BERLIN 2025 ESMO congress

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Perioperative atezolizumab with or without the immunomodulatory IMM-101 in patients (pts) with MSI-high (MSI-H) or MMR-deficient (dMMR) stage III colorectal cancer (CRC) ineligible for oxaliplatin-based chemotherapy: The randomised phase II ANTONIO-study (AIO-KRK-0220)

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Background

Pts with MSI-H/dMMR CRC are often older and are ineligible for oxaliplatin-based chemotherapy. This phase II study evaluates perioperative atezolizumab combined with IMM-101, a heat-killed Mycobacterium obuense, in locally advanced, non-metastatic MSI-H/dMMR CRC.

Methods

Pts with locally advanced MSI-H/dMMR CRC ineligible for oxaliplatin received atezolizumab (1200 mg i.v.) on day -28 and -7 and IMM-101 (1.0 mg intradermally) on day -35 and 0.5 mg on days -21 and -5 preoperatively. Surgery was planned 5 weeks after initiating immunotherapy. Adjuvant treatment included atezo (840 mg i.v.) and IMM-101 (0.5 mg) biweekly for up to one year. Primary endpoint was pathological regression (Dworak grades 3-4, < 10%viable tumor cells). Secondary endpoints included DFS, OS, and safety. Data cut-off: January 6, 2025.

Results

Of 20 planned pts, 13 were enrolled before trial discontinuation (due to IMM-101 supply issues); 8 received neoadjuvant atezo and IMM-101, while 5 received only atezo. Median age was 70 y (range 40-86), and 84.6% were female. ECOG PS were 46.2% (PS 0) and 53.9% (PS 1/2). Tumors were predominantly right-sided (92.3%), with 75% of all pts harboring a BRAFV600E mutation. Tumor stages included T1/2 (30.8%) and T3/4 (69.3%), with N1 (69.2%) and N2 (30.8%). Surgery was completed in 12 pts (92.3%) with a R0 resection rate of 83.3%. Median time to surgery was 44 days (range 22-52). MSI-H/dMMR status was confirmed in all enrolled pts. Pathological regression rates were 0% (Dworak 3-4), 25.0% (Dworak 2), and 75% (Dworak 1-0). Central reassessment showed 0% (Dworak 3-4), 42% (Dworak 2), and 58% (Dworak 1-0). Grade ≥3 TEAE occurred in 23.1%, primarily injection site reactions. One immune-mediated encephalitis was reported.

Conclusions

Neoadjuvant atezo and IMM-101 did not achieve substantial pathological regression in MSI-H/dMMR locally advanced CRC pts with a high rate of BRAFV600E mutation. Further analyses are underway to explore the reasons for the limited therapeutic efficacy observed in this study as well as the adjuvant outcome and long term efficacy.

Clinical trial identification

EudraCT 2020-002715-21.

Legal entity responsible for the study

AIO Studien GmbH.

Funding

Roche.

Disclosure

M.H.H. Schuler: Financial Interests, Personal, Invited Speaker: Amgen, Bristol Myers Squibb, Janssen, Roche, GSK, MSD; Financial Interests, Personal, Advisory Board: Amgen, AstraZeneca, Bristol Myers Squibb, GSK, Janssen, Novartis, Roche, Sanofi, Takeda, MSD, Regeneron, Immunocore; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb, AstraZeneca, Janssen; Non-Financial Interests, Principal Investigator, Member, Study Steering Board: Janssen; Non-Financial Interests, Principal Investigator, Member, Study Steering Committee: Amgen. A. Reinacher-Schick: Financial Interests, Personal, Invited Speaker: Roche, MSD, MCI Global, Pierre Fabre; Financial Interests, Personal, Advisory Board: Amgen, Roche, AstraZeneca, Pierre Fabre, Daiichi Sankyo, Boehringer Ingelheim, Servier, Aurikamed, MCI Deutschland; Financial Interests, Institutional, Funding: Roche, AIO Studien GmbH, Rafael Pharmaceutics, BioNTech, Genentech, Georg-August-Universität Göttingen (UMG). S. Kasper-Virchow: Financial Interests, Personal, Invited Speaker: BMS, MSD, Lilly, Merck, Amgen, Servier, Daiichi Sankyo, Pierre Fabre; Financial Interests, Personal, Advisory Board: GSK, Novartis, AstraZeneca; Financial Interests, Personal, Other, Adboard: Taiho Oncology; Financial Interests, Personal, Research Grant, IMAGINE Trial: BMS; Financial Interests, Personal, Coordinating PI, PIONEER and ANTONIO: Roche; Financial Interests, Personal, Coordinating PI, RAMTAS: Lilly; Non-Financial Interests, Advisory Role: BMS, MSD, Amgen, Merck, Lilly, Servier, AstraZeneca; Non-Financial Interests, Personal, Other, Travel Support: BeiGene; Non-Financial Interests, Member: ASCO, DGHO. All other authors have declared no conflicts of interest.