The Silver Tsunami

Percentage of the World Population Over 65, 1950-2050

Source: UN World Population Prospect, 2008
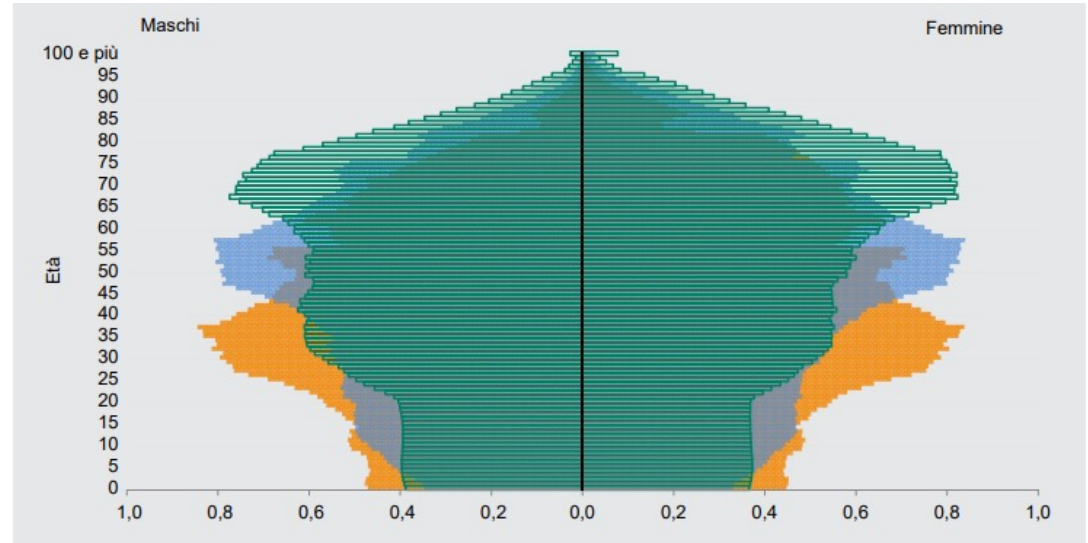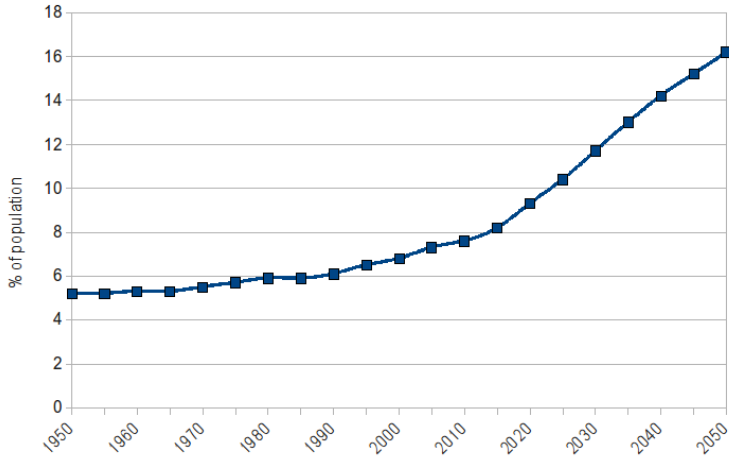
Fonte: Istat, Popolazione per sesso, età e stato civile e Previsioni della popolazione e delle famiglie, base 1.1.2021, scenario nazionale *ad hoc*
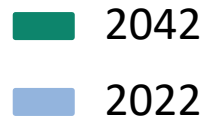
2042

2022

Over 65:
2022 - 14 milions (24%)
2042 - 19 milions (34%)

Lung cancer incidence rates

According to the most recent statistics in the US (SEER 2016–2020),
the median age at diagnosis is **71** years

Data source(s): SEER Incidence Data, November 2022

Lung cancer incidence rates

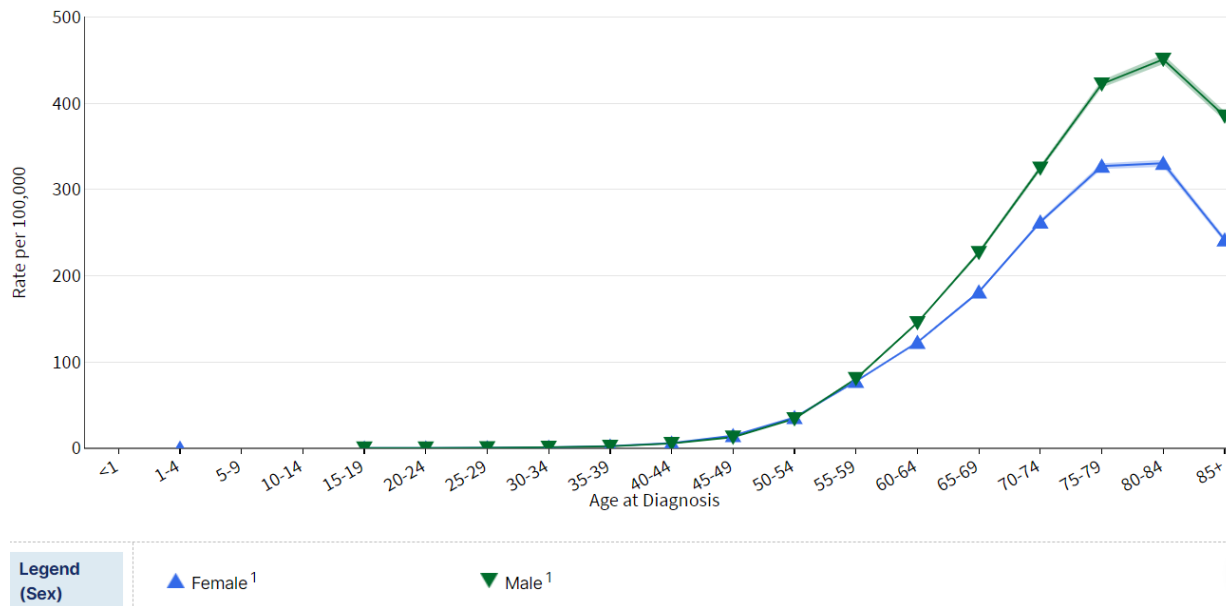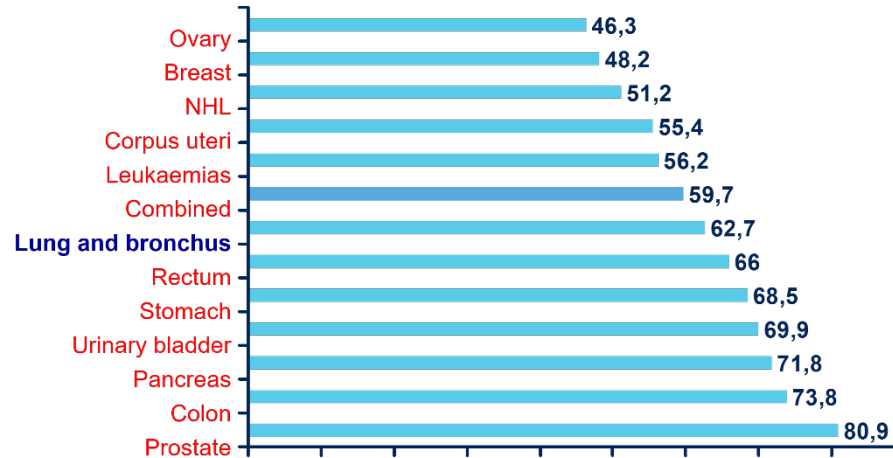
Proportion of patients aged >65 years with selected tumour (%)

