TG4010 Immunotherapy Combined with First-line Therapy in Advanced Non- Small Cell Lung Cancer (NSCLC). Phase 2b Results of the TIME Study

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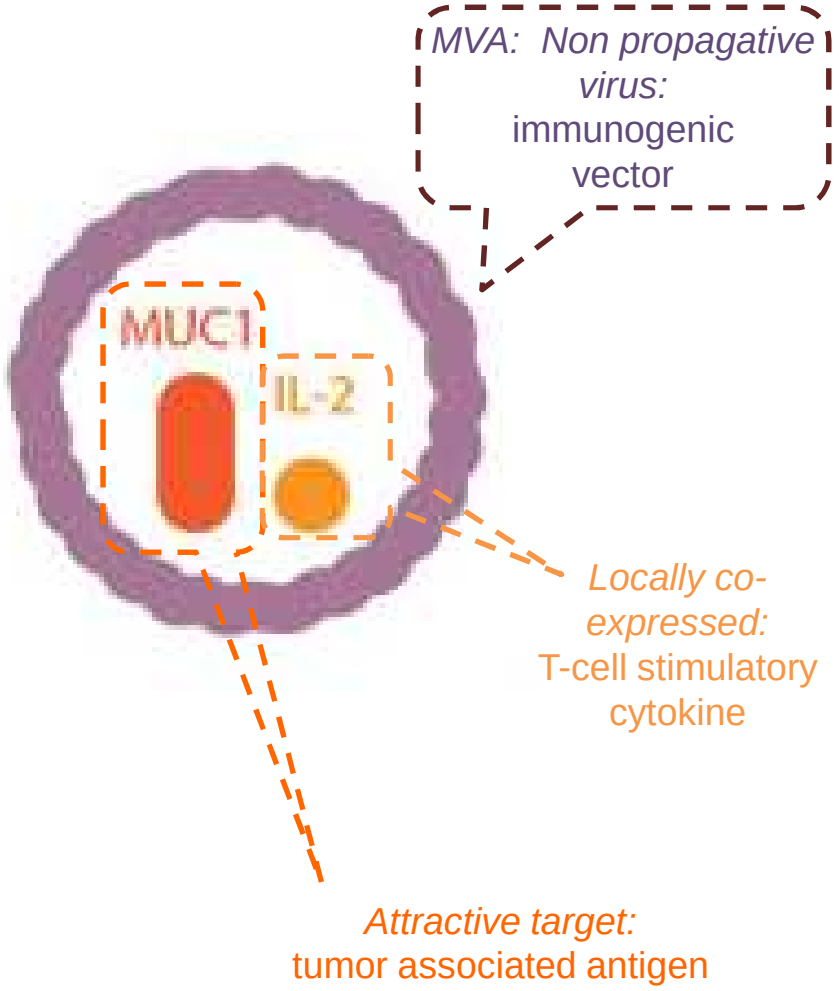
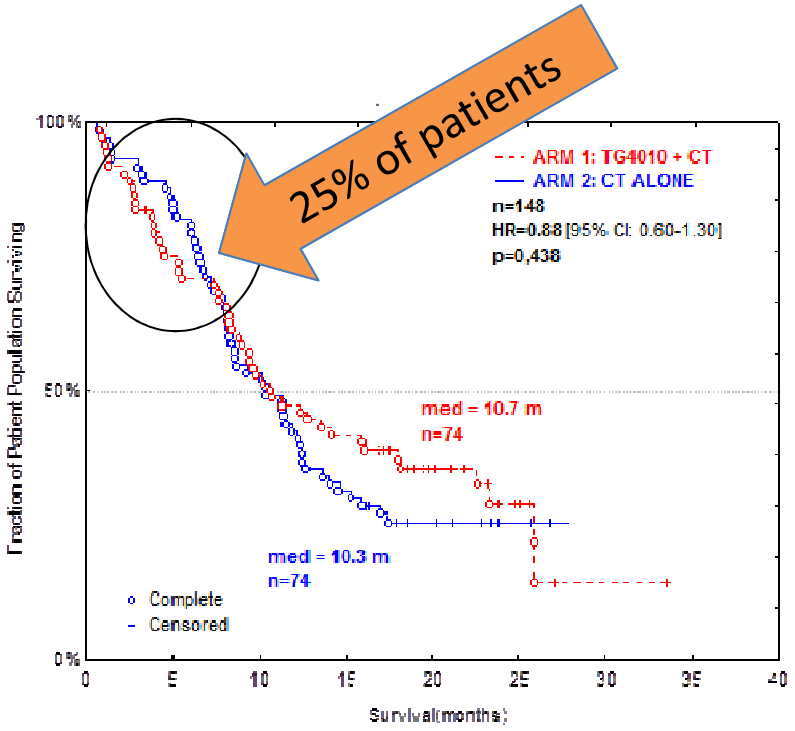
TG4010 Background

- Immunotherapeutic vaccine consisting of a viral vector (MVA) encoding the tumoral antigen MUC1 and IL2
- Different from other drug products targeting MUC1:
  - Encodes the full MUC1 cDNA sequence
  - Expresses IL2 , a potent stimulant of T-cell response

