Trial 709
The ISEL Study (IRESSA® Survival Evaluation in Lung Cancer)

Summary of Data
as of December 16, 2004

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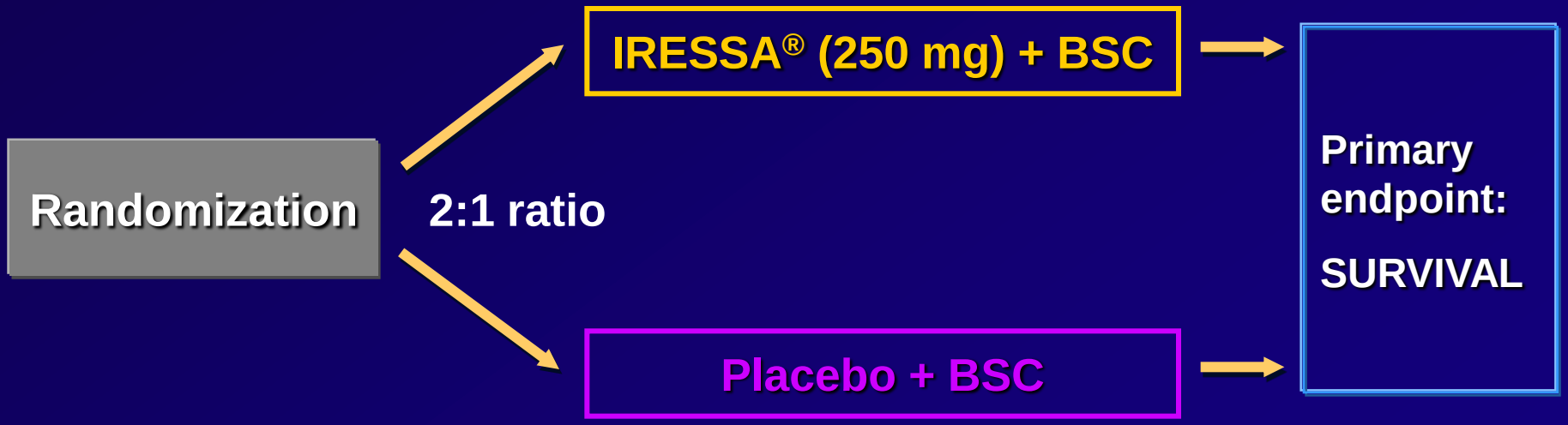
Trial 709– Clinical Trial Design

1692 patients in 210 centers across 28 countries
Stratified for histology, gender, intolerant/refractory and smoking history



Key Eligibility Criteria

- Histologically or cytologically confirmed non-small cell lung cancer
- Locally advanced or metastatic disease
- 1 or 2 prior chemotherapy regimens
- Intolerant to most recent chemotherapy regimen or have progressed on or within 90 days of their last chemotherapy cycle

Endpoints and Methods

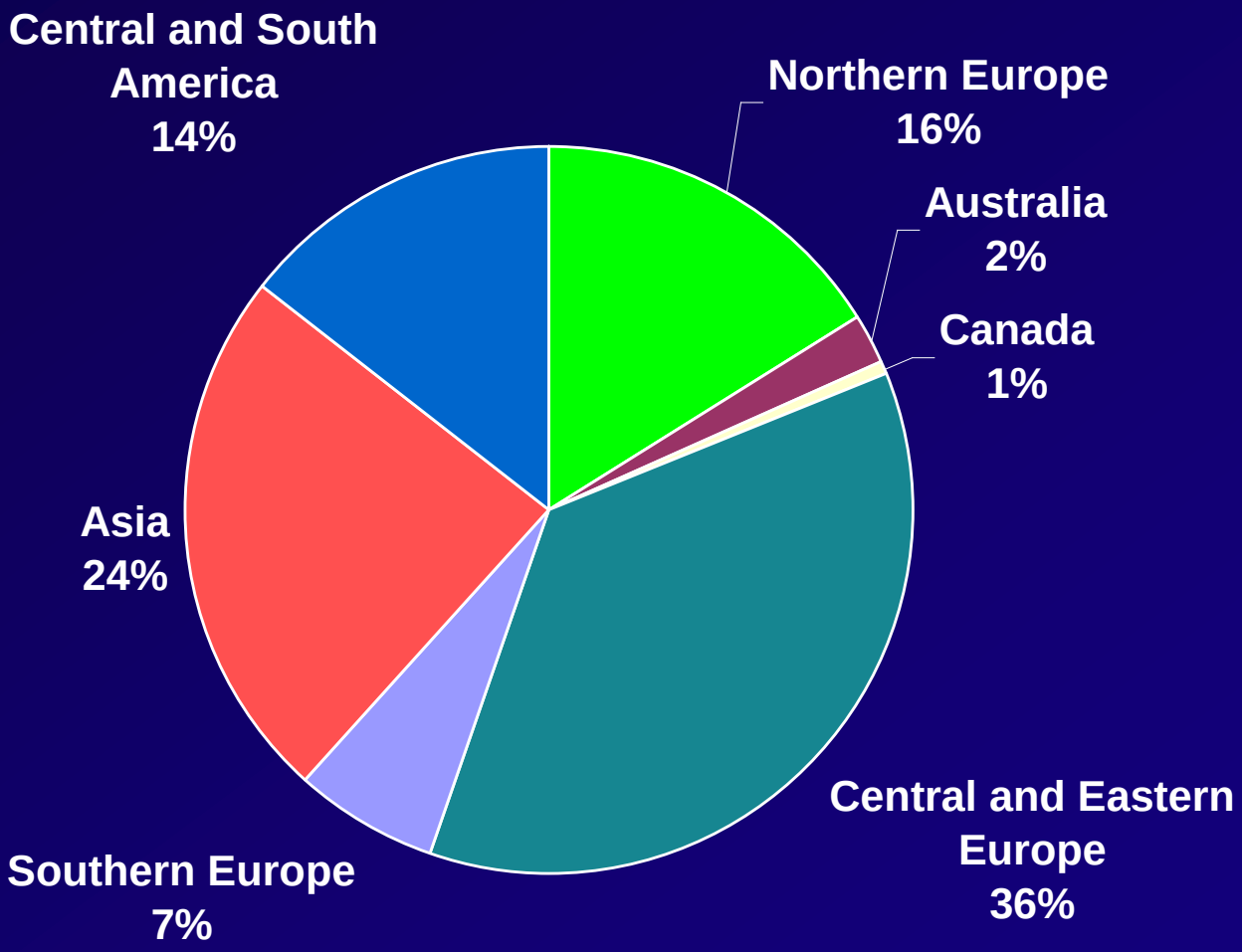
- Primary endpoint: overall survival
  - Stratified log-rank test
  - Cox regression supportive
- Overall and adenocarcinoma populations co-primary
  - At least 900 deaths for 90% power
- Secondary endpoints: time to treatment failure, objective response, QoL, symptoms, and safety
- Several pre-planned subgroup analyses
  - Outcomes in relation to clinical and biologic factors

