Gemcitabine-erlotinib versus gemcitabine-erlotinib-capecitabine in the first line treatment of patients with metastatic pancreatic cancer: Efficacy and safety results of a phase IIb randomized study from the Spanish TTD collaborative group

M. Benavides, J. Gallego, C. Guillén-Ponce, R. Vera, V. Iranzo, I. Ales, S. Arévalo, A. Pisa; A. Irigoyen, E. Aranda

On behalf of the Spanish Cooperative Group of Treatment of Digestive Tumors (TTD)

DISCLOSURE SLIDE

Advisory role: Amgen, Bayer, Merck, Roche, Sanofi

GECA trial

Background

Despite recent advances in various chemotherapeutic regimens and in the development of targeted therapies, metastatic pancreatic cancer (mPC) remains highly resistant to chemotherapy.

Gemcitabine plus capecitabine (GC) or plus erlotinib (GE) has been tested in phase III trials, with a statistically significant increase in ORR and PFS for GC and OS for GE.

GC plus erlotinib was tested in a phase II clinical trial, with a 32.6% PR, 6.5 months median PFS and a median OS of 12 months. (D.Oh et al. J Clin Oncol 2008. May 20; 26: suppl; abstr 4638)

GECA trial

Design

METASTATIC PANCREATIC CANCER

N: 120

→ **R**

1:1

GEMCITABINA

ERLOTINIB

GEMCITABINA

ERLOTINIB

CAPECITABINA

Disease progression or early withdrawal

Gemcitabine-erlotinib (GE)

G: 1000 mg/m2 d 1, 8 and 15

E: 100 mg/d po

Gemcitabine-erlotinib-capecitabine (GEC)

GE + Capecitabine: 830 mg/m2/12h, d1-21

- *Sponsor:* Spanish Cooperative Group for Digestive Tumour Therapy (*TTD)*
- *Study:* TTD-10-01
- *Principal investigators: Drs. Antonio Irigoyen y Manuel Benavides*
- *ClinicalTrials.gov identifier:* NCT01303029

GECA trial

Statistical Design

Sample Size:

- **PFS Superiority Trial:** HR=0,63 (med. PFS 3,75 vs 6 months)
- alpha error=0,05 one side ; Power=80%
- Logrank test, 12 months recruitment and 24 months follow up
- 120 patients: 60 per arm

Populations:

- ITT population: all randomized patients
- Safety population: all patients with, at least, one dose of treatment

Statistical Analysis:

- Descriptive statistics, 95% CI, and Kaplan-Meier plots

GECA trial

Study Objectives

- **Primary Endpoint: Progression free survival**

- **Secondary Endpoints:**

  Overall survival

  Objective response rate

  Duration of response

  Safety

  Efficacy according to rash

  Sub-study: Genetic profile and efficacy

GECA Trial

Eligibility criteria: main selection criteria

- Confirmed metastatic pancreatic cancer
- Informed consent
- Age ≥ 18 years
- ECOG performance status ≤ 2
- Measurable disease (RECIST v1.1)
- Life expectancy >12 weeks
- Chemotherapy-naïve metastatic disease
- Adjuvant chemotherapy more than 6 months before randomization

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Baseline Characteristics

	GE N=60	GEC N=60
Age (years), median (range)	64 [29, 78]	62 [31,77]
Sex: Male/Female	34/26	34/26
ECOG PS		
0 (%)	22 (36.6)	18 (30.0)
1 (%)	35 (58.3)	35 (58.3)
2 (%)	3 (5.0)	6 (10.0)
Unknown (%)	0	1 (1.6)
Metastases location		
Liver N (%)	43 (71.6)	**50** (83.3)
Lung N (%)	14 (23.3)	10 (16.6)
Peritoneum N (%)	**14**(23.3)	8 (13.3)
Bone N (%)	3 (5.0)	3 (5.0)

GECA Trial

SAFETY

	GE (N=58)	GEC (N=60)	
Related grade 3-4 AEs	55%	**72%**	**p=0.0494**
Neutropenia	15%	**43%**	**p=0.0008**
Thrombocytopenia	7%	10%	
Asthenia	10%	10%	
Mucose inflamation	0%	**9%**	**p=0.03**
GGT increase	**8%**	2%	
Diarrhea	5%	7%	
Anemia	8%	7%	
Hand-foot syndrome	0%	**5%**	

