Decennale di

HIGHLIGHTS in RADIOTERAPIA

Update degli Studi Practice Changing 2024

Undicesima Edizione

In memoria di Renzo Corvò

ROMA

30-31 gennaio 2025

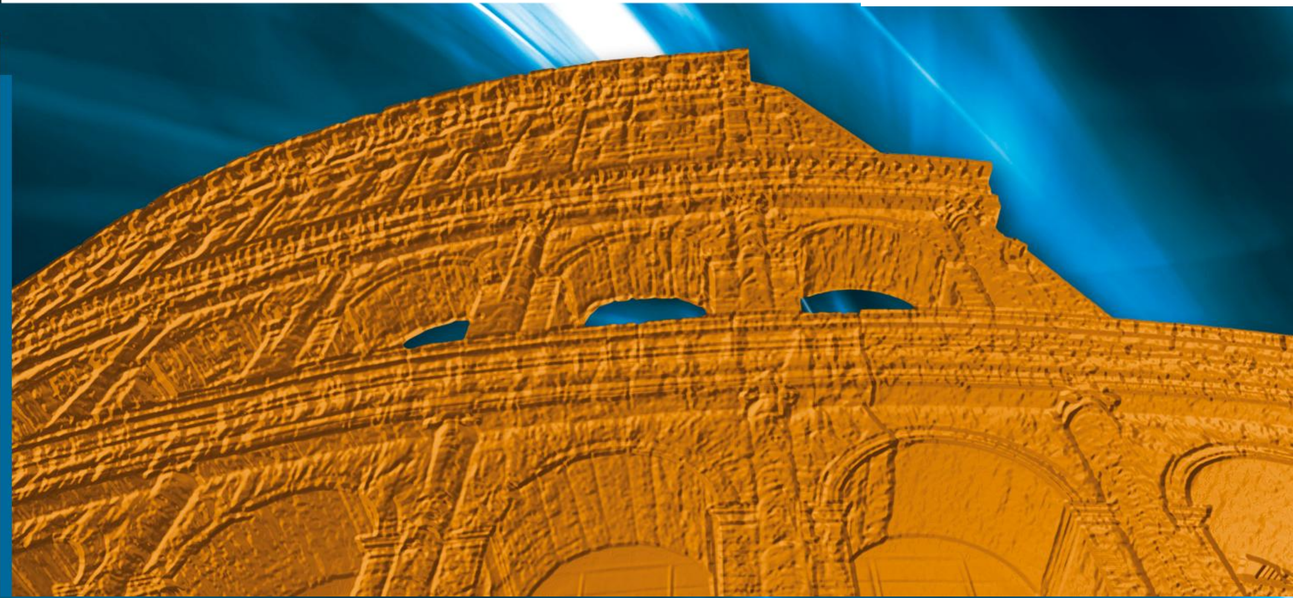
Starhotels Metropole

New evidence and practice changing treatments in Upper GI Tumors

D. Genovesi

A. D'Aviero

ISTITUTO di RADIOTERAPIA ONCOLOGICA CHIETI 1972 - 2022 50° ANNIVERSARIO



Early and Resectable locally advanced Esophageal & GEJ Tumors

RESEARCH SUMMARY

Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer

Kelly RJ et al. DOI: 10.1056/NEJMoa2032125

CLINICAL PROBLEM

For patients with locally advanced esophageal or gastroesophageal junction cancer, neoadjuvant chemoradiotherapy followed by surgery is a standard treatment. However, the risk of recurrence is high, especially among the 70 to 75% of patients without a pathological complete response, and clinicians lack proven adjuvant therapies for these patients.

CLINICAL TRIAL

A phase 3, double-blind, randomized, placebo-controlled trial to evaluate the efficacy of the checkpoint inhibitor nivolumab as adjuvant treatment after standard therapy.

794 adults who had received standard therapy for stage II or III esophageal or gastroesophageal junction cancer but had residual pathological disease were assigned within 4 to 16 weeks after surgery to intravenous nivolumab (30-minute infusions of 240 mg every 2 weeks for 16 weeks and then 480 mg monthly) or placebo for a maximum of 1 year. Median follow-up was 24.4 months.

RESULTS

Efficacy:

Median disease-free survival was 22.4 months with nivolumab and 11.0 months with placebo. Adjuvant nivolumab was also associated with longer metastasis-free survival.

Safety:

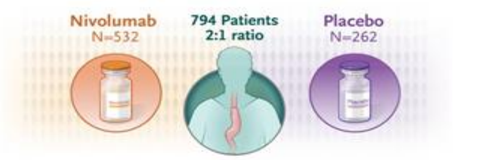
The safety profile of nivolumab was similar to that seen in other types of solid tumors. The most common high-grade nivolumab-related adverse events with potential immunologic cause were pneumonitis and rash.

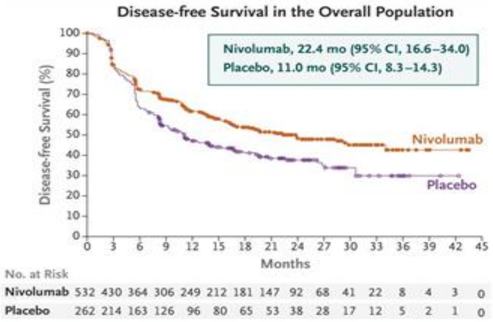
REMAINING QUESTIONS

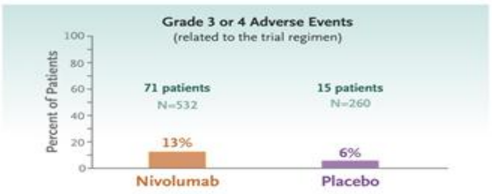
Further study is required to understand the following:

- The longer-term effects of nivolumab on overall survival
- Whether standard chemotherapy would be more effective if given with checkpoint inhibitors

Links: Full article | NEJM Quick Take | Editorial







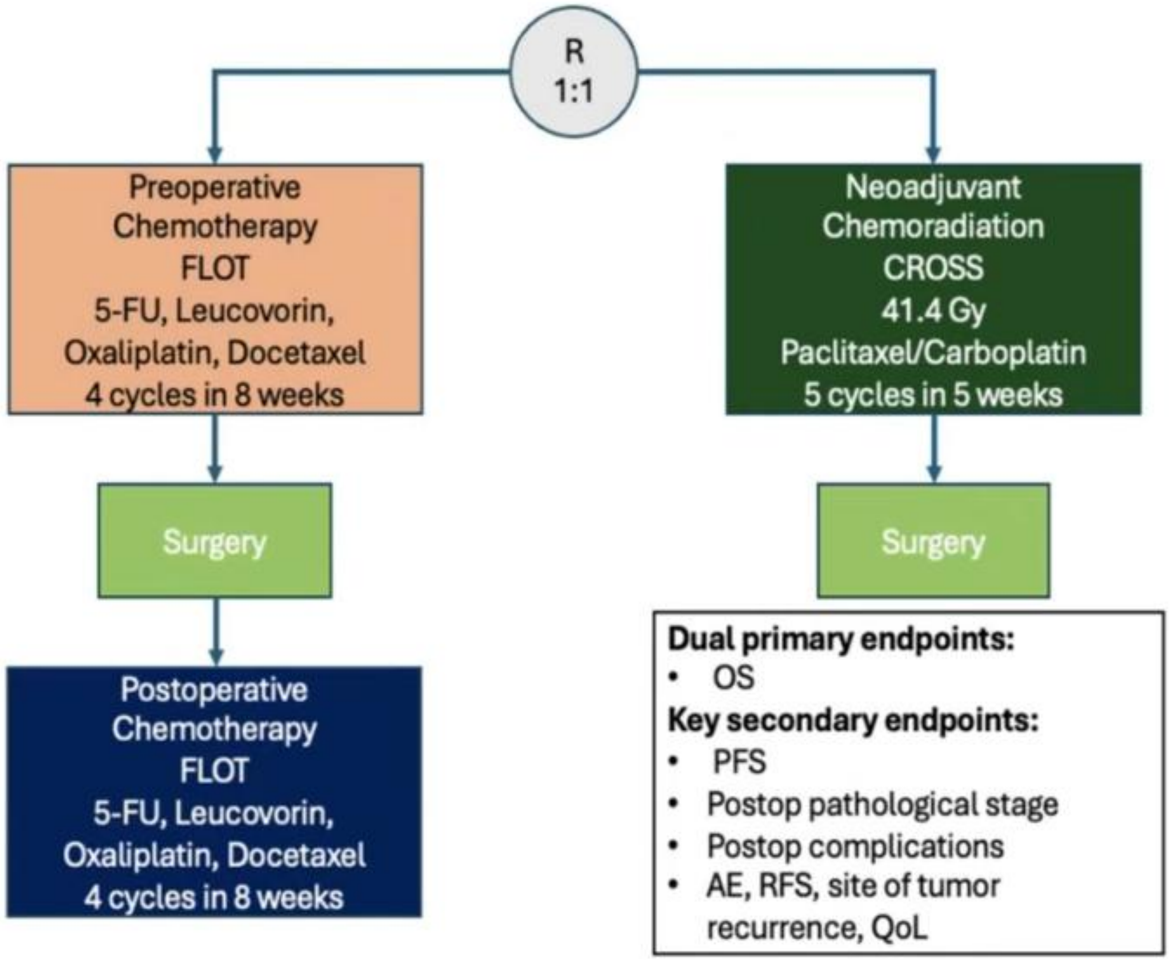
CONCLUSIONS

Adjuvant nivolumab significantly prolonged disease-free survival among patients with an incomplete pathological response after standard therapy for esophageal or gastroesophageal junction cancer.