Data Presented Today

- Patient data accruing up to October 29, 2004
- Preliminary data available for analysis mid-December 2004

- Median (range) follow up: 7 mo (3 to 15 mo)
- 969 (57%) deaths in the database

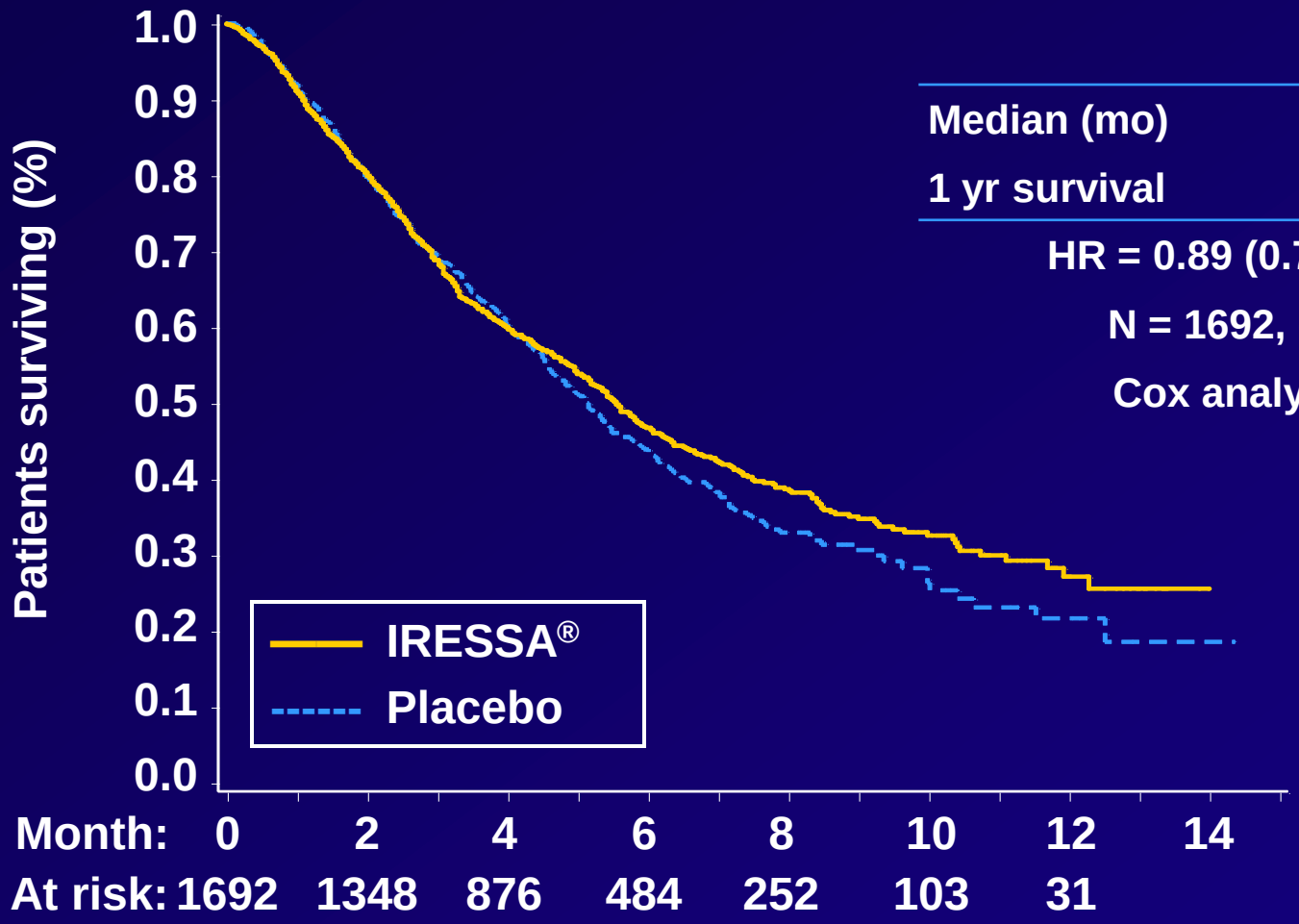
Regional Recruitment



Baseline Characteristics

- Median age 62 yr
- 67% Male
- 67% PS 0-1
- 22% Never smoked
- 20% Asian ethnicity
- 48% Adenocarcinoma
- 49% One prior chemotherapy
- 90% Refractory to most recent chemotherapy
- Treatment groups well balanced

