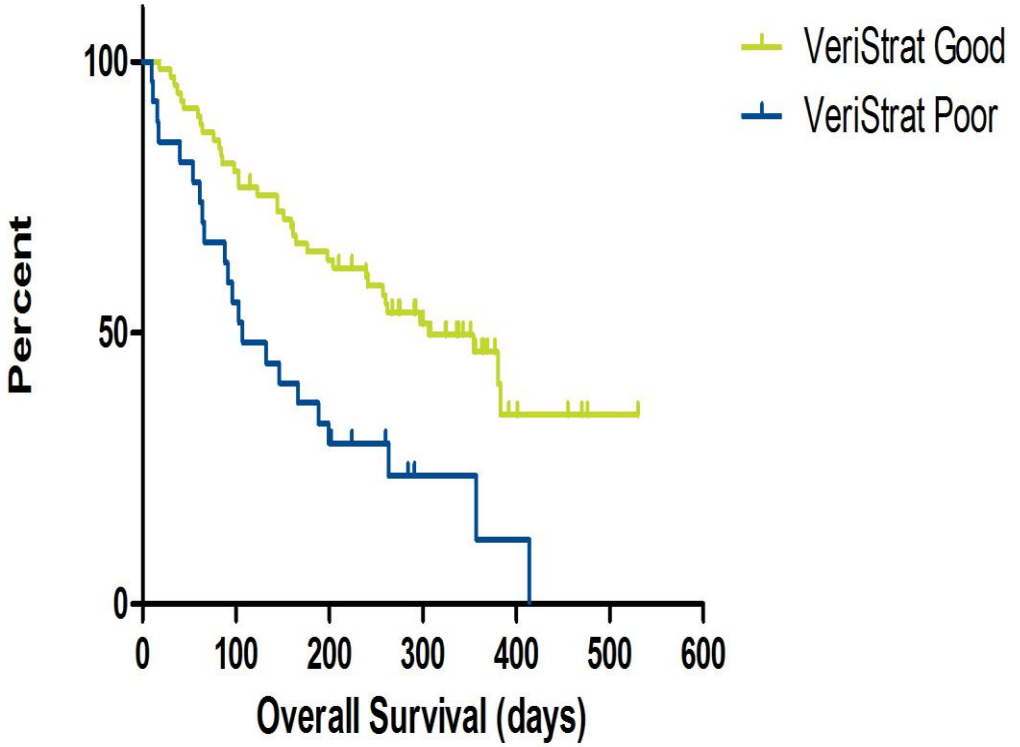
VeriStrat® Validation 2: ECOG 3503
1st line NSCLC Patients Treated with Erlotinib

ECOG 3503 (N=96)		
Median Survival = 257 days		
1 year survival = 37%		
VeriStrat Applied to ECOG 3503		
	VeriStrat Good 69	**VeriStrat Poor 27**
Events	36	22
Median Survival (days)	306	107
1 year survival (%)	47	12
	***p*=0.0007, HR=0.33**	



- In the VeriStrat Poor patient group, the risk of death was 3x that of the VeriStrat Good group after treatment with EGFR-TKIs.

Taguchi F et al. *J Natl Cancer Inst.* 2007;99:838-46.

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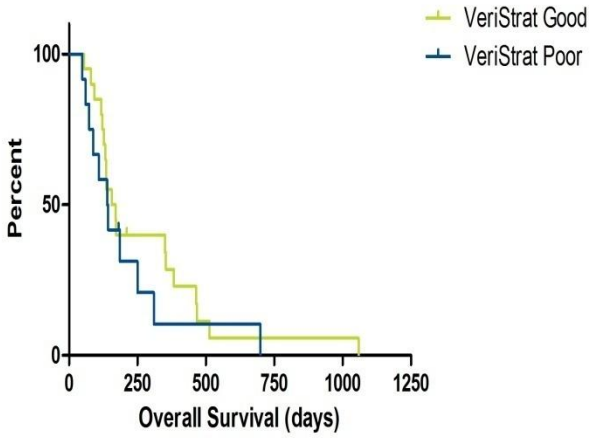
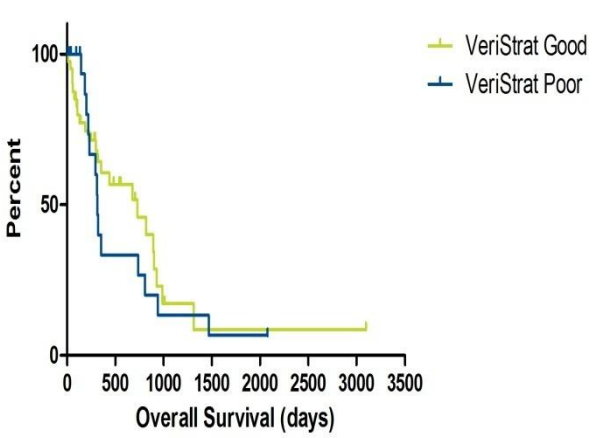
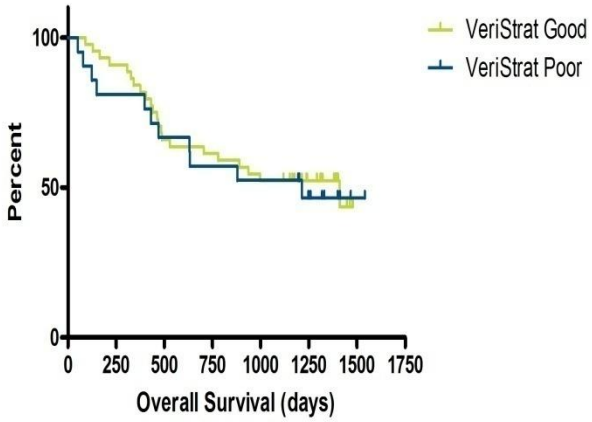
VeriStrat Validation: Predictive for EGFRIs?