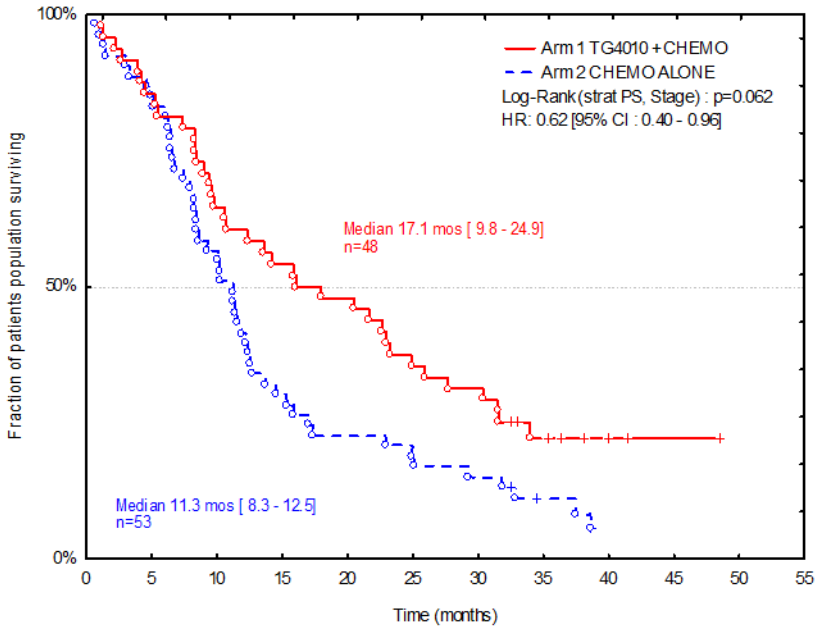


TG4010.09: Randomized Phase 2 Trial

- TG4010.09: Phase 2 randomized trial (n=148)
  - TG4010 + cis/gem versus cis/gem
  - Advanced NSCLC (IIIB “wet”)/IV)
  - Included only patients with MUC1+ tumors (by IHC)
- Retrospective Analysis:
  - Efficacy correlated with % of activated NK cells (CD16+ CD56+ CD69+ population defined as TrPAL)

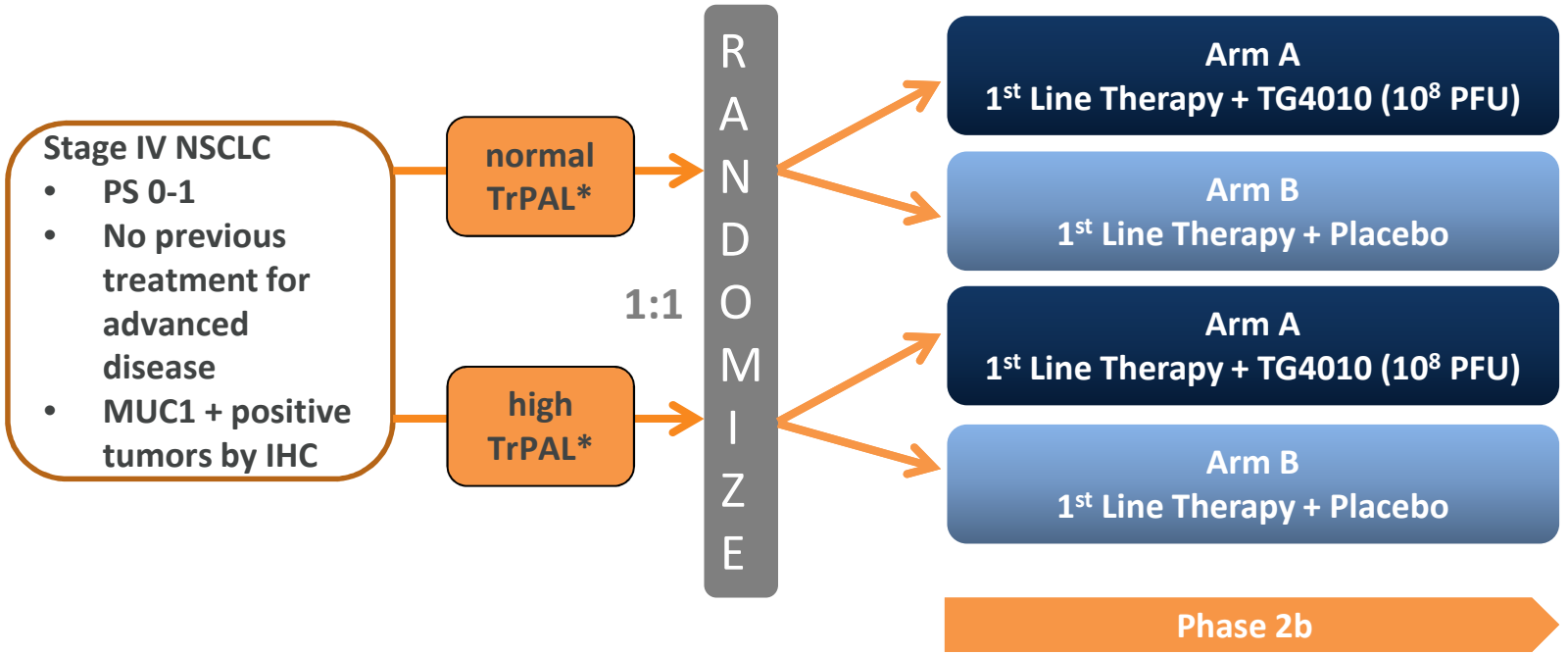


Survival: censor out 25% of study patients with elevated TrPAL



Quoix et al, Lancet Oncology 2011

TG4010.14: Study Design



Phase 2b

- Primary endpoint = PFS (Bayesian analysis)
- Prospective validation of the TrPAL biomarker
- Assessment of TG4010 in combinations of standard of care chemotherapy

N=222**

Phase 3

- Primary endpoint = OS
- Pivotal registrational trial

N=800

** enrollment complete

*TrPAL: CD16+, CD56+, CD69+ (based on Upper Limit of Normal)

TG4010.14: Treatment Regimens

TG4010 (1.0×10^8 PFU) or Placebo:

Subcutaneous injection weekly for 6 weeks and then once every 3 weeks until progression

1st Line Therapy:

Carboplatin + paclitaxel, or
Cisplatin + gemcitabine (for squamous histology), or
Cisplatin + pemetrexed (for non-squamous histology)

Bevacizumab was allowed at investigator's discretion
Maintenance therapy was allowed at investigator's discretion