Overall Population–Survival



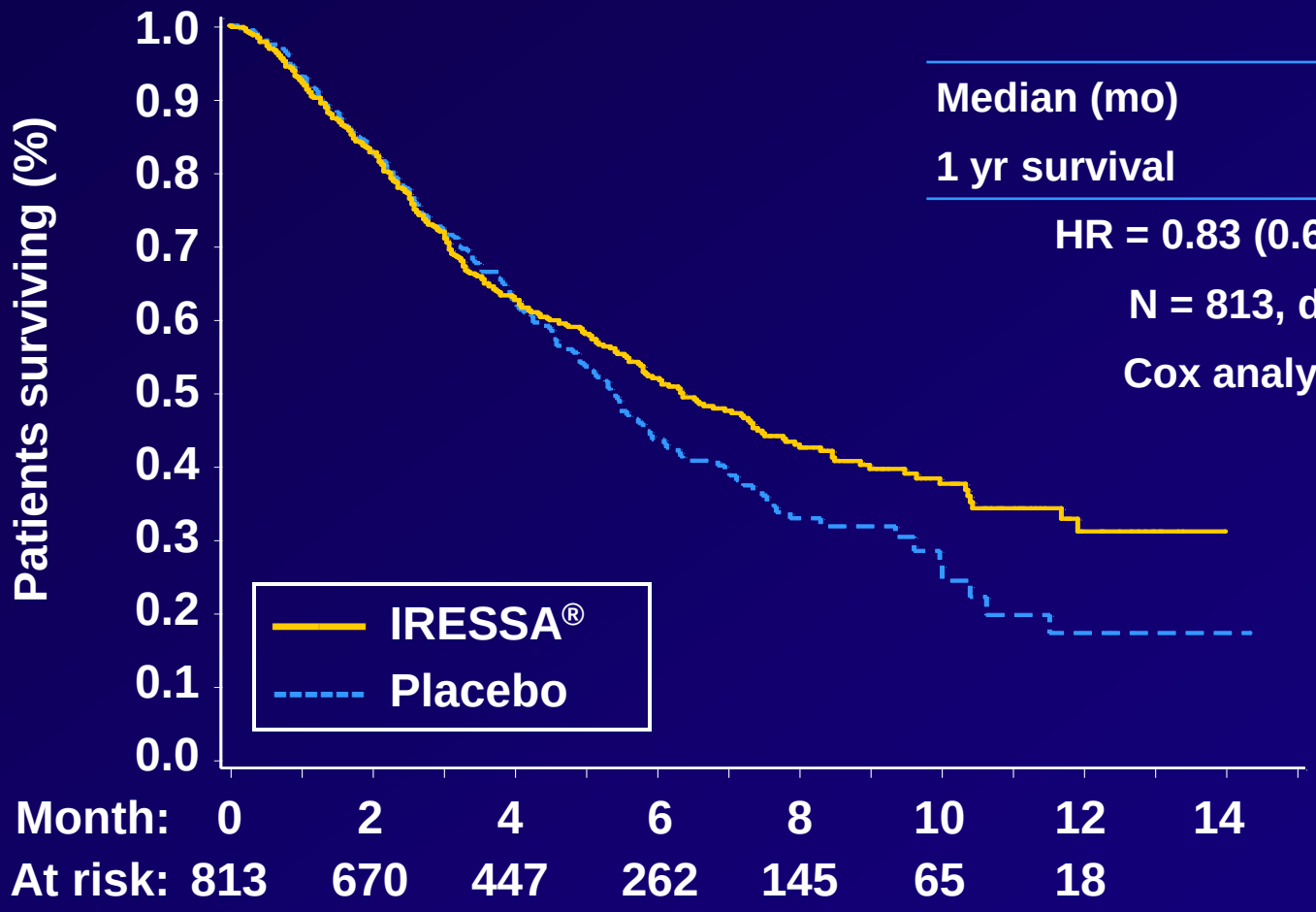
	IRESSA®	Placebo
Median (mo)	5.6	5.1
1 yr survival	27%	22%