Italian C
N=32 (20 Good, 12 Poor)
Events: 19 Good, 11 Poor
***p*=0.42, HR=0.72**



Vanderbilt
N=61 (41 Good, 20 Poor)
Events: 23 Good, 14 Poor
***p*=0.55, HR=0.81**



Polish
N=65 (44 Good, 21 Poor)
Events: 22 Good, 11 Poor
***p*=0.79, HR=0.90**

- VeriStrat did not show significant separation in chemotherapy-treated or post-surgery NSCLC patients

Taguchi F et al. *J Natl Cancer Inst*. 2007;99:838-46.

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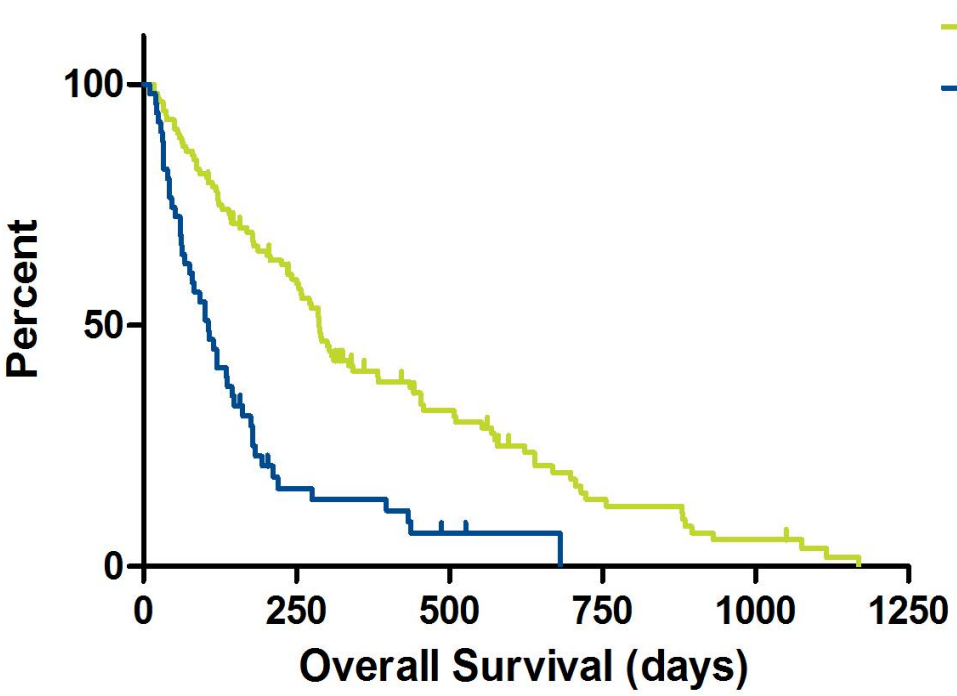
VeriStrat Correlates Outcomes Regardless of Clinical Characteristics: Hx of Smoking



Italian A,B + Japanese A,B Smokers
N=159 (108 Good, 51 Poor)
Events: 92 Good, 47 Poor
Median survival: 287 days (Good), 106 days (Poor)
***p*<0.0001, HR=0.28**

- In patients with a history of smoking, VeriStrat Good patients showed a significantly lower risk of death than VeriStrat Poor patients when treated with EGFR-TKI therapy

Taguchi F et al. *J Natl Cancer Inst*. 2007;99:838-46.