Ovary — 46,3
Breast — 48,2
NHL — 51,2
Corpus uteri — 55,4
Leukaemias — 56,2
Combined — 59,7
Lung and bronchus — 62,7
Rectum — 66
Stomach — 68,5
Urinary bladder — 69,9
Pancreas — 71,8
Colon — 73,8
Prostate — 80,9

More then 40% of lung cancer patients over 70 years

Yancik R, Cancer

Stage distribution by age
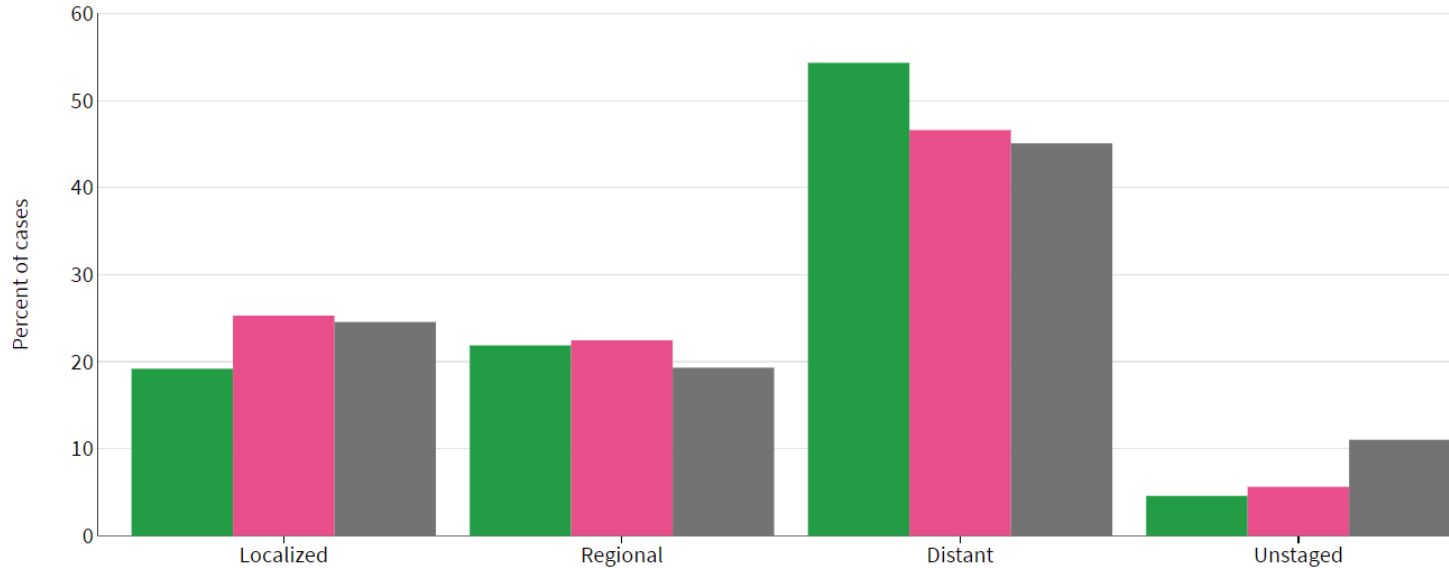
Locally advanced in about 20% of patients

Data source(s): SEER Incidence Data, November 2022

Heterogeneity of LA-NSCLC

By pathology…

Large cell carcinoma

Adenocarcinoma

EGFR
ALK
ROS-1
MET

Squamous cell carcinoma

PD-L1

Heterogeneity of LA-NSCLC

By stage…

ALL STAGE IIIA

De Leyn P, JTO 2009

Heterogeneity of LA-NSCLC

By stage and survival rates...

TABLE 1 The TNM staging system, version 8, demonstrating the heterogeneity of stage III