Early and Resectable locally advanced Esophageal & GEJ Tumors

ASCO 2024

ESOPEC: Comparing periop FLOT to neoadj CRT CROSS in Esoph Adeno



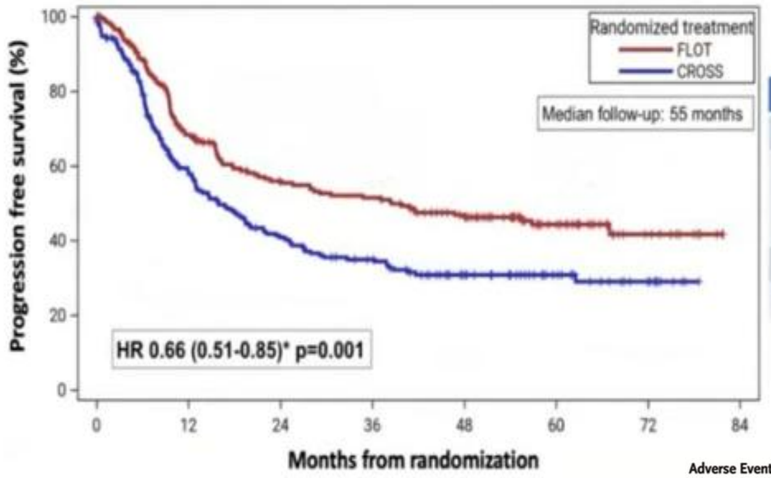
WHO	438 adults Median age, 63 years Men: 89%; Women: 11%
CLINICAL STATUS	Clinical stage cT1 cN+, cT2–4a cN+, or cT2–4a cN0 resectable esophageal adenocarcinoma without metastatic spread Tumors in the esophagus or near it and extending into the esophagus ECOG performance-status score of 0, 1, or 2 (range, 0 [full activity] to 5 [death]) Adequate hematologic, renal, hepatic, cardiac, and pulmonary function No previous radiotherapy or chemotherapy

Early and Resectable locally advanced Esophageal & GEJ Tumors

ASCO 2024

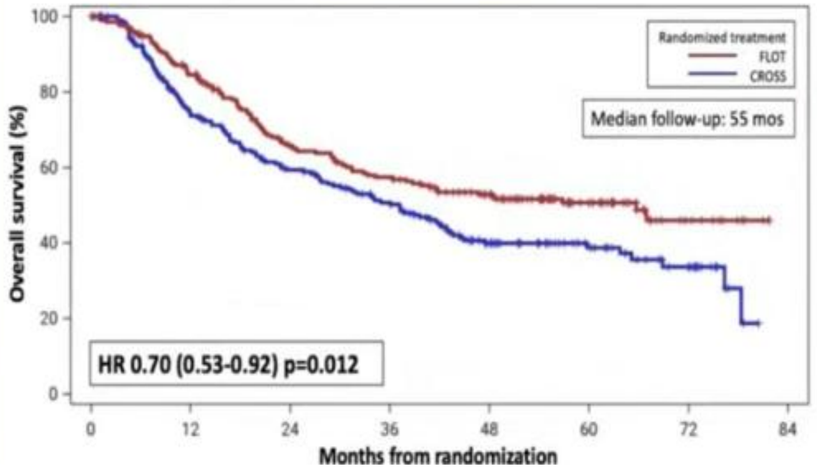
ESOPEC: Comparing periop FLOT to neoadi CRT CROSS in Esoph Adeno

Progression Free Survival

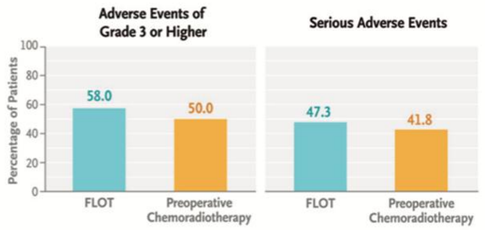


	FLOT	CROSS
Events	107	137
Median PFS time (months)	38 95% CI 21 – n.e.	37 95% CI 12 - 22
3 yr PFS rate	51.6 %	35.0%
5 yr PFS rate	44.4 %	30.9%

Overall Survival



	FLOT	CROSS
Events	97	121
Median OS time (months)	66 95% CI 36 – n.e	37 95% CI 28 - 43
3 yr OS rate	57.4 %	50.7%
5 yr OS rate	50.6 %	38.7%



The Kaplan–Meier estimate of mortality at 90 days after surgery was 3.1% in the FLOT group and 5.6% in the preoperative-chemoradiotherapy group.

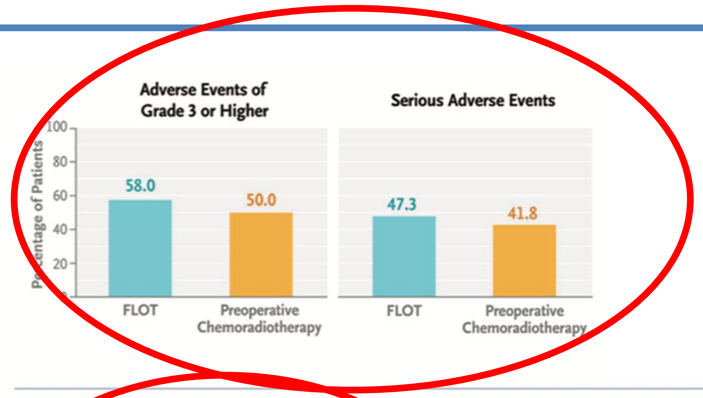
LIMITATIONS AND REMAINING QUESTIONS

- The trial was conducted entirely in Germany, which may limit the generalizability of the findings.
- Whether de-escalation to a chemotherapy doublet or a switch to preoperative chemoradiotherapy is preferable in patients with FLOT-related adverse events remains unanswered.

CONCLUSIONS

In patients with resectable esophageal adenocarcinoma, FLOT perioperative chemotherapy led to improved survival outcomes as compared with preoperative chemoradiotherapy.

REMARKS



LIMITATIONS AND REMAINING QUESTIONS

The trial was conducted entirely in Germany, which may limit the generalizability of the findings.

- Whether de-escalation to a chemotherapy doublet or a switch to preoperative chemoradiotherapy is preferable in patients with FLOT-related adverse events remains unanswered.

CONCLUSIONS

In patients with resectable esophageal adenocarcinoma, FLOT perioperative chemotherapy led to improved survival outcomes as compared with preoperative chemoradiotherapy.

- CROSS and NEOAEGIS: median OS 43 and 49 months vs. 39 months CRT in ESOPEC!!!
- Only 67.7% of pts received a full CTRT regime in ESOPEC vs. 92% and 87% of CROSS and NEOAEGIS studies: could make the difference in results!!!;
- Moreover, pts in CRT arm NOT have received adjuvant Immunotherapy although it currently represents the standard treatment !!!
- In the future, it will be necessary to take into account other elements, particularly the *Combined Positive Score (CPS):* the possibility or not of receiving complete perioperative chemotherapy to favor one or the other option. Pts selection!!!

SCIENCE PHASE III – ASCO 2025

Resectable locally advanced Esophageal Squamous Cell Carcinoma

LBA329 Oral Abstract Session

Preliminary results from the multicenter, randomized phase III trial (SCIENCE): Comparing chemotherapy plus sintilimab and chemoradiotherapy plus sintilimab versus chemoradiotherapy for neoadjuvant treatment in resectable locally advanced esophageal squamous cell carcinoma.

