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CANCERS OF THE UPPER GI TRACT

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Meeting Summary

Prospective randomized phase II study of FOLFIRI versus FOLFOX7 in advanced gastric adenocarcinoma: A Chinese Western Cooperative GI Oncology Group study

Feng Bi et al.

FOLFIRI VERSUS FOLFOX7 IN ADVANCED GASTRIC ADENOCARCINOMA

Patient population: Previously untreated metastatic or recurrent gastric adenocarcinoma patients with measurable disease

Design: mFOLFIRI (arm A) or mFOLFOX7 (arm B) every 2 weeks

The second-line treatment was mFOLFOX7 for arm A and mFOLFIRI for arm B.

Primary endpoint: PFS

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Prospective randomized phase II study of FOLFIRI versus FOLFOX7 in advanced gastric adenocarcinoma: A Chinese Western Cooperative Gastrointestinal Oncology Group study. Feng Bi et al.

FOLFIRI VERSUS FOLFOX7 IN ADVANCED GASTRIC ADENOCARCINOMA

Results:

	mFOLFIRI n = 54	mFOLFOX n = 74	p value
med PFS	2.9 mos	4.1 mos	0.109
Med OS	9.9 mos	12.0 mos	0.431
DCR	59.3%	66.3%	0.850
Med OS*	11.0 mos	20.2 mos	0.030
*subgroup analysis of the pts who completed both treatment lines per protocol			

Conclusions: There was no significant difference in the PFS or DCR. However, mFOLFOX7 followed by mFOLFIRI might have a better OS.

Prospective randomized phase II study of FOLFIRI versus FOLFOX7 in advanced gastric adenocarcinoma: A Chinese Western Cooperative Gastrointestinal Oncology Group study. Feng Bi et al.

Multicenter double-blind randomized Phase II: FOLFOX + ziv-aflibercept/placebo for patients with chemo-naïve metastatic esophagogastric adenocarcinoma (MEGA)

Peter C Enzinger et al.

FOLFOX + AFLIBERCEPT VS FOLFOX + PLACEBO IN 1ST LINE METASTATIC ESOPHAGEAL ADENOCARCINOMA

Patient population: Previously untreated metastatic esophageal or GE junction adenocarcinoma

Design: 2:1 randomization to receive either FOLFOX plus aflibercept vs FOLFOX

Primary endpoint: 6 months PFS

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Multicenter double-blind randomized Phase II: FOLFOX + ziv-aflibercept/placebo for patients with chemo-naïve metastatic esophagogastric adenocarcinoma (MEGA) Peter C Enzinger et al

FOLFOX + AFLIBERCEPT VS FOLFOX + PLACEBO IN 1ST LINE METASTATIC ESOPHAGEAL ADENOCARCINOMA

Results:

	FOLFOX + aflibercept n = 43	FOLFOX + placebo n = 21	p value
6 mo PFS	60.5%	57.1%	0.80
Med PFS	9.9 mos	7.3 mos	0.69
1-yr OS	58.7%	55.1%	0.80
Med OS	13.7 mos	18.7 mos	0.30
RR	61.1%	75.0%	0.33

Conclusion: aflibercept did not improve efficacy of FOLFOX

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Multicenter double-blind randomized Phase II: FOLFOX + ziv-aflibercept/placebo for patients with chemo-naïve metastatic esophagogastric adenocarcinoma (MEGA) Peter C Enzinger et al

GATSBY: A phase 2/3 study of T-DM1 vs a taxane in patients with previously treated HER2+ locally advanced or metastatic gastric/GE junction adenocarcinoma

Yoon-Koo Kang et al.

GATSBY: T-DM1 VS A TAXANE IN PTS WITH PREVIOUSLY PRE-TREATED HER2+ LOCALLY ADVANCED/METASTATIC GASTRIC/GE JUNCTION ADENOCARCINOMA

Patient population: locally advanced/metastatic HER2+ gastric/GE junction pre-treated with platinum + fluoropyrimidine + herceptin

Design:

- randomized 2:2:1 T-DM1 3.6 mg/kg q 3wk, T-DM1 2.4 mg/kg q wk, paclitaxel 80mg/m2 weekly or docectaxel 75 mg/m2 q 3 wk
- Weekly T-DM1 selected for further study by independent data monitoring committee

Primary Endpoint: OS

A randomized open-label, multicenter, adaptive phase 2/3 study of trastuzumab emtansine (T-DM1) versus a taxane (TAX) in patients with previously treated HER2+ locally advanced or metastatic gastric/GE junction adenocarcinoma. Yoon-Koo Kang et al