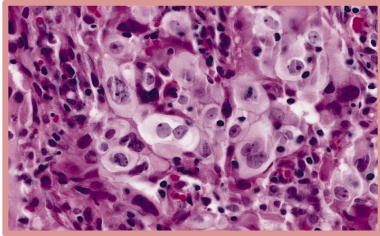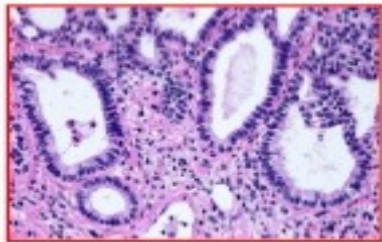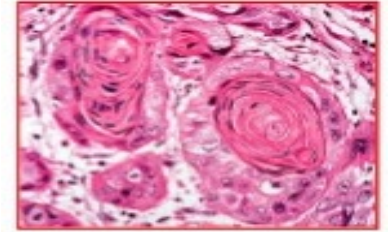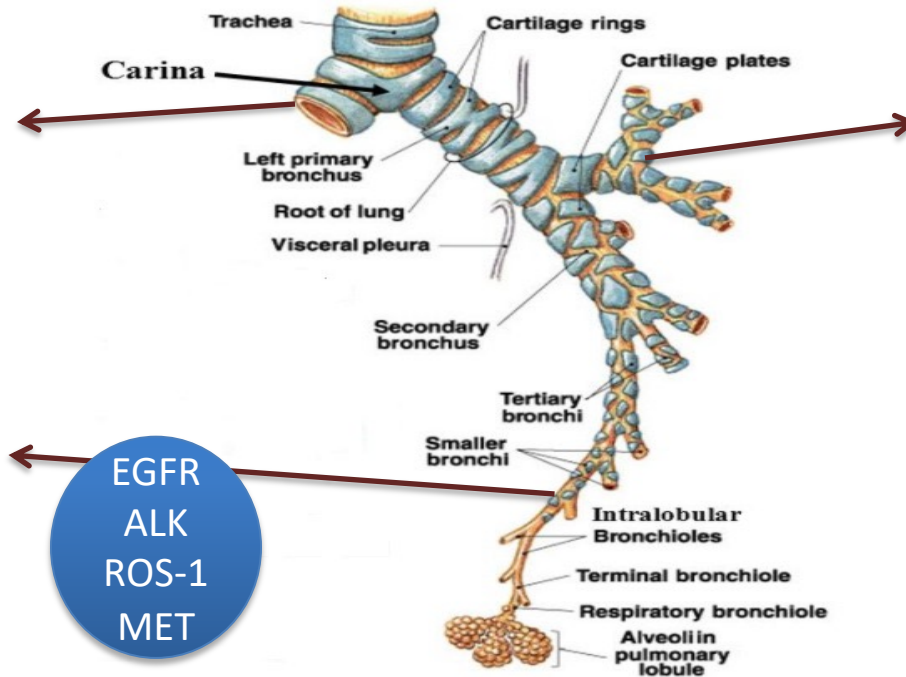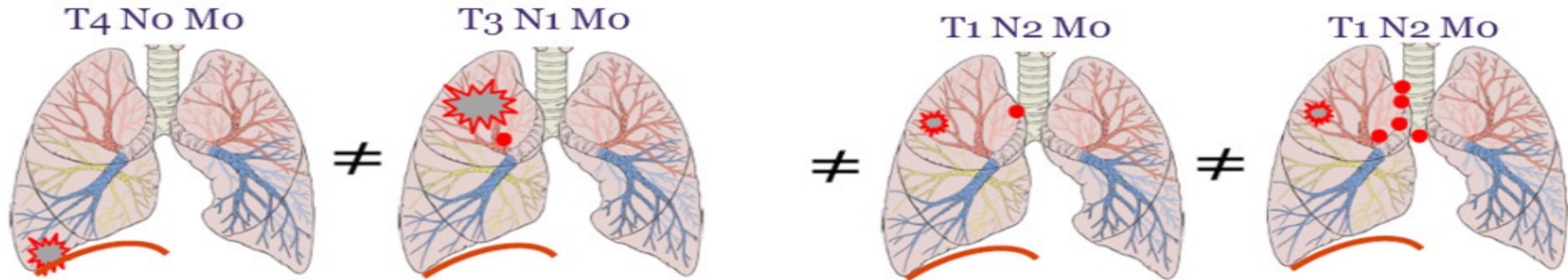| T/M and label	Description	N0	N1	N2	N3
T1					
T1a	≤1 cm	I A1	II B	III A	III B
T1b	>1–2 cm	I A2	II B	III A	III B
T1c	>2–3 cm	I A3	II B	III A	III B
T2					
T2a	Central, visceral and pleura	I B	II B	III A	III B
	>3–4 m	I B	II B	III A	III B
T2b	>4–5 cm	II A	II B	III A	III B
T3	>5–7 cm	II B	III A	III B	III C
	Invasive	II B	III A	III B	III C
	Satellite	II B	III A	III B	III C
T4	>7 cm	III A	III A	III B	III C
	Invasive	III A	III A	III B	III C
	Ipsilateral nodes	III A	III A	III B	III C
M1					
M1a	Contralateral nodes	IV A	IV A	IV A	IV A
	Pleura disseminated	IV A	IV A	IV A	IV A
M1b	Single	IV A	IV A	IV A	IV A
M1c	Multi	IV B	IV B	IV B	IV B

5-years OS

	Clinical stage	Pathological stage
I A1	92	90
I A2	83	85
I A3	77	80
I B	68	73
II A	60	65
II B	53	56
III A	36	41
III B	26	24
III C	13	12
IV A	10	
IV B	0	

Detterbeck FC, Chest 2017

BOLOGNA, 27-29 OTTOBRE 2023
PALAZZO DEI CONGRESSI

Associazione Italiana
Radioterapia e Oncologia clinica

Heterogeneity of LA-NSCLC

By patient…

Performance status
Co-morbidities
Cardio-pulmonary function
Compliance and family support

Geriatric Assessement

Functional Status
- Performance status (PS)
- Activities of daily living (ADL)
- Instrumental activities of daily living (IADL)

Comorbidity
- Comorbidity scales (Charlson; CIRS)

QoL
- Disease-specific questionnaires

Cognitive
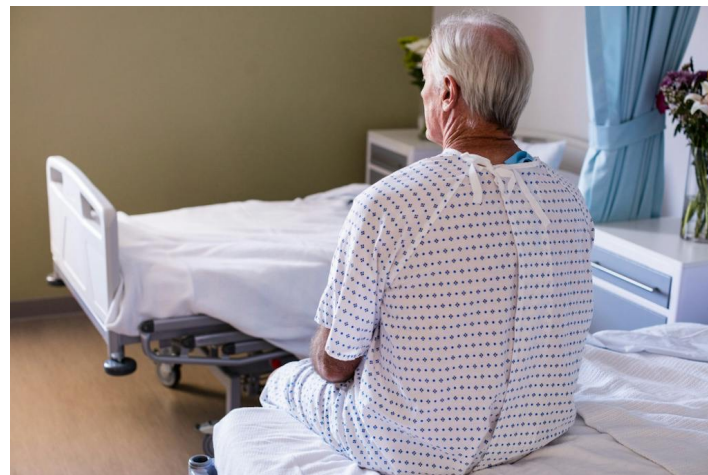- Folstein Minimental Status

Emotions
- Geriatric Depression Scale (GDS)
- Mini Mental State Examination
- MOCA

Social support network
Polypharmacy
Nutrition
- Mini Nutritional Assessment

FIT
VULNERABLE/FRAIL
UNFIT

Comprehensive Geriatric Assessement

Use of a Comprehensive Geriatric Assessment for the Management of Elderly Patients With Advanced Non–Small-Cell Lung Cancer: The Phase III Randomized ESOGIA-GFPC-GECP 08-02 Study

Romain Corre, Laurent Greillier, Hervé Le Caër, Clarisse Audigier-Valette, Nathalie Baize, Henri Bérard, Lionel Falchero, Isabelle Monnet, Eric Dansin, Alain Vergnenègre, Marie Marcq, Chantal Decroisette, Jean-Bernard Auliac, Suzanna Bota, Régine Lamy, Bartomeu Massuti, Cécile Dujon, Maurice Pérol, Jean-Pierre Daurès, Renaud Descourt, Hervé Léna, Carine Plassot, and Christos Chouaïd
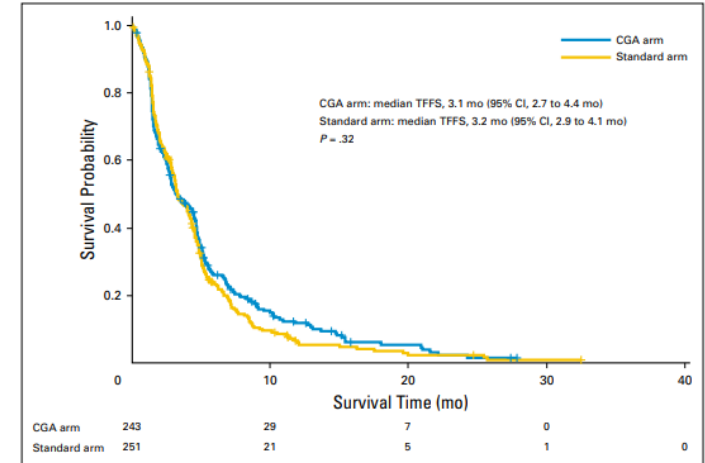
In elderly patients with advanced NSCLC, treatment allocation on the basis of CGA failed to improve the TFFS or OS but slightly reduced treatment toxicity

