P2.11-024: Efficacy Analysis for Molecular Subgroups in MARQUEE: a Randomized, Double-blind, Placebo-controlled, Phase 3 Trial of Tivantinib (ARQ 197) Plus Erlotinib versus Placebo plus Erlotinib in Previously Treated Patients with Locally Advanced or Metastatic, Non-squamous, Non-small Cell Lung Cancer (NSCLC)

SILVIA NOVELLO

Giorgio Scagliotti, Rodryg Ramlau, Adolfo Favaretto, Fabrice Barlesi, Wallace Akerley, Joachim Von Pawel, Sergey Orlov, Armando Santoro, David R. Spigel, Vera Hirsh, Frances Shepherd, Lecia V. Sequist, Jeffrey Ross, Dale Shuster, Hamim Zahir, Qiang Wang, Brian Schwartz, Richard Von Roemeling, Alan B. Sandler
MARQUEE Study Design

Key Eligibility Criteria
- Inoperable, locally advanced or metastatic NSCLC
- Non-squamous histology
- 1-2 prior systemic regimens, including mandatory prior platinum-based doublet therapy
- No prior EGFR TKI
- Tissue for biomarker analysis
- Stable brain metastases were permitted
- ECOG 0 or 1

Double-blind
- Randomize

1:1
- Placebo PO BID + Erlotinib @ 150 mg QD
- Erlotinib @ 360 mg PO BID

Stratification Factors
- Gender
- Smoking history
- # prior lines of systemic therapies
- EGFR genotype
- KRAS genotype

Abbreviations: BID, twice daily; EGFR, epidermal growth factor receptor; ITT, intent-to-treat; ORR, overall response rate; OS, overall survival; NSCLC, non-small cell lung cancer; PFS, progression-free survival; PO, orally; QD, once daily; wt, wild type; TKI, tyrosine kinase inhibitor.

Results in ITT Population  
\(n = 1048\) randomized

**A**  
**PFS**  
HR = 0.74 (95% CI, 0.64-0.85)  
\(P < .0001\)

**B**  
**OS**  
HR = 0.98 (95% CI, 0.84-1.15)  
\(P = .81\)

**Safety** (\(n = 1039\) treated): Neutropenia (Grade 3/4: 10.0% vs 1.0%), febrile neutropenia (3.3% vs 0.4%), and anemia (Grade 3/4: 6.5% vs 2.9%) were more common with tivantinib.
OS in MET Expression Subgroups

**MET High**
(n = 211)

HR = 0.70 (95% CI, 0.49-1.01)  
P = .03

**MET Low**
(n = 234)

HR = 0.90 (95% CI, 0.64-1.26)  
P = .53

**MET Unknown**
(n = 603)

HR = 1.13 (95% CI, 0.92-1.39)  
P = .21
OS in **EGFR** and **KRAS** Genotype Subgroups

**EGFR WT**
- \( n = 937 \)
- HR = 1.00 (95% CI, 0.85-1.18)
- \( P = .94 \)

**KRAS WT**
- \( n = 702 \)
- HR = 0.94 (95% CI, 0.77-1.14)
- \( P = .49 \)

**KRAS Mutant**
- \( n = 284 \)
- HR = 1.04 (95% CI, 0.78-1.40)
- \( P = .77 \)

EGFR Mutant subgroup results are immature.
Conclusions

- Tivantinib plus erlotinib did not improve OS in unselected non-squamous NSCLC, even though PFS was increased.
- Tivantinib improved PFS and OS in the MET High subgroup.
- Tivantinib had limited PFS benefit with no OS increase in the KRAS mutant subpopulation.
- Further investigation of tivantinib in MET High selected, non-squamous NSCLC is warranted.
- Tivantinib was well tolerated with neutropenia being the most common drug-related toxicity.