gastrointestinal tumours, colorectal

**POSEIDON PHASE II/III TRIAL: ABITUZUMAB COMBINED WITH CETUXIMAB PLUS IRINOTECAN AS SECOND-LINE TREATMENT FOR PATIENTS WITH KRAS WILD-TYPE METASTATIC COLORECTAL CANCER**


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**Aim:** Abituzumab (EMD 525797, DI17E6) is a humanized monoclonal IgG2 antibody specifically targeting the ανβ6 subunit of integrin receptors. POSEIDON is a Phase II/I open-label, randomized, controlled, multicenter trial (NCT01008475). Abituzumab ≤1000 mg combined with standard of care (SoC) revealed no dose-limiting toxicities in Phase I; here Phase II results are reported.

**Methods:** Pts were randomized 1:1:1 to abituzumab 500 mg (Arm A) or 1000 mg (Arm B) i.v. every 2-week cycle, combined with SoC (cetuximab [400 mg/m², day 1 cycle 1; then 250 mg/m² weekly] plus irinotecan [180 mg/m²/cycle]), or SoC alone (Arm C). Primary endpoint was investigator-assessed progression-free survival (PFS). Other objectives included overall survival (OS), safety and tolerability, and biomarker analysis. Eligible pts had confirmed wild-type colorectal cancer with distant metastasis and failure after oxaliplatin/fluoropyrimidine-containing treatment.

**Results:** In total, 216 pts were randomized: 73 to Arm A, 71 to Arm B, and 72 to Arm C; baseline characteristics were matched. Median PFS (investigator assessed) was 5.4 vs 5.6 vs Arm A vs Arm C, respectively (HR, 1.13 [95% CI, 0.78, 1.64]) and 5.6 mo with Arm B (HR, 1.11 [95% CI, 0.77, 1.61]). A trend for longer median OS was observed in Arms A and B, vs Arm C (15.0 and 14.4, vs 11.6 mo, respectively); response rates (RRs) were 27.4%, 25.4%, and 26.4%, respectively. Grade ≥3 treatment-emergent adverse events (TEAEs) were observed in 72%, 78%, and 67% of pts in Arms A, B, and C, respectively, and 13%, 10%, and 8% of TEAEs resulted in death (none considered abituzumab related). High integrin αvβ6 expression in the tumor tissue (98/197 analyzed pts) was associated with longer OS (HR, 0.48 [95% CI, 0.28, 0.82]) and better RR (31% vs 16%) for abituzumab-treated pts vs SoC. Additional data on circulating plasma proteins as candidate biomarkers and pharmacokinetics will be presented.

**Conclusions:** Although no difference in PFS was observed with the addition of abituzumab to SoC, abituzumab did prolong OS and doubled RR in pts with high tumor expression of αvβ6. The overall safety profile of abituzumab combined with SoC was acceptable.

**Disclosure:** C. Bokemeyer: Advisory Board: Merck-Serono, Sanofi Aventis Corporate-sponsored research: Merck Serono, Roche Pharma; E. Van Cutsem: Corporate-sponsored research: Research funding paid to my institution by Merckserono; B. Melichar: Advisory board: Merck, Roche, Sanofi, Lilly Other substantive relationships: honoraria for speeches Merck, Roche, Sanofi, Lilly; F. Rivera: Advisory board: Merck Serono Corporate-sponsored research: Merck Serono; Straub: Other substantive relationships: Employee of the trial sponsor; R. Bruns: Other substantive relationships: Employee of Merck KgA; S. Quaratino: Other substantive relationships: Employee of Merck KgA; J. Tabernero: Advisory board: Amgen, Imclone, Lilly, Merck KGaA, Millennium, Novartis, Roche, Sanofi, Celgene, Chugai and Taiho Other substantive relationships: Honoraria for presentations: Amgen, Merck KGaA, Novartis, Roche and Sanofi.All other authors have declared no conflicts of interest.