Corre R, et al., J Clin Oncol 2016

Comprehensive Geriatric Assessement

Evaluation of geriatric assessment and management on the toxic effects of cancer treatment (GAP70+): a cluster-randomised study

Supriya G Mohile, Mostafa R Mohamed, Huiwen Xu, Eva Culakova, Kah Poh Loh, Allison Magnuson, Marie A Flannery, Spencer Obrecht, Nikesha Gilmore, Erika Ramsdale, Richard F Dunne, Tanya Wildes, Sandy Plumb, Amita Patil, Megan Wells, Lisa Lowenstein, Michelle Janelsins, Karen Mustian, Judith O Hopkins, Jeffrey Berenberg, Navin Anthony, William Dale

(Lancet 2021)

Prospective randomized trial:

718 patients

Age ≥ 70 years (mean 77)

At least one altered geriatric parameter

Treated with chemotherapy

Primary outcome: G3-G4 toxicity

Secondary outcomes: treatment completion, quality of life

CGA
vs
no CGA

Associazione Italiana
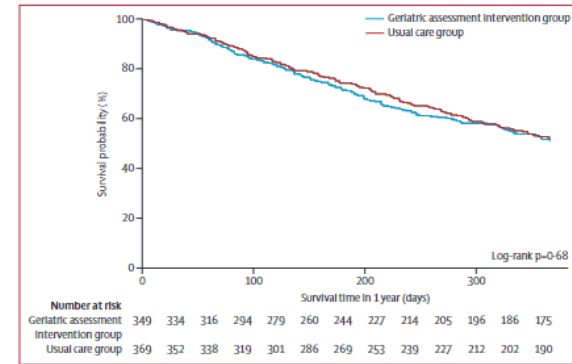Radioterapia e Oncologia clinica
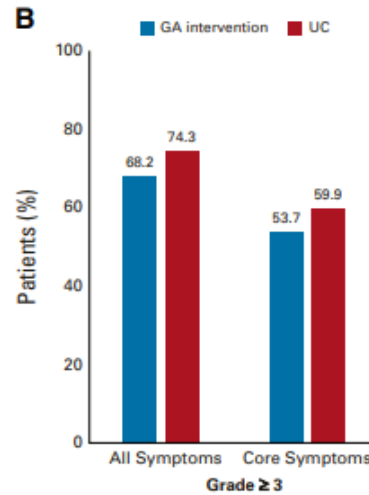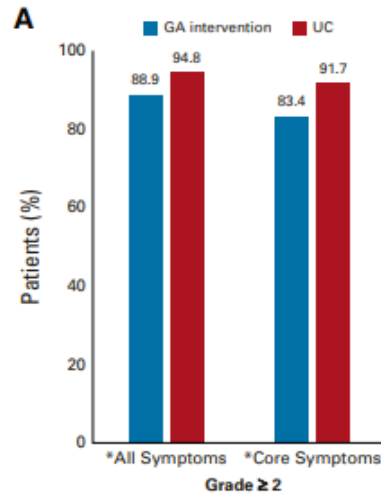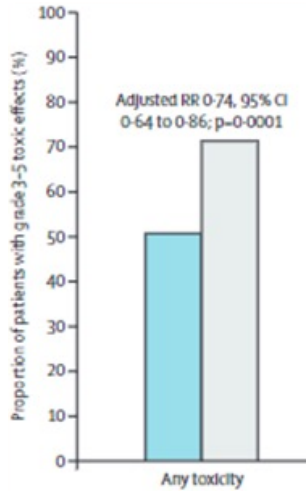
Comprehensive Geriatric Assessement

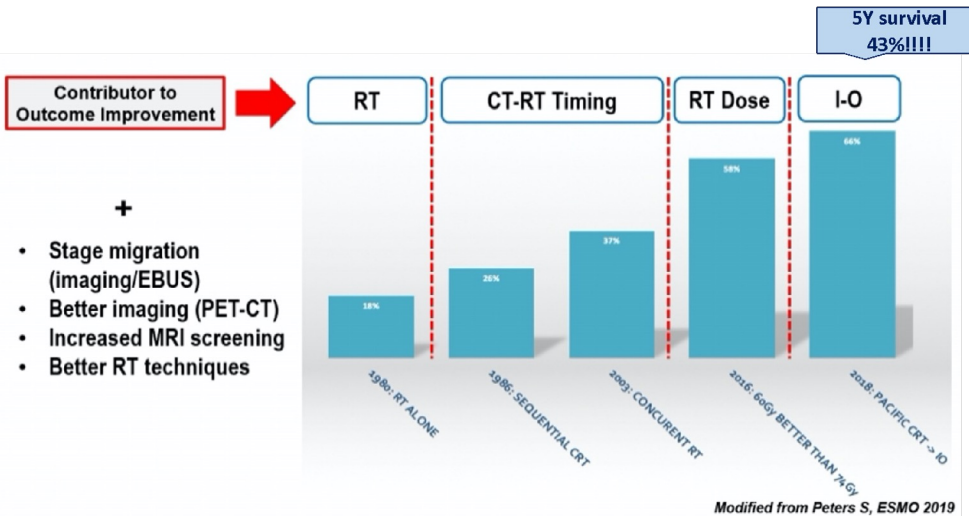Figure 4: Survival over 1 year by study group

A geriatric assessment intervention for older patients with advanced cancer reduced serious toxic effects from cancer treatment. No difference in OS.

Associazione Italiana
Radioterapia e Oncologia clinica

Screening Test: G8 questionnaire

	Items	Possible answers (score)
A	Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	0 : severe decrease in food intake
		1 : moderate decrease in food intake
		2 : no decrease in food intake
B	Weight loss during the last 3 months	0 : weight loss > 3 kg
		1 : does not know
		2 : weight loss between 1 and 3 kgs
		3 : no weight loss
C	Mobility	0 : bed or chair bound
		1 : able to get out of bed/chair but does not go out
		2 : goes out
E	Neuropsychological problems	0 : severe dementia or depression
		1 : mild dementia or depression
		2 : no psychological problems
F	Body Mass Index (BMI (weight in kg) / (height in m²)	0 : BMI < 19
		1 : BMI = 19 to BMI < 21
		2 : BMI = 21 to BMI < 23
		3 : BMI = 23 and > 23
H	Takes more than 3 medications per day	0 : yes
		1 : no
P	In comparison with other people of the same age, how does the patient consider his/her health status?	0 : not as good
		0.5 : does not know
		1 : as good
		2 : better
	Age	0 : >85
		1 : 80-85
		2 : <80
	TOTAL SCORE	**0 – 17**

If G8 total score > 14: Patient fit, no frailty risk

Treatment evolution pre-PACIFIC

5Y survival 43%!!!!