Xuefeng Leng, Wenwu He, Jiahua Lyu, Lei Gong, Tongchen Hu, Haining Zhou, Lin Peng, Guangyuan Liu, Kangning Wang, Qiang Fang, Yunxiang Qi, Yehan Zhou, Wencheng Zhang, Peng Tang, Tao Li, Yongtao Han; Department of Thoracic Surgery, Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, School of Medicine, University of Electronic Science and Technology of China, Chengdu, China; Sichuan Cancer Hospital, Chengdu, China; Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, School of Medicine, Chengdu, China; Tianjin Medical University Cancer Hospital & Institute, Tianjin, China; The People's Hospital of Leshan, Leshan, China; Department of Thoracic Surgery, Suining Central Hospital, Suining, China; Thocacic Surgery Department, Sichuan Cancer hospital institute/Sichuan Cancer Center/School of Medicine,University of Electronic Science and Technology of China, Chengdu, China; Radiotherapy Department, Sichuan Clinical Research Center for Cancer, Sichuan Cancer Hospital and Institute, Sichuan Cancer Center, Affiliated Cancer Hospital of University of Electronic Science and Technology of China, Chengdu, China; Tianjin Medical University Cancer Institute and Hospital/National Clinical Research Center for Cancer, Tianjin, China; Tianjin Medical University Cancer Institute & Hospital, National Clinical Research Center for Cancer, Tianjin, China; School of Medicine, University of Electronic Science and Technology of China, Chengdu, China

Background: Neoadjuvant chemotherapy (nCT) or chemoradiotherapy (CRT) followed by surgery is the standard treatment for resectable locally advanced esophageal squamous cell carcinoma (LA-ESCC). Despite significant advancements in therapeutic strategies, the rate of recurrence remains high. Therefore, this multicenter, randomized, Phase III trial (SCIENCE) aims to evaluate and compare the efficacy of nCT and nCRT plus Sintilimab, and nCRT alone in patients with resectable LA-ESCC. **Methods:** Eligible patients with thoracic ESCC and had not received any prior treatment. Patients were clinically staged as locally advanced (cT1N2-3M0 or cT2-4aN0-3M0). Participants were randomized in a 1:1:1 ratio to one of three neoadjuvant treatment groups: Group A: Sintilimab combined with nCT (nab-paclitaxel plus carboplatin) for two cycles. Group B: Sintilimab combined with concurrent nCRT (nab-paclitaxel plus carboplatin chemotherapy and radiotherapy using IMRT/IGRT totaling 41.4 Gy). Group C: Concurrent nCRT alone. Surgical resection was planned 6-8 weeks after the completion of neoadjuvant therapy. The co-primary endpoints were pathological complete response (pCR) rate, and event-free survival (EFS), evaluated by investigators according to RECIST 1.1 criteria. **Results:** Between November 2022 and June 2024, 146 patients were enrolled and randomized into three groups: Group A (n = 46), Group B (n = 45), and Group C (n = 55). The majority of patients were male (89.7%; 131/146), with most clinical stage III disease (72.6%; 106/146) and tumors located in the middle thoracic esophagus (51.4%; 75/146). All patients completed the neoadjuvant treatment and underwent surgical resection and achieving a 100% R0 resection rate. The pCR rates differed significantly among the groups, with Group A achieving a pCR rate of 13%, Group B 60%, and Group C 47.3%. Both Group B and C demonstrated significantly higher pCR rates compared to Group A, with Group B versus Group A showing a difference of 47% (95% CI, 27.8–62.2; OR = 10; 95% CI, 3.7–30.8; P < 0.0001) and Group C versus Group A showing a difference of 34.2% (95% CI, 16.4–49.1; OR = 6; 95% CI, 2.3–17.8; P = 0.0005). No perioperative deaths were reported. Treatment-emergent adverse events (TEAEs) of any grade were observed in 50% of patients in Group A, 86.7% in Group B, and 85.5% in Group C. Additionally, the incidence of Grade 3 or higher TEAEs during neoadjuvant treatment was 8.7% in Group A, 31.1% in Group B, and 36.4% in Group C. **Conclusion:** This Phase III trial demonstrates that nCRT, with or without Sintilimab, significantly enhances pCR rates compared to nCT with Sintilimab in LA-ESCC, without increasing surgical risks. Ongoing monitoring of EFS is necessary to validate these results. Clinical trial information: NCT05244798. Research Sponsor: None.

cT2-4 cN0-3 – cT1 cN2-3 ESOPH CANCER

- neo Carbo + nabPaclitaxel + Sintilimab
- nCRT 41.4/23) wCarbo-taxol + Sintilimab
- nCRT

- BETTER pCR CRT vs chemo (13% with chemo)
- Sintilimab + CRT vs CRT T pCR (60% v 47%) without added AEs

SCIENCE PHASE III – ASCO 2025

PRELIMINARY RESULTS

Results-Primary endpoints pCR

	Group A: Sint + nab-PC (n = 46)	Group C: nab-PC + RT (n = 55)	Group B: Sint + nab-PC + RT (n = 45)
pCR% (95% CI)	13 (4.9, 26.3)	47.3 (33.7, 61.2)	60 (44.3, 74.3)
Difference (95% CI), vs. Group A		34.2 (16.4, 49.1)	47 (27.8, 62.2)
OR (95% CI), vs. Group A		6 (2.3, 17.8)	10 (3.7, 30.8)
P value (vs. Group A)		0.0005	<0.0001

pCR rate: nab-PC + RT vs. Sint + nab-PC : 47.3% vs. 13%, (OR= 6, 95%CI, 2.3-17.8), *P*=0.0005

pCR rate: Sint + nab-PC + RT vs. Sint + nab-PC : 60% vs. 13%, (OR=10, 95% CI, 3.7-30.8), *P* <0.0001

ASCO Gastrointestinal Cancers Symposium #GI25 PRESENTED BY: Xuefeng Leng, Sichuan Cancer Hospital & Institute, UESTC, Chengdu, China

Results-Surgical complications

	Group A: Sint + nab-PC (n = 46)	Group C: nab-PC + RT (n = 55)	Group B: Sint + nab-PC + RT (n = 45)
Any events, n(%)			
No	13 (28.3)	28 (50.9)	24 (53.3)
Yes	33 (71.7)	27 (49.1)	21 (46.7)
Anastomotic leak, n (%)			
No	46 (100.0)	52 (94.5)	44 (97.8)
Yes	0 (0.0)	3 (5.5)	1 (2.2)
Postoperative hemorrhage, n (%)			
No	41 (89.1)	54 (98.2)	45 (100.0)
Yes	5 (10.9)	1 (1.8)	0 (0.0)
Pulmonary infection, n(%)			
No	15 (32.6%)	29 (52.7)	25 (55.6)
Yes	31 (67.4)	26 (47.3)	20 (44.4)

ASCO Gastrointestinal Cancers Symposium #GI25 PRESENTED BY: Xuefeng Leng, Sichuan Cancer Hospital & Institute, UESTC, Chengdu, China

ASCO KNOWLEDGE CONQUERS CANCER

Resectable locally advanced Esophageal Squamous Cell Carcinoma

Locally Advanced / Unresectable Esophageal & GEJ Tumors

International Journal of Radiation Oncology*Biology*Physics
Volume 111, Issue 3, Supplement, 1 November 2021, Page S5

7

Exclusive Chemoradiotherapy With or Without Radiation Dose Escalation in Esophageal Cancer: Multicenter Phase 2/3 Randomized Trial CONCORDE (PRODIGE-26)

G. Crehange [1], C. M'vondo [2], A. Bertaut [3], R. Pereira [4], E. Rio [5], D. Peiffert [6], K. Gnep [7], K. Benezery [8], P. Ronchin [9], G. Noel [10], L. Mineur [11], A. Drouillard [12], J. Blanc [3], M. Rouffiac [13], J. Boustani [14]

carcinoma, ECOG 0-2 and sufficient caloric intake. Patients were randomly assigned (1:1) to receive 50Gy in 25 fractions over 5 weeks (standard arm) or 66Gy in 33 fractions over 6.5 weeks (experimental arm). Elective nodal irradiation (40Gy) was delivered in both groups. Concomitant chemotherapy was FOLFOX-4 for 3 courses followed by 3 adjuvant courses. Random allocation to treatment groups was done by a central computerized randomization procedure by minimization, stratified by center, histology, weight loss, and technique of radiotherapy. The primary endpoint was 2-year locoregional progression-free survival (LRPFS).

Conclusion

Dose escalated chemoradiotherapy delivering 66Gy is not more toxic than 50Gy but did not improve locoregional progression-free survival. Chemoradiotherapy delivering 50Gy should be definitely admitted as a standard dose.

PARTIAL ACCESS | ORIGINAL REPORTS | June 08, 2021

Randomized Study on Dose Escalation in Definitive Chemoradiation for Patients With Locally Advanced Esophageal Cancer (ARTDECO Study)

Authors: Maarten C. C. M. Hulshof, MD, PhD, Elisabeth D. Geijsen, MD, Tom Rozema, MD, Vera Oppedijk, MD, Jeroen Buijsen, MD, PhD, J. Neelis, MD, PhD, Joost J. M. E. Nuyttens, MD, PhD, ... SHOW ALL ..., and Ate van der Gaast, MD, PhD | AUTHORS INFO & AFFILIATIONS

Publication: Journal of Clinical Oncology • Volume 39, Number 25 • https://doi.org/10.1200/JCO.20.03697

Patients and Methods

Patients with medically inoperable and/or irresectable esophageal carcinoma, referred for dCRT, were randomly assigned between a standard dose (SD) of 50.4 Gy/1.8 Gy for 5.5 weeks to the tumor and regional lymph nodes and a high dose (HD) up to a total dose of 61.6 Gy to the primary tumor. Chemotherapy consisted of courses of concurrent carboplatin (area under the curve 2) and paclitaxel (50 mg/m^2) in both arms once a week for 6 weeks. The primary end point was local progression-free survival.

