33P Final analysis of the Greek cohort of the AGENT phase III study arfolitixorin in metastatic colorectal cancer

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Background: The AGENT trial, a pivotal international randomized phase III study (NCT03750786; Tabernero et al., 2024), investigated arfolitixorin in metastatic colorectal cancer (mCRC). This study presents the final analysis focusing on the Greek patient subpopulation.

Methods: Patients with mCRC were randomized to receive arfolitixorin (Arm A: 120 mg/m2 given as two intravenous bolus doses) or leucovorin (Arm B: 400 mg/m2 as a single intravenous infusion), both in combination with 5-FU, oxaliplatin, and bevacizumab. Response assessments were conducted every 8 weeks by blinded independent central review (BICR), and toxicity was reported according to MedDRA Version 22.1. The primary endpoint was ORR per RECIST v1.1 by BICR. Key secondary endpoints included PFS, DoR, OS, and safety.

Results: A total of 59 patients were included, with 24 in Arm A and 35 in Arm B. The mean age was 63.8 years, all Caucasians, and 84.5% had ECOG PS 0. Molecular profiling for BRAF, KRAS, and NRAS revealed frequencies of 6.1%, 55.6%, and 7.8%, respectively. Compared to Arm B, patients in Arm A exhibited higher ORR [41.7% (95% CI:22.1%, 63.4%) vs. 37.1% (95% CI:21.5%, 55.1%)], superior DoR [18.6 (5.3, NR$) vs.9.9 (5.1, 14.8)], longer median PFS [13.1 vs. 7.6 months; HR (95% CI):0.554(0.261, 1.176)], and a trend toward improved OS [not reached vs. 28.6 months; HR (95% CI):0.732(0.325, 1.649)]. Grade $\geq$3 drug-related AE rates were similar between arms, with fatigue (53.4%), hematologic toxicity (53.4%), nausea (50%), and sensory neuropathy (27.6%) being the most frequently reported. However, only one patient discontinued treatment in Arm A compared to three in Arm B. Notably, efficacy and survival outcomes in this Greek analysis were inversely proportional to those of the overall study population, highlighting potential regional variations.

Conclusions: The AGENT trial did not demonstrate clinical superiority of arfolitixorin over leucovorin in first-line therapy for mCRC. Nonetheless, this analysis suggests potential benefits associated with arfolitixorin in the Greek population, possibly influenced by regional and genetic factors. Limitations, including the small sample size, warrant cautious interpretation of these findings.

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