Contributor to Outcome Improvement → RT | CT-RT Timing | RT Dose | I-O

+
- Stage migration (imaging/EBUS)
- Better imaging (PET-CT)
- Increased MRI screening
- Better RT techniques

1980: RT ALONE (18%), 1986: SEQUENTIAL CRT (26%), 2003: CONCURENT RT (37%), 2016: 60Gy BETTER THAN 74Gy (58%), 2018: PACIFIC CRT → IO (66%)

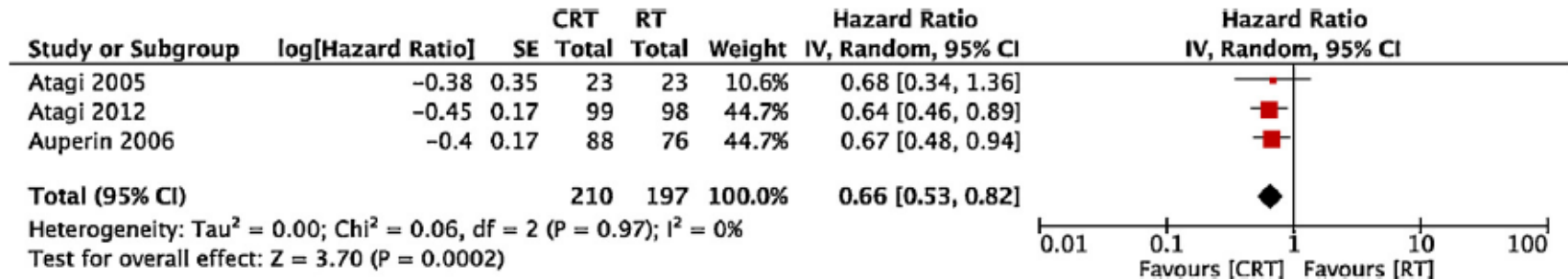Modified from Peters S, ESMO 2019

o   Sequential CT-RT > RT → **+ 3%** OS at 2y and 2% at 5y (HR 0.90) *[NSCLC Collaborative Group, BMJ 1995]*

Girard N, ESMO 2021
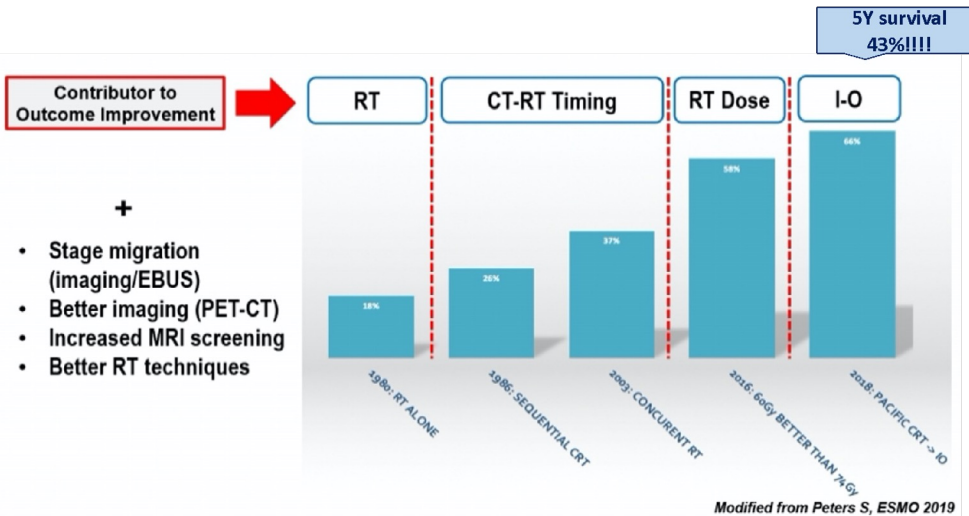
Meta-analysis CT-RT vs RT (elderly)

Chemoradiotherapy versus radiotherapy alone in elderly patients with stage III non-small cell lung cancer: A systematic review and meta-analysis

David E. Dawe [a,*], David Christiansen [a], Anand Swaminath [d], Peter M. Ellis [d], Janet Rothney [e], Rasheda Rabbani [c], Ahmed M. Abou-Setta [b,c], Ryan Zarychanski [a,b,c], Salaheddin M. Mahmud [b,c]

Study or Subgroup	log[Hazard Ratio]	SE	CRT Total	RT Total	Weight	Hazard Ratio IV, Random, 95% CI
Atagi 2005	−0.38	0.35	23	23	10.6%	0.68 [0.34, 1.36]
Atagi 2012	−0.45	0.17	99	98	44.7%	0.64 [0.46, 0.89]
Auperin 2006	−0.4	0.17	88	76	44.7%	0.67 [0.48, 0.94]
Total (95% CI)			210	197	100.0%	0.66 [0.53, 0.82]

Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.06, df = 2 (P = 0.97); I^2 = 0%
Test for overall effect: Z = 3.70 (P = 0.0002)

Dawe D, Lung Cancer 2016

Treatment evolution pre-PACIFIC

5Y survival 43%!!!!

Contributor to Outcome Improvement →

RT | CT-RT Timing | RT Dose | I-O

+
- Stage migration (imaging/EBUS)
- Better imaging (PET-CT)
- Increased MRI screening
- Better RT techniques

1980: RT ALONE | 1986: SEQUENTIAL CRT | 2003: CONCURRENT RT | 2016: 60Gy BETTER THAN 74Gy | 2018: PACIFIC CRT → IO

Modified from Peters S, ESMO 2019

- Sequential CT-RT > RT → **+ 3%** OS at 2y and 2% at 5y (HR 0.90) [NSCLC Collaborative Group, BMJ 1995]

- Concurrent CT-RT > Sequential → + 5.7% OS at 3y and **+ 4.5%** at 5y (HR 0.84) [Auperin et al, JCO 2010]

- Platinum-based CT 4 cycles

- No OS benefit from high dose RT [Bradley, Lancet 2015]

- No OS benefit integrating with biological agents

- No consolidation or maintenance CT after CT/RT

➢ **Concurrent CT/RT: 3-year OS about 30%**

Fit patients with PS 0 or 1, age < 70 or 75 years, without important comorbidities
[less than 50% of patients with unresectable stage III are eligible]