Conclusion

In dCRT for esophageal cancer, radiation dose escalation up to 61.6 Gy to the primary tumor did not result in a significant increase in local control over 50.4 Gy. The absence of a dose effect was observed in both AC and SCC.

ESMO 2024

Early Stage Resectable Gastric & GEJ Adenocarcinoma Tumors

ESMO Congress 2024 - Conference Calendar

Everything | Search For | Advanced Search

Calendar view | All Sessions | All Presentations | Final Programme (PDF) | All Posters | Industry Satellite Symposia

Proffered Paper session

LBA58 - A randomized phase III trial of perioperative chemotherapy (periop CT) with or without preoperative chemoradiotherapy (preop CRT) for resectable gastric cancer (AGITG TOPGEAR): Final results from an intergroup trial of AGITG, TROG, EORTC and CCTG

Presentation Number LBA58

Speakers Trevor Leong (Melbourne, Australia)

Authors Trevor Leong (Melbourne, Australia), Bernard M. Smithers (St Lucia, Australia), Michael Michael (Melbourne, Australia), Karin M. Haustermans (Leuven, Belgium), Rebecca Wong (Toronto, Canada), Val Gebski (Sydney, Australia), Rachel OConnell (Camperdown, Australia), John R. Zalcberg (Melbourne, Australia, VIC), Alex Boussioutas (Clayton, Australia), Michael Findlay (Auckland, New Zealand), David Willis (Birtinya, Australia), Alisha Moore (Waratah, Australia), Florian Lordick (Leipzig, Germany), Christopher O'Callaghan (Kingston, Canada), Carol Swallow (Toronto, Canada), Gail E. Darling (Halifax, Canada), Andrew Strickland (Clayton, Australia), Moishe Liberman (Montreal, Canada), Laurent Mineur (Avignon, France, CEDEX 2), John Simes (Sydney, Australia)

Lecture Time 08:30 - 08:40

Abstract

Background

In Western countries, the current standard of care for resectable gastric cancer is periop CT. There is much interest in preop CRT, but comparison to periop CT alone is lacking. In TOPGEAR we hypothesized that adding preop CRT to periop CT would improve pathological complete response (pCR) rates and ultimately overall survival (OS) compared to periop CT alone.

Methods

This international phase 3 trial randomized patients with resectable adenocarcinoma of the stomach and gastro-esophageal junction to periop CT alone, or with preop CRT. The periop CT alone group received 3 cycles of epirubicin/cisplatin/5-fluorouracil (ECF) or 4 cycles of fluorouracil/leucovorin/oxaliplatin/docetaxel (FLOT) both pre- and post-operatively. The preop CRT group received one less cycle of preop chemotherapy followed by chemoradiotherapy (45 Gy in 25 fractions radiation plus infusional 5-FU), and then the same postop chemotherapy. The primary endpoint was overall survival, and secondary endpoints included progression free survival (PFS), pCR rates, toxicity and quality of life.

Results

Between September 2009 and May 2021, 574 patients were enrolled from 70 sites across 15 countries in Australasia, Europe, and Canada; 288 to periop CT group and 286 to preop CRT group. Compared to periop CT alone, patients receiving preop CRT achieved a higher pCR rate (16.7% vs 8.0%), a higher rate of major pathological response (0 - <10% residual tumor: 49.5% vs 29.3%), and greater tumor downstaging following resection. After a median follow-up of 66.7 months, there was no significant difference in OS or PFS: median OS periop CT 49.4 months vs preop CRT 46.4 months; median PFS periop CT 31.8 months vs preop CRT 31.4 months. Preop CRT was not associated with increased perioperative treatment toxicity or a higher rate of surgical complications.

Conclusions

Despite improving pathological outcomes, the addition of preop CRT to periop CT does not improve overall survival compared to periop CT alone in patients with resectable gastric and gastro-esophageal junction adenocarcinoma.

Locally Advanced Resectable Gastric & GEJ Tumors

Delegates attending the ESMO Gastrointestinal Cancers Congress 2024 (26-29 June, Munich)

Final results of the KEYNOTE-585 study indicate that the current treatment standard for resectable G/GEJ should remain unchanged

As presented at the ESMO Gastrointestinal Cancers Congress 2024 (Munich, 26–29 June), final analysis of the KEYNOTE-585 study showed that event-free survival was not significantly improved with pembrolizumab plus CT compared with placebo plus CT or placebo plus FLOT in patients with untreated, locally advanced, **resectable gastric/gastro-oesophageal junction (G/GEJ) cancers** (LBA3). At a median follow-up of 59.9 months, neoadjuvant plus adjuvant treatment was associated with a median event-free survival (EFS) of 44.4 months with pembrolizumab plus cisplatin/fluorouracil-based chemotherapy (CT) versus 25.5 months with placebo plus CT (hazard ratio [HR] 0.81; 95% confidence interval [CI] 0.67–0.98) among the 804 patients involved in the study. Median overall survival (OS) was 71.8 months with pembrolizumab versus 55.7 months with placebo (HR 0.86; 95% CI 0.71–1.06). The pathological complete response (pCR) rates were 13.4% with pembrolizumab and 2.0% with placebo.

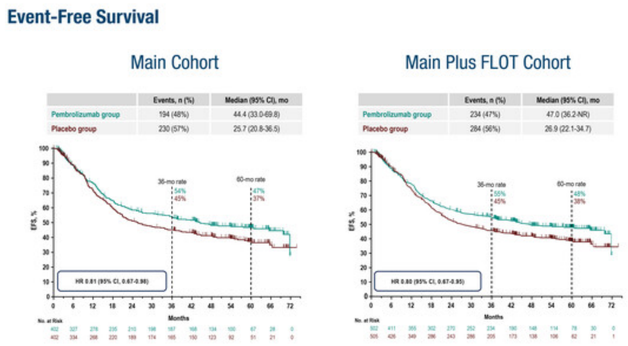
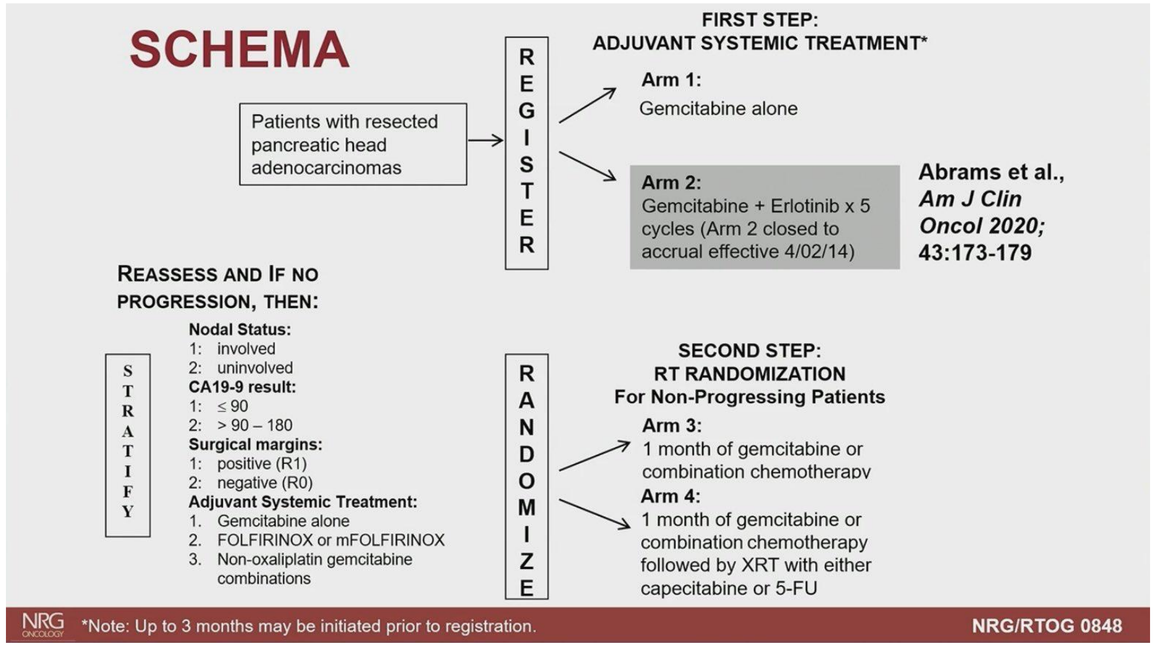
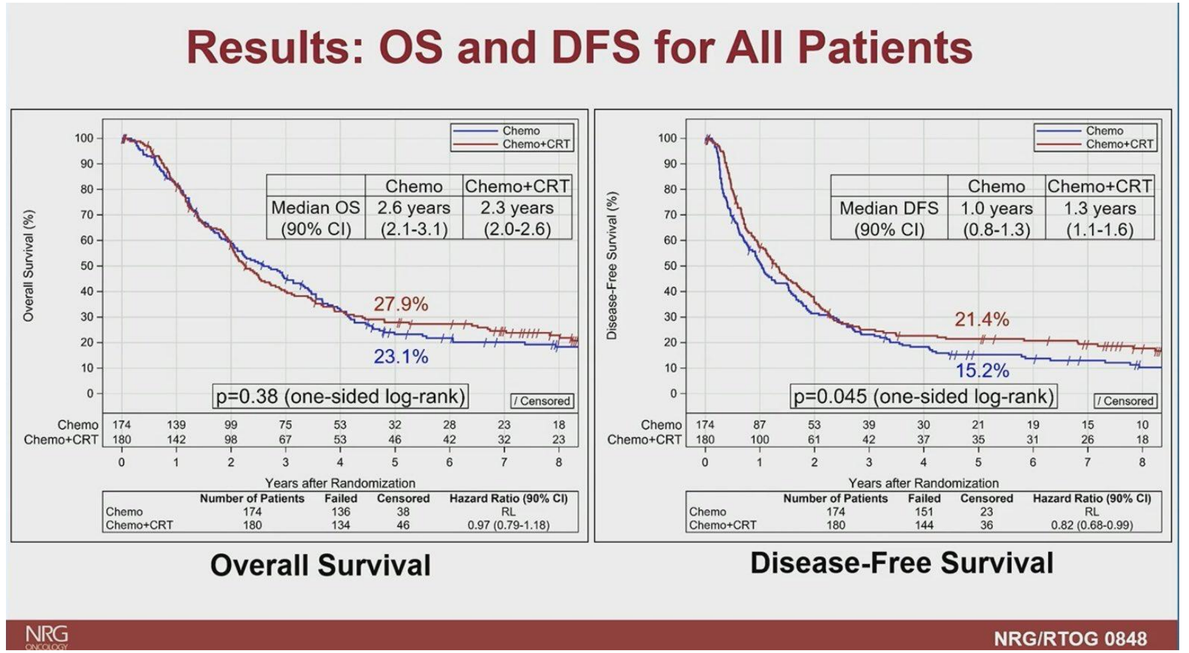


