HIGHLIGHTS IN RADIOTERAPIA
I lavori del 2019 che modificano la pratica clinica in radioterapia esclusiva ed associazione farmacologica

Roma, Centro Studi dell'Area Radiologica "Il Cardello"
23 gennaio 2020

I Sessione: Tumori del torace

Corrado Spatola
Università degli Studi di Catania
USD Radioterapia Oncologica

UNIVERSITÀ degli STUDI di CATANIA

Azienda Ospedaliero - Universitaria "Policlinico - Vittorio Emanuele"
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Tumori del torace

DICHIARAZIONE CONFLITTO DI INTERESSI

Relatore: CORRADO SPATOLA

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Consulenza ad aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Partecipazione ad Advisory Board (NIENTE DA DICHIARARE)
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)

Key points

- NSCLC - Early Stages
- NSCLC – Locally advanced
- NSCLC - Advanced disease
- Tecnica radioterapica – Tossicità
- SCLC
- Mesotelioma pleurico

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Tumori del torace

NSCLC – SBRT in Early Stage

Lancet Oncol. 2019 Apr;20(4):494-503. doi: 10.1016/S1470-2045(18)30896-9. Epub 2019 Feb 12.

Stereotactic ablative radiotherapy versus standard radiotherapy in stage 1 non-small-cell lung cancer (TROG 09.02 CHISEL): a phase 3, open-label, randomised controlled trial.

Ball D[1], Mai GT[2], Vinod S[3], Babington S[4], Ruben J[5], Kron T[6], Chesson B[7], Herschtal A[8], Vanevski M[8], Rezo A[9], Elder C[10], Skala M[11], Wirth A[7], Wheeler G[7], Lim A[12], Shaw M[7], Schofield P[13], Irving L[14], Solomon B[6]; TROG 09.02 CHISEL investigators.

BACKGROUND: Stereotactic ablative body radiotherapy (SABR) is widely used to treat inoperable stage 1 non-small-cell lung cancer (NSCLC), despite the absence of prospective evidence that this type of treatment improves local control or prolongs overall survival compared with standard radiotherapy. We aimed to compare the two treatment techniques.

METHODS: We did this multicentre, phase 3, randomised, controlled trial in 11 hospitals in Australia and three hospitals in New Zealand. Patients were eligible if they were aged 18 years or older, had biopsy-confirmed stage 1 (T1-T2aN0M0) NSCLC diagnosed on the basis of ^{18}F-fluorodeoxyglucose PET, and were medically inoperable or had refused surgery. Patients had to have an Eastern Cooperative Oncology Group performance status of 0 or 1, and the tumour had to be peripherally located. Patients were randomly assigned after stratification for T stage and operability in a 2:1 ratio to SABR (54 Gy in three 18 Gy fractions, or 48 Gy in four 12 Gy fractions if the tumour was <2 cm from the chest wall) or standard radiotherapy (66 Gy in 33 daily 2 Gy fractions or 50 Gy in 20 daily 2·5 Gy fractions, depending on institutional preference) using minimisation, so no sequence was pre-generated. Clinicians, patients, and data managers had no previous knowledge of

101 pts enrolled

SABR: 66 → Local Progression: 14%

Standard RT: 35 → Local Progression: 31%

No increased toxicity

(hazard ratio 0·32, 95% CI 0·13-0·77, p=0·0077)

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Tumori del torace

NSCLC – SBRT in Early Stage

ELSEVIER

Lung Cancer
Volume 138, December 2019, Pages 6-12

Stereotactic body radiotherapy versus percutaneous local tumor ablation for early-stage non-small cell lung cancer

Bryan J. Ager [a], Stacey M. Wells [a], Joshua D. Gruhl [a], Gregory J. Stoddard [b], Randa Tao [a], Kristine E. Kokeny [a], Ying J. Hitchcock [a]

National Cancer Database (NCDB) 2004-2014
15,792 patients
non-metastatic, node-negative invasive NSCLC with primary tumor size ≤5.0 cm who did not undergo surgery or chemotherapy

Highlights
- SBRT was much more common (93%) than percutaneous local tumor ablation (LTA)(7%).
- Higher OS was associated with SBRT versus percutaneous LTA in early-stage NSCLC.
- Improved OS was observed with SBRT for tumor sizes >2.0 cm (HR 0.72, p < .001)
- Patients with tumor sizes ≤2.0 cm had similar OS between treatments.

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Tumori del torace

NSCLC – SBRT in Early Stage

Dong et al. Radiation Oncology (2019) 14:195
https://doi.org/10.1186/s13014-019-1399-5

Radiation Oncology

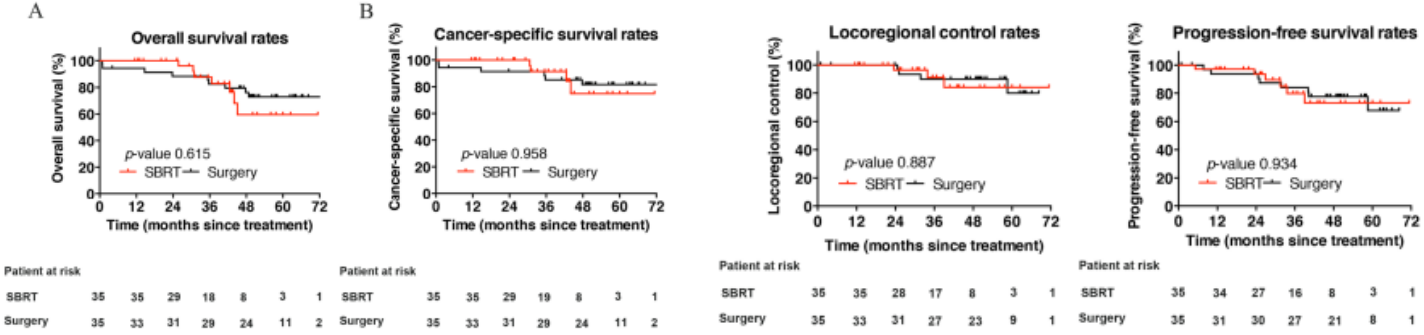
RESEARCH Open Access

Comparison of the outcomes of stereotactic body radiotherapy versus surgical treatment for elderly (≥70) patients with early-stage non-small cell lung cancer after propensity score matching

Baiqiang Dong[1,2†], Jin Wang[2†], Xuan Zhu[3], Yuanyuan Chen[2], Yujin Xu[2], Kainan Shao[2], Lei Zheng[4], Hangjie Ying[2], Ming Chen[1,2*] and Jianping Cao[1*]

Retrospective, single-center analysis
205 patients aged ≥70 years with stage I NSCLC
SBRT (BED>100 Gy) or surgery (Hangzhou, China)
January 2012 to December 2017
Propensity score matching analysis (35 pts each group)

Zhejiang Cancer Hospital (Hangzhou, China)



Surgery vs SBRT

3y-OS: 82,5% vs. 87,8%
5y-OS: 72,9% vs. 59,5%
(P=0,615)
3y-LRF: 90,0% vs. 91,1%
5y-LRF: 80,0% vs. 84,1%
(P=0,887)
Similar outcomes

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Tumori del torace

NSCLC – SBRT in Early Stage

JAMA Network | Open

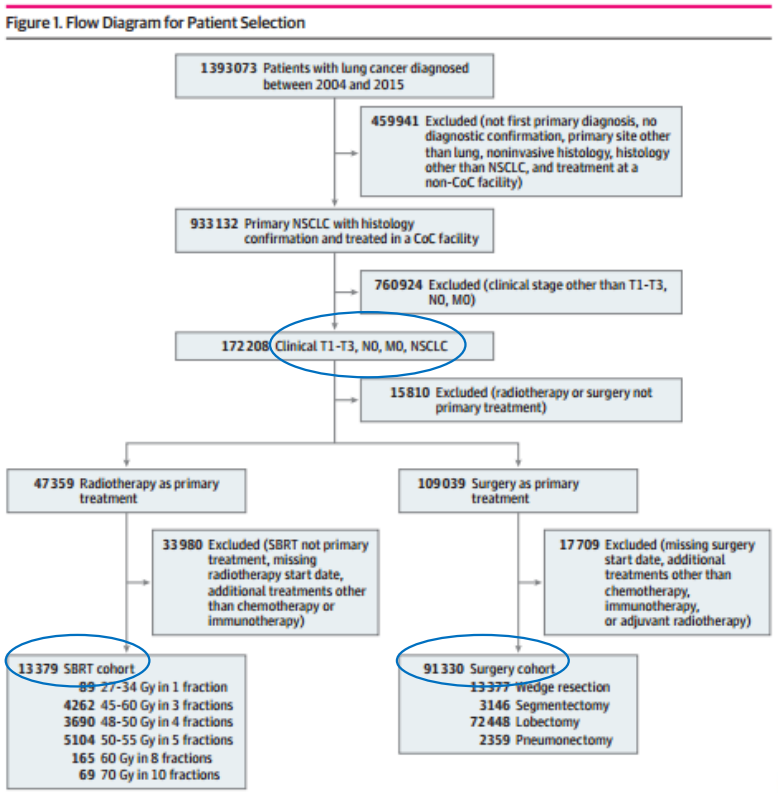
Original Investigation | Oncology

Comparison of Long-term Survival of Patients With Early-Stage Non–Small Cell Lung Cancer After Surgery vs Stereotactic Body Radiotherapy

Alexander Chi, MD; Wei Fang, PhD; Yeping Sun, MD; Sijin Wen, PhD

OBJECTIVE - DESIGN

- To compare long-term overall survival (OS) of patients with ES NSCLC after surgery vs SBRT when the extent of regional LNE in patients undergoing surgery is thoroughly considered
- Data from the US National Cancer Database
- ES NSCLC diagnosed between January 2004 and December 2015
- Analize after propensity score matching.



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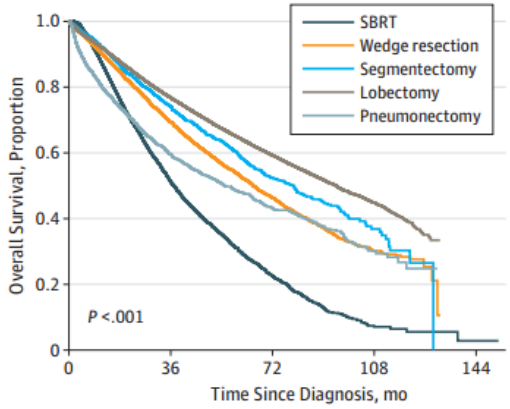
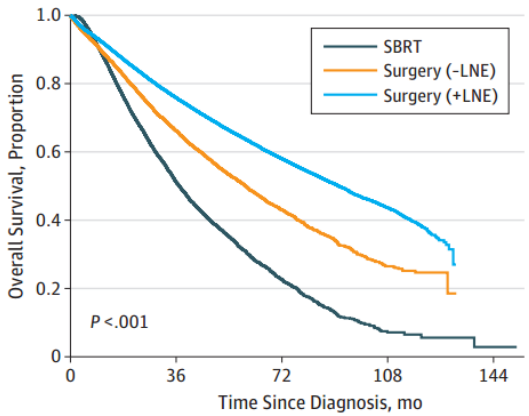
Tumori del torace

NSCLC – SBRT in Early Stage

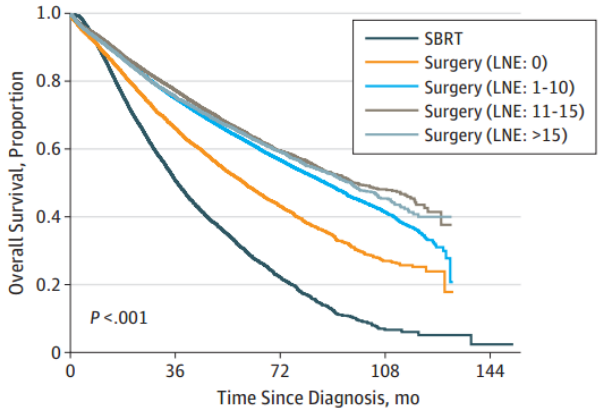
SBRT vs all surgical modalities



SBRT vs surgery with and without regional LNE



SBRT vs surgery with LNE of 0, 1-10, 11-15, and >15



- This study analyze the influence of regional lymph node assessment when comparing Surgery vs SBRT
- Overall, all surgical modalities studied were associated with superior long-term OS when compared with SBRT in patients with clinical stage T1 to T3, N0, M0 NSCLC
- This survival advantage is further enhanced by regional LNE, especially when more than 10 lymph nodes were examined