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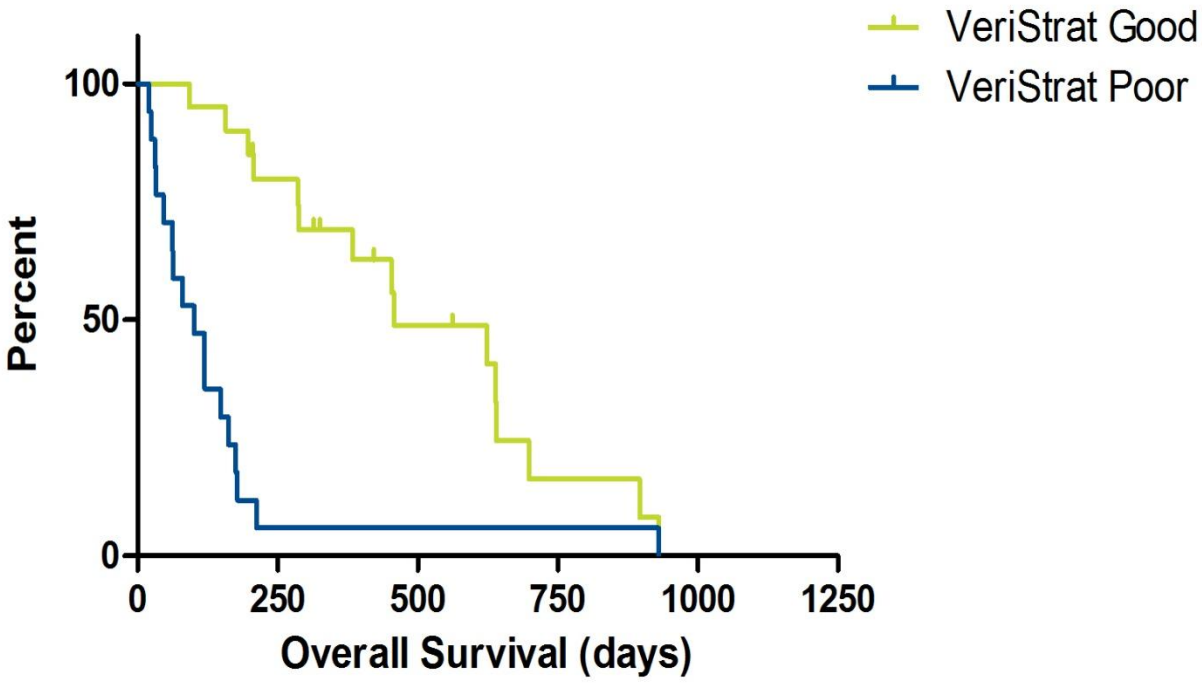
VeriStrat Correlates Outcomes Regardless of Clinical Characteristics: Histology



Italian A,B + Japanese A,B Squamous Histology
N=37 (20 Good, 17 Poor)
Events: 15 Good, 17 Poor
Median survival: 457 days (Good), 101 days (Poor)
***p*<0.0001, HR=0.17**

- In patients with squamous cell histology, VeriStrat Good patients showed a significantly lower risk of death than VeriStrat Poor patients when treated with EGFR-TKI therapy

Taguchi F et al. *J Natl Cancer Inst*. 2007;99:838-46.

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VeriStrat prediction of outcomes in advanced NSCLC patients treated with erlotinib or placebo in the NCIC CTG BR.21 trial

Carbone D, 2nd European Lung Cancer Conference, April 2010

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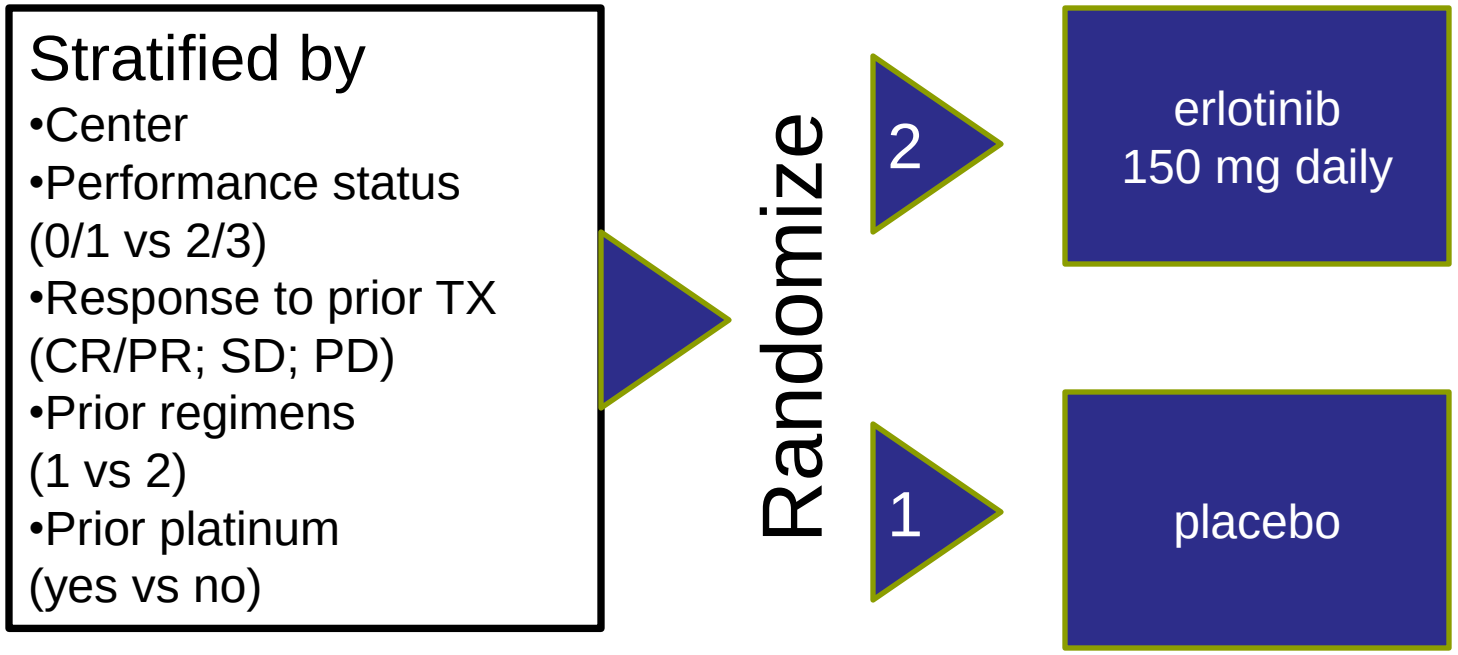
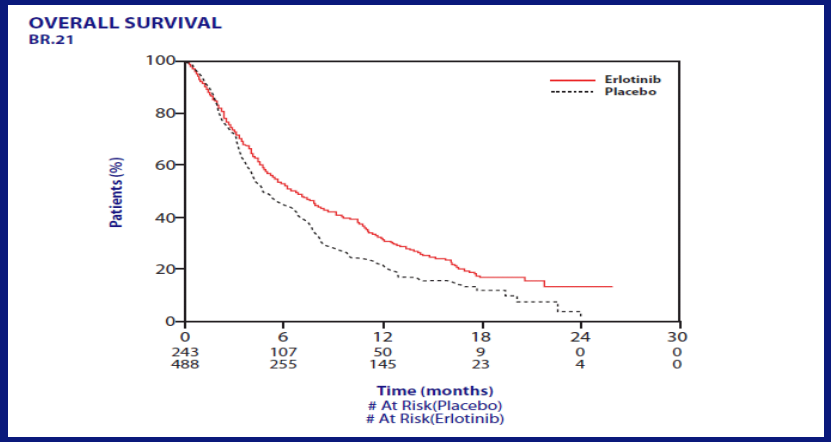
BR.21 Schema