TG4010.14: Patient Characteristics

	All Patients N=221*		Normal TrPAL N=170	
ITT population	TG4010 (n=110)	Placebo (n=111)	TG4010 (n=85)	Placebo (n=85)
Gender : Male (%)	64.5%	63.1%	70.6%	62.4%
Median age (yrs)	63	59	62	58
Former Smoker (%)	93.6%	89.2%	92.9%	87.1%
PS=1 (%)	69.1%	68.5%	68.2%	67.1%
Stage IV at diagnosis (%)	90.9%	93.7%	92.9%	92.9%

*N=221 at time of analysis (Aug 2014)

TG4010.14: Most Frequent AEs*

Most Frequent AEs (>20% in either arm)	Safety Population**	
	TG4010 (n=105)	Placebo (n=100)
Fatigue	54%	53%
Nausea	41%	37%
Neutropenia	42%	35%
Anaemia	37%	33%
Injection site reaction	31%	4%
Vomiting	25%	35%
Thrombocytopenia	19%	18%

Most Frequent AEs Grade 3/4 (>5% in either arm)	Safety Population**	
	TG4010 (n=105)	Placebo (n=100)
Neutropenia	31%	27%
Thrombocytopenia	11%	16%
Fatigue	11%	11%
Anaemia	8%	14%
Febrile neutropenia	3%	8%
Vomiting	3%	9%

Safety analyses based on Sep 2013 data cutoff (i.e. primary endpoint analysis in Normal TrPAL patient as per protocol) **
Patients who received at least one dose of TG4010 / placebo

TG4010.14 - Normal TrPAL Patients
BAYESIAN ANALYSIS

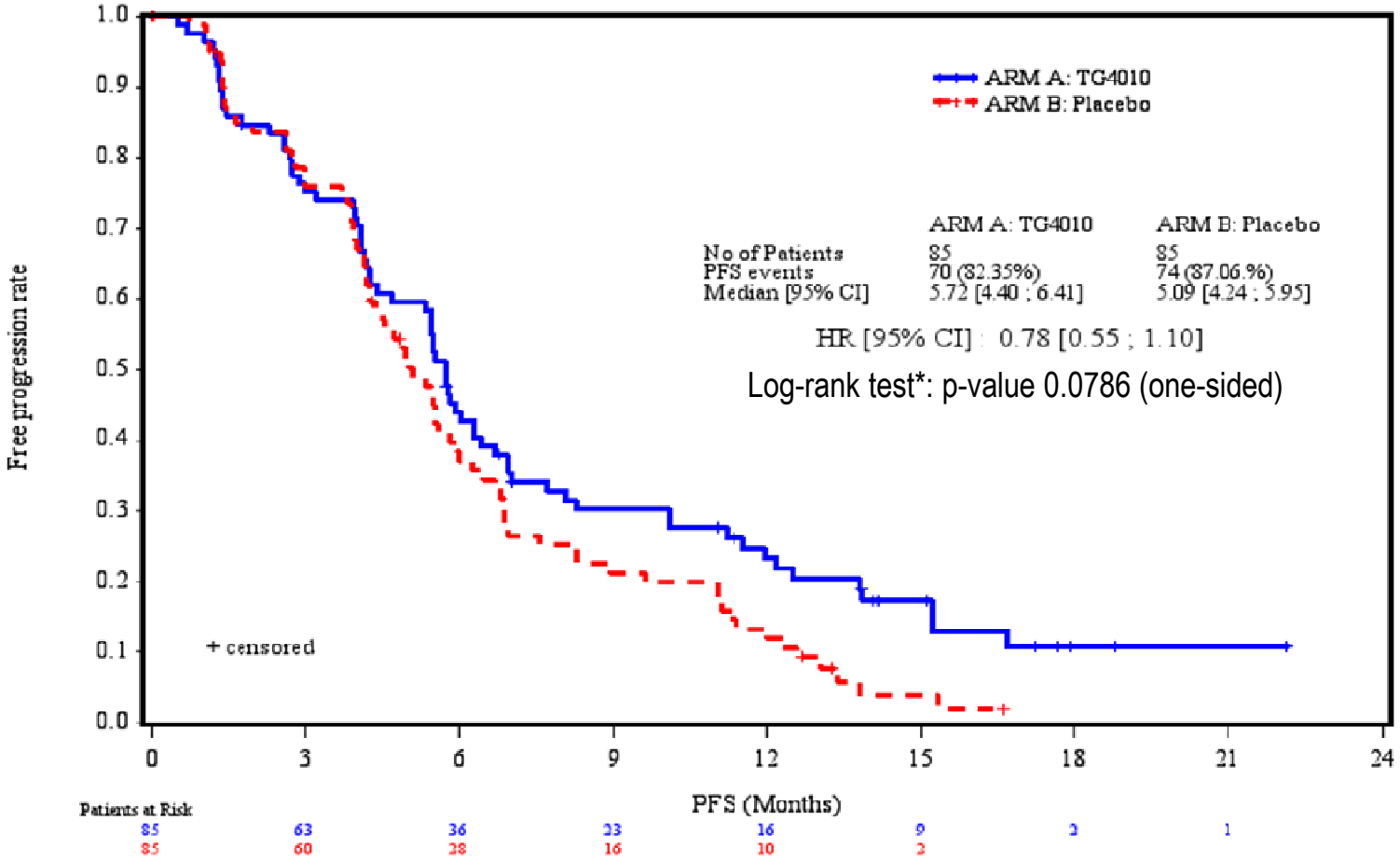
# events = 144 N=170	**ITT**
Hazard Ratio – PFS (CI)	0.74 (0.53, 1.02)
Probability (HR<1)	98.6%

→ Primary Endpoint is met.