Tumori del torace

NSCLC – SBRT in Early Stage

The Journal of Thoracic and Cardiovascular Surgery
JTCVS
AATS

< Previous Article | January 2019 Volume 157, Issue 1, Pages 362–373.e8 | Next Article >

A systematic review and meta-analysis of stereotactic body radiation therapy versus surgery for patients with non–small cell lung cancer

Christopher Cao, MD, PhD[a,b], Daniel Wang, MD[c], Caroline Chung, MD[c], David Tian, MD[b], Andreas Rimner, MD[d], James Huang, MD[a], David R. Jones, MD[a,*]

Metanalisi di 23 studi
National Institutes of Health (NIH)

SBRT is the preferred option for patients with inoperable early-stage NSCLC

For operable patients, comparative outcomes between SBRT and surgery for high-risk patients remain controversial

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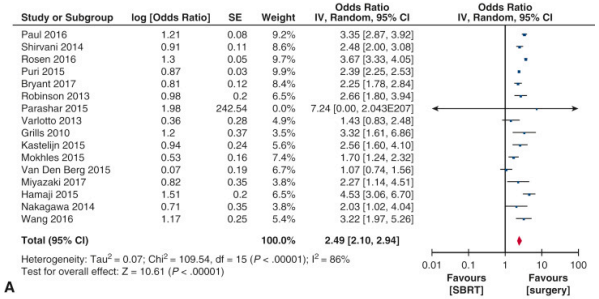
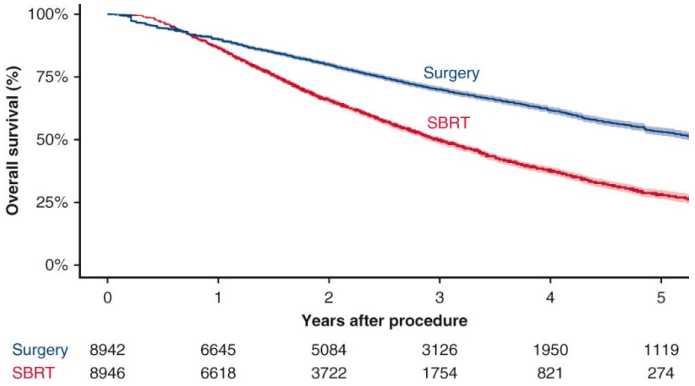
NSCLC – SBRT in Early Stage





Surgery is superior to SBRT in terms of:
Overall survival (OS),
Cancer-specific survival (CSS)
Disease-free survival (DFS)
Freedom from local relapse

- OS, OR non appaiato: 2,49 (P<0,00001); OR appaiato: 1,71 (P<0,00001);
- CSS, OR non appaiato: 2,44 (P<0,00001); OR appaiato: 1,78 (P=0,0006);
- DFS, OR non appaiato: 2,13 (P<0,00001); OR appaiato: 1,83 (P=0,03);
- libertà da recidiva locoregionale, OR non appaiato: 5,44 (P<0,005); OR appaiato: 2,91 (P=0,002).

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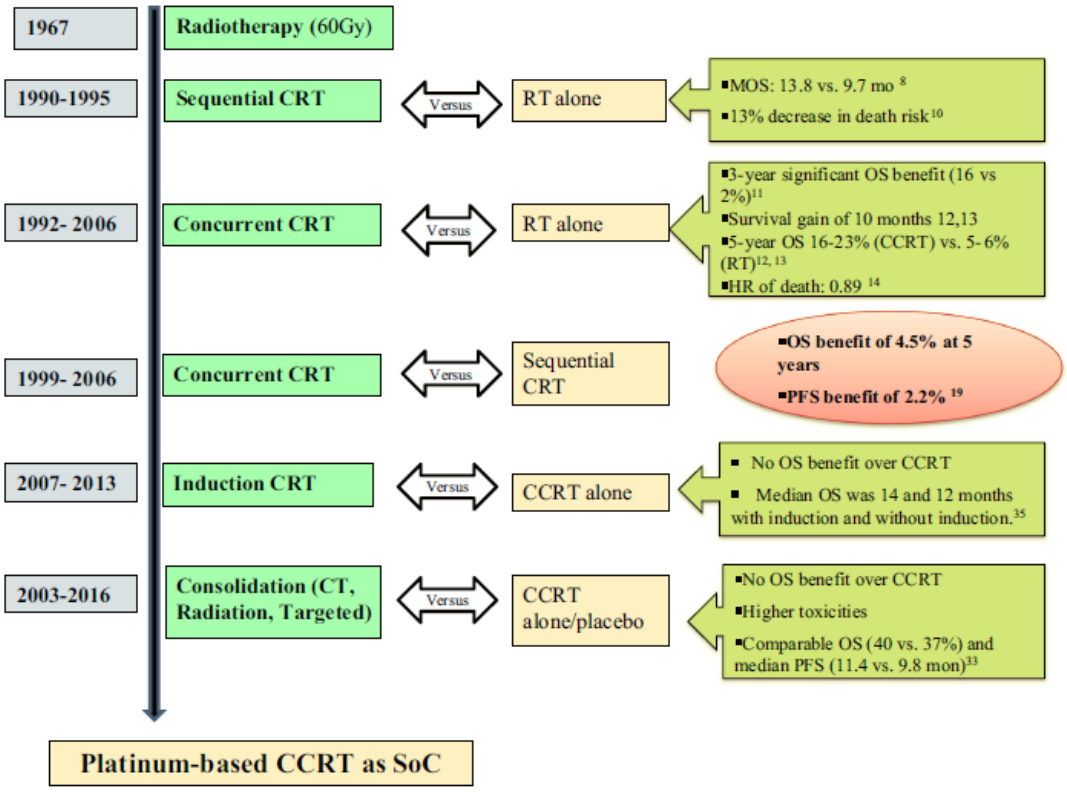
Tumori del torace

NSCLC - Locally advanced disease – Stato dell'Arte



Tumori del torace

NSCLC – Durvalumab in Stage III

PACIFIC: Study Design

Phase 3, Randomized, Double-blind, Placebo-controlled, Multicenter, International Study[1]

- Unresectable, Stage III NSCLC without progression after definitive platinum-based cCRT (≥2 cycles)
- 18 years or older
- WHO PS score 0 or 1
- If available, archived pre-cCRT tumor tissue for PD-L1 testing*

All-comers population (i.e. irrespective of PD-L1 status)

N=713 randomized

1–42 days post-cCRT

R

2:1 randomization, stratified by age, sex, and smoking history

Durvalumab 10 mg/kg q2w for up to 12 months N=476

Placebo 10 mg/kg q2w for up to 12 months N=237

Primary endpoints
- PFS by BICR using RECIST v1.1†
- OS

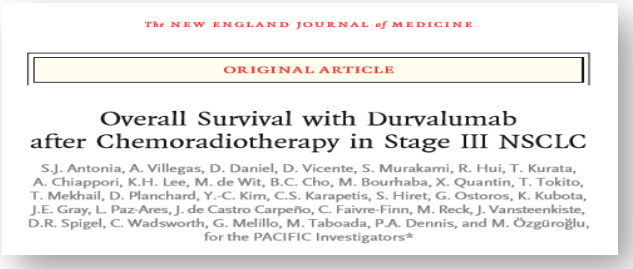
Key secondary endpoints
- ORR, DoR and TTDM by BICR
- PFS2 by investigator
- Safety
- PROs


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 16, 2017 VOL. 377 NO. 20

Durvalumab after Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

S.J. Antonia, A. Villegas, D. Daniel, D. Vicente, S. Murakami, R. Hui, T. Yokoi, A. Chiappori, K.H. Lee, M. de Wit, B.C. Cho, M. Bourhaba, X. Quantin, T. Tokito, T. Mekhail, D. Planchard, Y.-C. Kim, C.S. Karapetis, S. Hiret, G. Ostoros, K. Kubota, J.E. Gray, L. Paz-Ares, J. de Castro Carpeño, C. Wadsworth, G. Melillo, H. Jiang, Y. Huang, P.A. Dennis, and M. Özgüroğlu, for the PACIFIC Investigators*


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

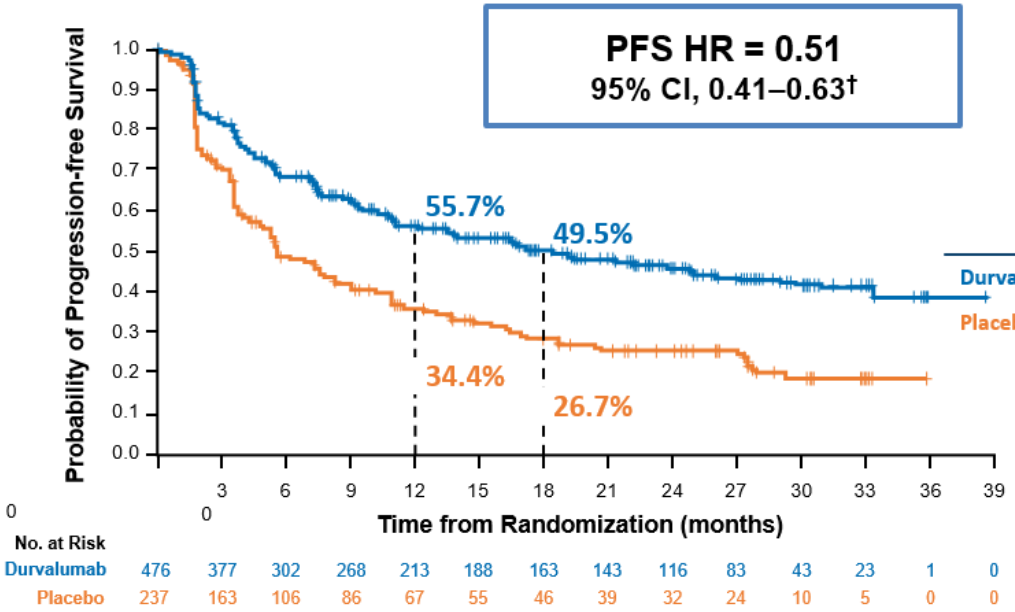
Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC

S.J. Antonia, A. Villegas, D. Daniel, D. Vicente, S. Murakami, R. Hui, T. Kurata, A. Chiappori, K.H. Lee, M. de Wit, B.C. Cho, M. Bourhaba, X. Quantin, T. Tokito, T. Mekhail, D. Planchard, Y.-C. Kim, C.S. Karapetis, S. Hiret, G. Ostoros, K. Kubota, J.E. Gray, L. Paz-Ares, J. de Castro Carpeño, C. Faivre-Finn, M. Reck, J. Vansteenkiste, D.R. Spigel, C. Wadsworth, G. Melillo, M. Taboada, P.A. Dennis, and M. Özgüroğlu, for the PACIFIC Investigators*

Scott JA et al, NEJM 2018
Scott JA et al, NEJM 2017

NSCLC – Durvalumab in Stage III

Updated Progression-free Survival by BICR* (ITT)