Shepherd et al. NEJM 2005

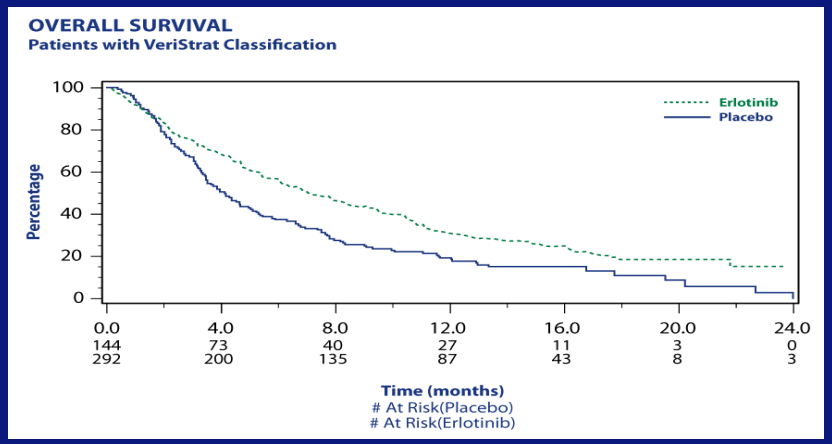
BR.21 OS



	Median Survival (mo)	1yr Survival (%)
erlotinib	6.7	31.2
placebo	4.7	21.5
Hazard ratio, 0.70 (0.58-0.85)		
P<0.001		

n = 731

BR.21 OS VS Subset



	Median OS (mos)	95% CI
erlotinib	7.0	6.1 - 8.4
placebo	4.1	3.5 - 5.1
Hazard ratio = 0.67 (0.54 – 0.83)		
P = 0.0003		

n = 441

Shepherd et al. NEJM 2005

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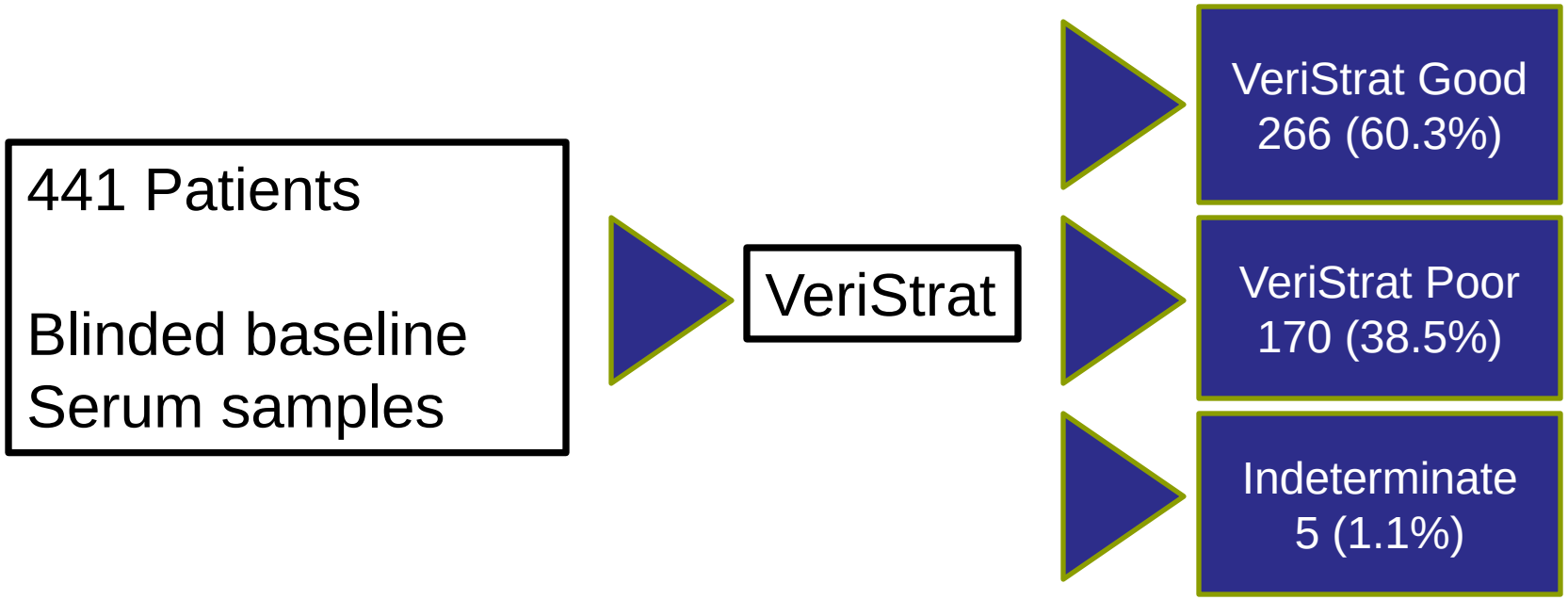
BR.21 VeriStrat Analysis: Methods