TG4010.14 - Normal TrPAL Patients
ITT

PFS

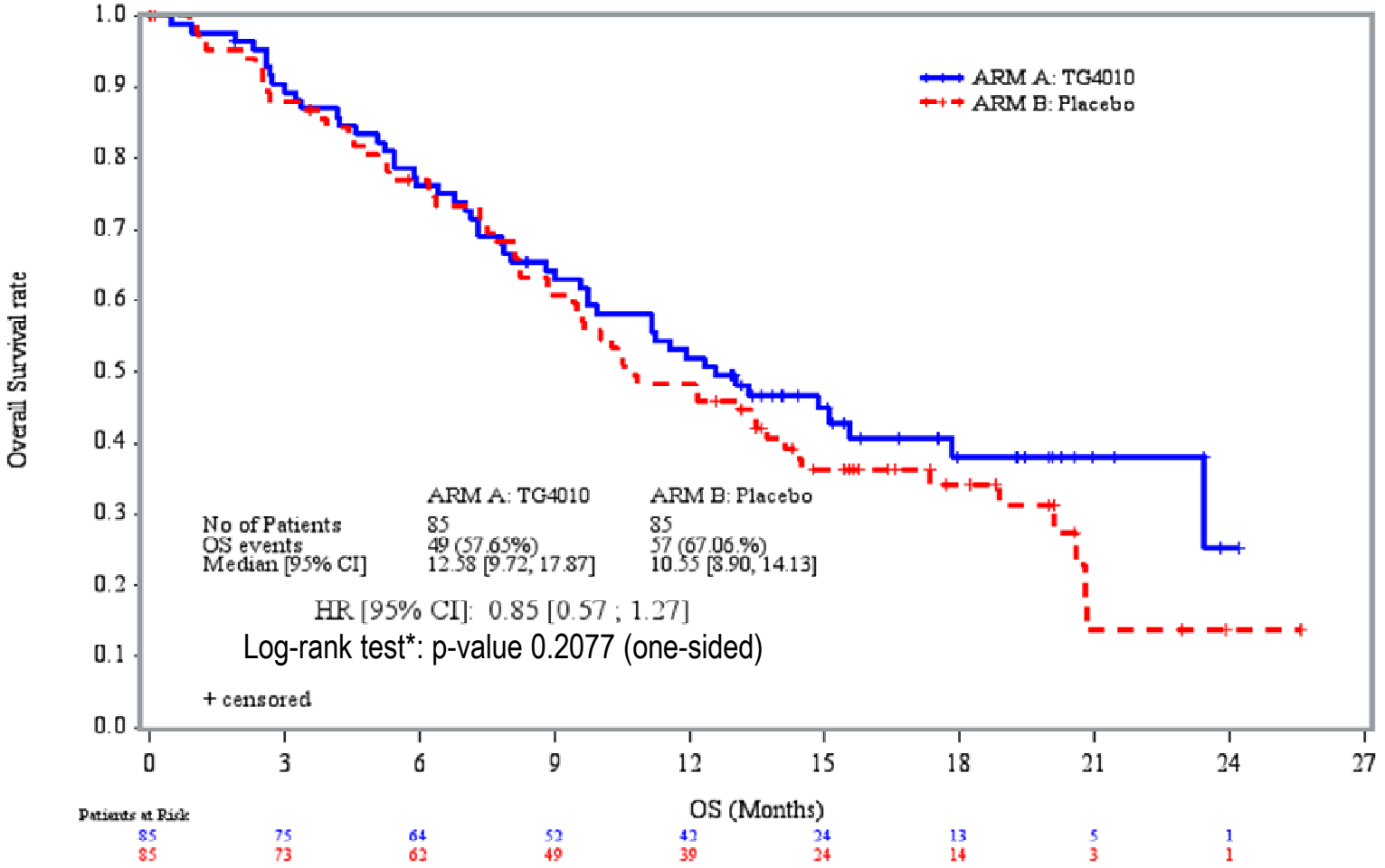
HR from stratified Cox model



TG4010.14 - Normal TrPAL Patients
ITT

OS

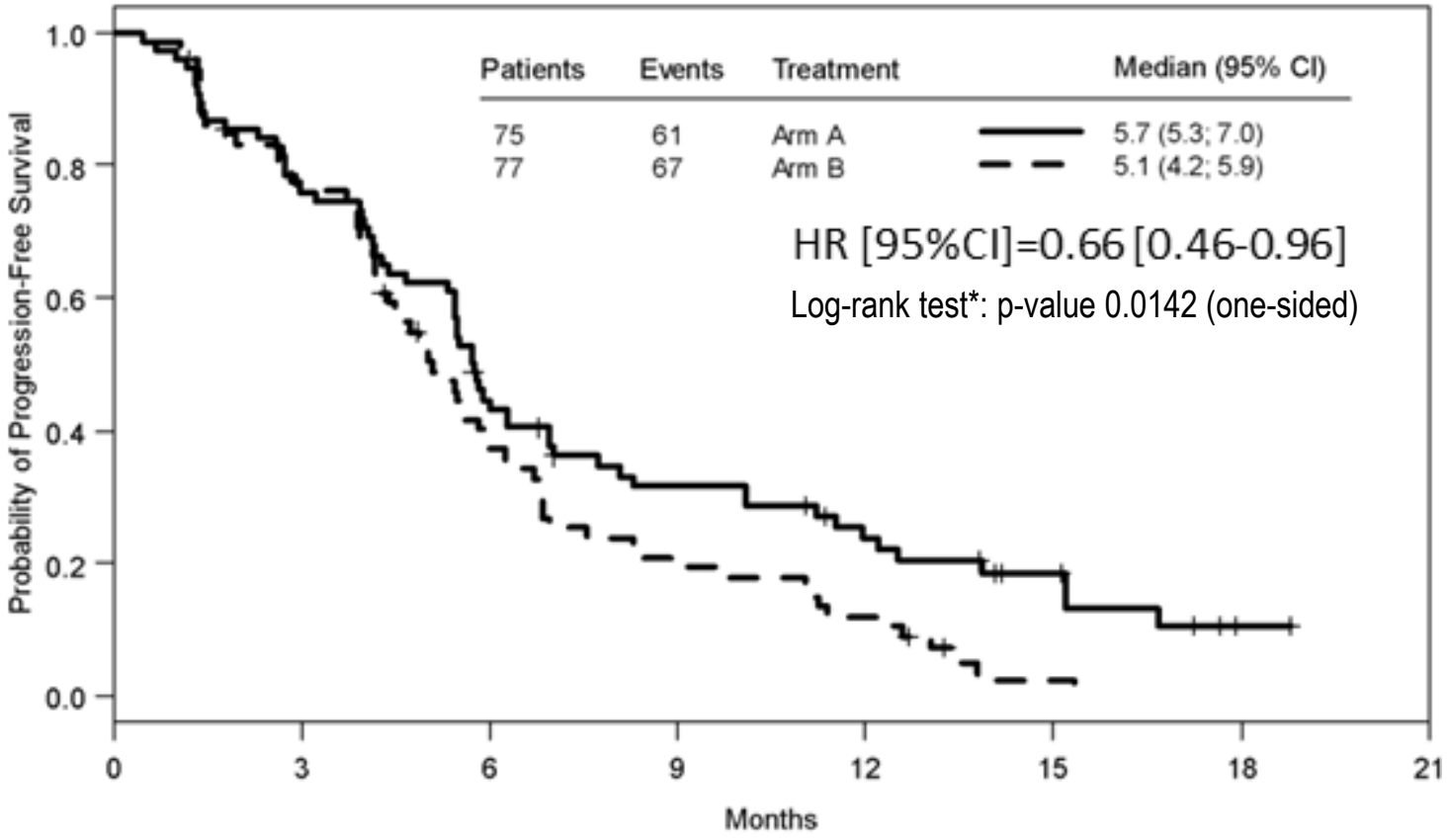
HR from stratified Cox model