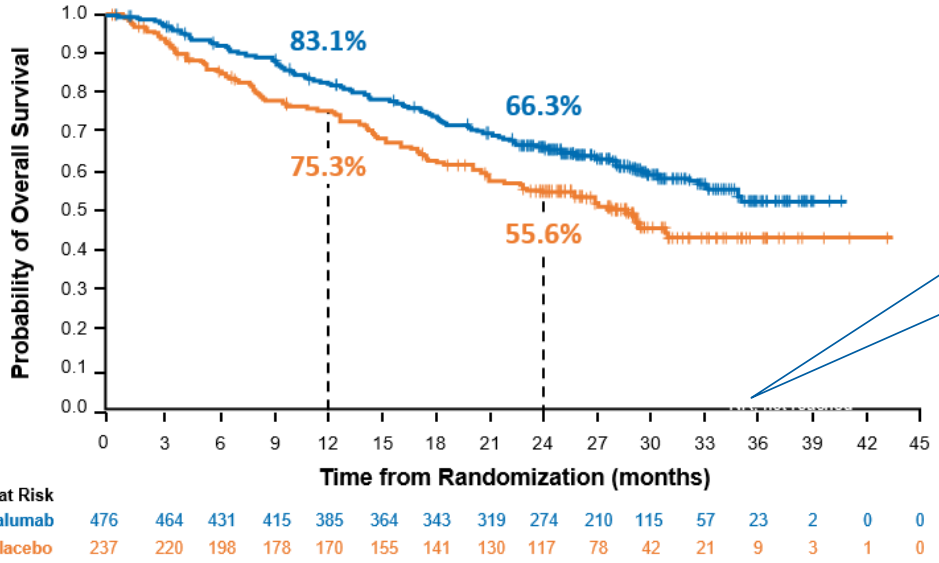


	No. of events / No. of patients (%)	Median PFS (95% CI) months
Durvalumab	243/476 (51.1)	17.2 (13.1–23.9)
Placebo	173/237 (73.0)	5.6 (4.6–7.7)

Scott JA et al, NEJM 2018
Scott JA et al, NEJM 2017

NSCLC – Durvalumab in Stage III

Overall Survival* (ITT)



ASCO 2019
Update from the PACIFIC trial

3-y OS: 57.0% versus 43.5%
MS: NR versus 29,1 mo

	No. of events / No. of patients (%)	Median OS (95% CI) months
Durvalumab	183/476 (38.4)	NR (34.7–NR)
Placebo	116/237 (48.9)	28.7 (22.9–NR)

Scott JA et al, NEJM 2018
Scott JA et al, NEJM 2017

NSCLC – Durvalumab in Stage III

Update from the PACIFIC trial

Con un addizionale anno di follow-up, gli ultimi risultati di durvalumab hanno mostrato un'efficacia costante e duratura, mantenendo una **riduzione del 31% del rischio di morte** vs placebo dopo RT-CT (Hr 0,69; Ic al 95%: 0,55 - 0,86)

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2020
Non-Small Cell Lung Cancer

NCCN Guidelines Index
Table of Contents
Discussion

Consolidation Therapy for Patients with Unresectable Stage III NSCLC, PS 0-1, and No Disease Progression After 2 or More Cycles of Definitive Chemoradiation
Durvalumab 10 mg/kg IV every 2 weeks for up to 12 months[7] (category 1)

*Regimens can be used as preoperative/adjuvant chemotherapy/RT.
†Regimens can be used as definitive concurrent chemotherapy/RT.
‡Durvalumab may be used after any of the concurrent chemo/RT regimens listed above for eligible patients.

Tumori del torace

NSCLC – Durvalumab in Stage III

Ann Oncol. 2019 Feb 1;30(2):161-165. doi: 10.1093/annonc/mdy553.

Position of a panel of international lung cancer experts on the approval decision for use of durvalumab in stage III non-small-cell lung cancer (NSCLC) by the Committee for Medicinal Products for Human Use (CHMP).

Peters S[1], Dafni U[2], Boyer M[3], De Ruysscher D[4], Faivre-Finn C[5], Felip E[6], Garrido P[7], Girard N[8], Guckenberger M[9], Haanen J[10], Le Pechoux C[11], Mornex F[12], Ozsahin M[13], Paz-Ares L[14], Planchard D[15], Raben D[16], Ramalingam S[17], Reck M[18], Smit E[19], Stahel R[20], Stenzinger A[21], Swanton C[22], Vallone S[23], Garassino MC[24].

- a causa delle raccomandazioni dell'EMA i pazienti europei con tumori PD-L1-negativi vengono privati di un trattamento potenzialmente salvavita
- la decisione dell'EMA si basa su un'analisi post-hoc non programmata, richiesta dagli organismi regolatori, di un piccolo sottoinsieme di pazienti dello studio PACIFIC, che non ha dimostrato in modo inequivocabile un beneficio in termini di sopravvivenza complessiva (overall survival, OS) nei pazienti PD-L1-negativi, anche se la popolazione intention-to-treat (ITT) ha evidenziato una OS significativamente migliore
- la mancanza di un beneficio inequivocabile in termini di OS non indica pericoli in questi pazienti
- non è approvato alcun altro trattamento post-chemioRT per i pazienti con tumori PD-L1-negativi

Tumori del torace

NSCLC - Locally advanced disease

original reports

Long-Term Results of NRG Oncology RTOG 0617: Standard- Versus High-Dose Chemoradiotherapy With or Without Cetuximab for Unresectable Stage III Non–Small-Cell Lung Cancer

Jeffrey D. Bradley, MD[1]; Chen Hu, PhD[2,3]; Ritsuko R. Komaki, MD[4]; Gregory A. Masters, MD[5]; George R. Blumenschein, MD[4]; Steven E. Schild, MD[6]; Jeffrey A. Bogart, MD[7]; Kenneth M. Forster, PhD[8]; Anthony M. Magliocco, MD[9]; Vivek S. Kavadi, MD[10]; Samir Narayan, MD[11]; Puneeth Iyengar, MD[12]; Clifford G. Robinson, MD[13]; Raymond B. Wynn, MD[14]; Christopher D. Koprowski, MD[15]; Michael R. Olson, MD[16]; Joanne Meng, MD[17]; Rebecca Paulus, BS[2]; Walter J. Curran Jr, MD[18]; and Hak Choy, MD[12]

Study Design (phase III Trial)
National Cancer Institute

Disegno fattoriale 2x2
496 pazienti con NSCLC in stadio III

60 Gy (Standard Dose) + CT

74 Gy (HIgh Dose) + CT

60 Gy (Standard Dose) + CT + Cetuximab

74 Gy (High Dose) + CT + Cetuximab

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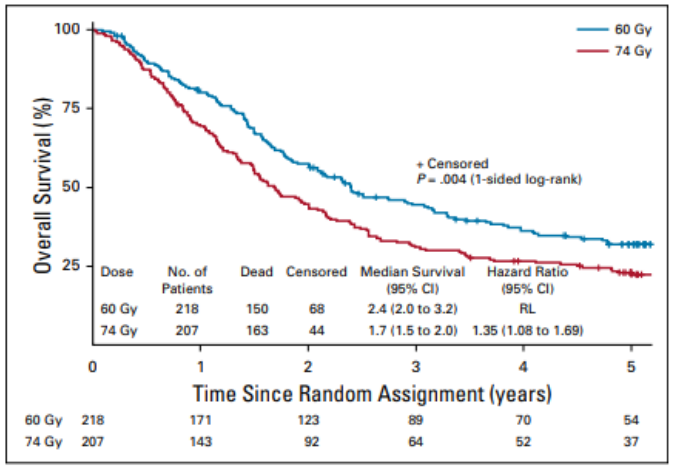
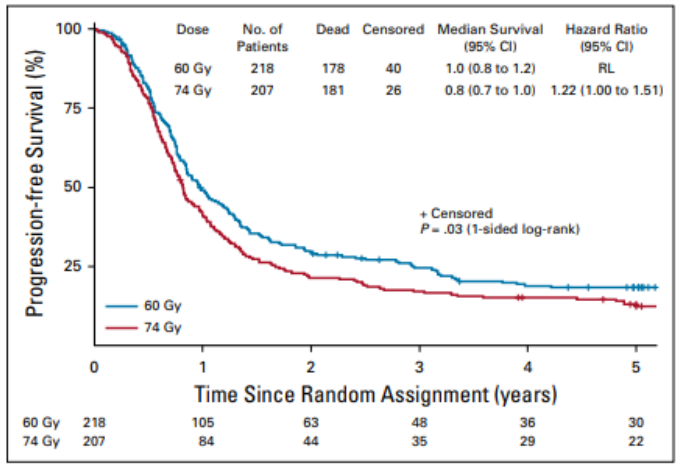
Tumori del torace

NSCLC - Locally advanced disease





Median Follow-up: 5,1 years

Median OS was 28.7 *vs* 20.3 months (*P* = .0072) in the SD and HD arms

5-year OS were **32.1%** *vs* 23%

PFS: 18.3% and 13% (*P* = .055)

The use of cetuximab conferred no survival benefit at the expense of increased toxicity

Tumori del torace

NSCLC - Locally advanced disease

TABLE 4. Multivariable Cox Model of Overall Survival

Covariate	Comparison	Dead of Total RL	Dead of Total Group 2	HR (95% CI)	P*
Radiation level	Standard dose (RL) *v* high dose	132 of 196	147 of 188	1.300 (1.020 to 1.660)	.0315
Tumor location	LLL or central node (RL) *v* neither LLL nor central node	172 of 226	107 of 158	0.860 (0.607 to 1.110)	.2395
Institution accrual volume	1-3 patients (RL) *v* ≥ 4 patients	122 of 149	157 of 235	0.740 (0.580 to 0.950)	.0170
Maximum related esophagitis/dysphagia grade	Maximum grade < 3 (RL) *v* maximum grade ≥ 3	230 of 328	49 of 56	1.540 (1.120 to 2.120)	.0079
Volume of PTV (log-transformed)	Continuous	279 of 384		1.323 (1.041 to 1.680)	.0219
Heart V5	Continuous	279 of 384		1.008 (1.002 to 1.013)	.0051

Factors associated with improved OS were:

- standard radiation dose
- tumor location
- institution accrual volume
- esophagitis/dysphagia
- planning target volume
- heart V5

CONCLUSION

- A **60-Gy** radiation dose with concurrent chemotherapy should remain the **standard of care**, with the OS rate being among the highest reported in the literature for stage III NSCLC
- Cetuximab had no effect on OS
- The 2-year OS rates in the control arm are similar to the PACIFIC trial : 59,6 vs 66,3% (approximately 5% benefit with Durvalumab at 5y)

Tumori del torace

Patterns of Disease Progression in Stage III NSCLC (ASTRO 2019)

LBA6

Patterns of Disease Progression with Durvalumab in Stage III Non-small Cell Lung Cancer (PACIFIC)

D. Raben,[1] A. Rimner,[2] S. Senan,[3] H. Broadhurst,[4] T. Pellas,[5] P.A. Dennis,[5] and C. Faivre-Finn[6]; [1]*University of Colorado Cancer Center, Aurora, CO,* [2]*Memorial Sloan Kettering Cancer Center, New York, NY,* [3]*Amsterdam University Medical Centers, Cancer Center Amsterdam, Amsterdam, Netherlands,* [4]*AstraZeneca, Alderly Park, United Kingdom,* [5]*AstraZeneca, Gaithersburg, MD,* [6]*The University of Manchester and The Christie NHS Foundation Trust, Manchester, United Kingdom*

International Journal of Radiation Oncology biology • physics

www.redjournal.org

Exploratory analyses from the phase III PACIFIC trial

- the site of first disease progression in most patients was inside the thorax, regardless of whether they received or did not receive immunotherapy with durvalumab

Fewer patients receiving durvalumab experienced local and/or distant disease progression:

- local-only (intrathoracic) disease progression occurred in 48.1% of the placebo group and 36.6% of the durvalumab group
- distant-only (extrathoracic) disease progression occurred in 13.1% and 6.9%, respectively

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23 gennaio 2020

Tumori del torace

Lung cancer: Applicazione Linee Guida

ATS Journals

Annals of the American Thoracic Society

Home > All AnnalsATS Issues > **Articles in Press**

Disparities in Receiving Guideline-Concordant Treatment for Lung Cancer in the United States

Erik F Blom , **Kevin ten Haaf** , **Douglas A Arenberg** , and **Harry J de Koning**
+ Author Information
https://doi.org/10.1513/AnnalsATS.201901-094OC **PubMed:** 31672025

Received: January 30, 2019 Accepted: October 16, 2019 Published Online: November 01, 2019

Adherence to the NCCN guidelines in the US

441,812 lung cancer cases in the National Cancer Database (2010-2014)

- Il 62,1% dei pazienti ha ricevuto il trattamento raccomandato (dal 50,4% nell'NSCLC in stadio avanzato al 76,3% nell'NSCLC locale).
- Il 16,3% dei pazienti ha ricevuto un trattamento meno intensivo rispetto a quello raccomandato (dal 6,4% nell'SCLC esteso al 21,6% nell'NSCLC localmente avanzato).
- Il 21,6% dei pazienti non ha ricevuto alcun trattamento (dal 10,3% nell'NSCLC locale al 31,4% nell'NSCLC in stadio avanzato).
- Il ricevimento del trattamento raccomandato diminuiva all'avanzare dell'età (età ≥80 anni rispetto a <50 anni, aOR: 0,12; IC 95%: 0,12–0,13).
- Nei pazienti con NSCLC locale i pazienti anziani avevano meno probabilità di essere sottoposti a trattamento chirurgico (aOR: 0,06; IC 95%: 0,05–0,06) e maggiore probabilità di ricevere radioterapia stereotassica corporea (aOR: 18,39; IC 95%: 14,09–23,99).

