Updated results of TRIBE2, a phase III, randomized strategy study by GONO in the first- and second-line treatment of unresectable mCRC.

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Abstract Disclosures

Background:
In the phase III TRIBE study FOLFOXIRI/bev significantly improved Response Rate (RR), PFS and OS when compared with FOLFIRI/bev as initial treatment of mCRC. However, the actual advantage by the triplet could be lower when compared with a pre-planned sequential strategy of doublets (FOLFOX, FOLFIRI). TRIBE2 (NCT02339116) is a phase III trial in which unresectable mCRC pts were randomized 1:1 to FOLFOX/bev followed by FOLFIRI/bev after PD (arm A) or FOLFOXIRI/bev followed by the reintroduction of the same regimen after PD (arm B). A pre-planned interim analysis showed a significant advantage for arm B in terms of PFS2, primary endpoint of the study, defined as the time from randomization to PD on any treatment given after first PD or death (PD2).

Methods:
The study had 80% power to detect a HR for PFS2 of 0.77 in favor of arm B with an overall 2-sided-α error of 0.05 (0.0131 and 0.0455 for the interim and final analyses, planned at 303 and 466 PFS2 events, respectively). Secondary endpoints included RR, 1st-PFS, i.e. the time from randomization to the first evidence of PD or death (PD1), 2nd-PFS, i.e. the time from PD1 to PD2, and OS.
Results:
From February 2015 to May 2017, 679 pts (arm A/B: 340/339) were enrolled in 58 Italian sites. Main pts’ characteristics were (arm A/B): right side 38%/38%, synchronous mets 89%/89%, RAS mutant 65%/63%, BRAF mutant 10%/10%. At a median follow up of 30.6 mos, 514 (arm A/B: 272/242) PD2, 594 (arm A/B: 303/291) PD1 and 408 (arm A/B: 217/191) OS events were collected. A significant advantage by upfront FOLFOXIRI/bev was confirmed in terms of PFS2 (19.1 vs 16.4 mos, HR 0.74, 95%CI 0.62-0.88, p<0.001), RR (62% vs 50%, OR 1.61, 95%CI 1.19-2.18, p=0.002) and 1st-PFS (12.0 vs 9.8 mos, HR 0.75, 95%CI 0.63-0.88, p<0.001). A significant OS benefit for pts in arm B was also observed (27.6 vs 22.6 mos, HR: 0.81, 95%CI: 0.67-0.98, p=0.033). Out of 594 pts with a PD1 event, 470 (79%, arm A/B: 251/219) received a treatment after PD. In the per-protocol analysis (N=323), pts in arm B showed significantly longer 2nd-PFS (6.5 vs 5.8 mos, HR 0.76, 95%CI 0.59-0.97, p=0.024).

Conclusion:
Upfront FOLFOXIRI/bev followed by the pre-planned reintroduction of the same agents after PD provided a statistically significant and clinically relevant PFS2 and OS benefit when compared with the pre-planned sequential administration of FOLFOX/bev and FOLFIRI/bev in unresectable mCRC patients. A median OS of 27.6 mos was reached despite the high percentage of pts with poor prognostic features (RAS and BRAF mutations, right side, synchronous mets). Clinical trial information: NCT02339116

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