GATSBY: T-DM1 VS A TAXANE IN PTS WITH PREVIOUSLY PRE-TREATED HER2+ LOCALLY ADVANCED/METASTATIC GASTRIC/GE JUNCTION ADENOCARCINOMA

Results:

	TAX n = 117	T-DM1 q wk n = 228	p value
Med OS	8.6 mos	7.9 mos	0.86
Med PFS	2.9 mos	2.7 mos	0.31
ORR	19.6%	20.6%	0.84
Gr3+ AE	78 (70.3%)	134 (59.8%)	

Conclusion: T-DM1 did not show superior efficacy to TAX

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A randomized open-label, multicenter, adaptive phase 2/3 study of trastuzumab emtansine (T-DM1) versus a taxane (TAX) in patients with previously treated HER2+ locally advanced or metastatic gastric/GE junction adenocarcinoma. Yoon-Koo Kang et al

CheckMate-032: Nivolumab monotherapy in advanced and metastatic gastric or gastroesophageal junction cancer

Dung T. Le et al.

CHECKMATE-032: NIVOLUMAB MONOTHERAPY IN ADVANCED AND METASTATIC GASTRIC OR GASTROESOPHAGEAL JUNCTION CANCER

Patient population: Patients with advanced/metastatic gastric or GE junction adenocarcinoma, irrespective of PD-L1 status

- 83% had 2 or more prior regimens

Design: Single-arm (n = 59) study

- Nivolumab 3 mg/kg IV q 3 weeks

Primary Endpoint: ORR

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Safety and activity of nivolumab monotherapy in advanced and metastatic (A/M) gastric or gastroesophageal junction cancer (GC/GEC): results from the CheckMate-032 study. Dung T. Le et al

CHECKMATE-032: NIVOLUMAB MONOTHERAPY IN ADVANCED AND METASTATIC GASTRIC OR GASTROESOPHAGEAL JUNCTION CANCER

Results:

ORR	14% (1 CR, 7 PR) 19% (11/59) with SD Disease control rate 33% mDuration of response 7.1 months
	PD-L1+ numerically higher response rate
6 month OS	49%
12 month OS	36%
Grade 3/4 AEs	17% (pneumonitis, fatigue, diarrhea, vomiting, hypothyroidism, elevated AST ALT AF)

Conclusion: Nivolumab therapy is well tolerated and shows encouraging activity in heavily pre-treated patients

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Safety and activity of nivolumab monotherapy in advanced and metastatic (A/M) gastric or gastroesophageal junction cancer (GC/GEC): results from the CheckMate-032 study. Dung T. Le et al

KEYNOTE-028: Phase 1b study of pembrolizumab (MK-3475) in cohort of patients with advanced esophageal carcinoma

Toshihiko Doi et al.

KEYNOTE-028: PEMBROLIZUMAB IN PATIENTS WITH ADVANCED ESOPHAGEAL CARCINOMA

Patient population:

- Patients with advanced SCC or adenocarcinoma of esophagus or GE junction
- PD-1 expression in tumor or stroma by IHC
    - 83 samples, 37 PD-1+ (44.6%), 23 treated
- Histology: 73.9% squamous (both histologies responded similarly)
- 87.0% received 2 or more prior therapies

Study design:

Pembrolizumab 10 mg/kg q 2 weeks

Primary Endpoint: ORR

Updated results for the advanced esophageal carcinoma cohort of the phase Ib KEYNOTE-028 study of pembrolizumab (MK-3475). Toshihiko Doi et al.

KEYNOTE-028: PEMBROLIZUMAB IN PATIENTS WITH ADVANCED ESOPHAGEAL CARCINOMA

Results:

ORR	30.4% (O CR, 7 PR)
SD	9.0% (Median duration of response 40 weeks)
	52.5% of patients had some degree of tumor shrinkage
Grade 3 AEs	4 patients (17.4%) had grade 3 AE's Most common AEs: decreased appetite, hypothyroidism

From Keynote-012:

- 50% survival at 11 months

Gene expression profiling for responders:

- IDO1, CXCL10, CXCL9, HLA-DRA, STAT1, IFN-g
- Increased responses with higher immune gene signature scores

Conclusion: manageable toxicity and durable anti-tumor activity in heavily pre-treated patients. Phase II & III trials in esophageal cancer are ongoing.

Updated results for the advanced esophageal carcinoma cohort of the phase Ib KEYNOTE-028 study of pembrolizumab (MK-3475). Toshihiko Doi et al.

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