Tumori del torace

Applicazione Linee Guida: Staging linfonodale

Chest. 2019 Oct 11. pii: S0012-3692(19)34007-3. doi: 10.1016/j.chest.2019.09.025. [Epub ahead of print]

Quality Gaps and Comparative Effectiveness in Lung Cancer Staging and Diagnosis.

Ost DE[1], Niu J[2], Zhao H[2], Grosu H[2], Giordano SH[2].

Author information

1 Departments of Pulmonary Medicine, The University of Texas MD Anderson Cancer Center. Electronic address: dost@mdanderson.org.
2 Health Services Research, The University of Texas MD Anderson Cancer Center.

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

- Studio retrospettivo su 15.914 pazienti affetti da tumore polmonare del Texas Cancer Registry e del database SEER, nel periodo 2004–2013
- Solo il 25,4% dei pazienti affetti da tumore polmonare con sospetto coinvolgimento linfonodale è sottoposto al campionamento dei linfonodi mediastinici come primo esame, come raccomandato dalle linee guida, e il 43% non viene sottoposto ad alcun campionamento
- Le cure conformi alle linee guida sono aumentate dal 23% al 34% durante il periodo dello studio (EBUS da 0,1% a 25%, mediastinoscopia da 54% a 64%)
- le cure conformi alle linee guida erano associate a meno complicanze o procedure invasive (toracotomie da 71% a 38%, biopsie TC guidate da 75% a 10%, pneumotorace da 22% a 5%)

Key points

- NSCLC - Early Stages
- NSCLC – Locally advanced
- NSCLC - Advanced disease
- Tecnica radioterapica – Tossicità
- SCLC
- Mesotelioma pleurico

Tumori del torace

NSCLC- Advanced disease

Definition of synchronous oligo-metastatic NSCLC

J Thorac Oncol. 2019 Aug 6. pii: S1556-0864(19)30655-0. doi: 10.1016/j.jtho.2019.07.025. [Epub ahead of print]

Definition of synchronous oligo-metastatic non-small cell lung cancer - a consensus report.

Dingemans AC[1], Hendriks LEL[2], Berghmans T[3], Levy A[4], Hasan B[5], Faivre-Finn C[6], Giaj-Levra M[7], Giaj-Levra N[8], Girard N[9], Greillier L[10], Lantuéjoul S[11], Edwards J[12], O'Brien M[13], Reck M[14], Smit EF[15], Van Schil P[16], Postmus PE[17], Ramella S[18], Lievens Y[19], Gaga M[20], Peled N[21], Scagliotti GV[22], Senan S[23], Paz-Ares L[24], Guckenberger M[25], McDonald F[26], Ekman S[27], Cufer T[28], Gietema H[29], Infante M[30], Dziadziuszko R[31], Peters S[32], Porta RR[33], Vansteenkiste J[34], Dooms C[34], de Ruysscher D[35], Besse B[36], Novello S[22].

EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

- Consensus del Lung Cancer Group EORTC su stadiazione NSCLC e definizione di malattia OM sincrona (sOM) come entità terapeutica speciale.
- La definizione di NSCLC sOM include un massimo di 5 metastasi e di 3 organi; il coinvolgimento dei linfonodi mediastinici non è considerato una sede di metastasi.
- La stadiazione richiede ^{8}F-FDG-PET-TC (con conferma istopatologica mediastinica se i risultati influenzano la strategia terapeutica), staging cerebrale, RM epatica (se mts isolata), toracoscopia (se mts pleurica solitaria).

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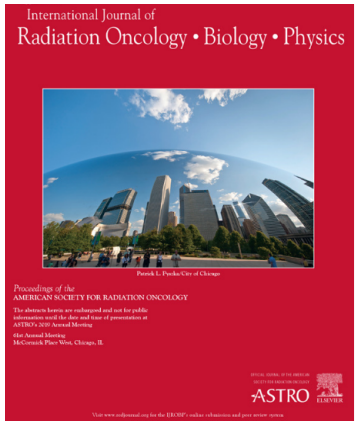
Tumori del torace

Advanced NSCLC: SBRT + Immunotherapy

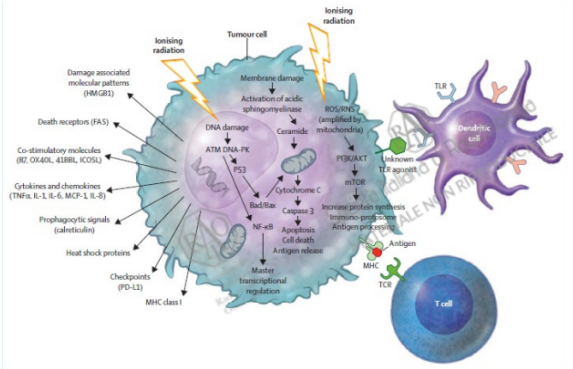


2019 ASTRO Annual Meeting

Final Results of a Phase II Prospective Trial Evaluating the Combination of Stereotactic Body Radiotherapy (SBRT) with Concurrent Pembrolizumab in Patients with Metastatic Non-Small Cell Lung Cancer (NSCLC)

A.M. Campbell[1], W.L. Cai[1], D. Burkhardt[2], S.N. Gettinger[3], S.B. Goldberg[4], M. Amodio[2], S. Kaech[5], S. Krishnaswamy[2], R.H. Decker[6]
74

- Patients (56) with metastatic non–small cell lung cancer (NSCLC) who have experienced disease progression on immunotherapy may benefit from stereotactic body radiotherapy (SBRT) in terms of progression-free survival
- The addition of SBRT after progression on immunotherapy resulted in increased PFS, a systemic response rate of 9.52%, and a disease control rate of 57.14%
- Improved PFS correlated with an increased TIL score: pts with elevated TIL scores (2-3) showed improved progression free survival (PFS), with a mean of 215 versus 59 days



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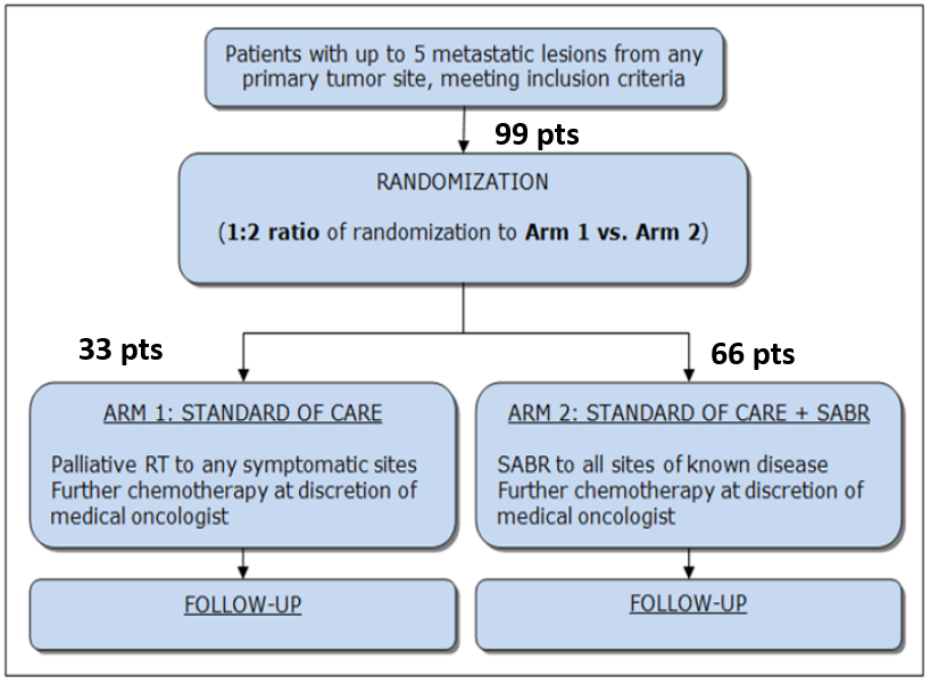
Tumori del torace

Advanced NSCLC: SBRT

SABR-COMET Schema



[Palma D et al, Lancet 2019]

Primary endpoint

- Overall Survival

Secondary endpoints

- Progression-free survival
- Toxicity (CTC-AE 4.0)
- Lesional control rate
- Quality of life (FACT-G)
- Number of cycles of further chemo

Lancet. 2019 May 18;393(10185):2051-2058. doi: 10.1016/S0140-6736(18)32487-5. Epub 2019 Apr 11.

Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial.

Palma DA[1], Olson R[2], Harrow S[3], Gaede S[4], Louie AV[4], Haasbeek C[5], Mulroy L[6], Lock M[4], Rodrigues GB[4], Yaremko BP[4], Schellenberg D[7], Ahmad B[4], Griffioen G[5], Senthi S[8], Swaminath A[9], Kopek N[10], Liu M[11], Moore K[3], Currie S[3], Bauman GS[4], Warner A[4], Senan S[8].

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3 Beatson West of Scotland Cancer Centre, Glasgow, UK.
4 London Health Sciences Centre, London, ON, Canada.
5 Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, Netherlands.
6 Nova Scotia Cancer Centre, Halifax, NS, Canada.
7 British Columbia Cancer, Surrey Centre, Surrey, BC, Canada.
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9 Juravinski Cancer Centre, Hamilton, ON, Canada.
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11 British Columbia Cancer, Vancouver Centre, Vancouver, BC, Canada.

Abstract

BACKGROUND: The oligometastatic paradigm suggests that some patients with a limited number of metastases might be cured if all lesions are eradicated. Evidence from randomised controlled trials to support this paradigm is scarce. We aimed to assess the effect of stereotactic ablative radiotherapy (SABR) on survival, oncological outcomes, toxicity, and quality of life in patients with a controlled primary tumour and one to five oligometastatic lesions.