Figure. Final analysis of the KEYNOTE-585 study showed that event-free survival was not significantly improved with pembrolizumab plus CT compared with placebo plus CT or placebo plus FLOT (ESMO Gastrointestinal Cancers Congress 2024, LBA3)

and/or PD-L1 expression." Smyth continues: "Next steps will be, to some extent, informed by the results of the ongoing MATTERHORN trial – **investigating the addition of durvalumab to perioperative FLOT** in resectable G/GEJ cancers – which is due to report in 2025."

Resected Pancreatic Head Adenocarcinoma





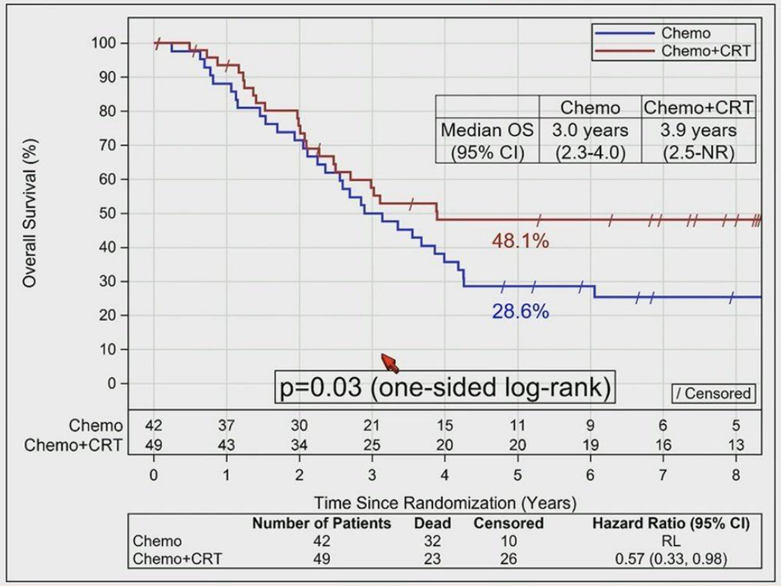
RTOG 0848 – ASCO 2024

- **DFS increase with RT**

- **DFS and OS increase in N0**

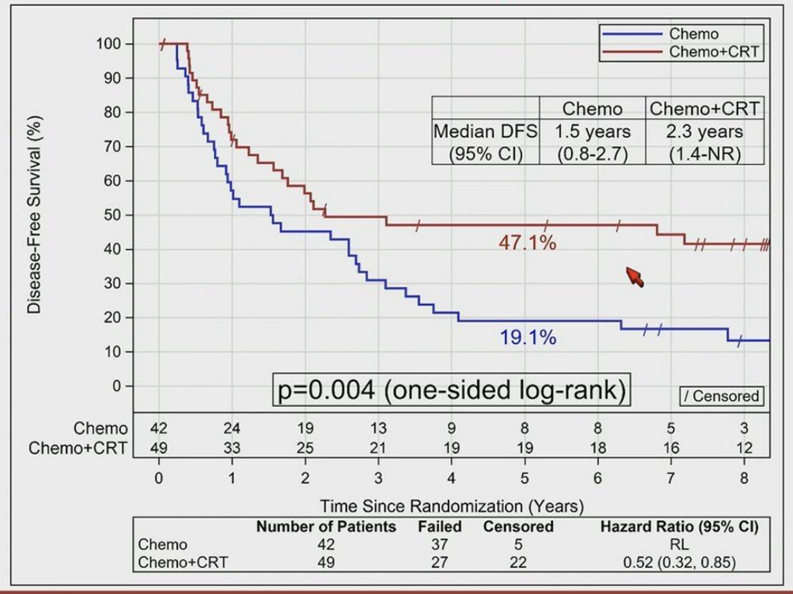
Resected Pancreatic Head Adenocarcinoma

Results: OS for Node Negative Patients



NRG ONCOLOGY NRG/RTOG 0848

Results: DFS for Node Negative Patients



NRG ONCOLOGY NRG/RTOG 0848

RTOG 0848 – ASCO 2024

- DFS increase with RT

- DFS and OS increase in N0

PRODIGE 44 – ESMO 2024

- mFOLFIRINOX +/- chemoRT (50.4 Gy) in **Borderline resectable pancreas cancer**;

- No dif in R0 resection (1^ endpt) or OS for all comers...

- pCR for chemoRT group was 29% (vs. 8%) & OS improved w chemoRT for pts undergoing resection (48 vs. 36 months)

POTENTIAL ROLE OF RT IN OS PROLONGATION

LBA62 - Preoperative modified FOLFIRINOX (mFOLFIRINOX) with or without chemoradiation (CRT) in borderline resectable pancreatic cancer (BRPC): Results from the randomized phase II trial PANDAS/PRODIGE 44

Presentation Number LBA62
Speakers Aurélien Lambert (Vandoeuvre-lès-Nancy, France)
Lecture Time 16:45 - 16:55

Abstract

Background

The role and the safety of CRT following mFOLFIRINOX administration in BRPC is unknown.