HR = 0.89 (0.78, 1.03), *P* = .11

N = 1692, deaths = 969

Cox analysis, *P* = .042

Adenocarcinoma Population–Survival



	IRESSA®	Placebo
Median (mo)	6.3	5.4
1 yr survival	31%	17%

HR = 0.83 (0.67, 1.02), *P* = .07

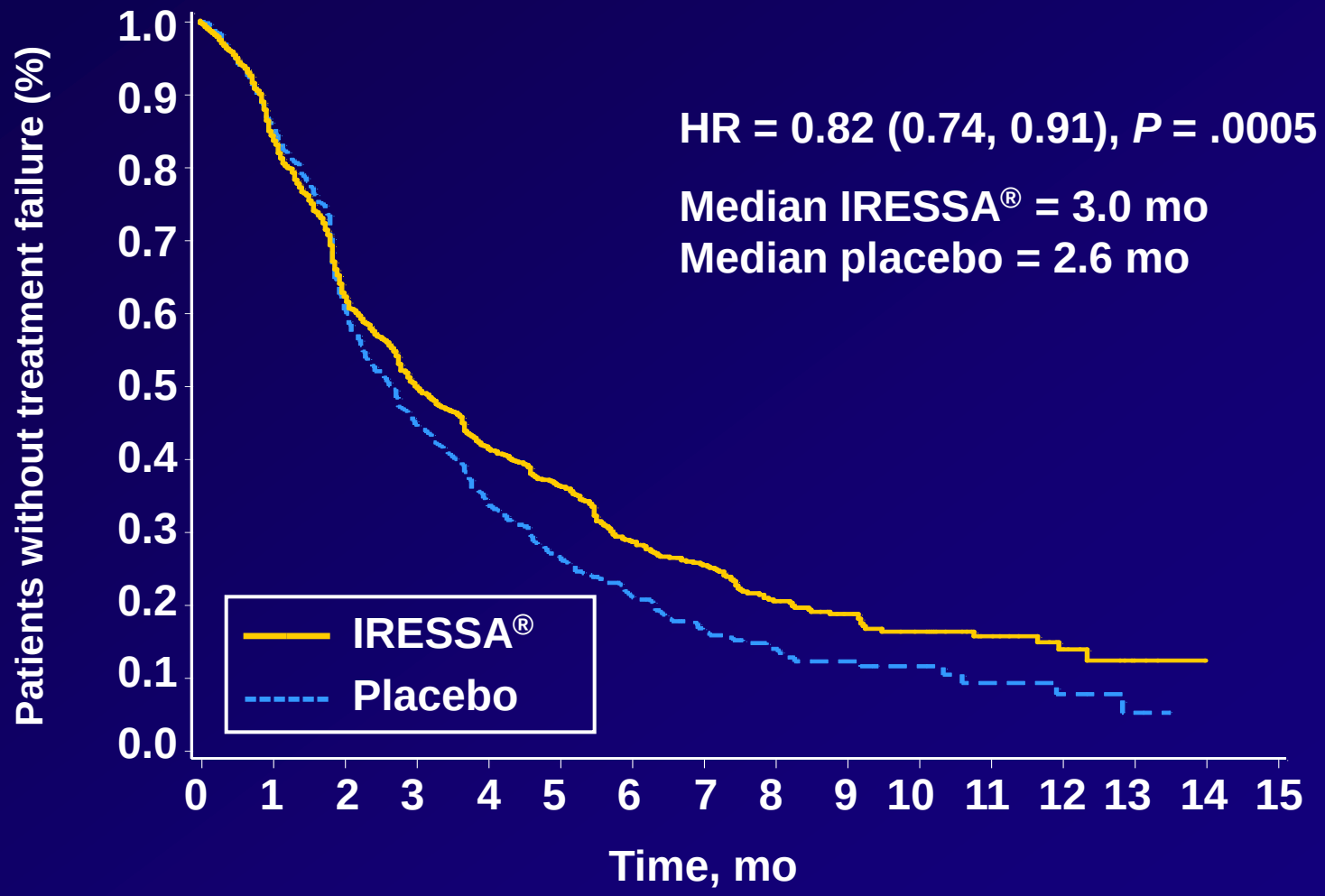
N = 813, deaths = 449

Cox analysis, *P* = .030

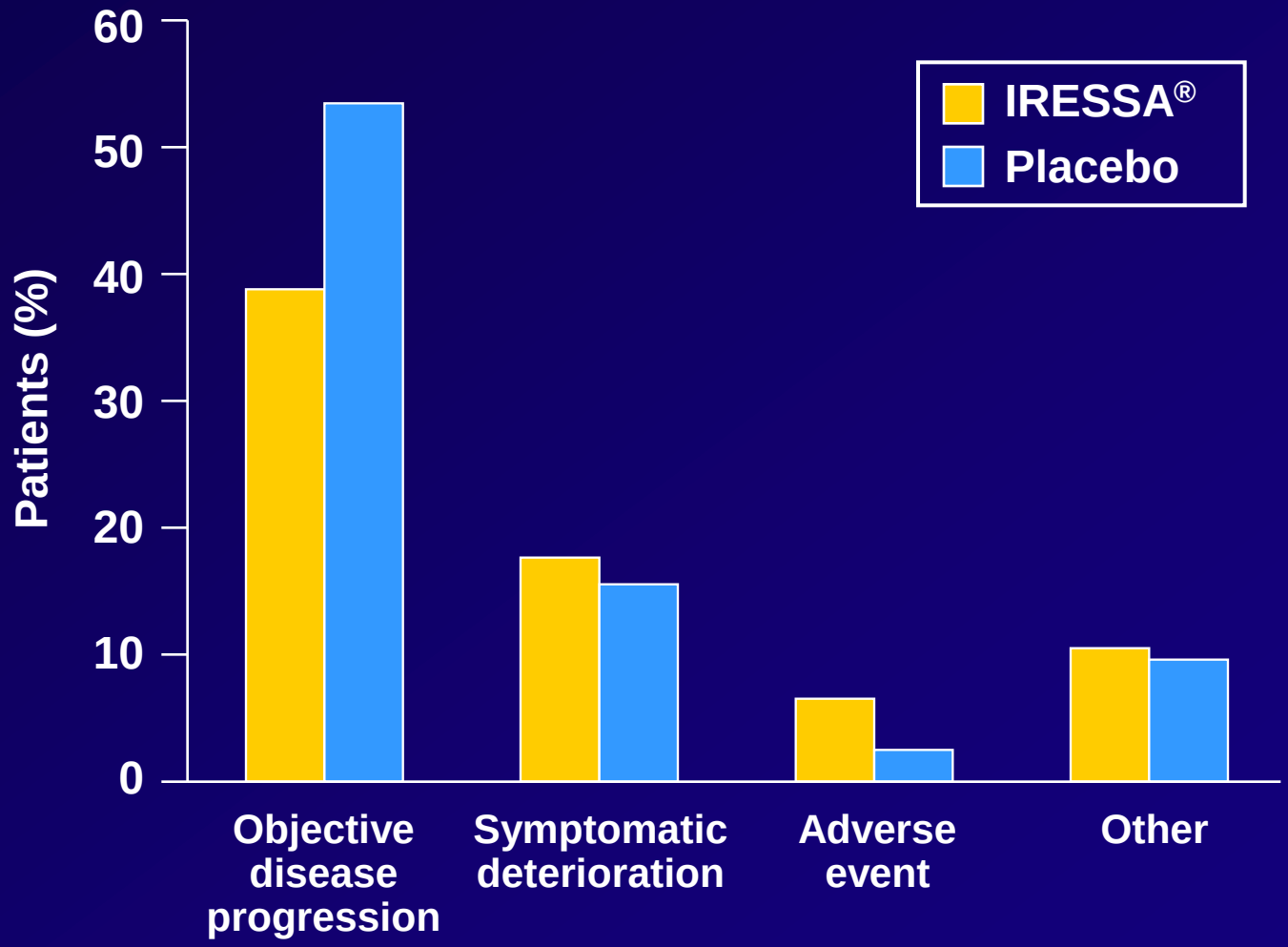
Significant Improvement In Objective Response Rate

	Patients, % (n/N)		Odds ratio (95% CI)	*P* value
	IRESSA®	Placebo		
