
Quality of life in patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer (AEOC) receiving either pazopanib monotherapy or placebo after first-line chemotherapy: AGO-OVAR16 results

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Disclosures

- Dr. Friedlander reports no conflict of interest
- Coauthors Meier, Lesoin, Kim, Poveda, Buck, Scambianone, and Shimada also report no conflict of interest
- Dr. du Bois has received honoraria from GlaxoSmithKline for a lecture related to trial accrual and he was Principal Investigator for the phase I/II trial that preceded this phase III trial
- S. Knoll is an employee of GlaxoSmithKline

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Editorial Assistance

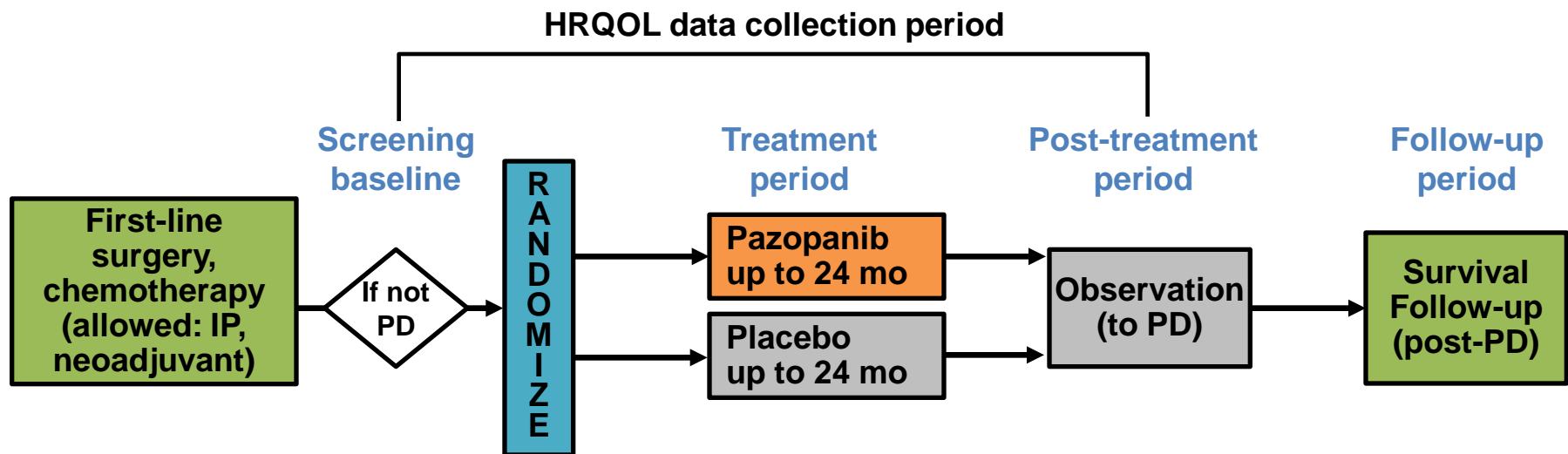
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Background

- Majority of advanced ovarian cancer patients relapse
 - median progression-free survival (PFS) 16 months from diagnosis¹
- Cochrane meta-analysis: no significant improvement in PFS or overall survival with maintenance chemotherapy²
- OVAR16: 5.6-month improvement in median PFS³
 - HR = 0.766; 95% CI: 0.643-0.911
- Health-related quality of life (HRQOL) and patient-reported outcomes in the patients from OVAR16 will be reported