Methods

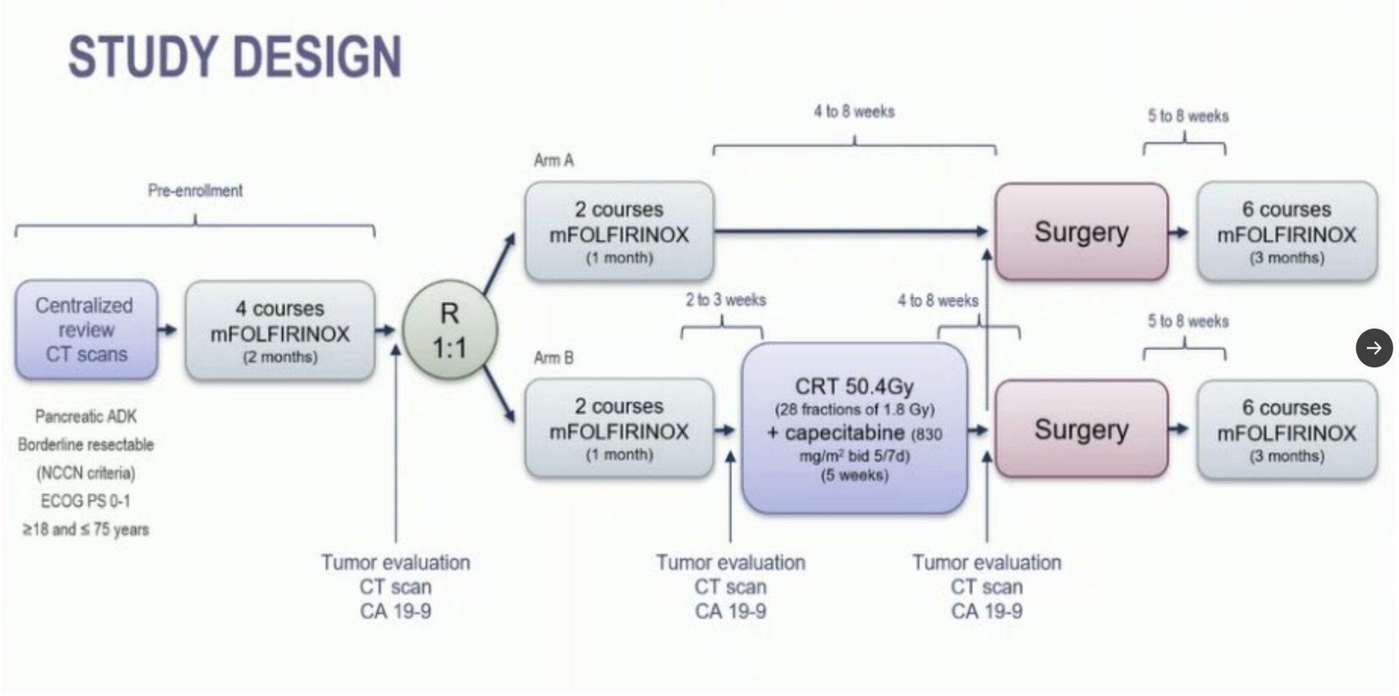
Patients (pts) with ECOG PS 0/1 and BRPC defined according to centrally-reviewed radiographic NCCN criteria received neoadjuvant mFOLFIRINOX for 4 cycles. Those who had tumour controlled at restaging were randomized between two additional cycles of mFOLFIRINOX (arm A) alone or followed by a CRT (50.4 Gy in 28 fractions with capecitabine 825mg/m2 BID 5 days a week) prior to surgery. Patients without disease progression then underwent a pancreatectomy and adjuvant chemotherapy for 3 months (gemcitabine or 5-FU/folinic acid before 6/2008, mFOLFIRINOX thereafter). The primary endpoint was R0 resection (ITT analysis). Main secondary endpoints were overall survival (OS), locoregional relapse-free survival, metastasis-free survival and toxicity.

Results

Among the 248 patients who were assessed for eligibility, 139 patients had a BRPC according to external radiographic review. Hundred and thirty patients were enrolled and 110 patients were finally randomized (54 pts arm A; 56 pts arm B). Median age (A: 66y, B: 61y), median CA 19-9 level (A: 65 U/ml, B: 169 U/ml) and ECOG PS (A: 62% PS 0, B: 52% PS 0) of registered pts were similar between arms. Thirty pts did not have a pancreatic resection due to tumor progression (7 pts arm A; 13 pts arm B), unresectable disease (1 pt arm A), physician or pt decision (4 pts arm A, 1 pt arm B), adverse event (1 in each arm), COVID-19 infection (1 pt arm A), or death (1 pt arm B). Thirty-seven pts (69%) in arm A and 31 pts (55%) in arm B had tumor resection. R0 resection was achieved in 20/37 pts (54.1%) in arm A and 18/31 pts (58.1%) in arm B. ypCR was observed in 3 pts (8.1%) in arm A and 9 (29%) in arm B. The median OS was 32.8 months (95%CI: 22.7 – 55.4) in arm A and 30 months (95%CI: 16.5 – nr) in arm B. Among pts who underwent pancreatectomy, the median OS was 35.7 months (95%CI: 22.2 – 55.4) and 47.9 months (95%CI: 23.3 – nr) in arm A and B, respectively.

Conclusions

Neoadjuvant mFOLFIRINOX was associated with favorable OS but mFOLFIRINOX with conventional CRT did not improve R0 nor OS compared to mFOLFIRINOX without preoperative CRT in patients with BRPC.



Palliative Pancreatic Cancer

The impact of celiac plexus radiosurgery on overall survival,

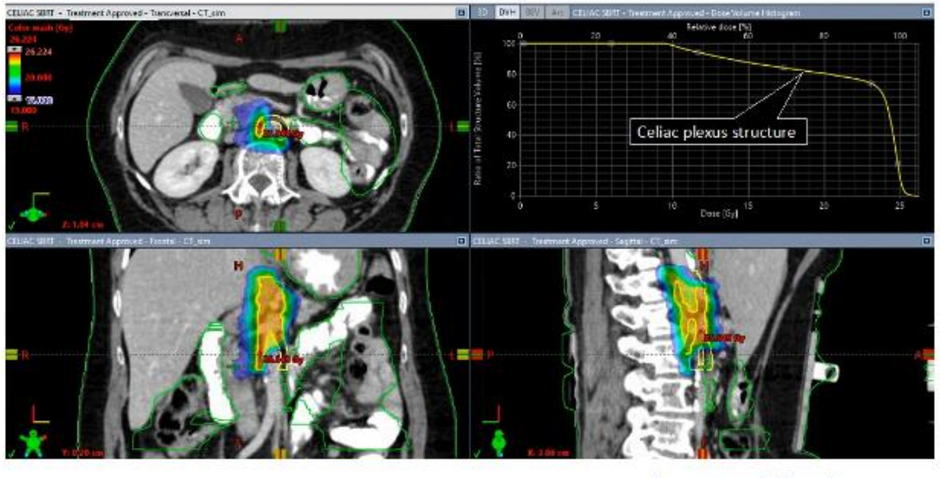
post-hoc analysis of a clinical trial

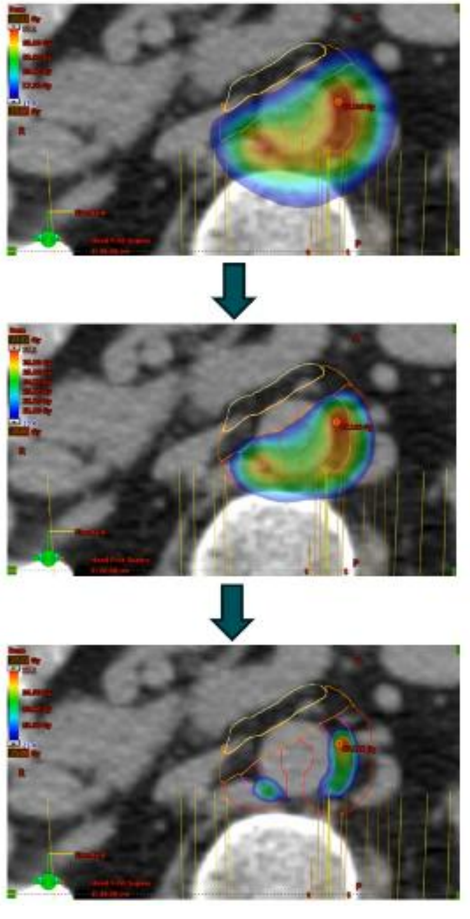
Yaacov R Lawrence, Marcin Miszczyk, Raphael Pfeffer, Laura A Dawson, Symon Zvi, Camilla Zimmermann, David Hausner, Michael Buckstein, Dayssy Diaz Pardo, Artur M Aguiar, Dror Limon, Sergey Dubinski, Aisling Barry, Ophir Morag, Gali Jacobson, Idan BarOrion, Tikva Meron, Adam P Dicker, Talia Golan, Maoz Ben-ayun

Primary purpose of palliative care is to improve quality of life.

Celiac plexus radiosurgery trial:

- patients with retroperitoneal pain at ≥5/10 despite analgesia
- single fraction 25 Gy
- 125 patients treated across eight hospitals in five countries.





Lawrence and Miszczyk

Results

Palliative Pancreatic Cancer

Primary endpoint:

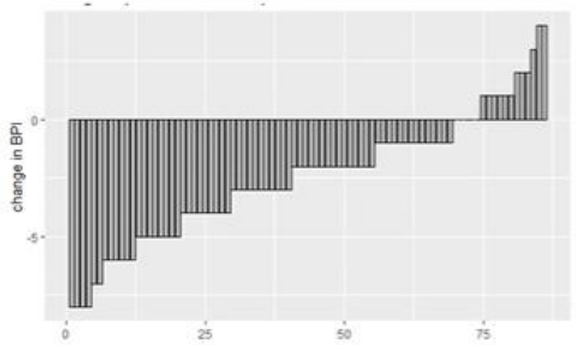
Palliative response rate* of 53.3% (95% CI: 42.5-63.9)

*Defined as 'complete or partial pain response' based upon a reduction of the BPI-SF average pain score of ≥2 points from baseline to 3-weeks post-treatment.

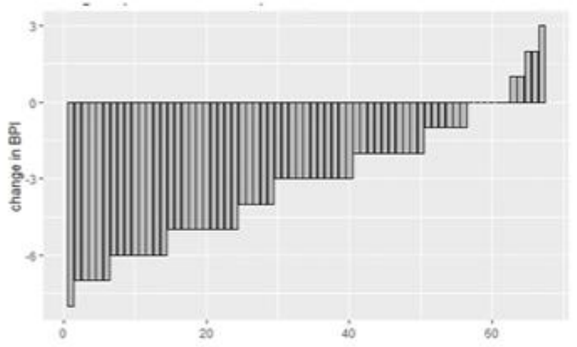
Secondary endpoints:

Treatment was well tolerated.