Girard N, ESMO 2021
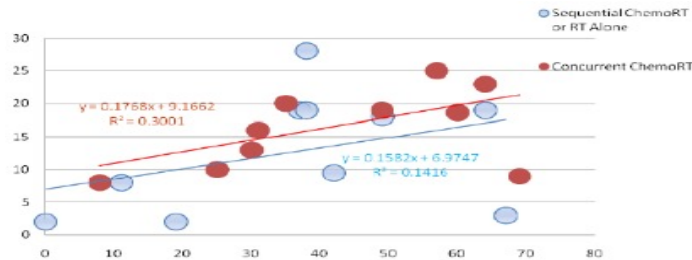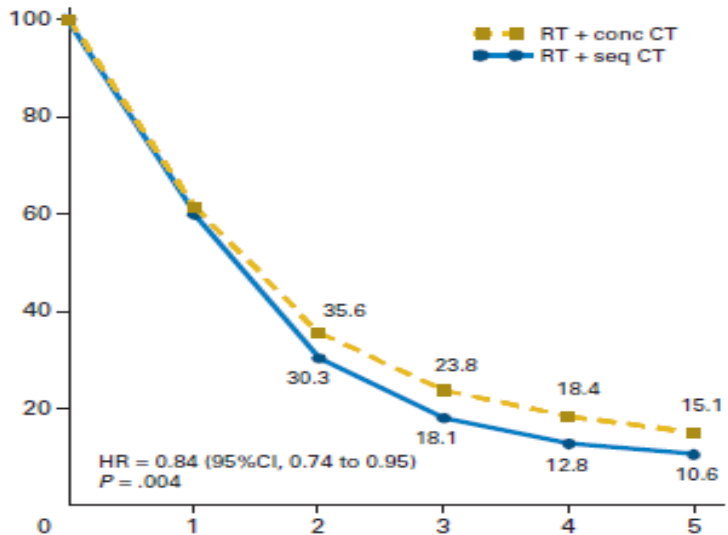
Meta-analysis CT-RT conc vs seq

HR = 0.84 (95%CI, 0.74 to 0.95)
P = .004

| | RT + conc CT |
| | RT + seq CT |

Table 2. Patient Characteristics

Characteristic	Concomitant Arm (n = 603)		Sequential Arm (n = 602)	
	No.	%	No.	%
Male sex	457	76	464	77
Median age, years	61.0		62.4	
Range	33-79		33-82	
< 60	273	45	246	41
60-64	114	19	111	18
65-69	140	23	130	22
≥ 70	76	13	113	19
Unknown	0		2	
Performance status				
0	309	52	297	50
1	278	46	293	49
2	13	2	9	1
Unknown	3		3	

y = 0.1768x + 9.1662
R² = 0.3001

y = 0.1582x + 6.9747
R² = 0.1416

○ Sequential ChemoRT or RT Alone
● Concurrent ChemoRT

Auperin A, JCO 2010

Sequential CT-RT

Concurrent systemic therapy with radiotherapy for the treatment of poor-risk patients with unresectable stage III non-small-cell lung cancer: a review of the literature

F. Cardenal[1*], E. Nadal[2], M. Jové[1] & C. Faivre-Finn[3]

- Only two phase III studies specifically including poor-risk patients have been published.
- There is an unmet need to develop well-designed clinical trials with tolerable combinations of systemic therapy and radiotherapy specifically tailored to this population.
- Such trials should incorporate careful comorbidity measurement and, in older adults, a validated geriatric assessment.

cancers

MDPI

Article

Elderly Patients with Locally Advanced and Unresectable Non-Small-Cell Lung Cancer May Benefit from Sequential Chemoradiotherapy

Magdalena Zaborowska-Szmit [1], Marta Olszyna-Serementa [1], Dariusz M. Kowalski [1], Sebastian Szmit [2,*] and Maciej Krzakowski [1]

Table 7. The key studies cited in the discussion.

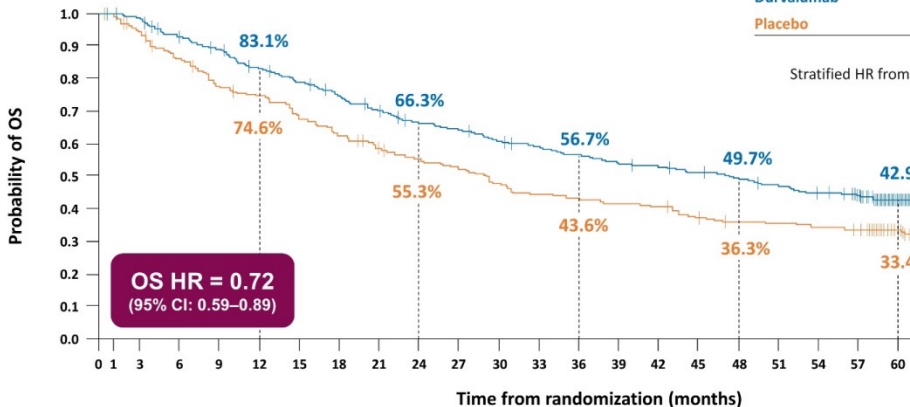| First Author of the Study	Design of the Study	Main Result or Conclusion
Atagi S. [9]	Patients: 71 years of age or older. Randomization: radiotherapy alone vs. chemoradiotherapy (concurrent use of carboplatin)	Terminated due to treatment-related deaths.
Stinchcombe T.E. [10]	16 phase II or III trials of concurrent chemoradiotherapy	Elderly patients under concurrent chemoradiotherapy had unbeneficial OS, higher rate of toxicity (including death).
Miller E.D. [11]	Patients: elderly (≥70 years old). Comparative effectiveness study of radiation therapy versus chemoradiation	Sequential chemotherapy and radiation resulted in a 9% mortality reduction in comparison to concurrent treatment.
Lee J.H. [22]	Patients: aged 70 years or more. Treatment: radical radiotherapy with or without chemotherapy	Simplified comorbidity score (SCS) was the independent prognostic factor for OS. Chemoradiotherapy was superior to radiotherapy in the fit elderly with SCS < 10.
Atagi S. [32]	Patients older than 70 years. Randomized, controlled, phase 3 trial: chemoradiotherapy (concurrent low-dose carboplatin) or radiotherapy alone,	Some elderly should be considered for chemoradiotherapy due to benefit of decreased mortality (HR = 0.68, $p = 0.0179$). Chemoradiotherapy was associated with more rate of grade 3–4 hematological toxicity.