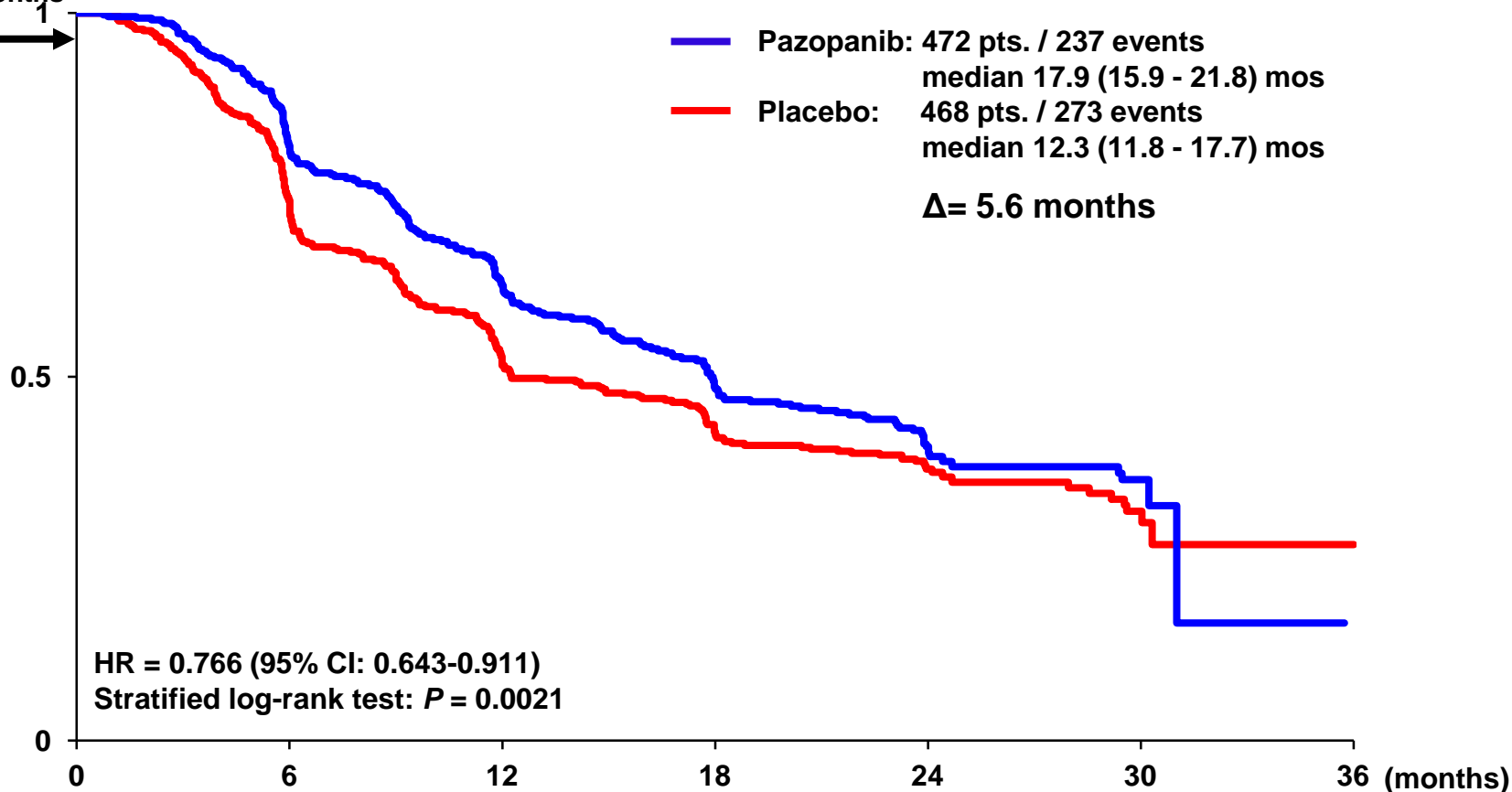
OVAR16 Study Design

- Randomized, double-blind, phase III trial (N=940)



OVAR16 Primary Endpoint: PFS by RECIST (Investigator Assessment)

Median time from
Diagnosis: 7 months



Patients	472	332	234	171	91	19
at risk	468	318	208	164	88	20

AEs Leading to Permanent Discontinuation of Study Treatment ($\geq 1\%$ of Patients in Either Arm)

Preferred Term, n (%)	Pazopanib (N=477)	Placebo (N=461)
Any event	159 (33)	26 (6)
Hypertension	38 (8)	6 (1)
Diarrhea	14 (3)	1 (<1)
AST increased	12 (3)	0
ALT increased	11 (2)	0
Neutropenia	11 (2)	1 (<1)
Hand-foot syndrome	8 (2)	1 (<1)
Nausea	6 (1)	0
Rash	6 (1)	0
Arthralgia	5 (1)	1 (<1)
Fatigue	5 (1)	1 (<1)
Neutrophil count decreased	5 (1)	0
Platelet count decreased	5 (1)	0
Pyrexia	5 (1)	0

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase

Health-Related Quality of Life

- Secondary endpoint: evaluate health-related quality of life (HRQOL) as measured by **EORTC QLQ-C30**, **OV28** and **EQ-5D** (captures health status across five dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression)
 - Data were collected at baseline, week 13, months 7, 10, 13, 16, 25 (end of treatment), and 31 (post-treatment)
- Pre-specified analyses examined HRQOL differences while on treatment
 - Mixed-model repeated measures analysis

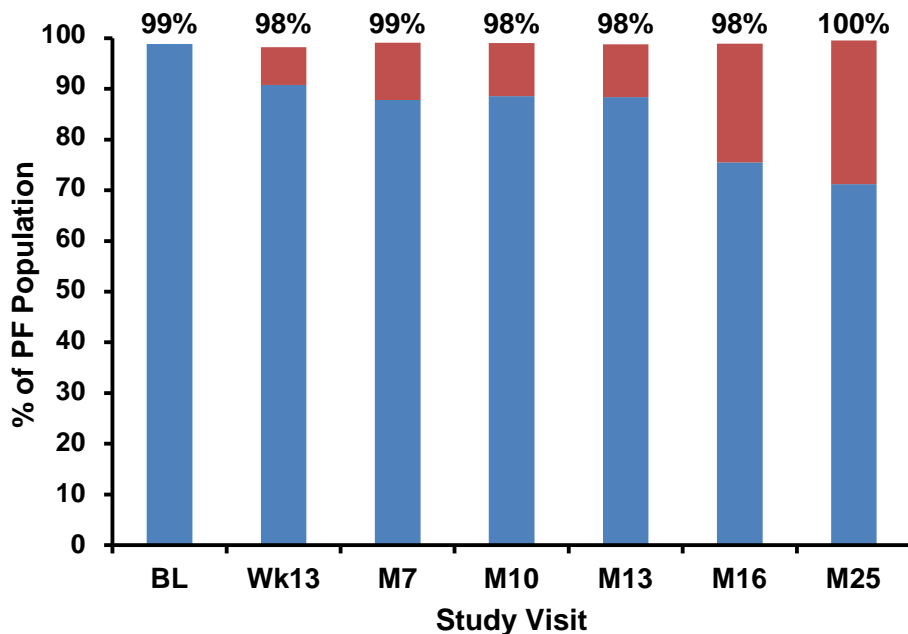
Maintenance therapy with pazopanib will result in a small but statistically significant decline in global HRQOL and more side effects during the time on treatment, but will be associated with an overall benefit to patients