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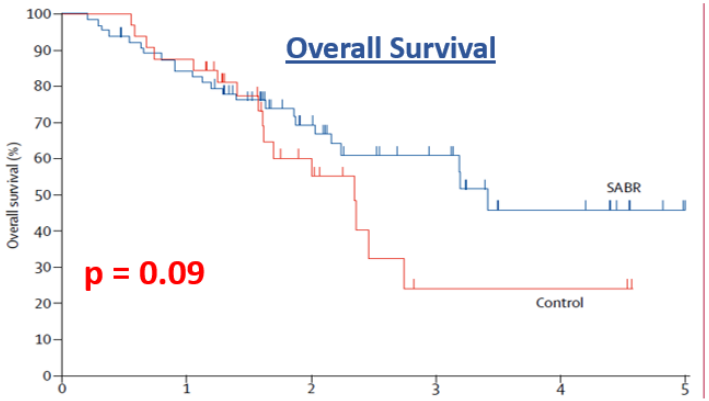
Tumori del torace

Advanced NSCLC: SBRT



Median Overall Survival

Control Arm: 28 months
(95% CI: 19- 33 months)
SABR Arm: 41 months
(95% CI: 26 months to 'not reached')

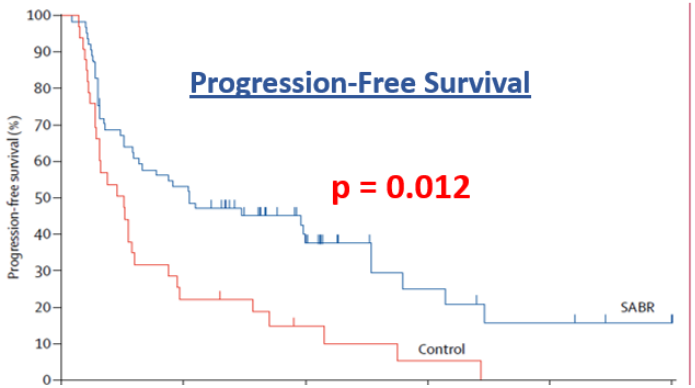
FINDINGS: 99 patients were randomised between Feb 10, 2012, and Aug 30, 2016. Of 99 patients, 33 (33%) were assigned to the control group and 66 (67%) to the SABR group. Two (3%) patients in the SABR group did not receive allocated treatment and withdrew from the trial; two (6%) patients in the control group also withdrew from the trial. Median follow-up was 25 months (IQR 19-54) in the control group versus 26 months (23-37) in the SABR group. Median overall survival was 28 months (95% CI 19-33) in the control group versus 41 months (26-not reached) in the SABR group (hazard ratio 0·57, 95% CI 0·30-1·10; p=0·090). Adverse events of grade 2 or worse occurred in three (9%) of 33 controls and 19 (29%) of 66 patients in the SABR group (p=0·026), an absolute increase of 20% (95% CI 5-34). Treatment-related deaths occurred in three (4·5%) of 66 patients after SABR, compared with none in the control group.

INTERPRETATION: SABR was associated with an improvement in overall survival, meeting the primary endpoint of this trial, but three (4·5%) of 66 patients in the SABR group had treatment-related death. Phase 3 trials are needed to conclusively show an overall survival benefit, and to determine the maximum number of metastatic lesions wherein SABR provides a benefit.

Median PFS

Control Arm: 6 months
(95% CI: 3.4- 7.1 months)
SABR Arm: 12 months
(95% CI: 6.9 - 30 months)

[Palma D et al, Lancet 2019]



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Tumori del torace

Advanced NSCLC: Radiotherapy in oligometastatic disease

Review Article

Changing equipoise in the landscape of radiation for oligometastatic lung cancer

Samuel R. Schroeder[1#], Michael Leenders[2#], Puneeth Iyengar[1], Dirk de Ruysscher[2]

Multiple prospective studies evaluating the role of Local Consolidative Therapy (LCT), mainly with **SBRT**, in oligometastatic NSCLC

Improved PFS and, in some cases, OS

Table 1 Completed studies

Study authors	Study design	Treatment setting	Patient eligibility	Study arm(s)	Results
De Ruysscher *et al.* (16,17)	Single arm phase II	Consolidation	Oligometastatic NSCLC (<5 sites), no response to systemic therapy required	Chemo with surgery or radiation for metastatic sites	Median PFS, OS 12.1 and 13.5 months, respectively
Gomez *et al.* (18,19)	Randomized phase II	Consolidation	Oligometastatic NSCLC (≤5 sites), EGFR mutations allowed (12% of patients)	Systemic therapy followed by local consolidative therapy (SABR, surgery, or chemoradiation) *vs.* maintenance treatment alone	Median PFS 14.2 *vs.* 4.4 months; OS 41.2 *vs.* 17 months
Iyengar *et al.* (20)	Randomized phase II	Consolidation	Oligometastatic NSCLC (≤6 sites including primary)	Chemo followed by SABR *vs.* maintenance treatment alone	Median PFS 9.7 *vs.* 3.5 months
Collen *et al.* (21)	Single arm phase II	Consolidation	Oligometastatic NSCLC (≤5 sites)	Chemo followed by SABR or SABR alone	Complete metabolic response (PET/CT) 30%; median OS 23.5 months
Petty *et al.* (22)	Single arm phase II	Consolidation	Oligometastatic NSCLC (≤5 sites)	Chemo followed by SABR if no evidence of progression	Median PFS, OS 11.2, 28.4 months, respectively
Arrieta *et al.* (23)	Single arm phase II	Consolidation	Oligometastatic NSCLC (≤5 sites), *EGFR/ALK* mutations allowed (43% of patients)	Systemic therapy followed by local consolidative therapy (conventional RT, SABR, surgery, chemoradiation, or RFA)	Median PFS 23.5 months, median OS NR; 51.4% of patients achieved CR by PET/CT, CR associate with significantly improved PFS (NR *vs.* 14.3 months) and OS (NR *vs.* 27.4 months)
Palma *et al.* (24)	Randomized phase II	Consolidation	Limited metastatic disease from any primary site (≤5 sites)	Standard of care plus SABR *vs.* standard of care alone	Median PFS 12 *vs.* 6 months; OS 41 *vs.* 28 months
Iyengar *et al.* (25)	Single arm phase II	Salvage	Limited metastatic NSCLC (≤5 sites), failed one line of systemic therapy	Erlotinib with SABR	Median PFS, OS 14.7, 20.4 months, respectively

PFS, progression-free survival; OS, overall survival; NSCLC, non-small cell lung cancer; SABR, stereotactic ablative radiotherapy; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase; CR, complete response; NR, not reached; PET/CT, positron emission tomography/computed tomography.

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Advanced NSCLC: Radiotherapy in oligometastatic disease

Factors that should drive use and timing of local therapy

- Metastatic presentation sequence (synchronous vs. metachronous)
- Extent of disease (number and distribution of sites)
- Quality of life goals
- Integration with Immunotherapy and/or Targeted therapies
- Recommend enrollment in phase III studies with OS endpoints

Table 2 Currently accruing phase III trials

Trial	Initiation year	Study design	Patient eligibility	Study arms	Primary endpoint
NRG LU 002 NCT03137771	2018	Randomized phase II/III	Oligometastatic NSCLC (≤3 sites), received 1st line systemic therapy without progression, immunotherapy allowed	Maintenance therapy plus SABR *vs.* maintenance therapy alone	Phase II: PFS; phase III: OS
SARON NCT02417662	2016	Randomized phase III	Oligometastatic NSCLC (≤3 sites), eligible to receive chemotherapy	Chemotherapy plus SABR *vs.* chemotherapy alone	OS
SABR-COMET 10 NCT03721341	2019	Randomized phase III	Limited metastatic disease from any primary site (4–10 metastatic sites)	Maintenance therapy plus SABR *vs.* maintenance therapy alone	OS
HALT NCT03256981	2017	Randomized phase II/III	Advanced NSCLC with actionable mutation and confirmed response to TKI treatment with ≤3 sites of progression	Maintenance TKI plus SABR *vs.* maintenance TKI alone	PFS

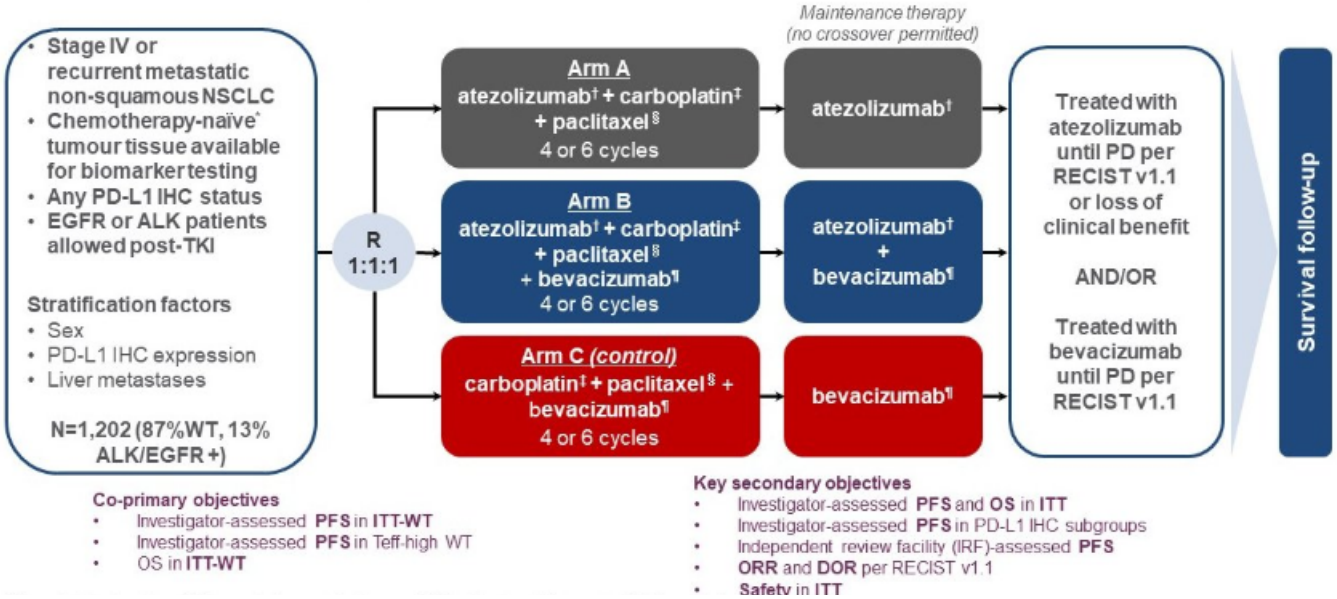
PFS, progression-free survival; OS, overall survival; NSCLC, non-small cell lung cancer; SABR, stereotactic ablative radiotherapy; TKI, tyrosine kinase inhibitor.

Tumori del torace

Advanced NSCLC: Atezolizumab in first line

2019 ASCO ANNUAL MEETING

IMpower150: study design



Vantaggio in termini di **sopravvivenza globale** (OS mediana=**13,3 vs 9,4 mesi**)

La sicurezza della combinazione di atezolizumab, bevacizumab e chemioterapia è risultata coerente con i **profili di sicurezza** noti dei singoli farmaci

Tumori del torace

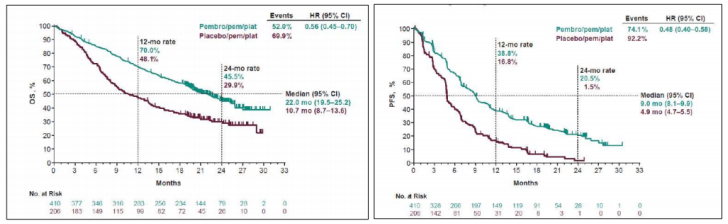
Advanced NSCLC: Pembrolizumab in first line

2019 ASCO ANNUAL MEETING

KEYNOTE-001
Phase 1 Trial of Pembrolizumab for Advanced NSCLC

Pembrolizumab in **monoterapia** ha dimostrato un **OS a cinque anni del 23,2%** in pazienti naïve al trattamento (n = 101) e del 15,5% in pazienti precedentemente trattati

KEYNOTE-189
Pembrolizumab +/- chemotherapy in NONSq-NSCLC



OS PFS

A 18,7 mesi di follow-up mediano l'aggiunta di pembrolizumab ha mantenuto i benefici in termini di **OS (22,0 vs 10,7 mesi)** e **PFS (9,0 mesi vs 4,9 mesi)**

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Tumori del torace

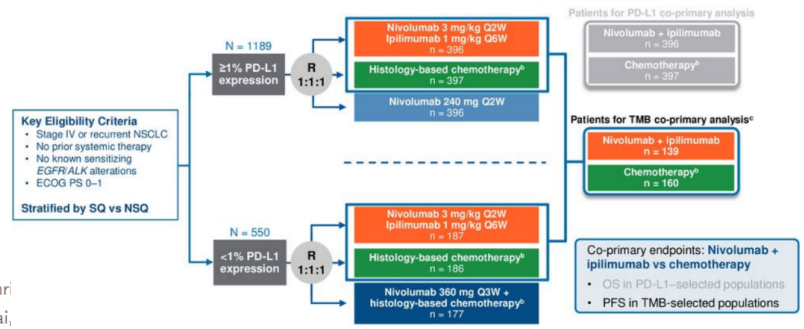
Advanced NSCLC: Nivolumab+Ipilimumab in first line (CheckMate 227 Study)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE FREE PREVIEW

Nivolumab plus Ipilimumab in Advanced Non–Small-Cell Lung Cancer

Matthew D. Hellmann, M.D., Luis Paz-Ares, M.D., Ph.D., Reyes Bernabe Caro, M.D., Ph.D., Bogdan Zurawski, M.D., Ph.D., Sang-We Kim, M.D., Ph.D., Enri Carcereny Costa, M.D., Keunchil Park, M.D., Ph.D., Aurelia Alexandru, M.D., Lorena Lupinacci, M.D., Emmanuel de la Mora Jimenez, M.D., Hiroshi Sakai, M.D., Istvan Albert, M.D., et al.