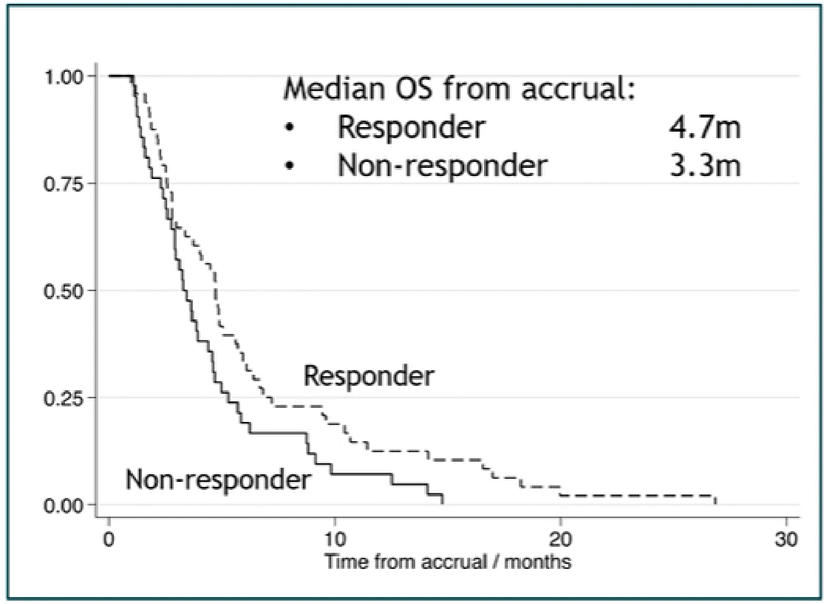
Mean 'average pain' decreased by 2.5 at three, and 3.2 points at six weeks.



Change in pain, 3 weeks vs baseline
(negative is better)



Change in pain, 6 weeks vs baseline
(negative is better)



- Better QoL with 1 single SABR fraction
- Better OS in responding patients

«The impact on overall survival of celiac plexus radiosurgery, post-hoc analysis of a clinical trial», Miszczyk

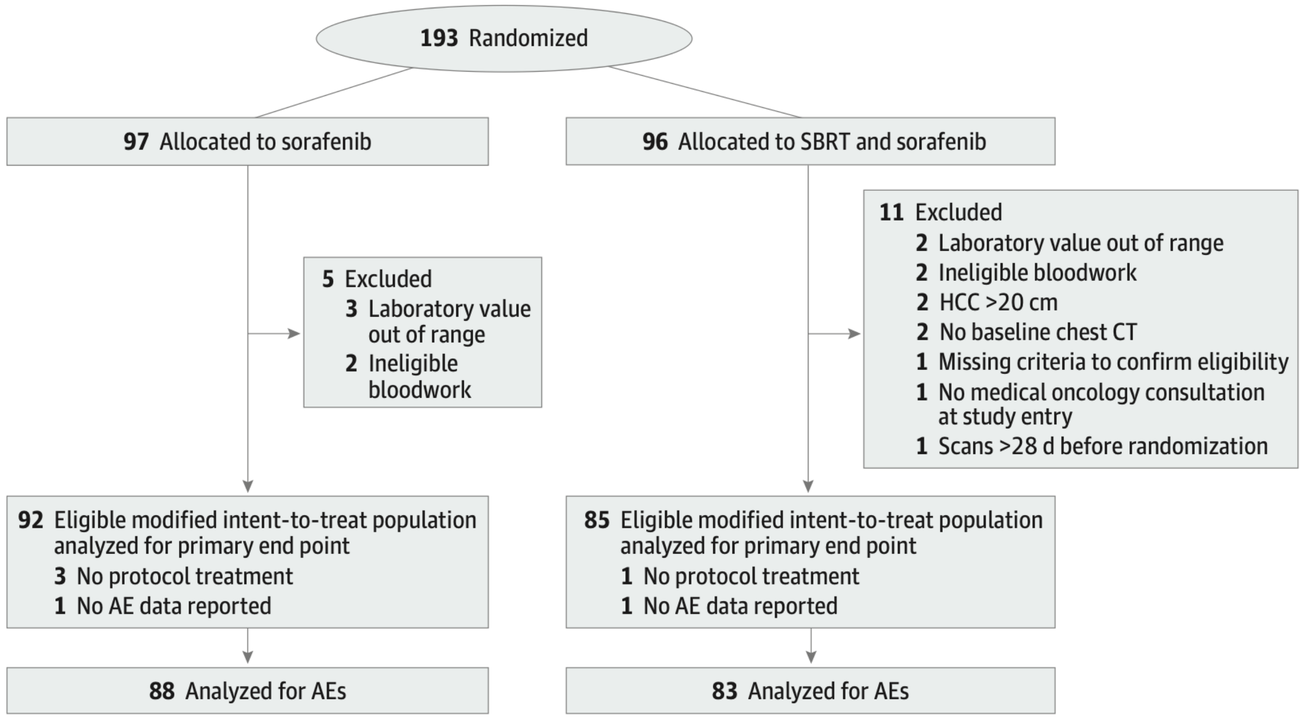
JAMA Oncology | Original Investigation

Stereotactic Body Radiotherapy vs Sorafenib Alone in Hepatocellular Carcinoma

The NRG Oncology/RTOG 1112 Phase 3 Randomized Clinical Trial

Laura A. Dawson, MD; Kathryn A. Winter, MS; Jennifer J. Knox, MD; Andrew X. Zhu, MD, PhD; Sunil Krishnan, MD; Chandan Guha, MD; Lisa A. Kachnic, MD; Michael T. Gillin, PhD; Theodore S. Hong, MD; Timothy D. Craig, PhD; Terence M. Williams, MD, PhD; Ali Hosni, MBBCh; Eric Chen, MD; Anne M. Noonan, MBBCh; Eugene J. Koay, MD; Rishi Sinha, MD; Michael I. Lock, MD; Nitin Ohri, MD; Jennifer A. Dorth, MD; Guila Delouya, MD; Anand Swaminath, MD; Jennifer Moughan, MS; Christopher H. Crane, MD

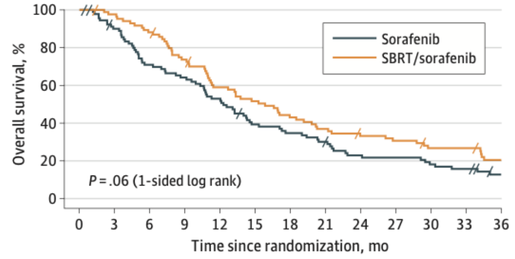
Figure 1. CONSORT Diagram



Hepatocellular Carcinoma

A Overall survival

Source	No. Total patients	Failed	Censored	Median OS (90% CI)	HR (90% CI)
Sorafenib	92	80	12	12.3 (10.6-14.3)	1 [Reference]
SBRT/sorafenib	85	73	12	15.8 (11.4-19.2)	0.77 (0.59-1.01)

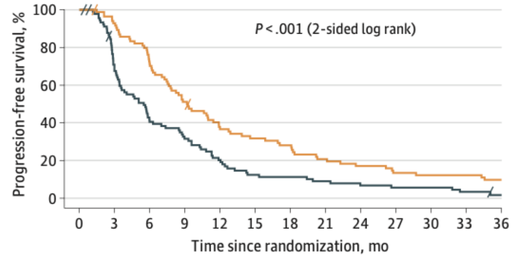


No. at risk

Sorafenib	92	80	63	57	47	34	30	25	19	18	15	13	8
SBRT/sorafenib	85	82	74	61	48	42	35	30	26	24	20	20	13

B Progression-free survival

Source	No. Total patients	Failed	Censored	Median PFS (95% CI)	HR (95% CI)
Sorafenib	92	88	4	5.5 (3.4-6.3)	1 [Reference]
SBRT/sorafenib	85	80	5	9.2 (7.5-11.9)	0.55 (0.40-0.75)

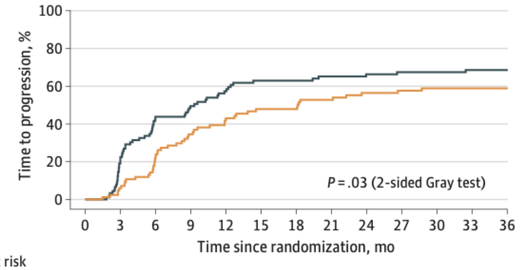


No. at risk

Sorafenib	92	60	36	28	18	11	10	8	6	5	5	3	1
SBRT/sorafenib	85	78	60	43	30	26	23	17	14	11	10	10	8