Specifically:

- Pazopanib will be associated with superior quality adjusted PFS
- Progressive disease results in a decline in quality of life
- Pazopanib will delay the time to second line therapy

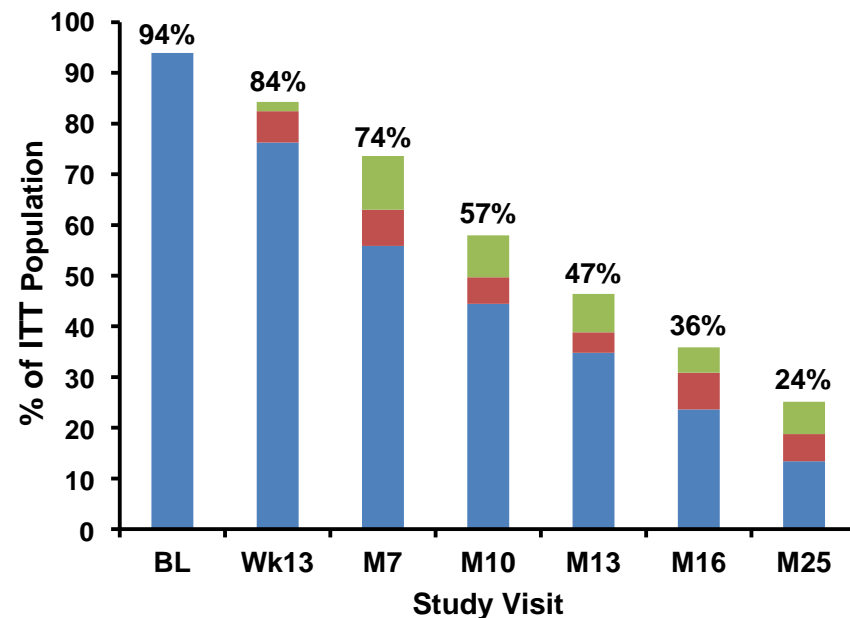
Proportion of EQ-5D Questionnaires Completed

