Gemcitabine plus erlotinib followed by capecitabine versus capecitabine plus erlotinib followed by gemcitabine: Interim toxicity analysis of a multicenter, randomized, cross-over phase III trial of the Arbeitsgemeinschaft Internistische Onkologie (AIO).

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Abstract:
Background: To date, only limited toxicity data are available for the combination of erlotinib (E; 150 mg/d) with either gemcitabine (G) or capecitabine (C) as first-line therapy for advanced pancreatic cancer (PC).

Methods: Within a prospective multicenter phase III trial, 281 patients (pts) with histologically confirmed advanced exocrine PC were randomly assigned to first-line treatment with either C (2000 mg/m²/d, d1-14 q3w) plus E (150 mg/d, arm A) or G (1000 mg/m² over 30 min weekly x 7, then d1, 8, 15 q4w) plus E (150 mg/d, arm B). In case of treatment-failure (e.g. disease progression or toxicity), pts were "crossed-over" to second-line treatment with the comparator cytostatic drug without E. The primary study endpoint was time to treatment failure of second-line therapy (TTF2).

Results: While the trial has completed recruitment, toxicity data (secondary endpoint) are available from the first 127 randomized pts. Sixty pts were randomized to arm A (55% male, 83% metastatic PC), 67 pts to arm B (55% male, 82% metastatic PC); median age was 64 years. During first-line therapy, pts received a median number of 3 treatment cycles (range 0-13) in both arms; overall 456 treatment cycles were applied (arm A: 218, arm B: 238). Regarding chemotherapy, a treatment delay was observed in 12% of the cycles in arm A and in 22% of the cycles in arm B. Dose reductions of the cytostatic drug were performed in 18% and 27% of treatment cycles, respectively. E dose reductions were performed in 6% and 11% of all cycles. Grade 3/4 hematological toxicity was <15% in both arms; in arm A, grade 3/4 diarrhea was observed in 9% of pts (arm B: 7%), grade 3/4 skin rash in 4% (12%) and grade 3/4 hand-foot syndrome in 7% (0%), respectively. Nine pts in arm A (7 of them due to PC) and 8 pts in arm B (6 due to PC) died within 60 days after randomization. Conclusion: G/E and C/E were both tolerated well and toxicity was manageable. This first analysis suggests that treatment with E 150 mg/d is feasible in combination with G or C.