Serum available for 441 of 731 patients

VeriStrat classification assigned to 99% of patients

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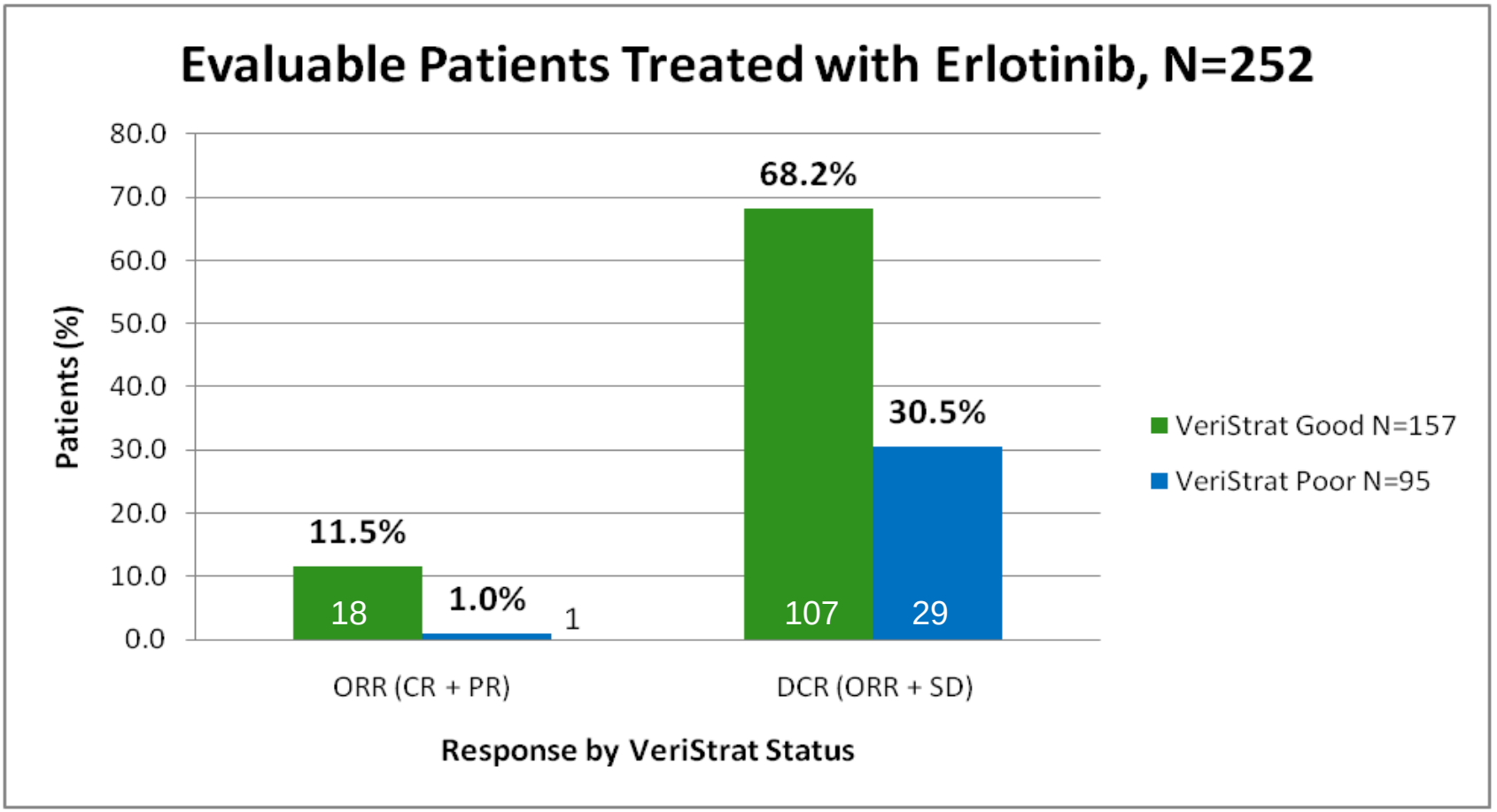
VeriStrat is Predictive of ORR and DCR