Safety population N=118. Two patients in the GEC arm were not included in the safety population, since they did not initiate study treatment

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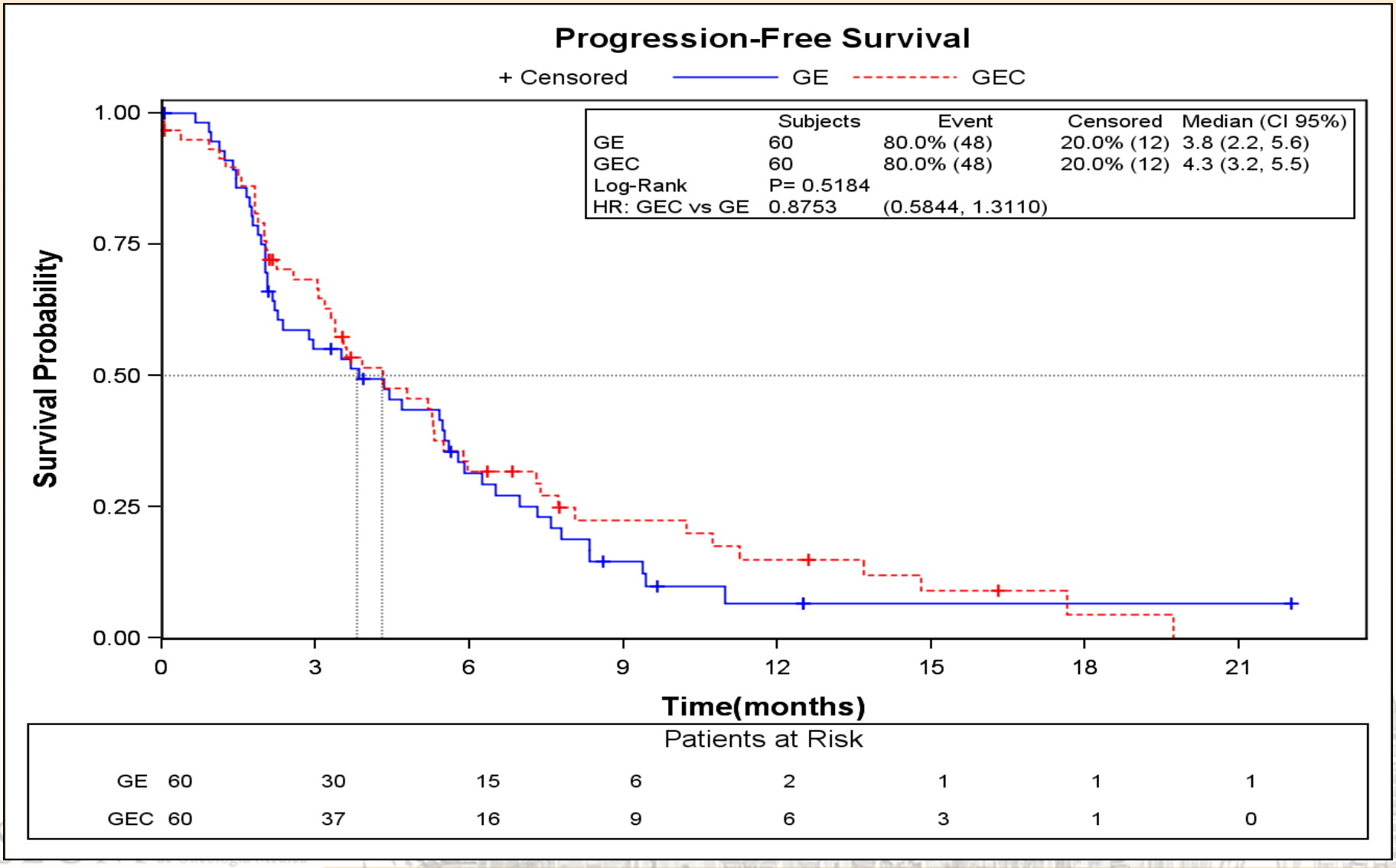
Results: primary endpoint