Objective response rate	7.7% (74/961)	1.2% (6/483)	7.03 (3.0, 16.4)	< .0001

Significant Improvement In Time to Treatment Failure



Fewer Treatment Failures on IRESSA®



Preliminary Quality-of-Life Data– Change in Mean Scores (FACT-L)

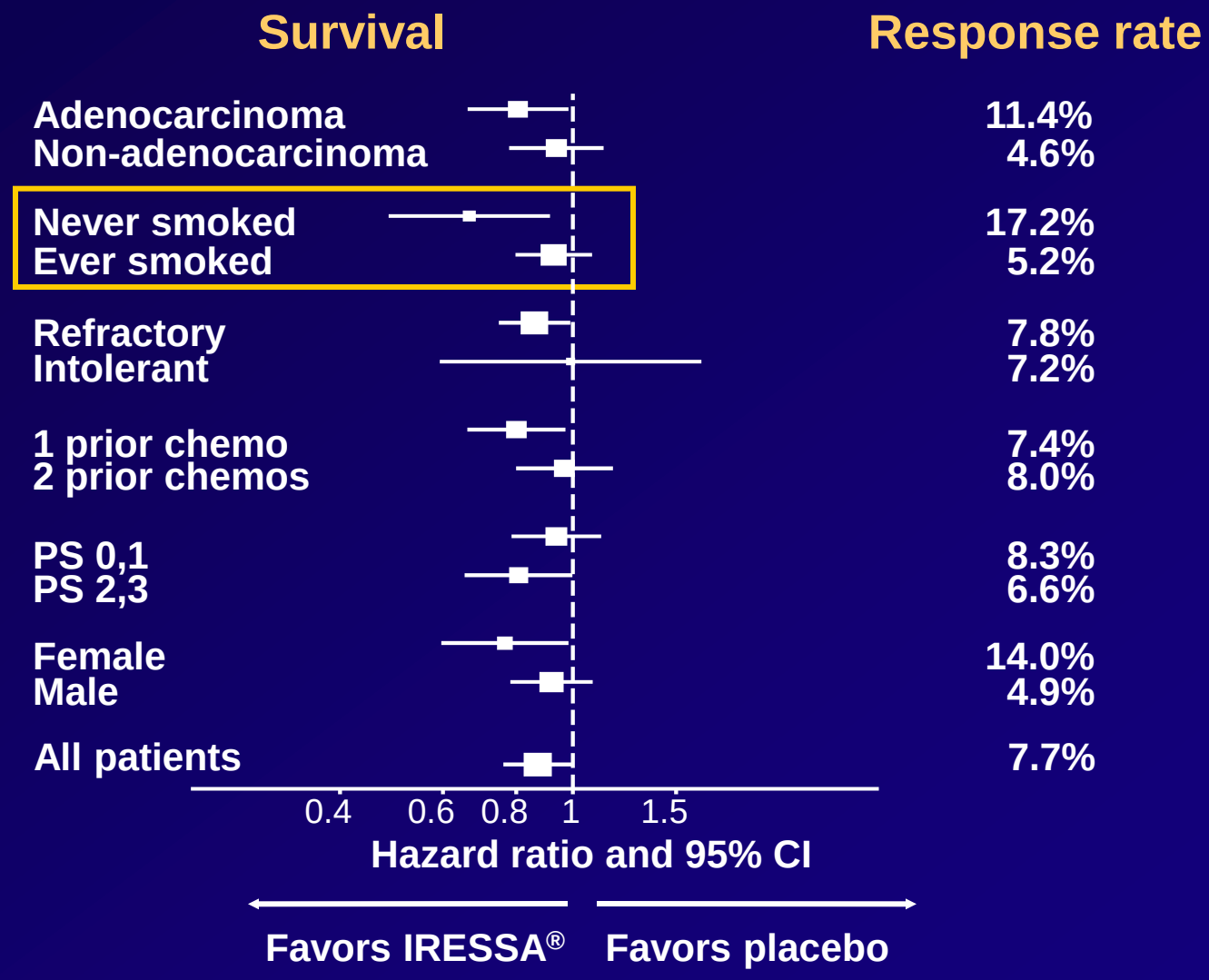
	Possible range of scores†	Mean score		
		IRESSA® (n = 858)	Placebo (n = 425)	*P* value
Symptoms (lung cancer subscore)	0 to 28	16.9	16.4	.02
Overall quality of life	0 to 144	83.8	82.3	.07
Trial outcome index	0 to 84	47.5	46.5	.11