•VeriStrat status was predictive of objective response rate (p=0.002) and disease control rate (p=0.0001)

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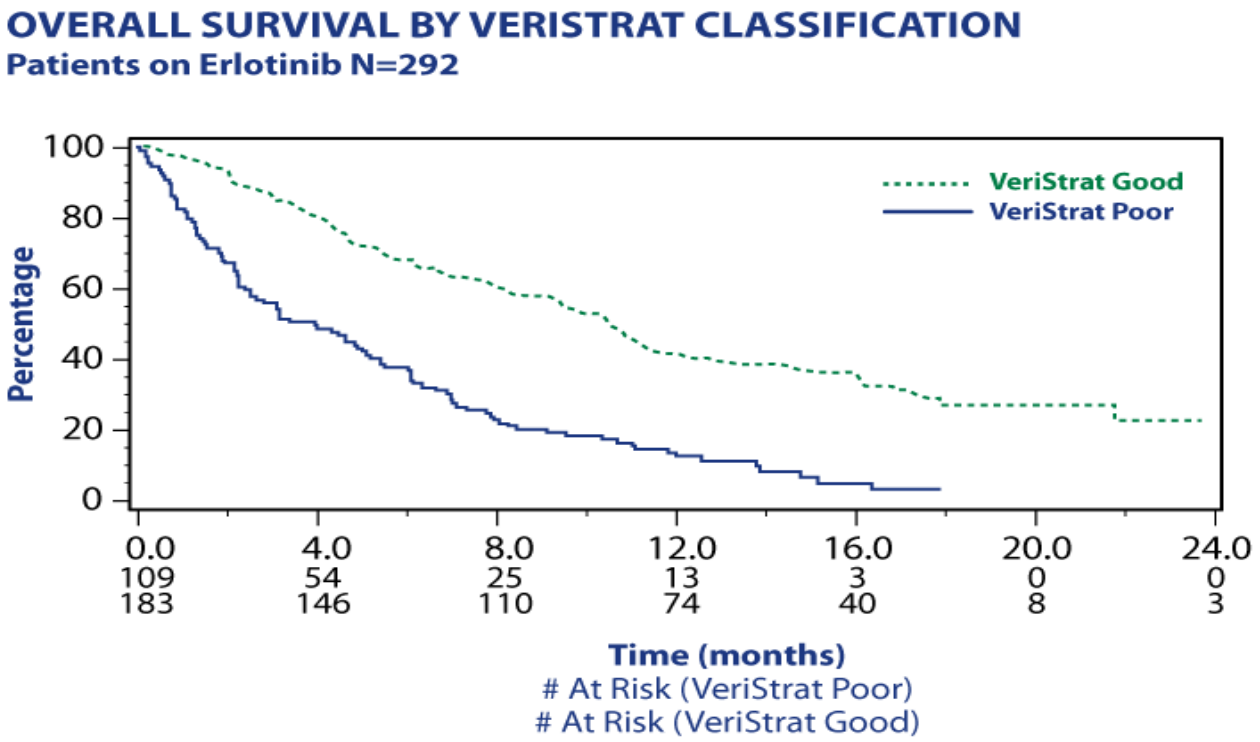
BR.21 – VeriStrat OS in Treatment Arm



	Median OS (mos)	95% CI
VeriStrat Good	10.5	9.1 – 11.4
VeriStrat Poor	4.0	2.5 – 5.2
Hazard ratio = 0.37 (0.28 – 0.48)		
P < 0.0001		