CONCLUSIONS

*First-line treatment with nivolumab plus ipilimumab resulted in a **longer duration of overall survival** (17.1 vs 13,9 months) than did chemotherapy in patients with NSCLC, independent of the PD-L1 expression level.*

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Tumori del torace

Advanced EGFR-mutated NSCLC: Osimertinib

FLAURA study
(N=556)

- Locally advanced, not amenable to curative surgery or radiotherapy, or metastatic NSCLC
- EGFRm disease (exon 19 deletion or L858R)
- No prior anticancer therapy
- Stable, asymptomatic CNS metastases were allowed*

EGFR TKI comparator (n=277):
Gefitinib 250 mg orally, once daily
OR
Erlotinib 150 mg orally, once daily

TAGRISSO (n=279)
80 mg orally, once daily

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

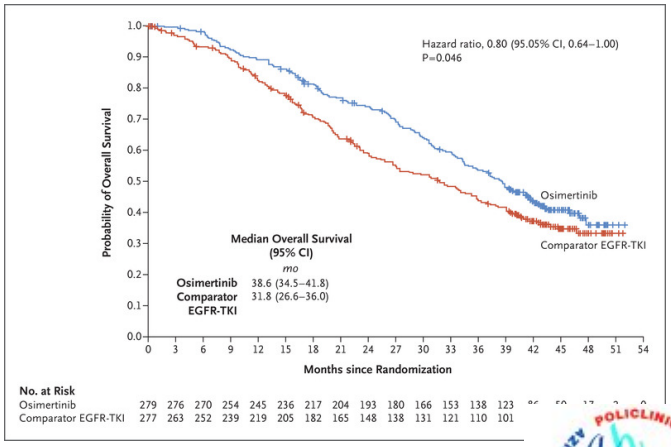
Overall Survival with Osimertinib in Untreated, *EGFR*-Mutated Advanced NSCLC

S.S. Ramalingam, J. Vansteenkiste, D. Planchard, B.C. Cho, J.E. Gray, Y. Ohe, C. Zhou, T. Reungwetwattana, Y. Cheng, B. Chewaskulyong, R. Shah, M. Cobo, K.H. Lee, P. Cheema, M. Tiseo, T. John, M.-C. Lin, F. Imamura, T. Kurata, A. Todd, R. Hodge, M. Saggese, Y. Rukazenkov, and J.-C. Soria, for the FLAURA Investigators*

Table 1. Overall Survival and Continuation of First-Line Trial Drug.*

Variable	Osimertinib (N=279)	Comparator EGFR-TKI (N=277)
Overall survival — % (95% CI)		
At 12 mo	89 (85–92)	83 (77–87)
At 24 mo	74 (69–79)	59 (53–65)
At 36 mo	54 (48–60)	44 (38–50)
Patients continuing to receive first-line trial drug — no. (%)		
At 12 mo	194 (70)	131 (47)
At 24 mo	118 (42)	45 (16)
At 36 mo	78 (28)	26 (9)

* In the comparator group, patients received one of two tyrosine kinase inhibitors of epidermal growth factor receptor (EGFR-TKI): gefitinib or erlotinib.



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Costi terapie antitumorali più recenti

- Sono stati studiati farmaci per trattare tumori solidi registrati dall'Agenzia europea per i medicinali (European Medicines Agency, EMA) dal 2004 al 2017
- Il valore aggiunto è stato misurato secondo la v1.1 dell'ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) e la scala Added Therapeutic Benefit Rank (ASMR) dell'Alta Autorità della Salute (High Authority of Health, HAS) francese
- Il 48% e il 70% dei farmaci avevano uno scarso valore aggiunto

"La maggior parte dei nuovi farmaci antitumorali aveva uno scarso valore aggiunto, quindi medici e pazienti non dovrebbero presupporre che solo perché un farmaco è nuovo, sarà migliore"

[Marino P. The price of added value for new anti-cancer drugs in France 2004-17. Abstract 1629O_PR, ESMO 2019. Presented at ESMO: 2019 Annual Meeting (Barcelona, Spain)]

Key points

- NSCLC - Early Stages
- NSCLC – Locally advanced
- NSCLC - Advanced disease
- Tecnica radioterapica – Tossicità
- SCLC
- Mesotelioma pleurico

Tumori del torace

Tecnica radioterapica - Adaptive RT

ELSEVIER

Seminars in RADIATION ONCOLOGY

Anatomical Adaptation—Early Clinical Evidence of Benefit and Future Needs in Lung Cancer

James Kavanaugh, MS, Geoffrey Hugo, PhD, Cliff G. Robinson, MD, and Michael C. Roach, MD

Semin Radiat Oncol 29:274–283

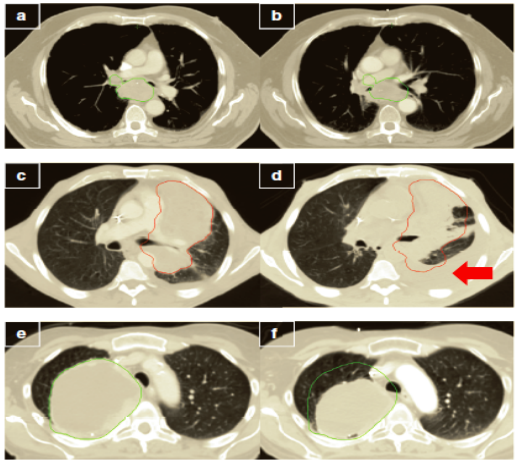

Figure 1 Common anatomical changes, including geometric displacement (a, b), pleural effusion (c,d), and tumor regression (e, f), in 3 patients with NSCLC undergoing definitive chemoradiation therapy that would require consideration for adaptive radiotherapy. The gross tumor volume contour defined on the initial planning CT is delineated in each image, with the midtreatment patient anatomy illustrated by images b, d, and f. The effusion is shown by the arrow in (d).

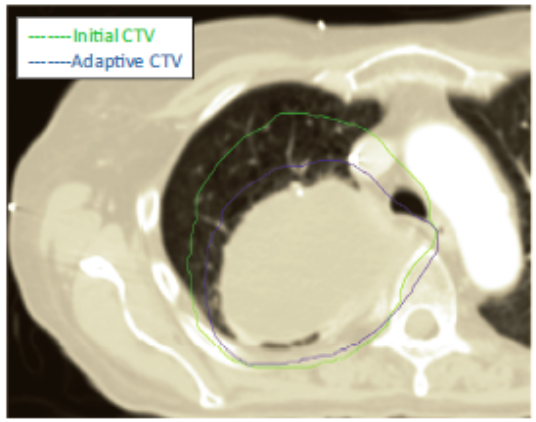

Figure 2 A midtreatment CT scan illustrating substantial tumor regression. The volume between the initial CTV and adaptive CTV represents regions that may still contain subclinical disease.

Conclusions

The role of adaptive radiotherapy in the treatment of locally advanced stage III lung cancer offers the potential to improve therapeutic outcomes, whether through dose escalation or organ-at-risk sparing. Numerous smaller studies have investigated several methods in applying ART to the lung cancer patient population and results from large prospective clinical trials will hopefully provide consensus on the method, utility, and efficacy of implementing ART in a clinical setting. Additional development into standardization and automation of the ART workflow, specifically in identifying when ART is warranted and in reducing the manual clinical effort needed to produce an adaptive plan, will be paramount making it feasible for the broader radiation therapy community.

Tumori del torace

Constraints di dose

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2020
Non-Small Cell Lung Cancer

NCCN Guidelines Index
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Discussion

Table 5. Normal Tissue Dose-Volume Constraints for Conventionally Fractionated RT with Concurrent Chemotherapy*

OAR	Constraints in 30–35 fractions
Spinal cord	Max ≤50 Gy
Lung	V20 ≤35%–40%†; MLD ≤20 Gy
Heart	V50 ≤25%; Mean ≤20 Gy
Esophagus	Mean ≤34 Gy; Max ≤105% of prescription dose; V60 ≤17%; contralateral sparing is desirable
Brachial plexus	Median dose ≤69 Gy

HIGHLIGHTS IN RADIOTERAPIA
I lavori del 2019 che modificano la pratica clinica
in radioterapia esclusiva ed associazione farmacologica
Roma, Centro Studi dell'Area Radiologica "Il Cardello"
23 gennaio 2020

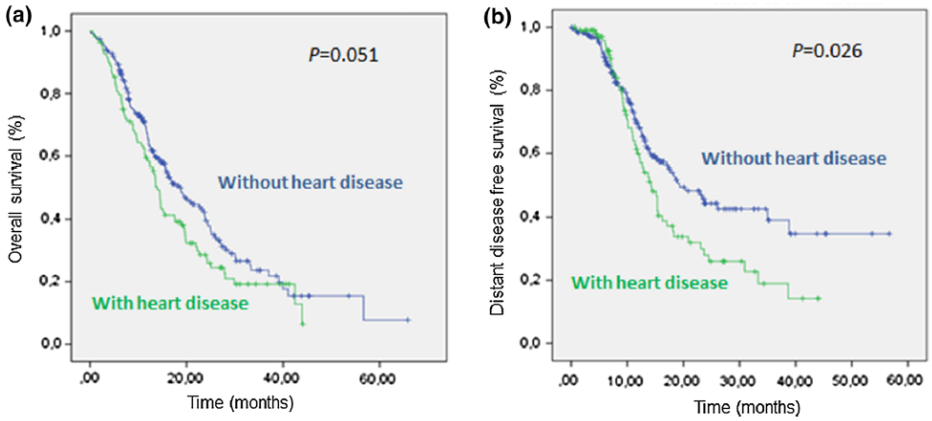
Tumori del torace

NSCLC and Heart

Clin Transl Oncol. 2019 Sep;21(9):1220-1230. doi: 10.1007/s12094-019-02047-5. Epub 2019 Jan 24.

Cardiovascular disease and survival in non-small cell lung cancer: a multicenter prospective assessment.

Herrero Rivera D[1], Nieto-Guerrero Gómez JM[2], Cacicedo Fernández de Bobadilla J[3], Delgado D[2], Rivin Del Campo E[4], Praena-Fernández JM[5], Bernabé Caro R[1], Ortiz Gordillo MJ[2,6], Fernández Fernández MC[2], Lopez Guerra JL[7,8].



