Impact of depth of response of induction therapy on maintenance therapy in patients with RAS wild-type metastatic colorectal cancer: An analysis of the PanMa trial (AIO KKR 0212)


Study design and Background

Background

Depth of response (D0R) is associated with improved progression-free survival (PFS) and overall survival (OS) in patients with RAS wild-type (WT) metastatic colorectal cancer (mCRC). There are limited data on the relevance of D0R to induction therapy for consecutive maintenance treatment. Thus, the impact of D0R to induction with 6 cycles of FOLFOX4 (FUSP), capecitabine and panitumumab (Pmab) in the efficacy of maintenance therapy (PFS or OS) was assessed.

Methods

Computed tomography and magnetic resonance imaging were used for central pathologic assessment. D0R was defined as change of tumor diameter from baseline (pre-induction) to baseline (post-induction). Cox regression models and rank-sum tests estimated hazard ratios including 95% confidence intervals of D0R (as a binary outcome) in both arms (Pmab- and FUFA-based maintenance therapy).

Results

Out of 248 patients in the full analysis set 211 were evaluable for central review and D0R analysis (arm A, n=106; arm B, n=105). Median D0R was similar in both treatment arms (42.7% [arm A] vs. 42.2% [arm B]). Cox regression analysis demonstrated a significant correlation of initial D0R with both consecutive PFS (p=0.023) and OS (p=0.046) in the Pmab-arm while in patients receiving FUFA alone this association was not observed. There was no predictive value of D0R groups on efficacy according to treatment arm.

Conclusions

In RAS WT mCRC treated in within the PanMa trial, D0R to induction therapy has a prognostic impact on subsequent maintenance treatment. This effect appears pronounced in patients receiving Pmab-based maintenance therapy.

Methods, Results and Conclusions

Methods

A

B

C

D

Overall depth of response (FUSP+aPmab, n=106; FUFA, n=105)

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The Figure 3 shows the depth of response (D0R) to induction therapy and maintenance therapy. A) D0R to maintenance therapy for FUSP+Pmab and FUFA alone. In the baseline median DFS (95% CI) was 10.1 and 9.8 months, respectively, in arm A and arm B, respectively. The median time-to-event (TTE) for DFS was 10.6 months in arm A and 9.8 months in arm B. The median OS was 10.6 months in arm A and 9.8 months in arm B. The median PFS was 10.1 months in arm A and 9.8 months in arm B. The median OS was 10.6 months in arm A and 9.8 months in arm B.

Results

Out of 248 patients receiving maintenance therapy, 211 were evaluable for D0R analyses.

- Total D0R in all patients was 95.5%. D0R of induction therapy (42.5%) accounted for the largest proportion (75.2%) of the total D0R.

- While greater D0R to induction was significantly associated with longer PFS (HR 0.67, 95% CI 0.52–0.93; p=0.03) and OS (HR 0.38, 95% CI 0.28–0.51, p<0.001), no significant interaction of D0R with maintenance therapy arms was observed.

CONCLUSIONS

Overall D0R was similar to other EGFR-based regimens.

D0R achieved by induction therapy accounted for three quarters of the total shrinkage supporting des-escalation strategies without substantial compromising efficacy.

D0R to induction was prognostic but not predictive for efficacy of consecutive maintenance therapy.

REFERENCES