Progression-free (PF) Population



■ on treatment ■ off treatment

Intent-to-treat (ITT) Population



■ PF on treatment ■ PF off treatment ■ PP

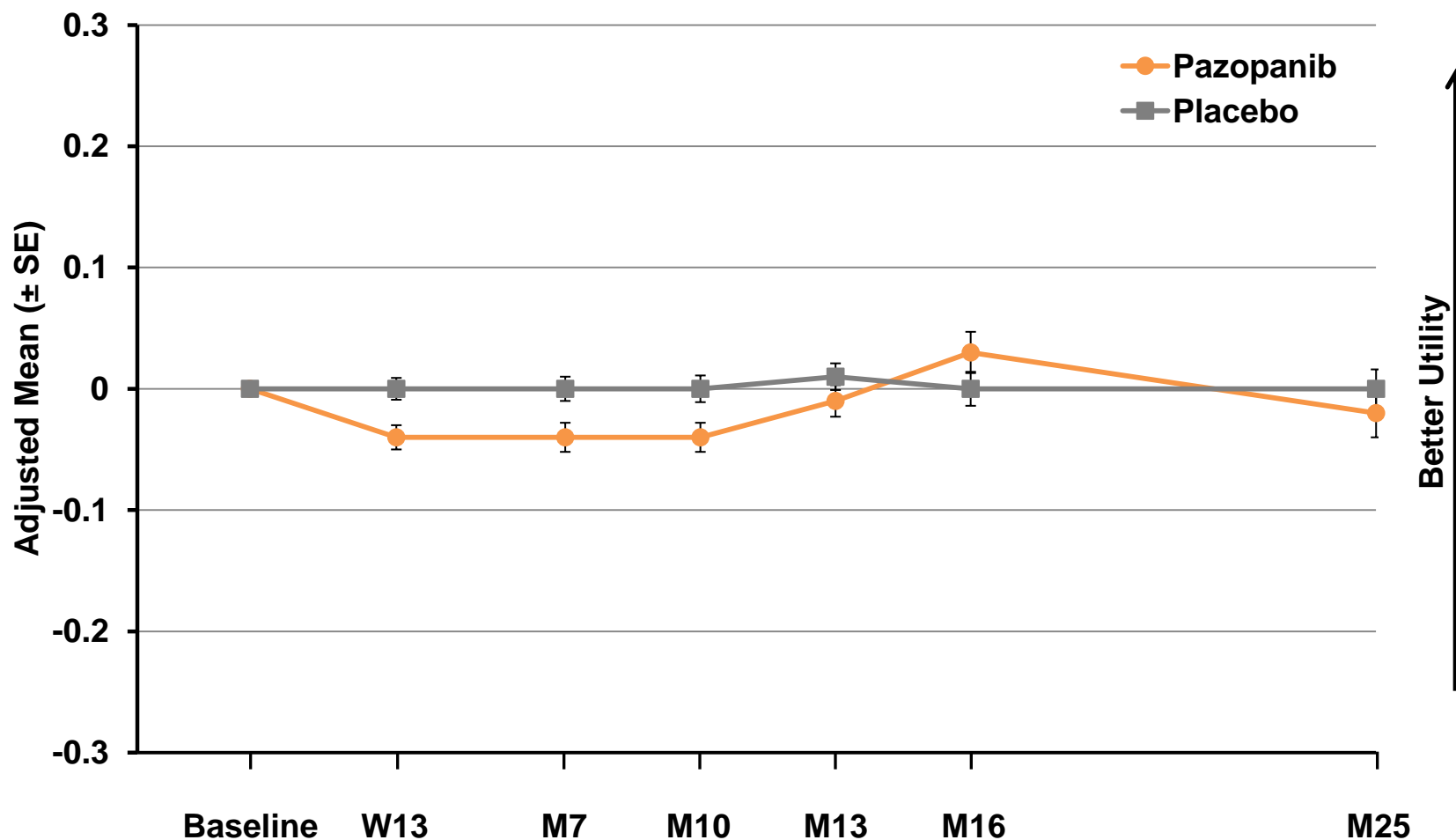
Prespecified Analyses per Protocol

- Difference in change from baseline in HRQOL scores between treatment groups*
 - QLQ-C30 Global Health Status
 - OV-28 subscales
 - EQ-5D

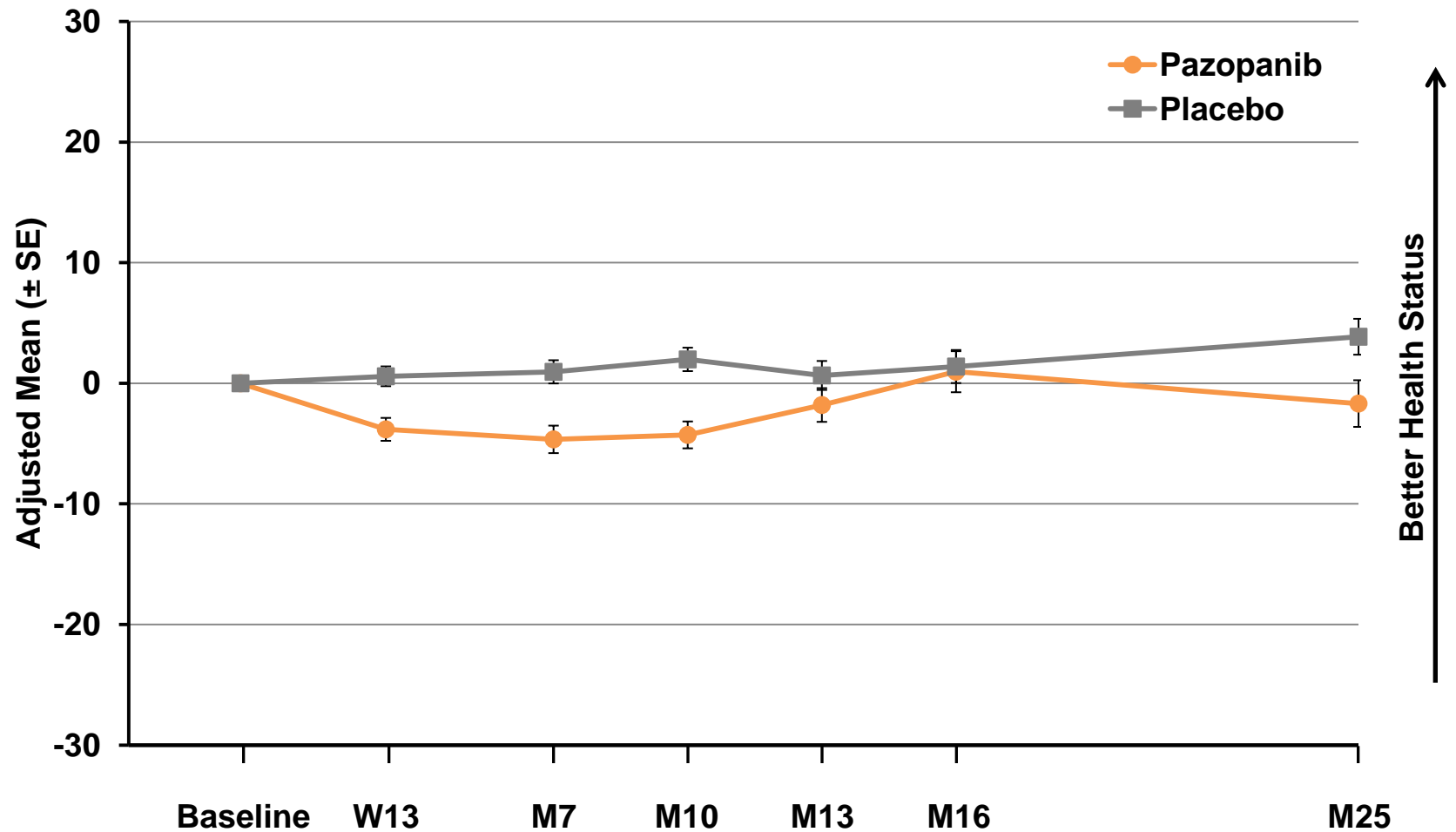
*Mixed model repeated measure analysis

Interpretation of clinical significance followed Cocks et al 2011 and Pickard et al 2007

