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Ipilimumab or FOLFOX in combination with nivolumab and trastuzumab in previously untreated HER2 positive locally advanced or metastatic esophagogastric adenocarcinoma (EGA): Results of the randomized phase II INTEGA trial (AIO STO 0217)

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Background

In 1st line EGA, the addition of PD-1 inhibitors to chemotherapy improved outcome in selected patient populations. The INTEGA trial compared different immunotherapy regimens in 1st line HER2+ EGA.

Methods

INTEGA is a randomized exploratory phase II investigator initiated trial with two experimental arms. Patients (pts) with previously untreated (for advanced disease) HER2+ (local status - IHC3+ or 2+/ISH+) EGA were randomized to receive trastuzumab (trast) and nivolumab (nivo) (240mg or 1mg/kg with ipi) in combination with either ipilimumab (ipi) (4x 3mg/kg every 3 weeks) (arm A) or mFOLFOX6 (arm B) for up to 12 months. The 1° endpoint was to increase the 12month overall survival rate (OSR@12) from 55% (trast/chemo - ToGA regimen) to 70% in each arm.

Results

Between March 2018 and May 2020 a total of 97 pts were enrolled and 88 randomized (44 per arm) in 21 German sites. Baseline characteristics were female/male 18/70, median age 61 (range 41-80), ECOG 0/1 54/34, GEJ/stomach 66/22, prior surgery for primary tumor in 24 patients and were well balanced between groups. Central posthoc biomarker analysis (ongoing) yet showed PD-L1 CPS>1 in 55 and >5 in 41 pts and HER2 positivity in 76 pts while 8 were negative (incl. one failed ISH). The 1° endpoint of 70% OSR@12 was reached in arm B, but not in arm A (57%) (Table). Treatment related grade 3/4 AE/SAE occurred in 29/15 pts in arm B and in 20/17 pts in arm A. Liquid biopsy analyses showed strong correlation of high ctDNA load with shorter PFS/OS and emergence of truncating HER2 mutations on trast.Table: LBA54

	All (n=88)		CPS>1 (n=55)		CPS>5 (n=41)	
	Arm A	Arm B	Arm A	Arm B	Arm A	Arm B
ORR	32%	56%	38%	65%	29%	68%
mPFS	3.2 mo	10.7 mo	2.2 mo	11 mo	2 mo	11 mo
PFSR@12	15%	37%	15%	34%	7%	37%
mDOR	5.8 mo	9.2 mo	-	-	-	-
mOS	16.4 mo	21.8 mo	16.4 mo	21.8 mo	12.5 mo	22.4 mo
OSR@12	57%	70%	54%	70%	51%	69%

mPFS – median PFS, PFSR@12 - PFS rate at 12 months, mDOR - duration of response, OSR@12 - OS rate at 12 months, mo - months

Conclusions

Trast/nivo/FOLFOX showed increased efficacy compared to the ToGA regimen, whereas trast/nivo/ipi did not improve OS over trast/chemo. Subgroupanalyses are ongoing and will be presented.

Clinical trial identification

NCT03409848.

Legal entity responsible for the study

AIO Studien gGmbH.

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Disclosure

A. Stein: Financial Interests, Institutional, Research Grant: BMS; Financial Interests, Personal and Institutional, Invited Speaker: BMS; Financial Interests, Personal and Institutional, Advisory Board: BMS. All other authors have declared no conflicts of interest.