TG4010.14 – Prospective Definition of 75th Percentile: Low TrPAL* Patients ITT

PFS

HR from stratified Cox model



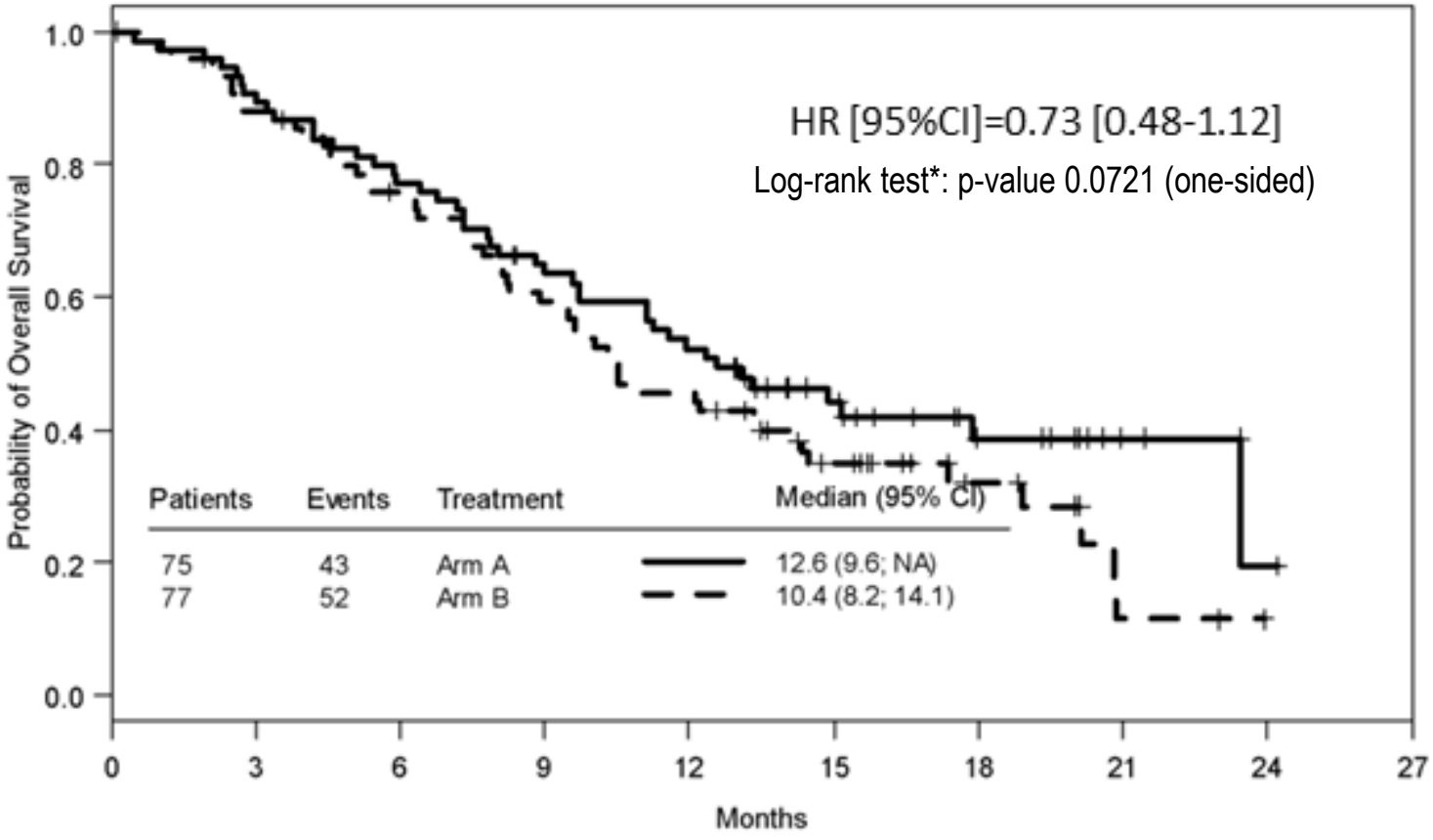
Number at risk								
Arm A	75	56	32	21	14	8	1	0
Arm B	77	54	25	13	8	1	0	0