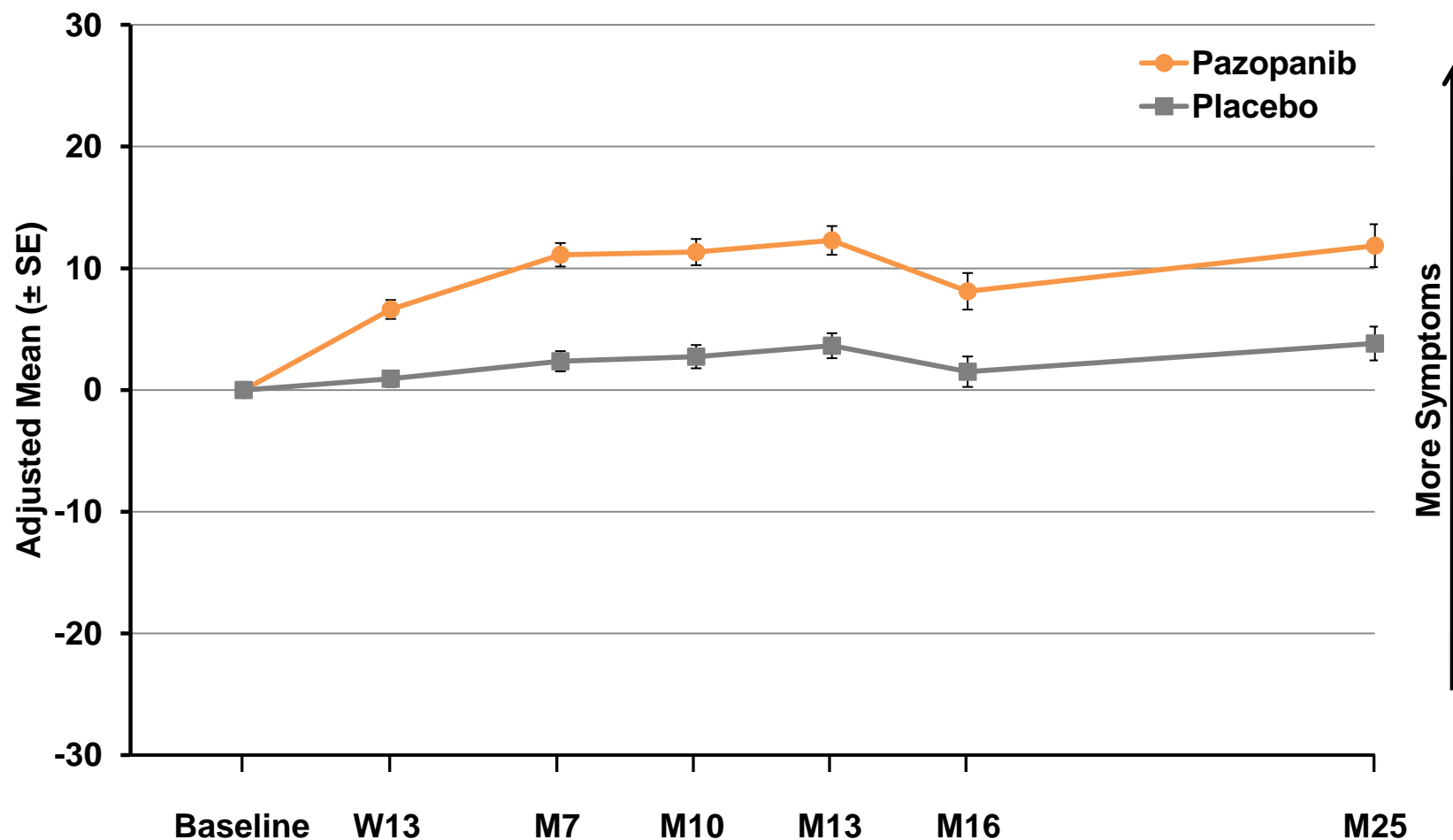
EQ-5D Utility Index



QLQ-C30 Global Health Status



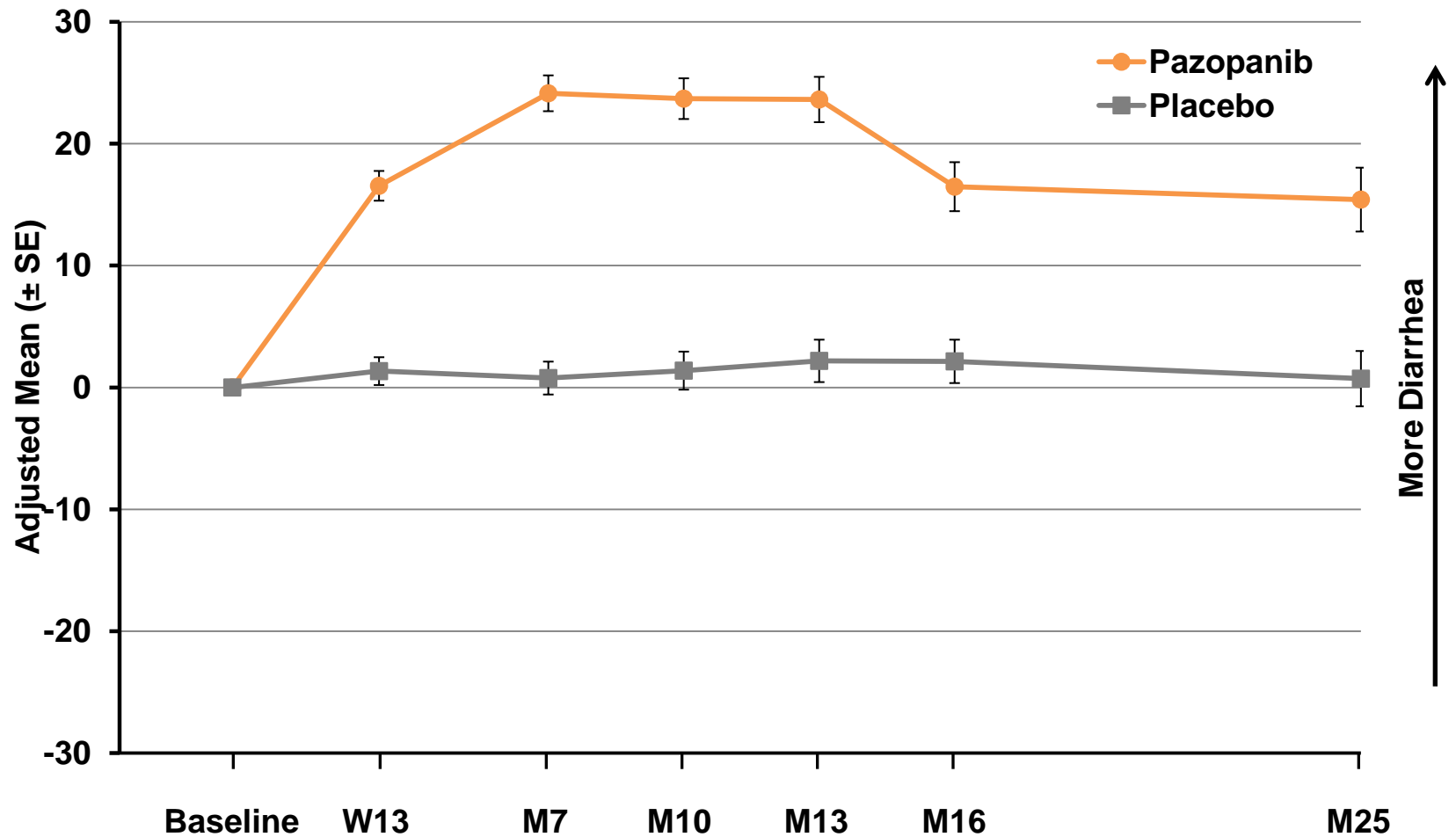
QLQ-OV28 Abdominal / GI Symptoms



