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FOLFOX plus nivolumab and ipilimumab versus FOLFOX induction followed by nivolumab and ipilimumab in patients with previously untreated advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction: Results from the randomized phase II Moonlight trial of the AIO

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Background

FOLFOX plus nivolumab (nivo) has become standard of care for first-line therapy of patients (pts) with esophagogastric adenocarcinomas. To reduce toxicity, there is a need to evaluate if short-term induction chemotherapy followed by immunotherapy as an alternating treatment is as effective, while more tolerable. The aim of this second part of the Moonlight trial was to evaluate if mFOLFOX induction therapy followed by nivo plus ipilimumab (ipi) is less toxic but equally effective compared to both regimens combined together. Results of the other study parts will be presented elsewhere.

Methods

The AIO-STO-0417 trial (Moonlight) is a four-arm investigator-initiated trial, whereof two arms (A1/A2) are presented here. Pts were randomized 1:2 to FOLFOX plus nivo 240 mg; q2w and ipi 1 mg/kg; q6w administered in parallel (arm A1; parallel treatment) or three cycles of mFOLFOX induction treatment followed by nivo and ipi (arm A2; sequential treatment). PD-L1 expression was centrally assessed. Primary endpoint was progression-free survival at 6 months (PFS@6), main secondary endpoints were OS, PFS, objective response rate (ORR) and safety.

Results

Ninety patients were randomized (30 pts to arm A1 and 60 pts to A2). Baseline characteristics were: median age 62y, GEJ, 51%, intestinal type, 33%. Forty-one percent had PD-L1 CPS≥1 (available in 74% of pts). Pts received a median of 11 cycles in A1 vs 7 cycles in A2. Adverse events of grade ≥3 were seen in 93% of the pts for arm A1 and 73% for arm A2, serious adverse events (SAE) in 70% in arm A1 and 62% in A2. Median follow-up was 7.3 mo. PFS@6 was 57% in arm A1 vs 28% in A2 (p=.012) with median PFS 8.4 vs 4.0 mo, respectively (p=.006). Median OS was not yet reached in A1 vs 9.1 mo in A2, ORR was 47% vs 30%, respectively. The results were similar in the PD-L1+ group.

Conclusions

FOLFOX chemotherapy plus nivolumab and ipilimumab administered in parallel was clearly more effective than FOLFOX induction followed

by nivo and ipi. Although associated with lower toxicity, our study doesn't support the use of sequential treatment in the first-line setting.

Clinical trial identification

EudraCT-No. 2017-002080-18 NCT03647969.

Legal entity responsible for the study

Institut für Klinische Krebsforschung IKF GmbH at Krankenhaus Nordwest.

Funding

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Disclosure

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