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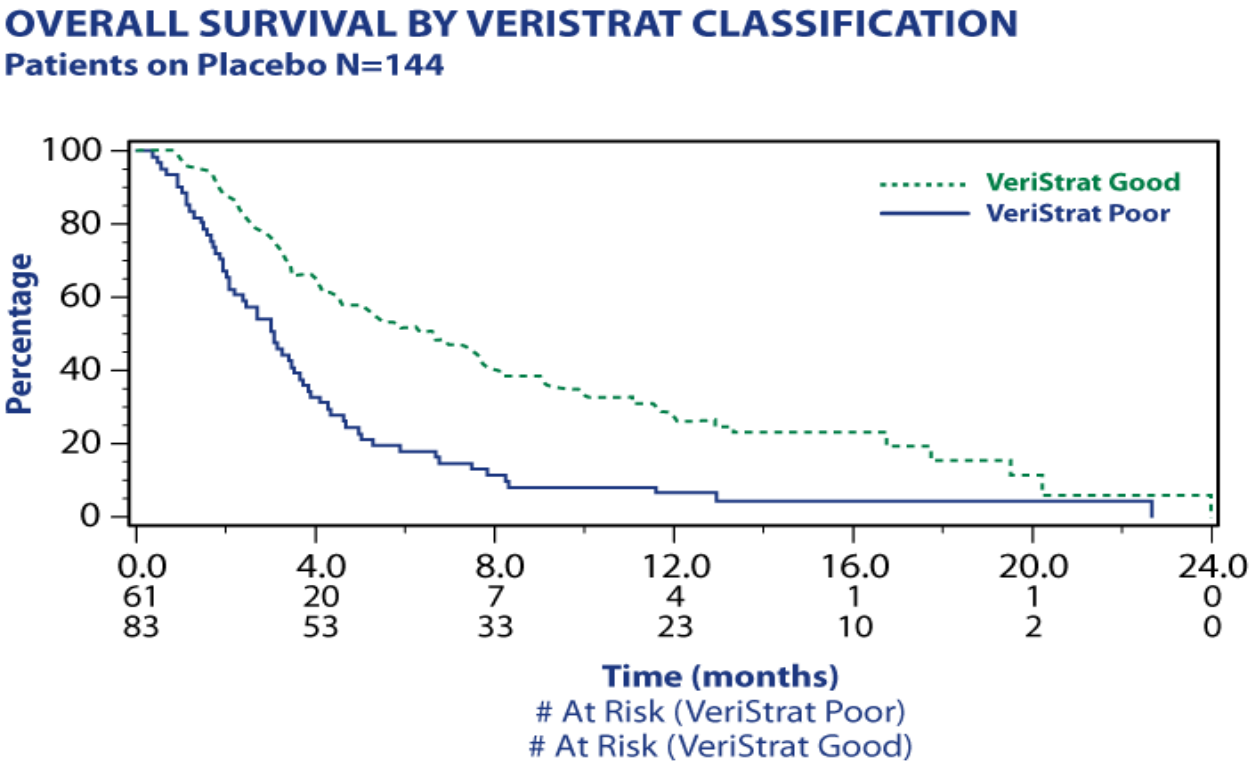
BR.21 – VeriStrat OS in Placebo Arm



	Median OS (mos)	95% CI
VeriStrat Good	6.6	4.4 – 8.2
VeriStrat Poor	3.1	2.2 – 3.7
Hazard ratio = 0.44 (0.31 – 0.63)		
P < 0.0001		

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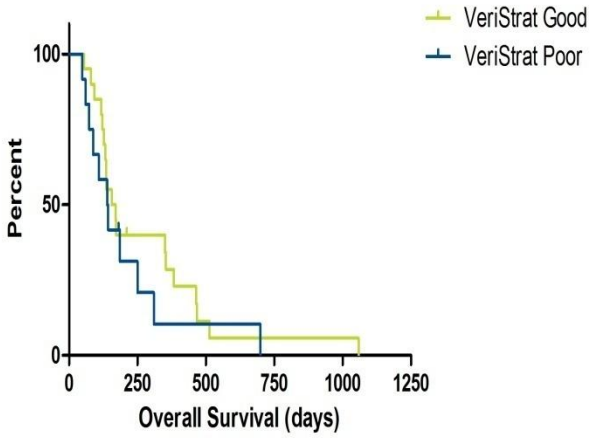
VeriStrat Does Not Correlate with Outcomes for Patients Treated with Chemotherapy



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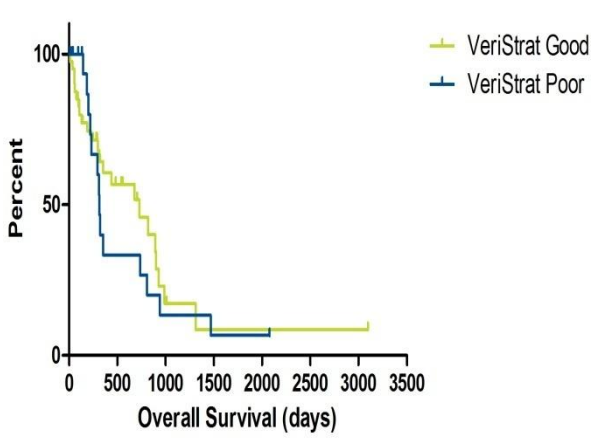

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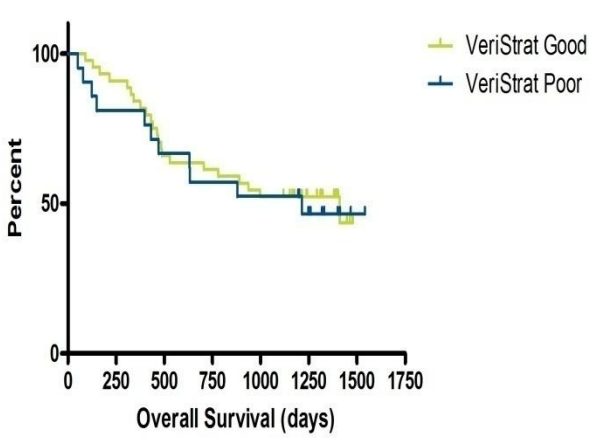

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BR.21: VeriStrat Status Independent of Tissue Markers