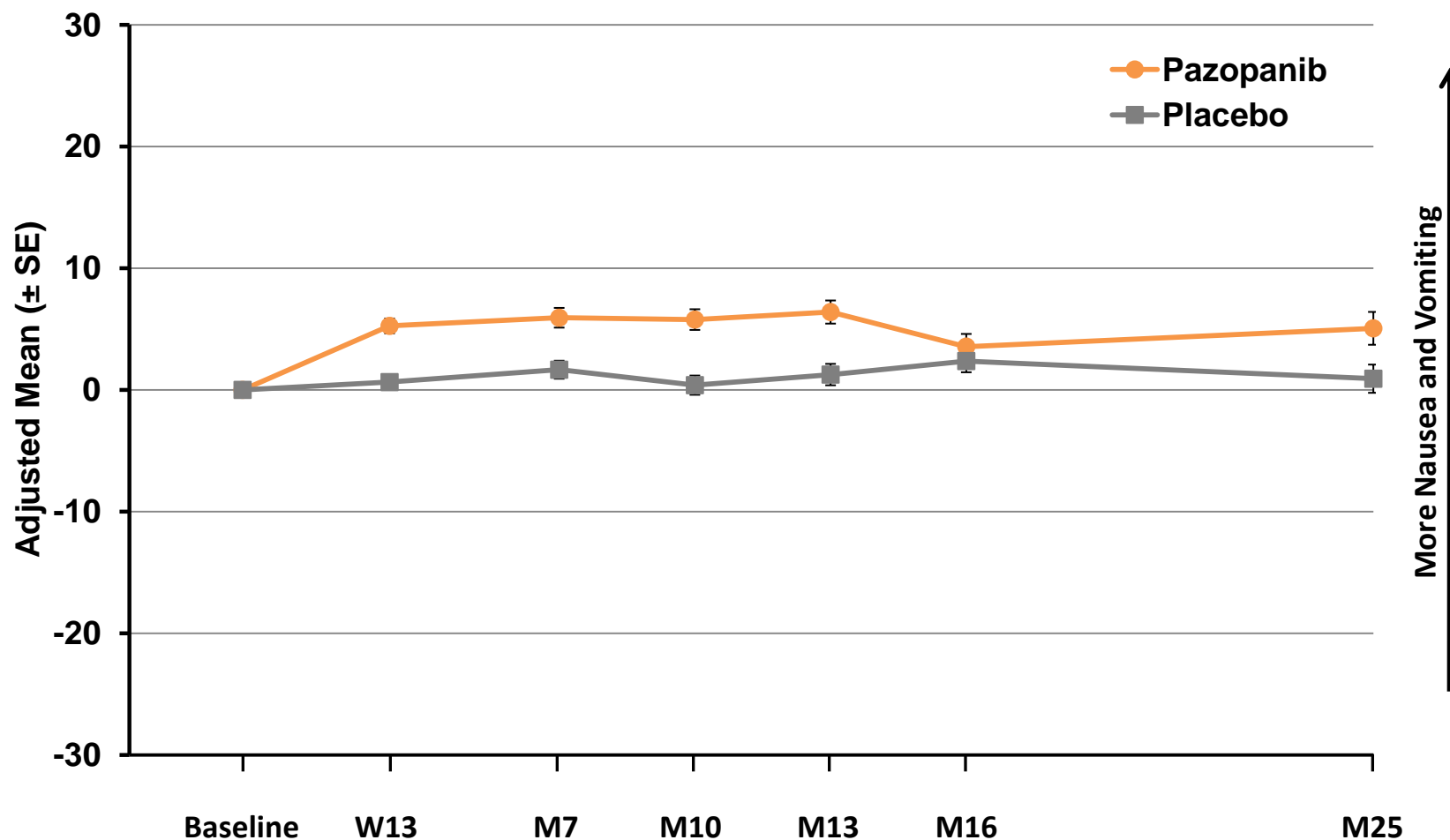
Post Hoc / Exploratory Analyses

Evaluate the trade-offs between treatment efficacy and treatment-related toxicity