C Time to progression

Source	No. Total patients	Failed	Censored	Competing risk	HR (95% CI)
Sorafenib	92	62	4	26	1 [Reference]
SBRT/sorafenib	85	51	5	29	0.69 (0.48-0.99)



No. at risk

Sorafenib	92	60	36	28	18	11	10	8	6	5	5	3	1
SBRT/sorafenib	85	78	60	43	30	26	23	17	14	11	10	10	8

The median OS was 12.3 months (90% CI, 10.6-14.3) with sorafenib vs 15.8 months (90% CI, 11.4-19.2) following SBRT and sorafenib (hazard ratio [HR], 0.77; 90% CI, 0.59-1.01; 1-sided *P* = .06);

Adjusting for stratification factors, OS was improved with SBRT (HR, 0.72; 95% CI, 0.52-0.99; 2-sided *P* = .04);

Median PFS was improved from 5.5 months (95% CI, 3.4-6.3) with sorafenib to 9.2 months (95% CI, 7.5-11.9) with SBRT and sorafenib (HR, 0.55; 95% CI, 0.40-0.75; 2-sided *P* < .001)

– ASCO 2024

Hepatocellular Carcinoma

- *TACE + TKI + SBRT*
  Vs.
- *TACE + TKI*

- Better OS with SBRT (17.9 vs 9.6 m)

- 6months PFS SBRT (78% vs 36%)

Stereotactic body radiotherapy (SBRT) combined with transcatheter arterial chemoembolization (TACE) and tyrosine kinase inhibitors (TKIs) versus TACE and TKIs alone for unresectable hepatocellular carcinoma (uHCC) with portal vein tumor thrombus (PVTT): A randomized controlled trial.

Jiayu Duan, Jitao Zhou, Chang Liu, Hanyu Jiang, Jin Zhou, Kunlin Xie, Hong Wu, Yong Zeng, Xin Wang; Division of Abdominal Tumor Multimodality Treatment, Department of Radiation Oncology, State Key Laboratory of Biotherapy and Cancer Center, West China Hospital, Sichuan University, Chengdu, China; Department of Liver Transplantation Center, Chengdu, China; Department of Radiology, West China Hospital, Sichuan University, Chengdu, China; Division of Liver Surgery, Department of General Surgery and Laboratory of Liver Surgery, and State Key Laboratory of Biotherapy and Collaborative Innovation Center of Biotherapy, Chengdu, China; Department of Liver Transplantation Center, State Key Laboratory of Biotherapy and Cancer Center, West China Hospital, Sichuan University, and Collaborative Innovation Center of Biotherapy, Chengdu, China

Background: TKIs-based systemic therapy is a primary treatment option for uHCC. Clinical studies have established the effectiveness and safety of radiotherapy (RT) in patients with PVTT, who typically have a poor prognosis. Previous research has shown that combining TACE and RT can extend survival in HCC patients with PVTT compared to sorafenib treatment. This study aimed to explore the efficacy and safety of combined local therapy (TACE plus SBRT) and TKIs in HCC patients with PVTT. **Methods:** This single-center, randomized controlled study enrolled patients aged ≥18 years with HCC and PVTT. Additional eligible criteria included ECOG PS 0-1, Child-Pugh score ≤B7, no extrahepatic metastasis on CT scan, and normal liver volume ≥700cc. Patients were randomly assigned to either the SBRT+TACE+TKIs group (Group A) or the TACE+TKIs group (Group B). SBRT was administered at 35-45 Gy in 5 fractions, 3 fractions per week. TKIs (sorafenib 0.4g bid; donafenib 0.2g bid; or lenvatinib 8mg/12mg qd, depending on body weight) were paused during the perioperative period of TACE (up to 4 times). The primary endpoint was the 6-month progression-free survival (PFS) rate, with secondary endpoints including objective response rate (ORR), overall survival (OS), disease control rate (DCR) and treatment-related adverse events (TRAEs). Treatment response was evaluated using mRECIST. **Results:** A total of 90 patients with uHCC were enrolled from June 2019 to October 2023 in this trial, with baseline characteristics presented in the Table. As of January 5th 2024, the median follow-up time was 14.5 months [IQR, 2.43-55]. The 6-month PFS rate was significantly higher in Group A (78%) compared to Group B (36%, *P*=0.0245). Group A also showed prolonged median PFS (9.75 vs. 4.89 months, HR=1.703 [95%CI, 1.045-2.777], *P*=0.0245) and OS (17.93 vs. 9.61 months, HR=1.869 [95%CI, 1.059-3.266], *P*=0.017). Improved ORR was observed in the SBRT group (74.4% vs. 40.5%, *P*=0.0015). DCR was 81.4% in Group A and 66.7% in Group B (*P*=0.1211). The most common grade 3/4 TRAEs were hypertension (Group A: 17.8%, Group B: 13.3%, *P*=0.5608), ALT elevation (Group A: 26.7%, Group B: 22.2%, *P*=0.6237), and AST elevation (Group A: 22.2%, Group B: 15.6%, *P*=0.4191). There was one treatment-related death in Group B due to liver failure. **Conclusions:** In uHCC patients with PVTT, the combination of SBRT and TACE-TKIs showed significant survival benefit without the identification of any severe safety concerns. Clinical trial information: ChiCTR1900025300. Research Sponsor: None.

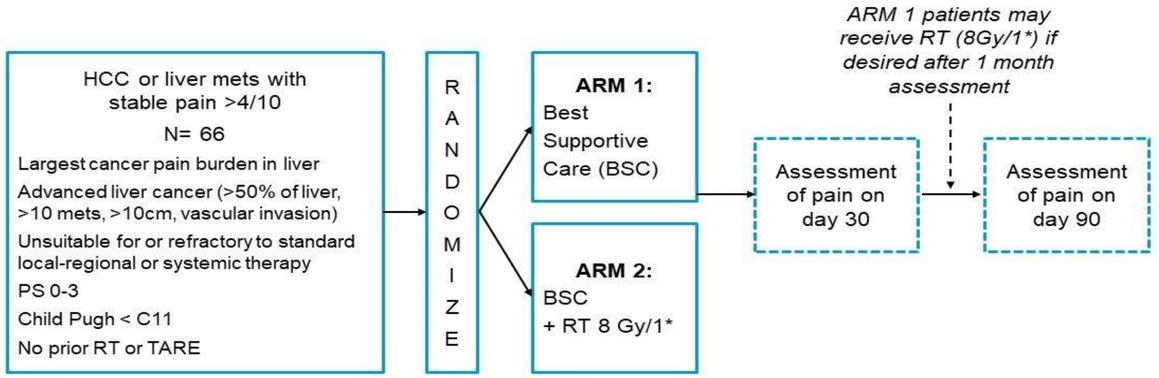
	Group A (n=45)	Group B (n=45)	*P* value
Age (years), median (range)	55(21-54)	54(31-67)	0.838
Hepatitis B Virus Infection, n (%)	40(88.9)	38(84.4)	0.821
Child-Pugh A, n (%)	43(95.6)	32(88.9)	0.452
PVTT I/II/III/IV, n	2/12/26/5	1/20/24/0	0.06

CCTG HE1

Palliative radiotherapy versus best supportive care in patients with painful hepatic cancer (CCTG HE1): a multicentre, open-label, randomised, controlled, phase 3 study

Laura A Dawson, Jolie Ringash, Alysa Fairchild, Paul Stos, Kristopher Dennis, Aamer Mahmud, Teri Lynn Stuckless, Francois Vincent, David Roberge, Matthew Follwell, Raimond K W Wong, Derek J Jonker, Jennifer J Knox, Camilla Zimmermann, Philip Wong, Aisling S Barry, Marc Gaudet, Rebecca K S Wong, Thomas G Purdie, Dongsheng Tu, Christopher J O'Callaghan

CCTG HE.1: WHOLE LIVER RT VS BSC



*Patients also receive anti-emetic pre-RT (dexamethasone 4 mg, granisetron 1 mg or equivalent)

Planned sample size: 45 evaluable patients (≈ 60 accrued), 2 sided alpha <0.05, power 80% to show improvement in 5% (BSC arm) to 40% (RT arm)

@KrishanJethwa

Dawson ASCO GI 2023

CCTG HE.1: WHOLE LIVER RT VS BSC

Endpoint	% pts with improvement		
	RT	BSC	P Value
BPI "worst" pain (primary endpoint)	67%	22%	P=0.004
BPI "pain at its least"	63%	28%	P=0.03
BPI "percentage relief in pain by treatment"	59%	25%	P=0.04
Sensitivity analysis all pts, BPI "worst" pain	48%	12%	P=0.002*

*Sensitivity analysis – treating with no 1-month assessment as having "no improvement"

@KrishanJethwa

Dawson Lancet Oncol 2024

CCTG HE1

Phase 3 RCT refractory HCC or liver metastasis with associated pain > 4/10
Randomized:
Best Supportive care (BSC)
VS.
Single fraction palliative liver RT + BSC
RT associated with:
- ⇧Pain response
-⇧QoL
- Trend to ⇧OS