BEVACIZUMAB BEYOND PROGRESSION IN METASTATIC COLORECTAL CANCER PATIENTS RECEIVING A FIRST-LINE TREATMENT CONTAINING BEVACIZUMAB: UPDATE OF BEBYP TRIAL BY GONO

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Background: Retrospective data suggested that the continuation of bevacizumab (BV) with second-line chemotherapy (CT) beyond the first progression in patients (pts) who received the anti-VEGF monoclonal antibody (moAb) as part of the first-line treatment can improve the outcome. Recently, results of the AIO/AMG ML18147 study demonstrated an improved overall survival (OS) by continuing BV beyond progression.

Methods: This phase III study randomized pts with unresectable metastatic colorectal cancer (mCRC) and measurable disease according to RECIST criteria, treated in first-line with BV plus fluoropyrimidine, FOLFIRI, FOLFOX or FOLFOXIRI, to receive a second-line CT with mFOLFOX6 or FOLFIRI (depending on first-line CT) with or without BV. A CT scan was performed every 8 weeks until progression. The primary end-point was progression free survival (PFS). To detect a HR for PFS of 0.70 with an α and β error of 0.05 and 0.20 respectively, the study required 249 events. Assuming an accrual time of 24 months and a follow-up of 12 months we planned to randomize 262 pts.

Results: Considering the results of the AIO/AMG ML18147 trial that showed an improved OS with the prosecution of BV beyond progression, the study accrual was stopped prematurely. A total of 185 pts were randomized and 184 pts were included in the ITT analysis (1 pt randomized in error). Pts characteristics for arm A (CT alone) and arm B (CT plus BV) were the following: number 92/92, gender M75%-F25%/M57%-F43%, median age 66 (38-75)/62 (38-75) years, PS = 0 82%/82%, multiple site of disease 76%/77%, and liver-only disease 15%/13%. At the first analysis (median follow up of 18 months) the study met its primary endpoint by demonstrating an improvement in PFS in the BV containing arm. We updated results and at a median follow up of 22 months the improvement in PFS for the experimental arm was confirmed with a median PFS of 5.2 months for arm A and 6.7 months for arm B (HR = 0.66; 95% CI 0.49–0.90; unstratified p = 0.007).

Subgroup analyses showed a consistent benefit in all the subgroups including gender and first-line PFS. Response rates (RECIST) were 18% and 21% (p = 0.71) in arm A and B, respectively. Toxicity profile was consistent with previously reported data. The OS data are still immature, with 56 events in arm A and 54 in arm B and the median OS is 16.0 months and 16.5 months respectively (HR = 0.83; 95% CI 0.57–1.22; unstratified p = 0.34).

Conclusion: This study demonstrates an improvement in PFS by continuing BV in second-line in pts who had received CT + BV in first-line.