Progression Free Survival



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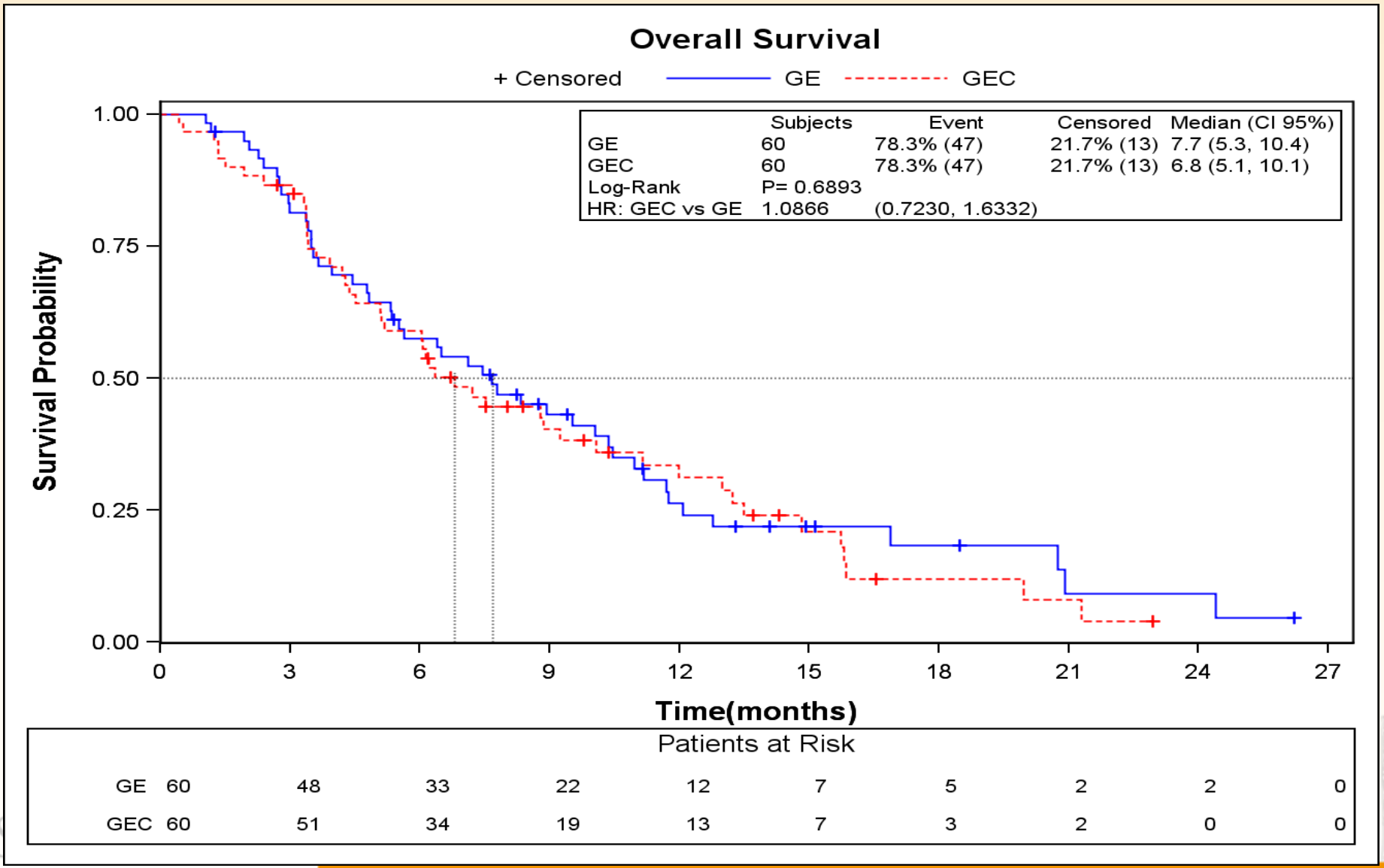
Results: secondary endpoint

