

AB027. PS01.09. In-progress: phase 1b study of anetumab ravtansine in patients with mesothelin-expressing malignancies

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Background: Mesothelin is expressed in a wide variety of tumors, including mesothelioma, ovarian, pancreatic, gastric/GEJ, non-small cell lung cancer (NSCLC), triple-negative breast cancer, cholangiocarcinoma, and thymic carcinomas. Indeed, in tissue samples from 34 patients with thymic carcinomas assessed for mesothelin expression, approximately three quarters were positive and of those approximately half had high expression (Thomas *et al. Lung Cancer* 2016;101:104). Anetumab ravtansine (BAY 94-9343), is a novel fully human anti-mesothelin IgG1 antibody conjugated to the maytansinoid tubulin inhibitor DM4 and has shown encouraging anti-tumor activity in mesothelioma and ovarian cancer patients in a phase I study. We will therefore conduct a signal generating study with anetumab ravtansine in six additional high unmet medical need malignancies with mesothelin expression (NCT03102320).

Methods: Eligibility criteria include: ≥ 18 years, unresectable

locally advanced or metastatic recurrent or relapsing disease, one or more prior lines of therapy, and availability of tumor tissue for mesothelin expression testing. Mesothelin-positive patients with selected adenocarcinomas (NSCLC, triple negative breast, gastric including gastroesophageal junction) and thymic carcinoma will receive anetumab ravtansine as monotherapy at 6.5 mg/kg IV on a 21-day cycle. Patients with cholangiocarcinoma will receive anetumab ravtansine in combination with cisplatin (25 mg/m² IV day 1 and 8 on a 21-day cycle for up to 6 cycles) and patients with pancreatic adenocarcinoma will receive anetumab ravtansine in combination with gemcitabine (1,000 mg/m² IV day 1 and 8 on a 21-day cycle). A safety run-in phase (18–24 patients each) will be conducted for the combination regimens prior to enrolling patients in the main study phase. The primary objective of the main phase of the study is objective response rate (ORR) of anetumab ravtansine as monotherapy or combination therapy in patients with either of two mesothelin expression levels: high ($\geq 30\%$ positive tumor cells with moderate and stronger membrane staining intensity) and low-mid ($\geq 5\%$ all intensities and $< 30\%$ positive tumor cells with moderate and stronger membrane staining intensity). Secondary objectives include safety, disease control rate, duration of response, durable response rate, and progression-free survival (PFS). Approximately 348 patients will be enrolled.

Keywords: Mesothelin; antibody drug conjugate

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