QLQ-C30 Diarrhea (ITT)



QLQ-C30 Nausea and Vomiting (ITT)

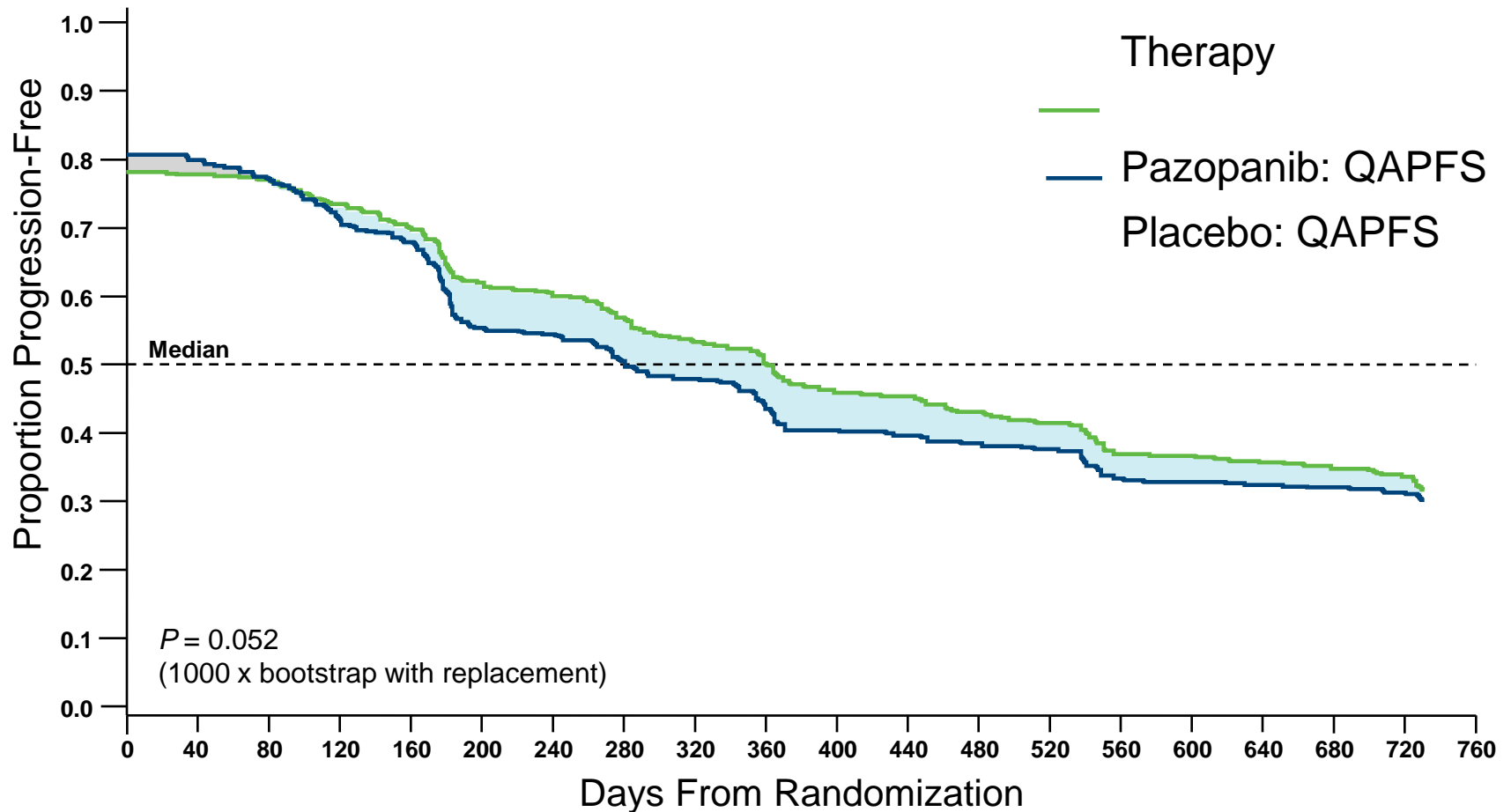


Post Hoc Analysis

Quality-adjusted PFS (QAPFS)