* ≤ Q3 (3 lowest quartiles)

TG4010.14 – Prospective Definition of 75th Percentile: Low TrPAL Patients ITT

OS

HR from stratified Cox model

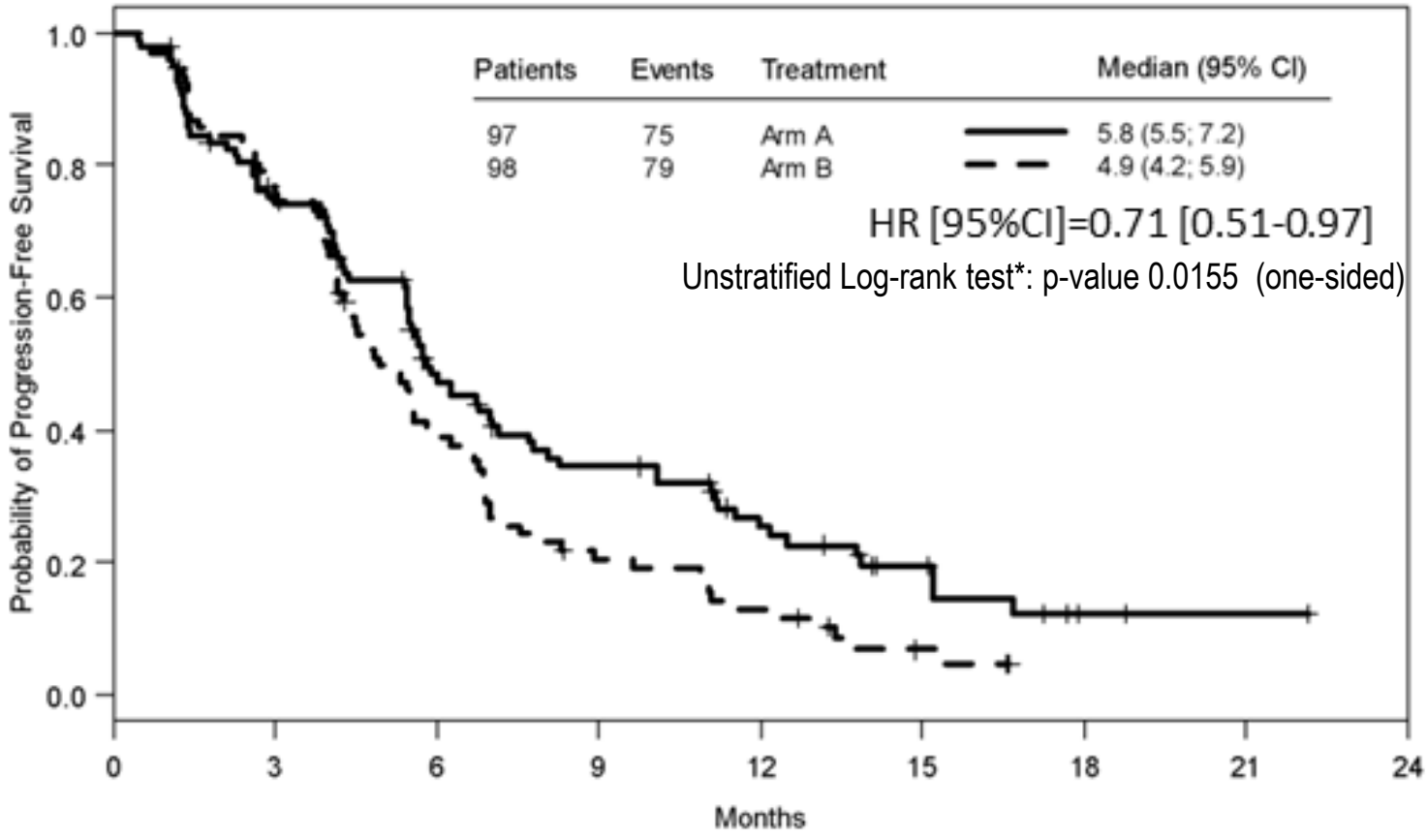


Number at risk										
Arm A	75	66	57	46	37	21	11	4	1	0
Arm B	77	66	55	43	33	20	10	2	0	0

