Where Science Becomes Hope

IMMUNO-ONCOLOGY IN PERIOPERATIVE THERAPY FOR EARLY GASTROESOPHAGEAL CANCER: TO ADD OR NOT TO ADD?

Do not add

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QUESTIONS AND ASSUMPTIONS

What do we consider “early” gastroesophageal cancer? T>1, N+

Are we confined to a particular histology? No

What are we adding? Single agent immune checkpoint inhibitor.

What are we adding it to? TBD

Are we including MSI-H disease? No

Do we know the CPS score? No

IMMUNE CHECKPOINT INHIBITOR THERAPY IS USED IN THE TREATMENT OF ESOPHAGOGASTRIC CANCER.

Adjuvant nivo in eso, GEJ (R0, s/p neoadj chemoRT, no path CR). **CheckMate 577**. DFS benefit. ?OS

Nivolumab added to 1L FOLFOX if CPS >=5. **CheckMate 649**. OS benefit.

Pembrolizumab (and trastuzumab) to 1L FOLFOX if her2/neu overexpressed. **KEYNOTE 811**. OS benefit.

CURRENT STANDARD OF CARE. A REVIEW.

Chemoradiotherapy for Oesophageal Cancer Followed by Surgery Study (CROSS).

Site	Esophageal, GEJ
Histology	AdenoCa (75%), SCC (23%), other
T stage	T3 (approx. 80%).
N stage	N1 (approx. 64%)
Intervention	Preop chemoradiation (weekly carbo/taxol)
Control	Surgery

	Chemoradiation + surgery (n=178)	Surgery (N=188)	
R0 resection	92%	69%	P<0.001
pCR	29%	N/A	
AdenoCA	23%		
SCC	49%		
mDFS	Not reached	24.2 mo	HR 0.50 (0.36, 0.69)
mOS	49.4 m	24.0 m	HR 0.66 (0.50, 0.87)

N ENGL J MED 366;22 NEJM.ORG MAY 31, 2012

NOT STANDARD OF CARE. EA2174 (ASCO 2024)

Site	Esophageal, GEJ
Histology	AdenoCa
T stage/N stage	T1N1-3 or T2-3N0-2
Intervention	Preop chemoradiation (weekly carbo/taxol) + nivolumab (week 1, week 3) then surgery
Control	Preop chemoradiation (weekly carbo/taxol) then surgery

	ChemoRT + nivo (n=137)	ChemoRT (n=138)	
Went to surgery	76.1%	81%	
pCR	24.8%	21.0%	P=0.27
mDFS	TBD	TBD	
mOS	TBD	TBD	

2nd randomization into adjuvant nivo versus nivo + ipi

The addition of nivo to neoadjuvant carboplatin, paclitaxel and radiation does not improve the pCR rate in pts with resected E/GEJ adenocarcinoma.

Eads et al. JCO 42(16) supp.

CURRENT STANDARD OF CARE. A REVIEW. CONTINUED

FLOT4-Arbeitsgemeinschaft Internistische Onkologie (AIO).

Site	Gastric, GEJ
Histology	AdenoCa
T stage / N stage	cT2 or cN+
Intervention	Periop FLOT (4 cycles)
Control	Periop ECF/ECX (3 cycles)

	FLOT (n=356)	ECF/ECX (n=360)	
Surgery	94%	87%	
R0	85%	78%	
ypT1	25%	15%	P=0.0008
ypN0	46%	41%	P=0.025
Gr 3 or 4 tox	7%	26%	
mDFS	30 m	18 m	HR 0.75 (0.62 -0.94)
mOS	50 m	35 m	HR 0.77 (0.63-0.94)

El-Batran et al. Lancet 2019;393:1948-57

NOT STANDARD OF CARE. DANTE/FLOT8

DANTE/FLOT8-Arbeitsgemeinschaft Internistische Onkologie (AIO).

Site	Gastric, GEJ
Histology	AdenoCa
T stage / N stage	cT2 or cN+
Intervention	Periop FLOT + atezo (4 cycles)
Control	Periop FLOT (4 cycles)

	FLOT + atezo	FLOT	
Surgery			
R0			
pCR	23%	14%	
Gr 3 or 4 tox			
mDFS	?	?	
mOS	?	?	

Zhu et al. JCO, 42 (4):373

NOT STANDARD OF CARE (YET). ESOPEC

Site	Esophagus
Histology	AdenoCa
T stage / N stage	cT1cN+ or T2-4Nanything
Intervention	FLOT
Control	CROSS regimen

	FLOT (n=221)	CROSS (217)	
Surgery	191/207	180/196	
R0	180/191	171/190	
pCR	19.3%	13.5%	
Gr 3 or 4 tox			
mOS	66 m	37 m	
3 yr OS rates	57.4%	50.%	HR 0.70 (0.53 – 0.92)

Hoeppner et al. JCO 42(17). 2024

NOT STANDARD OF CARE (YET). ESOPEC

	FLOT (n=221)	CROSS (217)	
Surgery	191/207	180/196	
R0	180/191	171/190	
pCR	19.3%	13.5%	
Gr 3 or 4 tox			
mOS	66 m	37 m	
3 yr OS rates	57.4%	50.%	HR 0.70 (0.53 – 0.92)

Hoeppner et al. JCO 42(17). 2024

THERE IS A ROLE FOR IMMUNE CHECKPOINT INHIBITOR THERAPY IN THE TREATMENT OF GASTROESOPHAGEAL CANCERS. JUST NOT IN THE NEODJUVANT SETTING. YET.

No evidence

No evidence

No evidence

Generally well tolerated but not without its issues.

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