FACT-L = Functional assessment of cancer treatment-lung.
†Higher scores indicate more a favorable status.

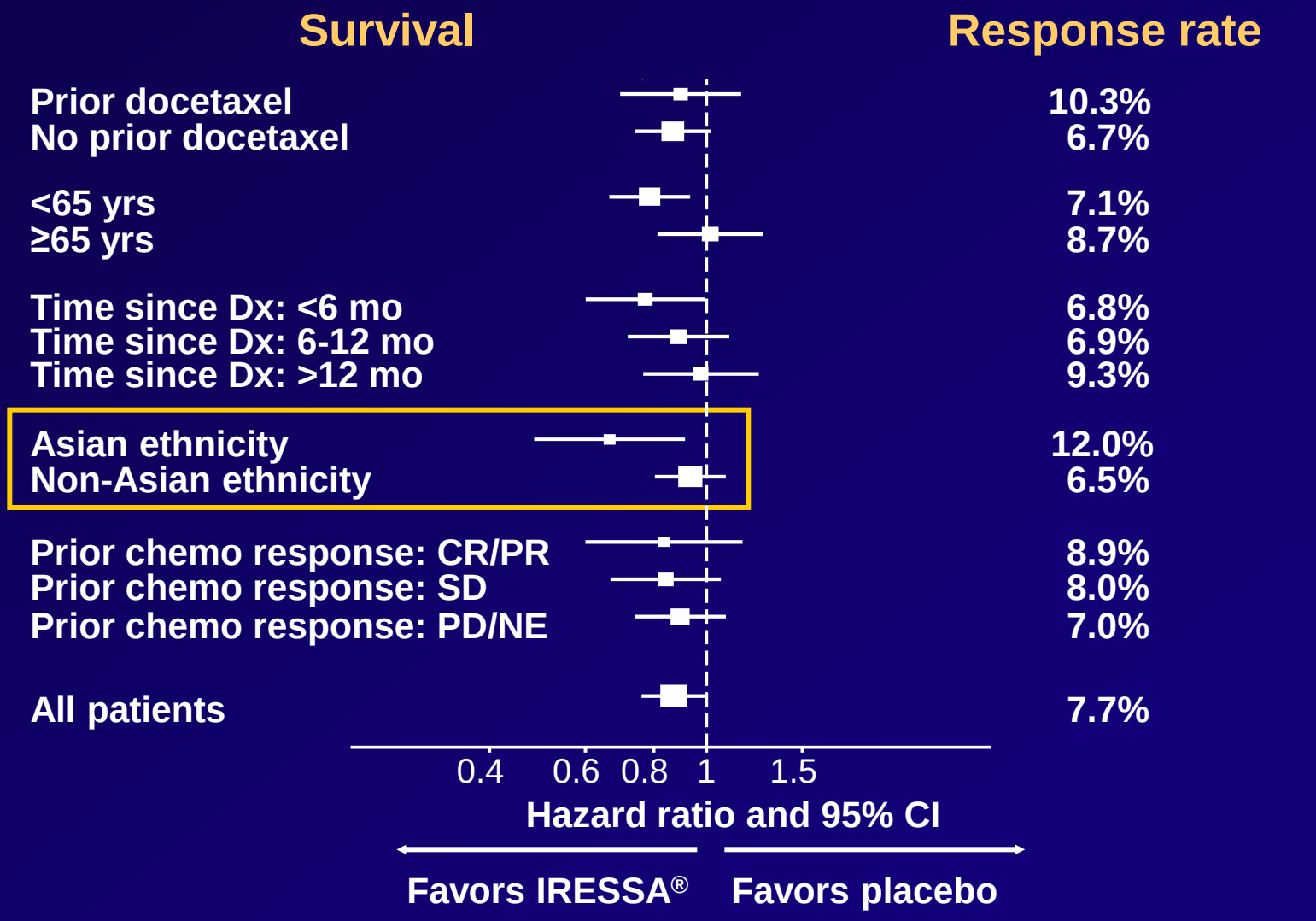
Pre-Planned Subset Analyses

- Subset identified up front on basis of Phase II results and findings on other drugs in class
- Rigorous statistical approach
  - Treatment by subset interactions
  - Effects in subsets
- Confidence that differences, if seen, are due to the drug and not the play of chance

