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MEETING SUMMARY

**WCGIC, JUNE 28TH TO JULY 1ST 2017, BARCELONA, SPAIN
ASCO, JUNE 2ND TO 6TH 2017, CHICAGO, USA**

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CANCERS OF THE UPPER GI TRACT

**PERIOPERATIVE CHEMOTHERAPY WITH
DOCETAXEL, OXALIPLATIN, AND
FLUOROURACIL/LEUCOVORIN (FLOT) VERSUS
EPIRUBICIN, CISPLATIN, AND FLUOROURACIL
OR CAPECITABINE (ECF/ECX) FOR RESECTABLE
GASTRIC OR GASTROESOPHAGEAL JUNCTION
(GEJ) ADENOCARCINOMA (FLOT4-AIO): A
MULTICENTER, RANDOMIZED PHASE 3 TRIAL**

AL-BATRAN ET AL

FLOT 4

- Patients with resectable (T2+N0+) gastric/GEJ tumors
 - 56% GEJ
 - 79-83% had T3+ disease
 - 78-81% had N+ disease
 - Randomized to receive
 - FLOT x 4 → surgery → FLOT x 4
(5-FU/LV + oxaliplatin + docetaxel q 2 weeks)
- OR**
- ECF/ECX x 3 → surgery → ECF/ECX x 3

FLOT 4

	mPFS	mOS (EP)	Resection	R0 resection
FLOT (n=356)	30 mos	50 mos	94%	84%
ECF/ECX (n=360)	18 mos	35 mos	87%	77%
HR	0.75	0.77		
P value	0.004	0.012	0.001	0.011

- Perioperative morbidity and mortality rates were similar
- Benefit of FLOT4 arm observed among all subgroups
- No difference in SAE rates
- Toxicities
 - FLOT significantly higher rates of
 - Diarrhea, infections, neutropenia, sensory complications
 - ECF/ECX significantly higher rates of
 - Nausea, vomiting, thromboembolic events, anemia

FLOT is a new standard of care for perioperative management of gastric/GEJ cancers

KEYNOTE-059

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- **Cohort 1:** Cohort 1: Efficacy and safety of pembrolizumab (pembro) monotherapy in patients with previously treated advanced gastric cancer. *Fuchs et al*
 - **Cohort 2:** Safety and efficacy of pembrolizumab (pembro) plus 5-fluorouracil (5-FU) and cisplatin for first-line (1L) treatment of advanced gastric cancer. *Bang et al*
 - **Cohort 3:** Safety and efficacy of pembrolizumab (pembro) monotherapy for first-line (1L) treatment of patients with PD-L1-positive advanced gastric/gastroesophageal cancer. *Kang et al*
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KEYNOTE-059

Title	N	PD-L1+	ORR	DCR	mDOR	mPFS	mOS
Cohort 1 (2 nd line pembro)	259	57%	11.6%	27%	8.4 mos	2.0 mos	
Cohort 2 (1 st line pembro + cisplatin + 5-FU/cape)	25	64%	60%	80%	5 mos	6.6 mos	20.8 mos
Cohort 3 (1 st line pembro PD- L1+)	31	100%	26%	55%		3 mos.	6 mo PFS 72.6% 12 mo PFS 61.7%

Responses were seen irrespective of PD-L1+, but higher in PD-L1+

KEYNOTE-059

	N	Gr 3+ AEs	Immune-related Gr 3+ AEs	
Cohort 1 (2 nd line pembro)	259	17%	4.6%	
Cohort 2 (1 st line pembro + cisplatin + 5-FU/cape)	25	76%	12%	No new safety signals
Cohort 3 (1 st line pembro PD-L1+)	31	23%	10%	

Phase III studies are ongoing

**NIVOLUMAB ± IPIILIMUMAB IN PTS WITH
ADVANCED/METASTATIC CHEMOTHERAPY-
REFRACTORY (CTX-R) GASTRIC (G),
ESOPHAGEAL (E), OR GASTROESOPHAGEAL
JUNCTION (GEJ) CANCER:
CHECKMATE 032 STUDY**

JANJIGIAN et al

OTT et al

CHECKMATE 032

- Patients with advanced/metastatic gastroesophageal cancer with progression on 1+ lines of therapy including a fluoropyrimidine and a platinum
- 3 cohorts
 - Nivolumab 3 mg/kg
 - Nivolumab 1 mg/kg + ipilimumab 3 mg/kg
 - Nivolumab 3 mg/kg + ipilimumab 1 mg/kg

CHECKMATE 032

	GEJ/esoph	3+ lines of therapy	<1% PD-L1
Nivo 3	68%	49%	62%
Nivo 1 + ipi 3	55%	46%	76%
Nivo 3 + ipi 1	65%	38%	70%

CHECKMATE 032

	ORR primary endpoint	DCR	SAEs
Nivo 3	12%	32%	5%
Nivo 1 + ipi 3	24%	41%	35%
Nivo 3 + ipi 1	8%	37%	17%

RR higher in PD-L1+ patients, but responses occurred regardless of PD-L1 expression

CHECKMATE 032

	mPFS	PFS 6 mo	PFS 12 mo	mOS	OS 6 mo	OS 12 mo
Nivo 3	1.4 mos	17%	8%	6.2 mos	39%	25%
Nivo 1 + ipi 3	1.4 mos	24%	17%	6.9 mos	35%	28%
Nivo 3 + ipi 1	1.6 mos	12%	10%	4.8 mos	24%	13%

Phase III studies are ongoing

GASTROESOPHAGEAL UPDATES

CONCLUSION

- FLOT has become a new standard of care for perioperative management of gastric/GEJ cancers
 - Will replace ECF/ECX
 - Pembrolizumab alone or in combination with chemotherapy shows promising activity in advanced gastric/GEJ cancers, awaiting phase III trial results
 - Nivolumab +/- ipilimumab also shows promising activity in gastroesophageal cancers, awaiting phase III trial results
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