TG4010.14 – Non-squamous Patients
ITT

PFS

HR from unstratified Cox model

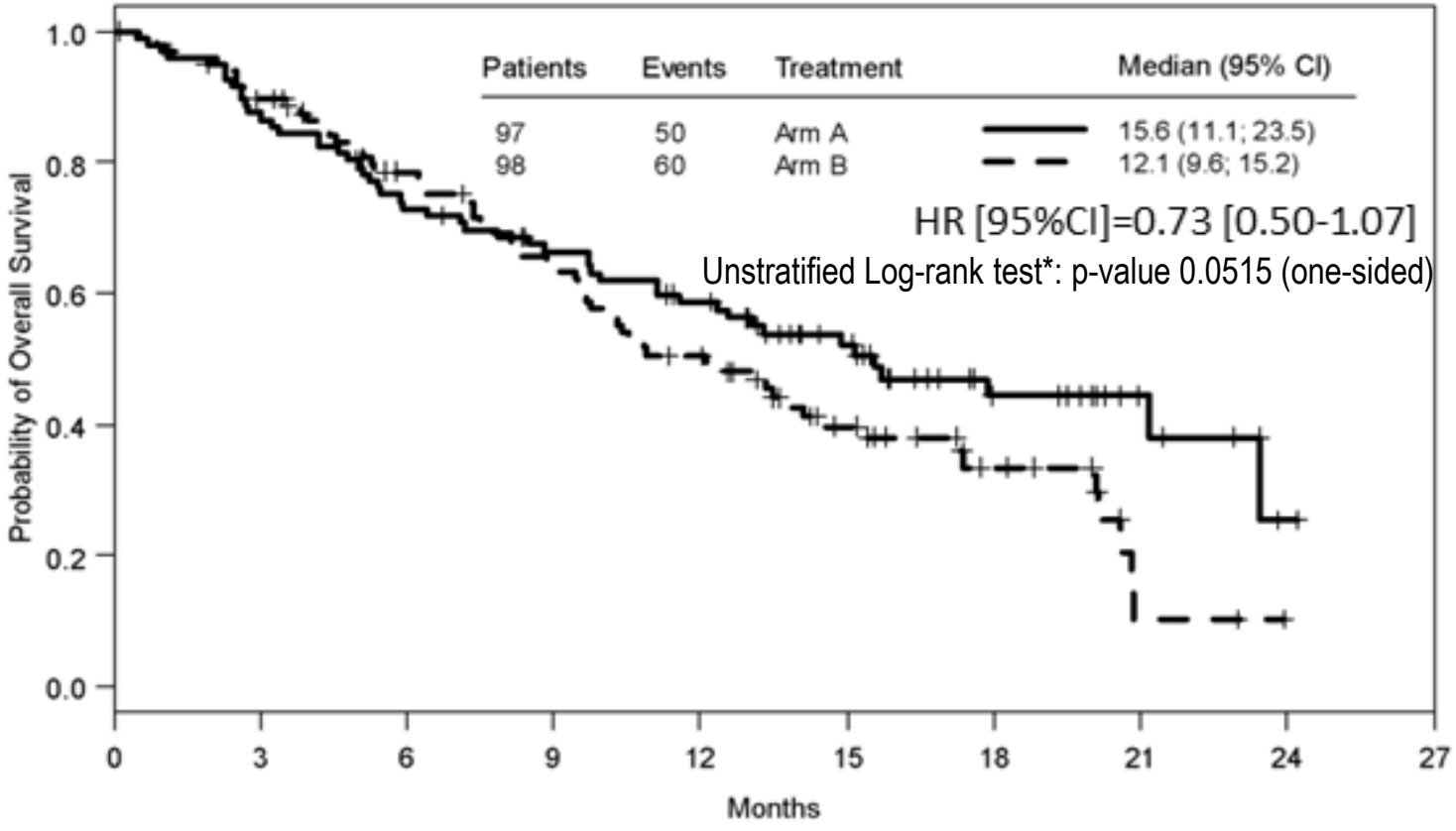


Number at risk									
Arm A	97	71	43	29	18	9	2	1	0
Arm B	98	65	32	16	10	3	0	0	0