Overall Survival



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Results: secondary endpoint

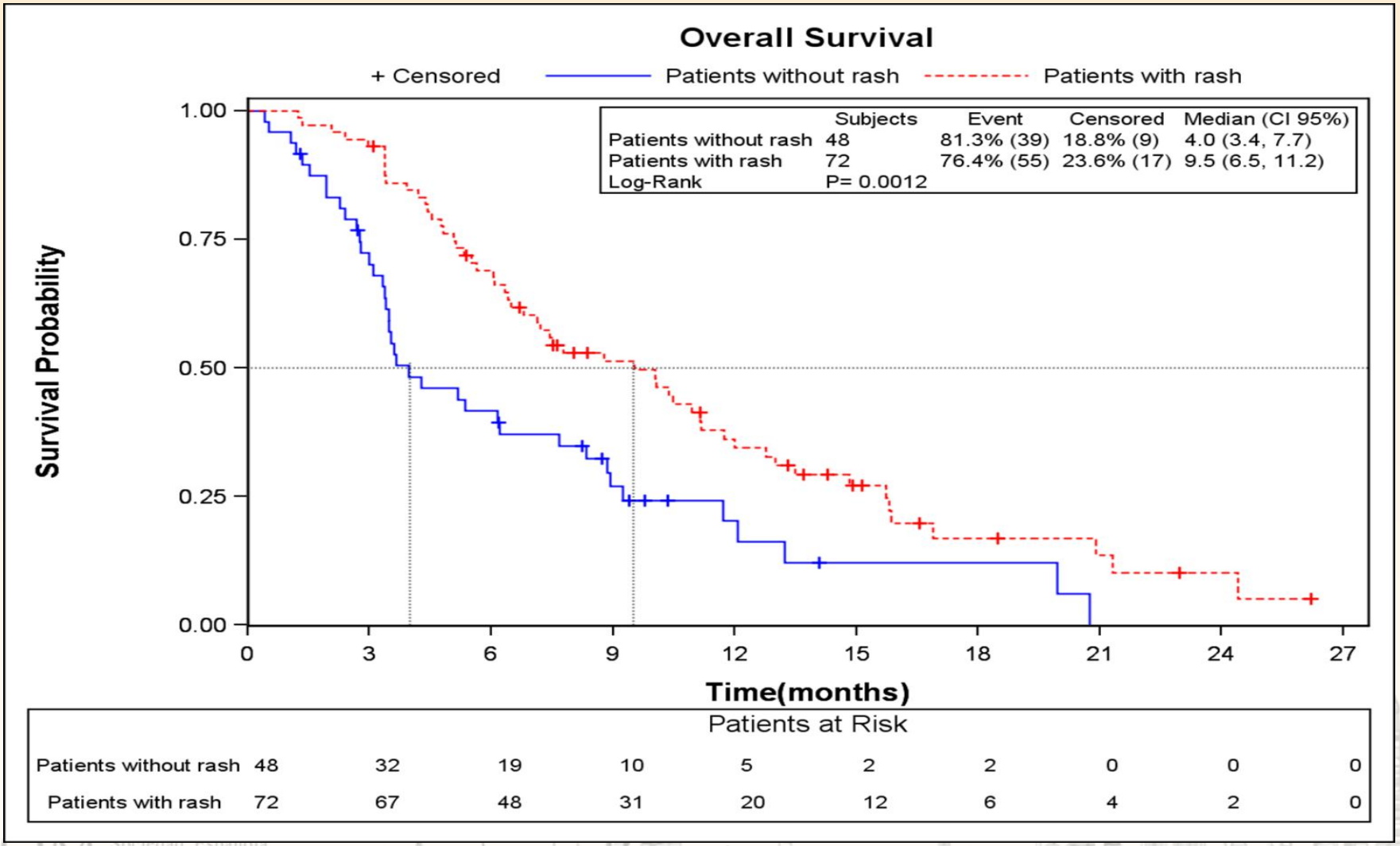
Confirmed response rate

Best confirmed response rate		GE N=60	GEC N=60	P value test*
PR	N(%)	**7 (11.67)**	**9 (15.00)**	**0.5810**
SD	N(%)	26 (43.33)	30 (50.00)	
PD	N(%)	23 (38.33)	16 (26.67)	
NE	N(%)	4 (6.67)	5 (8.33)	