Elderly population in RCT

Clinical study	Phase	Setting	Regimens	Main results	Overall population (n)	Elderly population (n, %)
Albain et al, 2009 [5]	III	Curative treatment of stage IIIA NSCLC	Chemo-RT induction followed by surgery versus definitive Chemo-RT	PFS benefit for surgery arm	429	63 (15.9)*
Eberhardt et al, 2015 [20]	III	Curative treatment of stage IIIA-B NSCLC	Chemo-RT induction followed by surgery versus definitive Chemo-RT	Equal PFS and OS between arms	246	116 (47)**
Pless et al, 2015 [34]	III	Curative treatment of stage IIIA (N2) NSCLC	Chemo-RT induction followed by surgery versus Neoadjuvant Chemotherapy followed by surgery	Radiotherapy did not add any benefit to induction chemotherapy followed by surgery	232	NA
Schild et al, 2003 [48]	III	Curative treatment of unresectable stage III NSCLC	Chemotherapy (Etoposide plus Cisplatin) and either RT once daily or split-course RT twice daily	Elderly patients have survival rates equivalent to younger individuals	244	63 (25.8)*
Antonia et al, 2018 [8]	III	Curative treatment of unresectable stage III NSCLC	Definitive Chemo-RT followed by durvalumab for 1 year or not	PFS and OS benefit for the durvalumab arm	713	322 (45.2)***

* over 70 years of age; ** over 60 years of age; *** over 65 years of age

PACIFIC: 5-years update

	No. of events/ total no. of patients (%)	Median OS (95% CI), months
Durvalumab	264/476 (55.5)	47.5 (38.1–52.9)
Placebo	155/237 (65.4)	29.1 (22.1–35.1)
	Stratified HR (95% CI): 0.72 (0.59–0.89)	

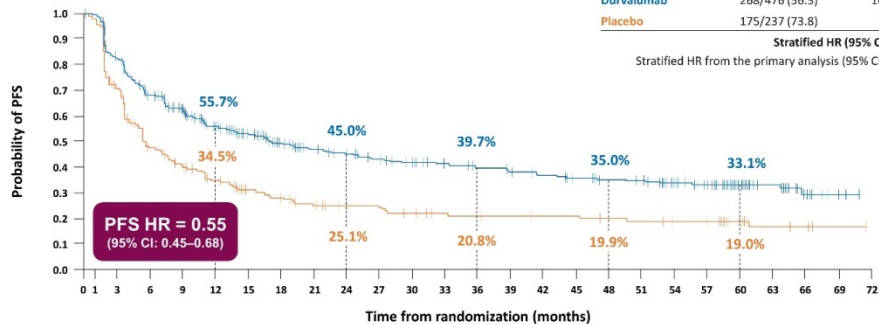Stratified HR from the primary analysis (95% CI):[1,2] 0.68 (0.53–0.87)

Spigel D et al, ASCO 2021

	No. of events/ total no. of patients (%)	Median PFS (95% CI), months
Durvalumab	268/476 (56.3)	16.9 (13.0–23.9)
Placebo	175/237 (73.8)	5.6 (4.8–7.7)
	Stratified HR (95% CI): 0.55 (0.45–0.68)	

Stratified HR from the primary analysis (95% CI):[1] 0.52 (0.42–0.65)

Pneumonitis or radiation pneumonitis with durvalumab was mostly low grade, and the incidence of G3 or 4 was well balanced between the groups (*3.4% durvalumab vs 2.6% placebo*)

PACIFIC: prognostic factors for OS

Age, years	≥ 65	210/322 (65.2)	< 65	209/391 (53.5)	1.30 (1.06 to 1.59)[a]
Disease stage[b]	IIIB	182/319 (57.1)	IIIA	227/377 (60.2)	1.03 (0.84 to 1.26)
Best response to prior treatment[c]	CR/PR	195/365 (53.4)	SD	216/338 (63.9)	0.88 (0.72 to 1.08)
Tumor histologic type	Squamous	205/326 (62.9)	Nonsquamous	214/387 (55.3)	1.28 (1.04 to 1.58)[a]
WHO PS	1[d]	233/365 (63.8)	0	186/348 (53.4)	1.23 (1.01 to 1.50)[a]
Prior platinum CT agent[e]	Cisplatin	215/395 (54.4)	Carboplatin	190/301 (63.1)	0.84 (0.69 to 1.03)
Race	Asian	95/192 (49.5)	White	310/494 (62.8)	0.63 (0.49 to 0.81)[a]
	Black or African American	7/14 (50.0)			0.81 (0.38 to 1.73)
	Other[f]	7/13 (53.8)			0.91 (0.41 to 1.99)
Sex	Male	304/500 (60.8)	Female	115/213 (54.0)	1.27 (1.01 to 1.61)[a]
Smoking status	Smoker	384/649 (59.2)	Nonsmoker	35/64 (54.7)	0.83 (0.56 to 1.22)
Time from CRT to random assignment, days	≥ 14	312/531 (58.8)	< 14	107/182 (58.8)	0.97 (0.77 to 1.22)
EGFR or ALK aberration status	Positive[g]	25/43 (58.1)	Negative	275/482 (57.1)	1.06 (0.69 to 1.64)
	Unknown	119/188 (63.3)			0.95 (0.73 to 1.23)
PD-L1 expression level	TC ≥ 25%	78/159 (49.1)	TC < 25%	175/292 (59.9)	0.82 (0.62 to 1.07)
	Unknown	166/262 (63.4)			1.19 (0.92 to 1.54)

Spigel D et al, ASCO 2021
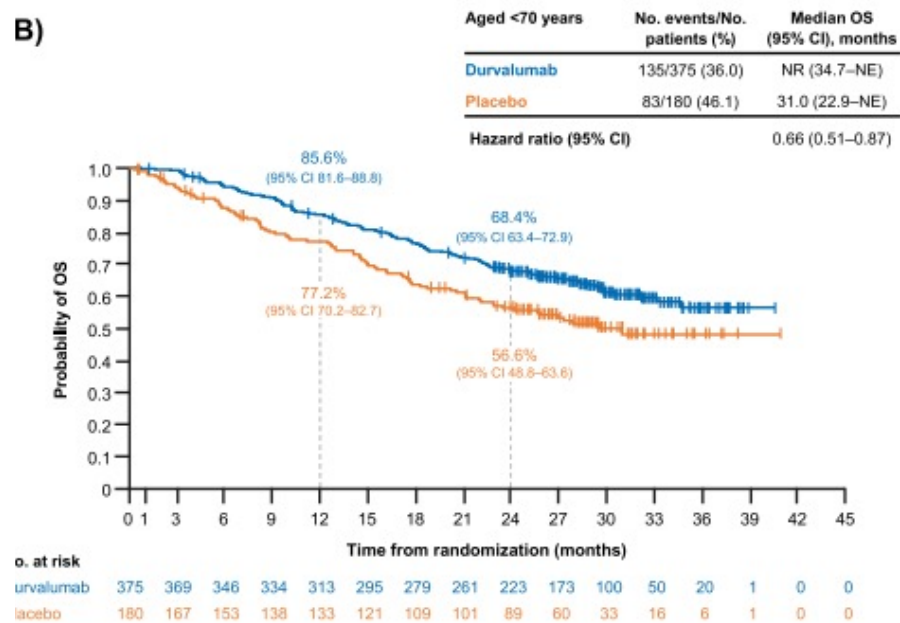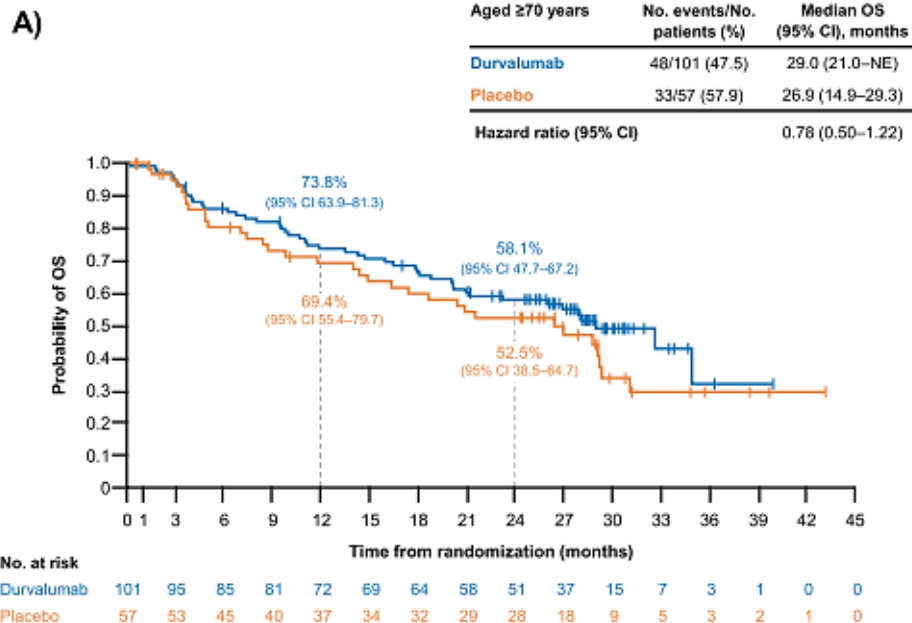
PACIFIC: elderly patients