TG4010.14 – Non-squamous Patients
ITT

OS

HR from unstratified Cox model

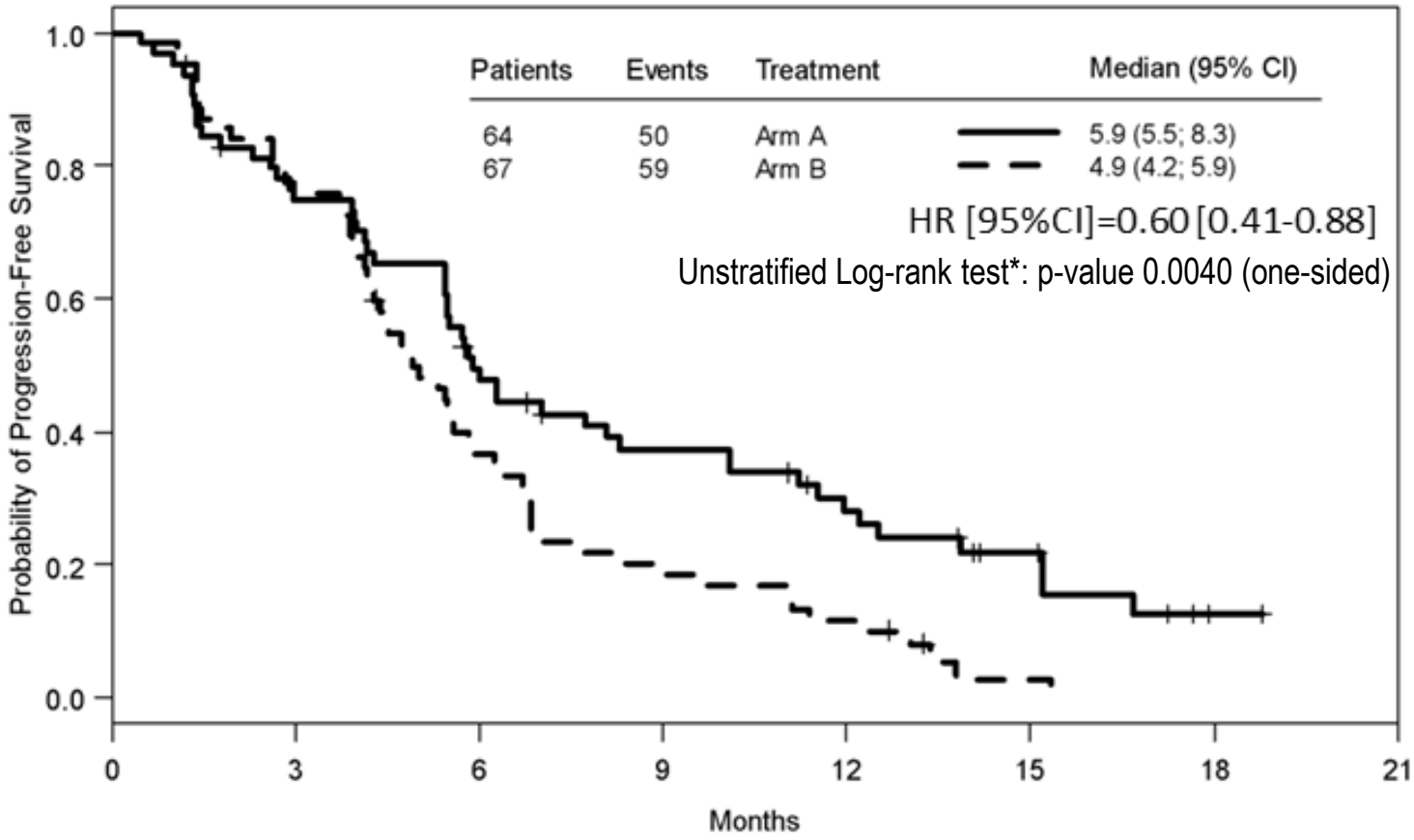


Number at risk										
Arm A	97	83	69	60	51	33	15	7	1	0
Arm B	98	85	68	54	42	25	13	2	0	0

TG4010.14 – Low TrPAL, Non-squamous Patients ITT

PFS

HR from unstratified Cox model

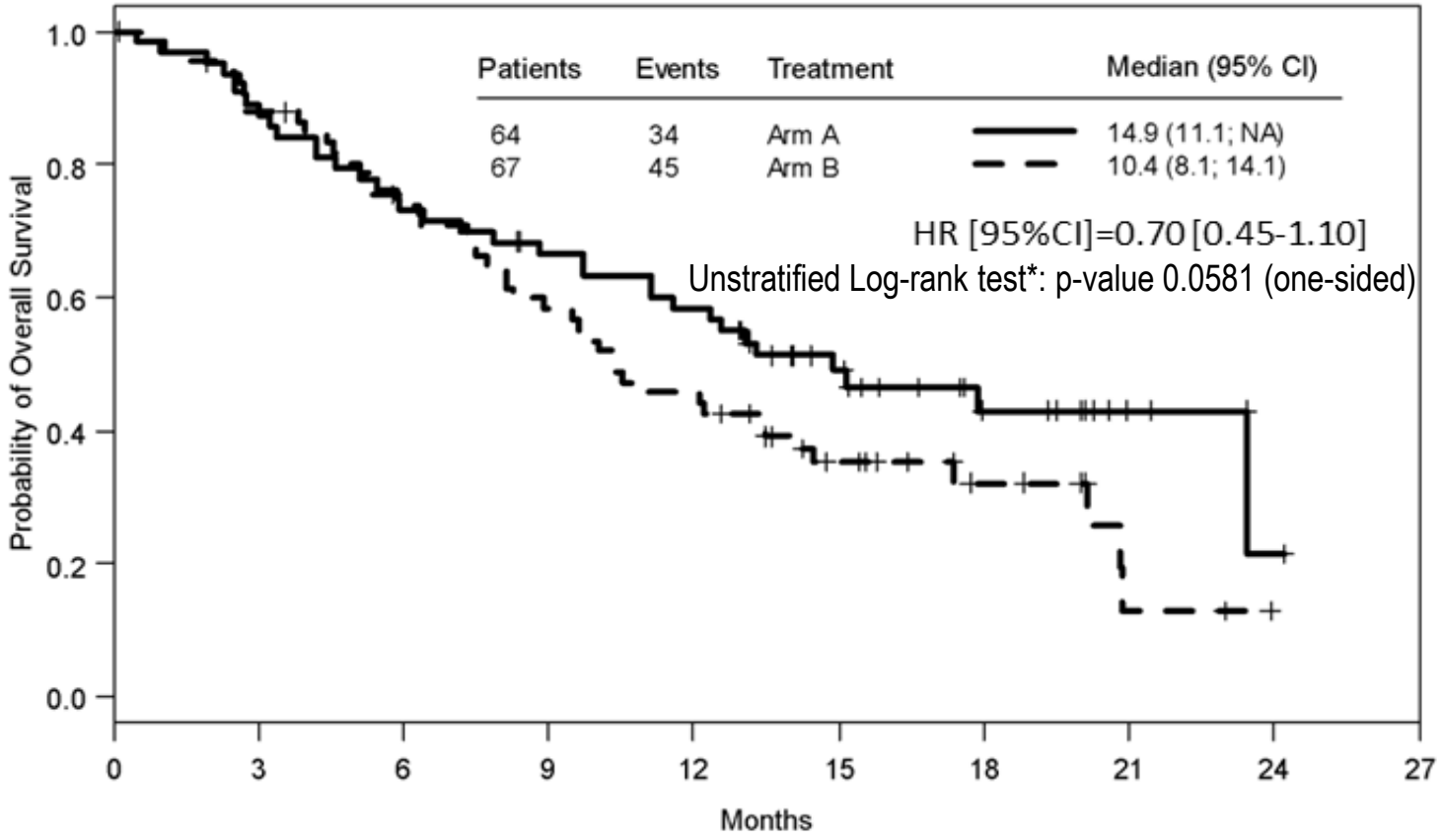


Number at risk								
Arm A	64	47	30	21	14	8	1	0
Arm B	67	47	22	11	7	1	0	0

TG4010.14 – Low TrPAL, Non-squamous Patients ITT

OS

HR from unstratified Cox model



Number at risk										
Arm A	64	55	46	40	35	21	11	4	1	0
Arm B	67	58	48	37	29	17	9	2	0	0

Summary

- Primary endpoint was achieved in patients with normal TrPAL (at baseline):
  - Bayesian probability demonstrates that TG4010 improves PFS
- TG4010 was well tolerated
- Subgroup analyses show that TG4010 significantly improved PFS in patients with non-squamous carcinoma, both in the overall population and in the patients with Low TrPAL
- Although still maturing, Overall Survival showed improvement consistent with that observed for PFS

➔ Phase 3 part of the trial is currently being planned