		VeriStrat Good (n=266)	VeriStrat Poor (n=170)	P Value
EGFR Mutation				
N = 14	Mutations	10 (71%)	4 (29%)	0.62
N = 116	Wild Type	68 (59%)	48 (41%)	
N = 306	Unknown	188 (61%)	118 (39%)	
EGFR FISH				
N = 43	FISH +	24 (56%)	19 (44%)	0.76
N = 56	FISH -	34 (61%)	22 (39%)	
N = 337	Unknown	208 (62%)	129 (38%)	
KRAS Mutation				
N = 20	Mutations	13 (65%)	7 (35%)	0.93
N = 111	Wild Type	67 (60%)	44 (40%)	
N = 305	Unknown	186 (61%)	119 (39%)	

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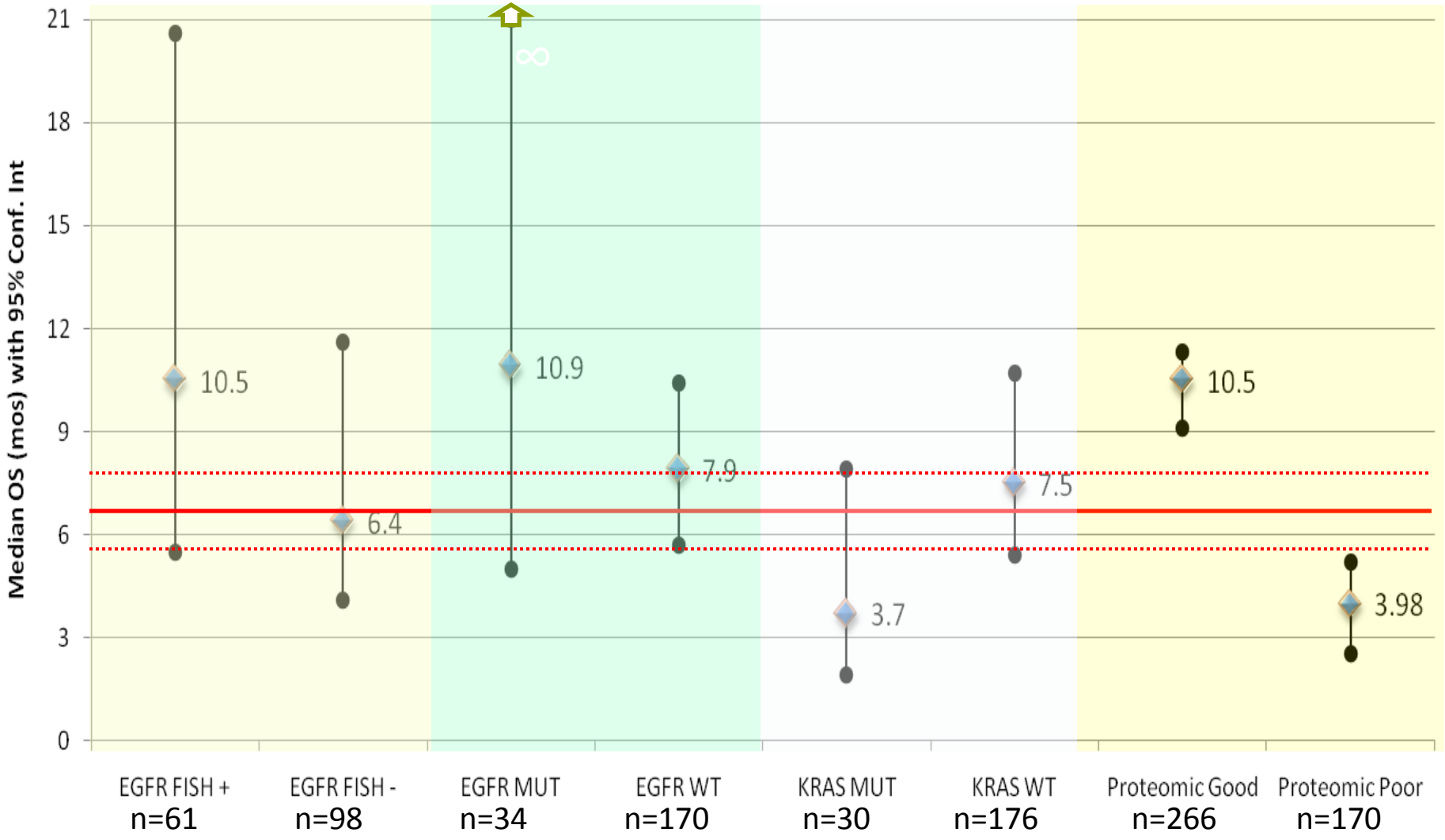
BR.21- Median OS erlotinib arm by biomarker



____indicates median OS unselected patients BR21 with 95% Conf. Int.
Median OS = 6.7 mos (CI: 5.5 -7.8)

Adapted from Zhu JCO 2008
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BR.21 VeriStrat Analysis: Summary

- VeriStrat is serum test for 2nd line + NSCLC patients
- VeriStrat is predictive of DCR and ORR in the erlotinib arm and has a strong prognostic component
- VeriStrat Good patients had significantly better overall survival than VeriStrat Poor patients
  - VeriStrat Good patients had a median OS of 10.5mos
  - VeriStrat Poor patients had no statistically significant benefit from erlotinib therapy
- VeriStrat is independent of known prognostic factors and does not correlate with EGFR/KRAS mutations or EGFR FISH

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