* Fisher test

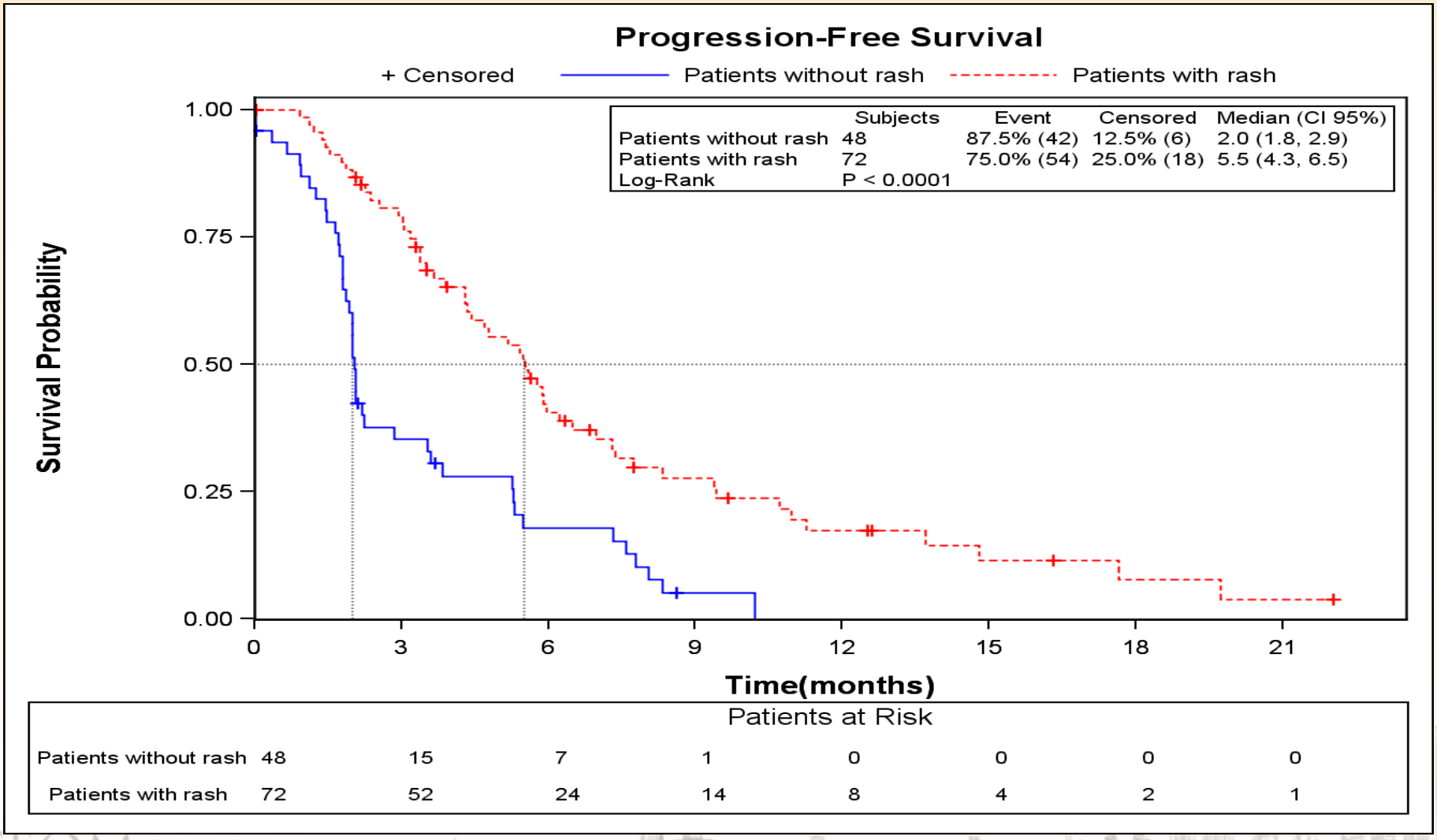
GECA trial

OS according to rash (G ≥1 vs G=0)



GECA trial

PFS according to rash (G ≥1 vs G=0)



GECA trial

PFS and OS according to rash (G ≥1 vs G=0) and treatment

	GEC		GE	
	Rash G ≥1	No Rash (G=0)	Rash G ≥1	No Rash (G=0)
PFS	5.9	2.0	5.5	2
OS	8.8	4.3	10	4

GECA trial: Conclusions

PFS was not different between GEC and GE arms and it did not meet the criterion for statistical significance.

Response rate (RR) and OS were similar between the two arms without statistically significant differences

Skin rash strongly predicted erlotinib efficacy (PFS and OS).

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