- 345 NSCLC pts from 2013 to 2017
- 32% with baseline heart disease (HD), 43% hypertension, 13% tromboembolism (VTE)
- 84% were treated with platinum-based chemotherapy (CT), 87% received thoracic RT (60 Gy)

CONCLUSIONS

HD and VTE are associated with a higher risk of mortality and distant metastasis in NSCLC patients. Chronic inflammation associated with CVDs could be an additional pathophysiologic factor in the development of distant metastasis

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HIGHLIGHTS IN RADIOTERAPIA
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Tumori del torace

Cardiac Toxicity

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 73, NO. 23, 2019

Cardiac Radiation Dose, Cardiac Disease, and Mortality in Patients With Lung Cancer

Katelyn M. Atkins, MD, PhD,[a] Bhupendra Rawal, MS,[b] Tafadzwa L. Chaunzwa, BS,[c,d] Nayan Lamba, BA,[e] Danielle S. Bitterman, MD,[a] Christopher L. Williams, PhD,[d] David E. Kozono, MD, PhD,[d] Elizabeth H. Baldini, MD, MPH,[d] Aileen B. Chen, MD, MPP,[d] Paul L. Nguyen, MD,[d] Anthony V. D'Amico, MD, PhD,[d] Anju Nohria, MD,[f] Udo Hoffmann, MD,[g] Hugo J.W.L. Aerts, PhD,[d,h] Raymond H. Mak, MD[d]

- Analisi retrospettiva su 748 pazienti con NSCLC in stadio II–III sottoposti a RT toracica (66 Gy) e una dose cardiaca mediana (MHD) di 12,3 Gy.
- Follow-up mediano di 20,4 mesi.

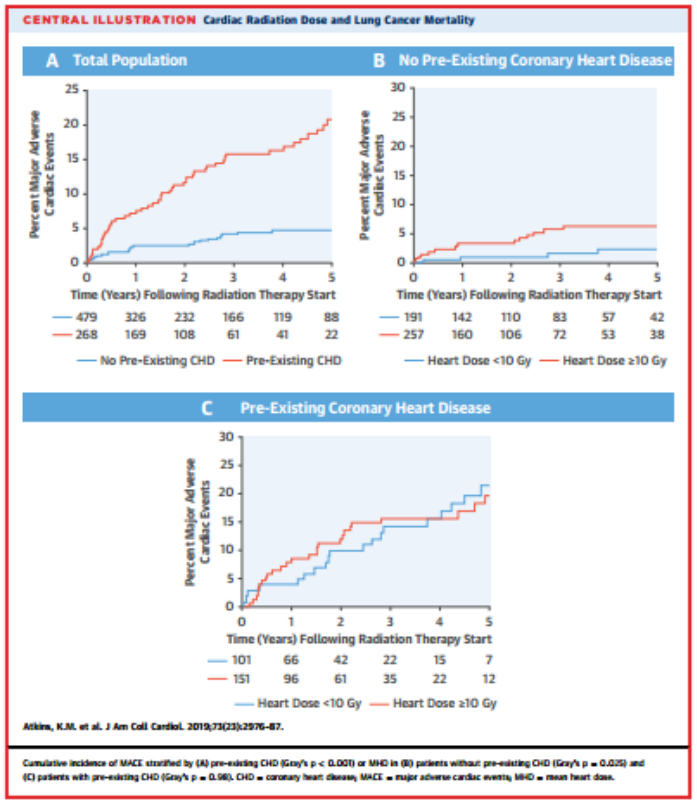
BACKGROUND Radiotherapy-associated cardiac toxicity studies in patients with locally advanced non-small cell lung cancer (NSCLC) have been limited by small sample size and nonvalidated cardiac endpoints.

OBJECTIVES The purpose of this analysis was to ascertain whether cardiac radiation dose is a predictor of major adverse cardiac events (MACE) and all-cause mortality (ACM).

METHODS This retrospective analysis included 748 consecutive locally advanced NSCLC patients treated with thoracic radiotherapy. Fine and Gray and Cox regressions were used to identify predictors for MACE and ACM, adjusting for lung cancer and cardiovascular prognostic factors, including pre-existing coronary heart disease (CHD).

Tumori del torace

Cardiac Toxicity



- Il 10,3% dei pazienti ha sviluppato ≥1 MACE (major cardiac adverse event), evento più probabile nei pazienti positivi per coronaropatie (coronary heart disease, CHD; 18,7% vs. 5,6%; P> 0,0001)
- Nei pazienti CHD-negativi il trattamento con MHD ≥10 Gy rispetto a <10 Gy era associato a un rischio signicativamente maggiore di MACE (HR: 3,01; P=0,025) e di mortalità per qualunque causa (HR: 1,34; P=0,014).

La MHD è un predittore indipendente di MACE e di mortalità per qualunque causa entro 2 anni dalla radioterapia per NSCLC

Constraints:
MHD< 15 Gy V50< 25% V5≤ 60%

Key points

- NSCLC - Early Stages
- NSCLC – Locally advanced
- NSCLC - Advanced disease
- Tecnica radioterapica – Tossicità
- SCLC
- Mesotelioma pleurico

HIGHLIGHTS IN RADIOTERAPIA
I lavori del 2019 che modificano la pratica clinica
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Roma, Centro Studi dell'Area Radiologica "Il Cardello"
23 gennaio 2020

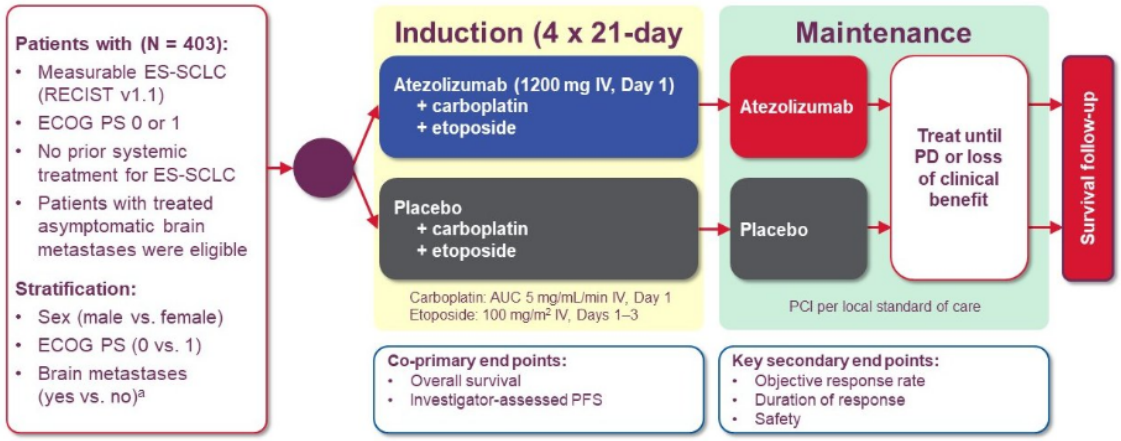
Tumori del torace

SCLC- Atezolizumab nell'ED

2019 ASCO ANNUAL MEETING

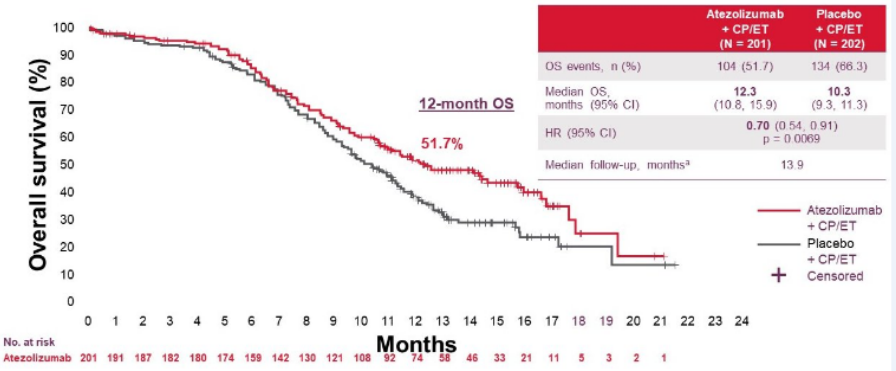
BARCELONA 2019 ESMO congress

IMpower133: Global Phase 1/3, double-blind, randomized, placebo-controlled trial evaluated atezolizumab + carboplatin + etoposide in 1L ES-SCLC



[a] Only patients with treated brain metastases were eligible. ECOG PS, Eastern Cooperative Oncology Group Performance Status; IV, intravenous; PCI, prophylactic cranial irradiation; PD, progressive disease; PFS, progression-free survival; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors.

Overall survival



	Atezolizumab + CP/ET (N = 201)	Placebo + CP/ET (N = 202)
OS events, n (%)	104 (51.7)	134 (66.3)
Median OS, months (95% CI)	12.3 (10.8, 15.9)	10.3 (9.3, 11.3)
HR (95% CI)	0.70 (0.54, 0.91) p = 0.0069	
Median follow-up, months[a]	13.9	

[a] Clinical data cutoff date: April 24, 2018, 11 months after the last patient was enrolled. CI, confidence interval; HR, hazard ratio; CP/ET, carboplatin + etoposide.

Patients alive at 18 months: 34% versus 21%

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Tumori del torace

SCLC- Durvalumab nell'ED

Lancet. 2019 Oct 4. pii: S0140-6736(19)32222-6. doi: 10.1016/S0140-6736(19)32222-6. [Epub ahead of print]

Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial.

Paz-Ares L[1], Dvorkin M[2], Chen Y[3], Reinmuth N[4], Hotta K[5], Trukhin D[6], Statsenko G[7], Hochmair MJ[8], Özgüroğlu M[9], Ji JH[10], Voitko O[11], Poltoratskiy A[12], Ponce S[13], Verderame F[14], Havel L[15], Bondarenko I[16], Kazarnowicz A[17], Losonczy G[18], Conev NV[19], Armstrong J[20], Byrne N[20], Shire N[21], Jiang H[21], Goldman JW[22]; CASPIAN investigators.

IASLC 2019 World Conference on Lung Cancer
September 7-10, 2019 | Barcelona, Spain

Randomised, open-label, phase 3 trial: 209 sites across 23 countries (CASPIAN)
Untreated ES-SCLC: durvalumab plus platinum–etoposide (268 pts) vs platinum–etoposide alone (269 pts)

durvalumab 1500 mg concomitant and in maintenance

Durvalumab plus platinum–etoposide was associated with a significant improvement in:
median overall survival: 13,0 vs 10,3 months (HR 0·73 (95% CI 0·59–0·91; p=0·0047)
patients alive at 18 months: 34% (26·9–41·0) versus 25% (18·4–31·6)

Tumori del torace

SCLC- Durvalumab nell'ED

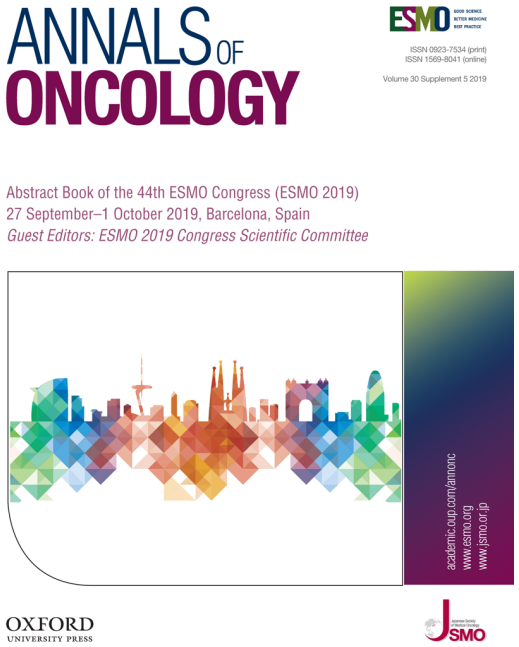
LBA89 **PD-L1 expression, patterns of progression and patient-reported outcomes (PROs) with durvalumab plus platinum-etoposide in ES-SCLC: Results from CASPIAN**