-
- QAPFS is the product of time without progression and patient reported utility as estimated by EQ-5D¹
 - Summary measure of the trade-off between treatment efficacy and it's impact on QOL
 - Positive result would support maintenance pazopanib from the patient perspective

Quality-Adjusted PFS (QAPFS)



Post Hoc Analysis

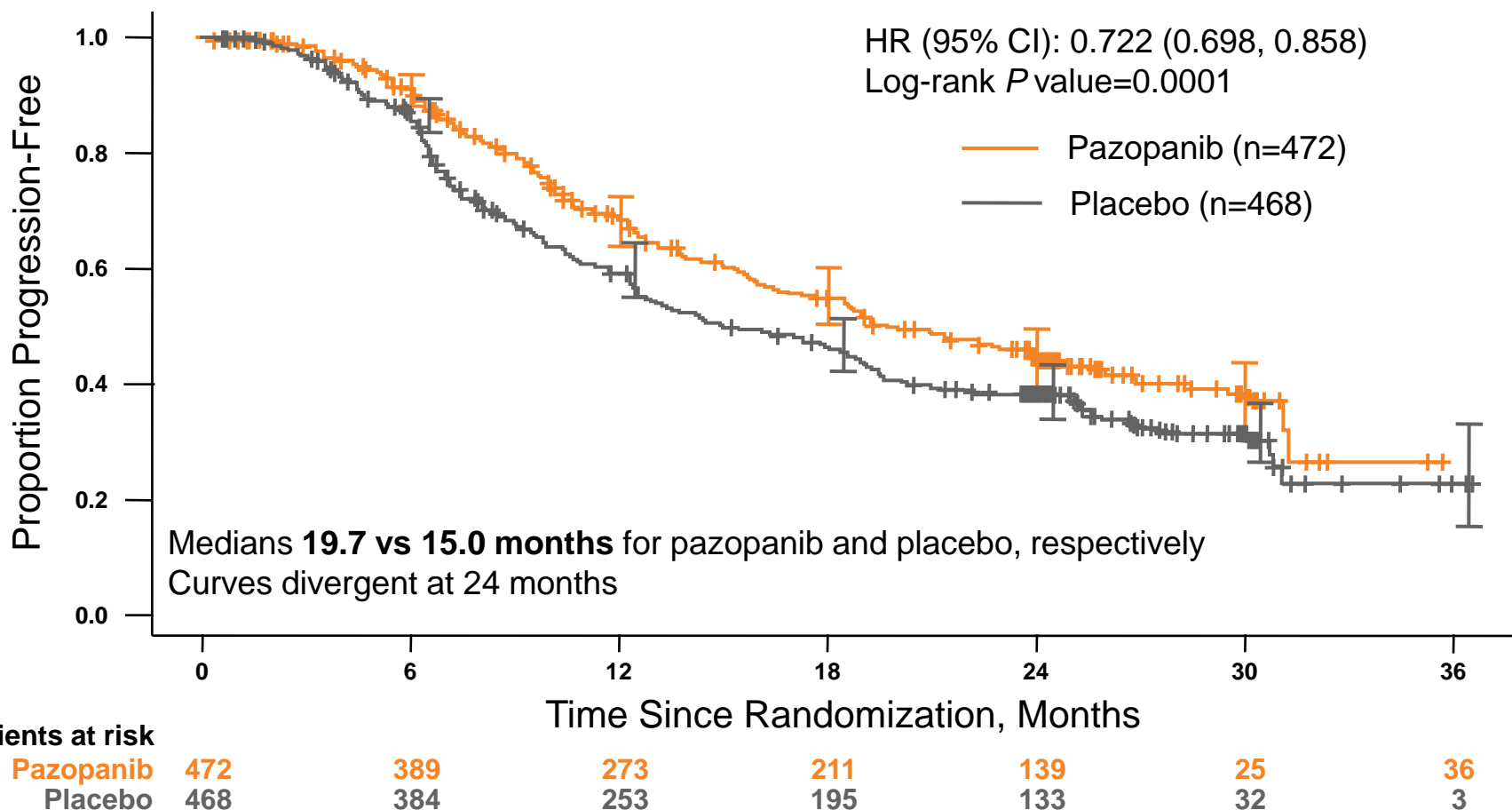
QLQ-C30 after progression

- QLQ-C30 Global Health Status (GHS) deteriorates with progression
 - 8.6 points difference between pre- and post-progression ($P < 0.0001$)*

*paired t-test; analysis included patients with pre- and post-progression data pooled across treatment arms (N=**206**)

Post Hoc Analysis

Time to Subsequent Anticancer Therapy



Conclusions

- Maintenance therapy with pazopanib results in
 - an improvement in median PFS of 5.6 months
 - a small decrement in overall HRQOL for patients on treatment
 - a significant increase in patient-reported diarrhea
- Progression results in worse HRQOL and initiation of further chemotherapy
- Quality-adjusted PFS supports the net value of maintenance therapy
- Limitations of post-hoc analyses
 - highlight the importance of including a priori HRQOL hypotheses in future studies

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