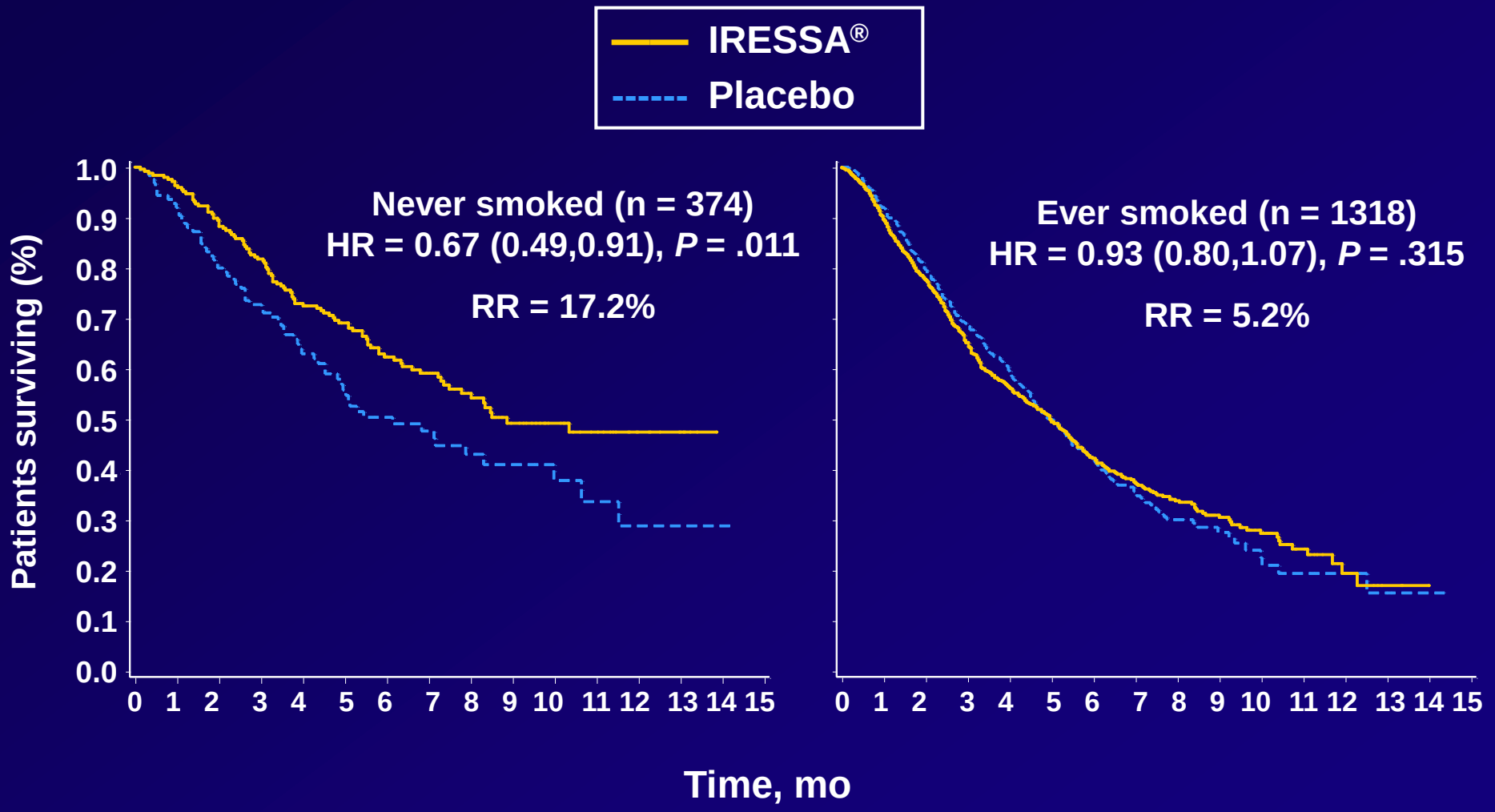
Effects in Subsets (1)