L. Paz-Ares[1], J.W. Goldman[2], M.C. Garassino[3], M. Dvorkin[4], D. Trukhin[5], G. Statsenko[6], K. Hotta[7], J.H. Ji[8], M.J. Hochmair[9], O. Voitko[10], L. Havel[11], A. Poltoratskiy[12], G. Losonczy[13], N. Reinmuth[14], Y. Shrestha[15], N. Patel[16], H. Mann[17], H. Jiang[18], M. Özgüroğlu[19], Y. Chen[20]

Una minoranza di pazienti con ES-SCLC ottiene un beneficio clinicamente rilevante dall'immunoterapia

L'espressione di PD-L1 è bassa e non ha alcun effetto significativo sugli esiti clinici (no biomarkers)

Trattare tutti i pazienti è costoso rispetto ai benefici ottenuti ed espone i pazienti a tossicità inutili



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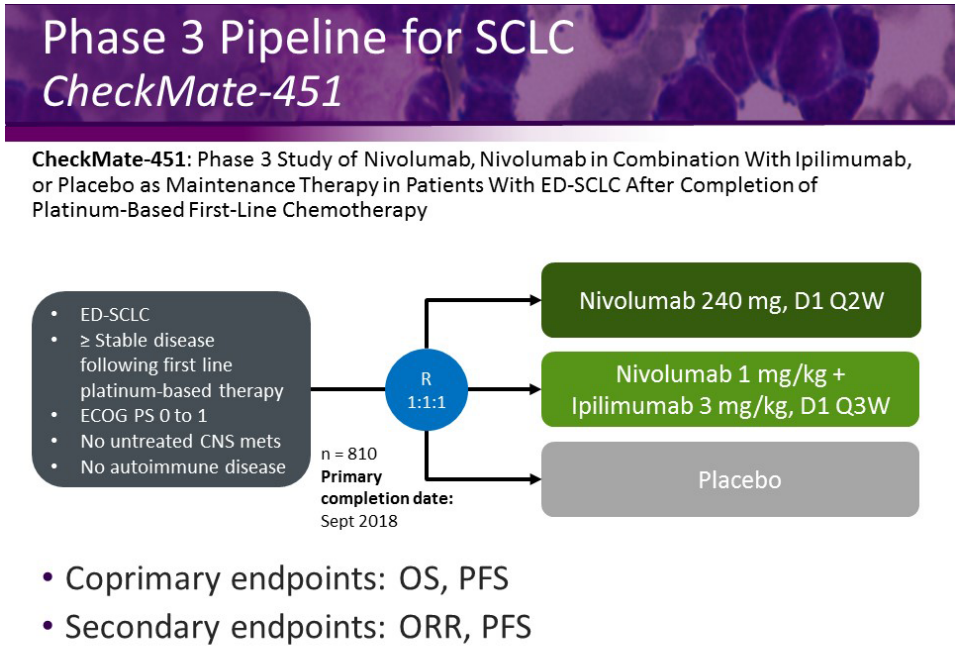
SCLC- Nivolumab-Ipilimumab nell'ED



834 pazienti senza progressione dopo 4 cicli di chemioterapia sono stati randomizzati alla terapia combinata di **mantenimento** con nivolumab e ipilimumab, o a nivolumab in monoterapia, o al placebo

L'endpoint primario di sopravvivenza complessiva non viene significativamente prolungato

Tumori del torace

SCLC - PCI nell'ED

JAMA Network | Open

Research Letter | Oncology

Evolving Practice Patterns in the Use of Prophylactic Cranial Irradiation for Extensive-Stage Small Cell Lung Cancer

Olsi Gjyshi, MD, PhD; Ethan B. Ludmir, MD; Todd A. Pezzi, MD, MBA; David Boyce-Fappiano, MD; Amy E. Dursteler, MD; Timur Mitin, MD, PhD; Steven H. Lin, MD, PhD

Lancet Oncol. 2017 May;18(5):663-671. doi: 10.1016/S1470-2045(17)30230-9. Epub 2017 Mar 23.

Prophylactic cranial irradiation versus observation in patients with extensive-disease small-cell lung cancer: a multicentre, randomised, open-label, phase 3 trial.

Takahashi T[1], Yamanaka T[2], Seto T[3], Harada H[4], Nokihara H[5], Saka H[6], Nishio M[7], Kaneda H[8], Takayama K[9], Ishimoto O[10], Takeda K[11], Yoshioka H[12], Tachihara M[13], Sakai H[14], Goto K[15], Yamamoto N[16].

Linee Guida NCCN: **equivalenza tra la sorveglianza con RM e PCI nell'ES-SCLC**

Survey ASTRO (569 su 3851 soci) sull'uso di PCI conseguente allo studio Takahashi, Lancet Oncol. 2017

L'uso di PCI tra i medici che conoscevano lo studio è diminuito dal 72% al 44%(pre vs post-pubblicazione)

Il tasso di continuazione dell'uso di PCI era dell'85% tra i medici che non conoscevano lo studio del 2017

- **il 47% dei rispondenti arruolerebbe pazienti affetti da SCLC in stadio limitato ed ES-SCLC**;
- il 15% arruolerebbe solo pazienti affetti da SCLC in stadio limitato;
- il 20% arruolerebbe solo pazienti affetti da ES-SCLC

Key points

- NSCLC - Early Stages
- NSCLC – Locally advanced
- NSCLC - Advanced disease
- Tecnica radioterapica – Tossicità
- SCLC
- Mesotelioma pleurico

Tumori del torace

Pleural Mesothelioma – Role of Radiotherapy

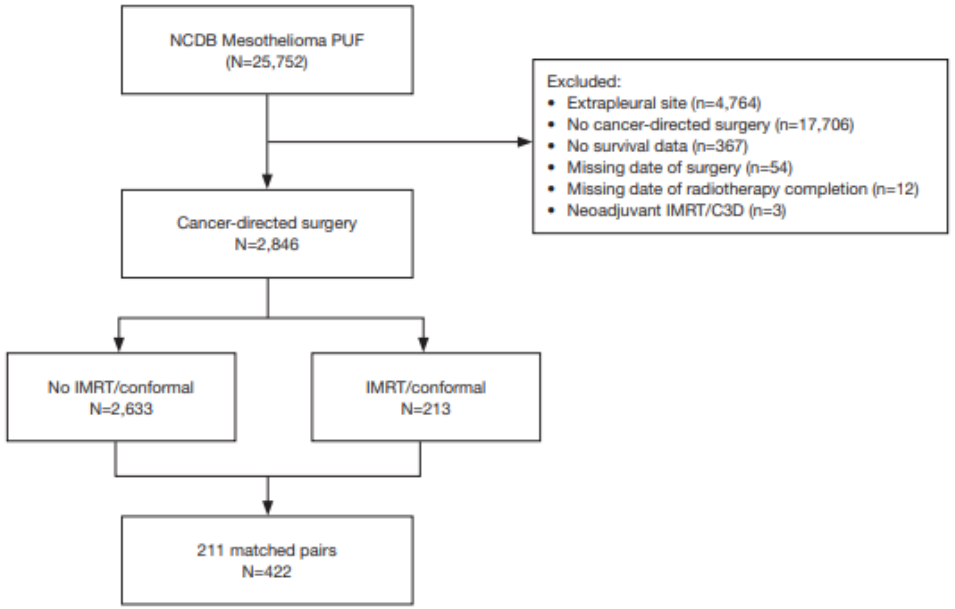
Journal of Thoracic Disease, Vol 11, No 4 April 2019

Original Article

Defining the role of adjuvant radiotherapy for malignant pleural mesothelioma: a propensity-matched landmark analysis of the National Cancer Database

David B. Nelson[1#], David C. Rice[1#], Kyle G. Mitchell[1], Anne S. Tsao[2], Ara A. Vaporciyan[1], Mara B. Antonoff[1], Wayne L. Hofstetter[1], Garrett L. Walsh[1], Stephen G. Swisher[1], Jack A. Roth[1], Daniel R. Gomez[3], Reza J. Mehran[1#], Boris Sepesi[1#]

[1]Department of Thoracic and Cardiovascular Surgery, [2]Department of Thoracic/Head and Neck Medical Oncology, [3]Department of Radiation Oncology, The University of Texas MD Anderson Cancer, Houston, TX, USA



- 2,846 patients were identified with MPM who received cancer-directed surgery between 2004-2013
- Adjuvant radiation included IMRT or 3D-CRT

Tumori del torace

Pleural Mesothelioma – Role of Radiotherapy

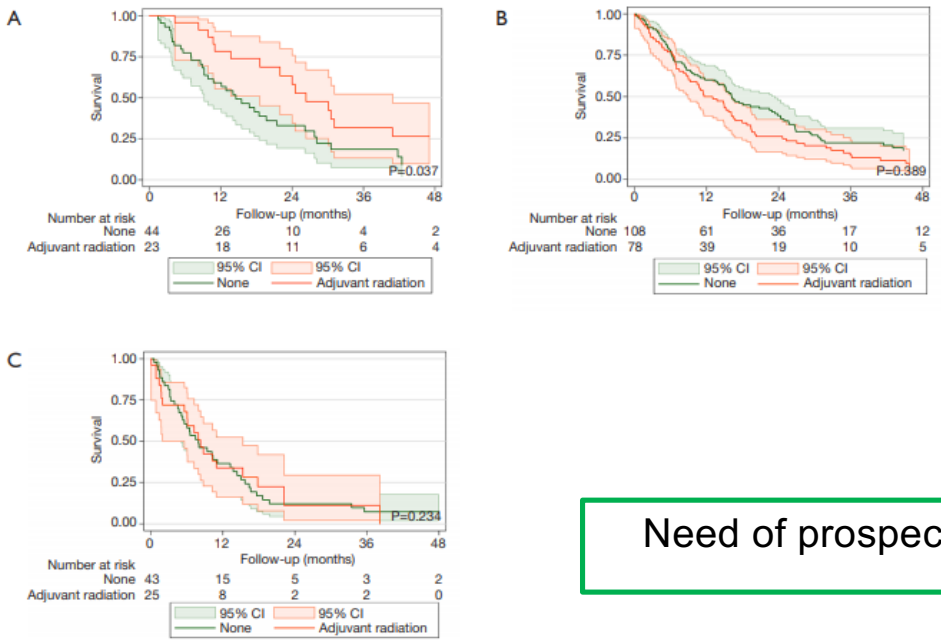


Figure 2 Overall survival after adjuvant radiation: propensity matched landmark analysis. (A) Stages I–II; (B) stage III; (C) stage IV.

- Adjuvant radiation was associated with improved survival for stage I-II pts [hazard ratio (HR) 0.52, P=0.035], whereas no similar effect was observed for those who were stage III or IV (P=0.190 and P=0.562, respectively).
- Sarcomatoid histology (HR 1.80, P=0.018) and stage IV disease (HR 1.65, P=0.033) were associated with worse survival.

Need of prospective trials to investigate utility of multimodality therapy

Nelson et al, J Thorac Dis 2019

Pleural Mesothelioma – Role of Radiotherapy

Radical Hemi-thoracic Radiotherapy vs. Palliative Radiotherapy for Malignant Pleural Mesothelioma

- Phase 3 study, 108 pts were randomized
- Radical hemithoracic radiotherapy (RHR) with IMRT and PET-guidance, to deliver up to 50 to 60 Gy, in patients undergoing non-radical lung-sparing surgery and chemotherapy
- Total mean lung dose < 22 Gy
- The intention-to-treat analysis showed a 2- year OS rate of 58% in the RHR arm vs. 28% in the PR arm (p=0.003)
- RHR doubles survival compared with palliative radiotherapy in patients with malignant pleural mesothelioma (MPM)
- Toxicity: G 3-4 pneumonitis in 5 pts

[Minatel E, Trovo M et al, ESTRO 38 – 2019, *Abstract OC-0500]*

Tumori del torace

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