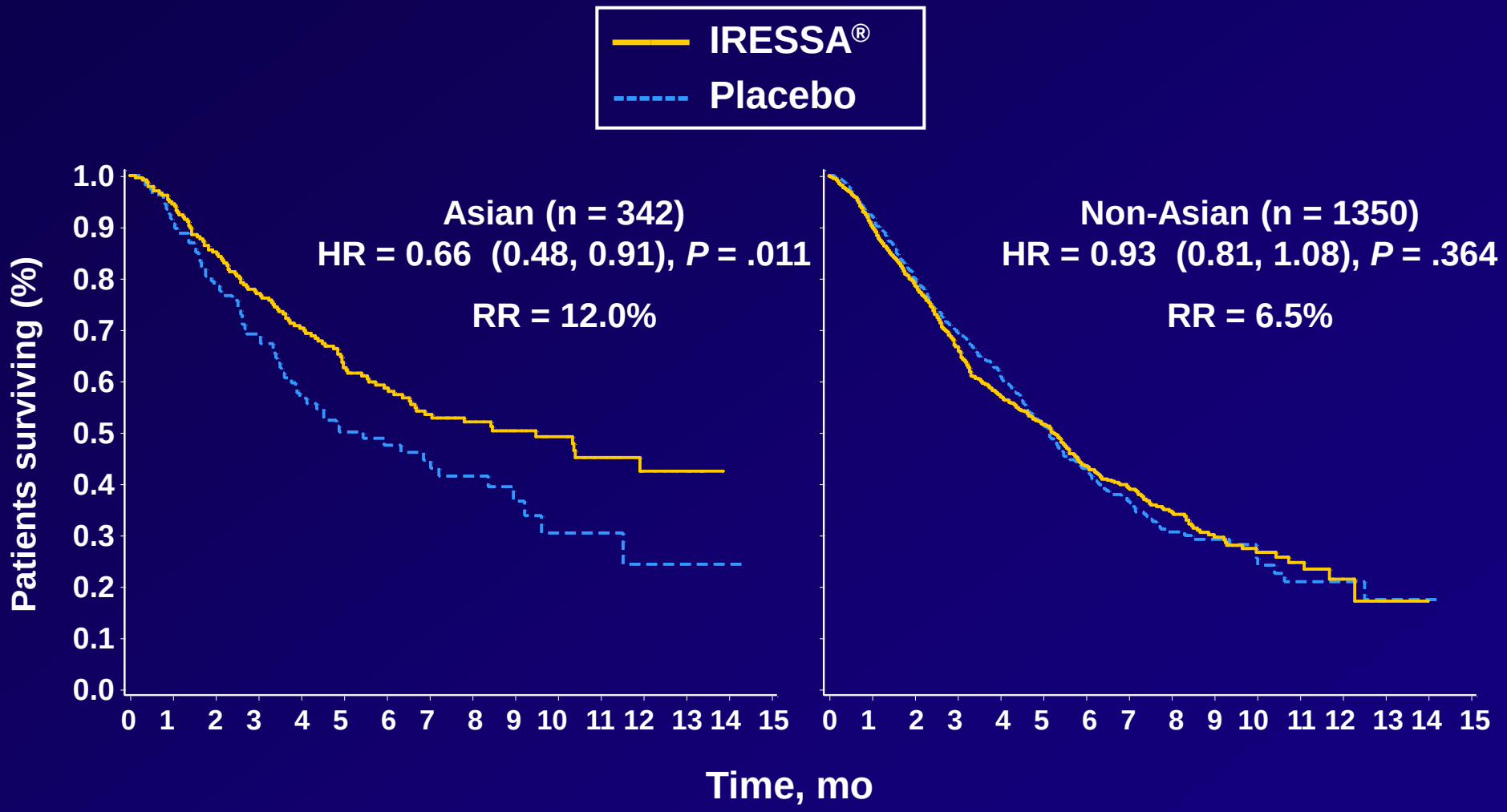
Effects in Subsets (2)



Survival by Smoking History



Survival by Ethnic Origin



Safety Data

- Adverse event profile consistent with established safety profile for IRESSA®
- Rash (35% vs. 9%) and diarrhea (27% vs. 9%) most common adverse events
- No difference in serious adverse events
- Few (5% vs. 4%) withdrawals due to adverse events
- No difference in incidence of interstitial lung disease (ILD)-like events (1.1% vs. 0.9%)

Adverse Events Occurring in ≥5% of the Trial Population or Difference in Incidence of ≥3 (1)

	IRESSA® N = 1126		Placebo N = 562	
	All grades	Grade 3/4	All grades	Grade 3/4
Rash	35%	1.2%	9%	0.2%
Diarrhea	27%	3.0%	9%	1.0%
Nausea	17%	0.8%	16%	0.4%
Anorexia	15%	2.0%	12%	2.0%
Vomiting	14%	1.0%	10%	0.4%
Dry skin	11%	0	4%	0

Adverse Events Occurring in ≥5% of the Trial Population or Difference in Incidence of ≥3% (2)

	IRESSA® N = 1126		Placebo N = 562	
	All grades	Grade 3/4	All grades	Grade 3/4
Constipation	10%	1.0%	13%	2.0%
Pruritus	7%	0.2%	5%	0.2%
Pyrexia	7%	0.6%	5%	0.4%
Asthenia	7%	2.0%	6%	1.0%
Cough	7%	0.2%	8%	0.7%
Dyspnea	7%	3.0%	8%	4.0%
Acne	4%	0.1%	1%	0

Final, Validated Data Show No Change

- Preliminary data validated as of February 2, 2005
- 976 deaths on or before October 29, 2004
- Findings based on preliminary data unchanged
  - Overall population HR = 0.89, *P* = .09
  - Adenocarcinoma subset HR = 0.84, *P* = .09

Further Follow-up Recommended by the Independent Data Monitoring Committee

- Median follow-up 10 months, 70% deaths
- Data consistent with planned, protocoled analysis
  - Overall HR = 0.89, *P* =.07
  - Adenocarcinoma HR = 0.84, *P* = .07
  - Continued variability despite increased crossover

Trial 709 Data as of December 16, 2004

- Trial 709 showed some improvement in survival; however, the difference did not reach statistical significance
- Preliminary data highlights efficacy and variability in terms of survival outcome