Durvalumab After Concurrent Chemoradiotherapy in Elderly Patients With Unresectable Stage III Non–Small–Cell Lung Cancer (PACIFIC)

Exploratory analysis, between-treatment comparisons of PFS, OS, TTDM, ORR, the incidence of new lesions, post discontinuation disease-related anticancer therapy, safety, and PROs were performed in subgroups **of patients aged ≥70 and <70 years** at study baseline (a post-hoc age threshold)
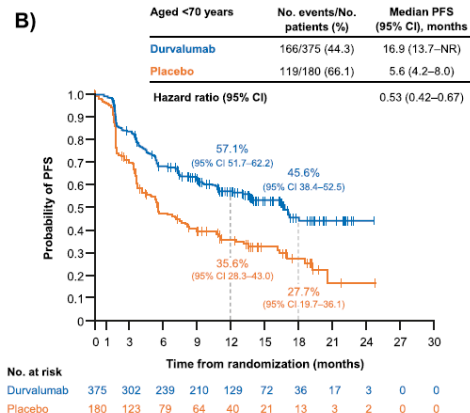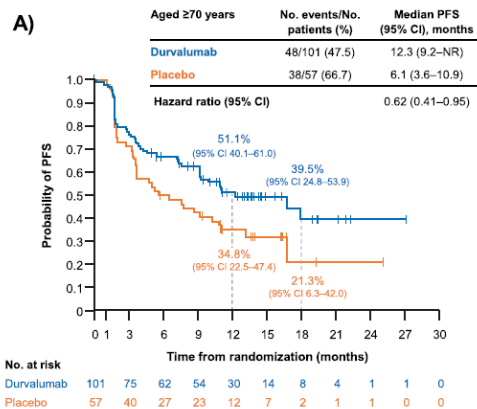
Socinski et al. *Clinical Lung Cancer 2021*

PACIFIC: elderly patients

Socinski et al. *Clinical Lung Cancer 2021*

PACIFIC: elderly patients

	Aged ≥70 Years		Aged <70 Years	
AE Category*	**Durvalumab (N = 101)**	**Placebo (N = 55)**	**Durvalumab (N = 374)**	**Placebo (N = 179)**
Any-grade all-causality AEs, n (%)	100 (99.0)	53 (96.4)	360 (96.3)	169 (94.4)
Grade 3/4	42 (41.6)	14 (25.5)	113 (30.2)	52 (29.1)
Outcome of death	11 (10.9)	7 (12.7)	10 (2.7)	8 (4.5)
Leading to discontinuation	22 (21.8)	9 (16.4)	51 (13.6)	14 (7.8)
Serious AEs, n (%)	43 (42.6)	14 (25.5)	95 (25.4)	40 (22.3)
Immune-mediated AEs, n (%)[a]	20 (19.8)	8 (14.5)	96 (25.7)	11 (6.1)
AEs leading to dose delay, n (%)	51 (50.5)	16 (29.1)	152 (40.6)	56 (31.3)
Pneumonitis/radiation pneumonitis[b]				
Any grade[c]	33 (32.7)	18 (32.7)	128 (34.2)	40 (22.3)
Grade 1	10 (9.9)	6 (10.9)	57 (15.2)	19 (10.6)
Grade 2	13 (12.9)	5 (9.1)	59 (15.8)	17 (9.5)
Grade 3	8 (7.9)	3 (5.5)	9 (2.4)	3 (1.7)
Grade 5	2 (2.0)	4 (7.3)	3 (<1)	1 (<1)
Leading to discontinuation	9 (8.9)	5 (9.1)	21 (5.6)	5 (2.8)

Table 3 Adverse Events in Patients Aged ≥70 Years and <70 Years

Socinski et al. *Clinical Lung Cancer 2021*

Radiation technique

Table 3. Outcomes at 2 Years by Radiation Therapy Technique

Outcome	3D-CRT, % (95% CI)	IMRT, % (95% CI)	P
Overall survival	49.4 (42.9 to 55.5)	53.2 (46.4 to 59.6)	.597
Progression-free survival	27.0 (21.5 to 32.7)	25.2 (19.7 to 31.1)	.595
Local failure	37.1 (31.0 to 43.1)	30.8 (24.8 to 36.9)	.498
Distant metastases	49.6 (43.2 to 55.8)	45.9 (39.2 to 52.3)	.661

IMRT
vs
3D-CRT

Table 4. CTCAE ≥ Grade 3 Radiation-Related Adverse Events of 3D-CRT and IMRT

≥ Grade 3 Toxicity	3D-CRT, % (No.)	IMRT, % (No.)	P
No. of patients	254	228	
Pneumonitis	7.9 (20)	3.5 (8)	.039
Esophagitis/dysphagia	15.4 (39)	13.2 (30)	.534
Weight loss	2.8 (7)	3.9 (9)	.419
Cardiovascular	8.3 (21)	4.8 (11)	.131

IMRT was associated with lower rates of severe pneumonitis and cardiac doses in clinical trial RTOG 0617, which supports routine use of IMRT for locally advanced NSCLC.

Chun SG, JCO 2017

Radiation technique

BOLOGNA, 27-29 OTTOBRE 2023
PALAZZO DEI CONGRESSI

Esophageal sparing

Assessment of a Contralateral Esophagus–Sparing Technique in Locally Advanced Lung Cancer Treated With High-Dose Chemoradiation
A Phase 1 Nonrandomized Clinical Trial
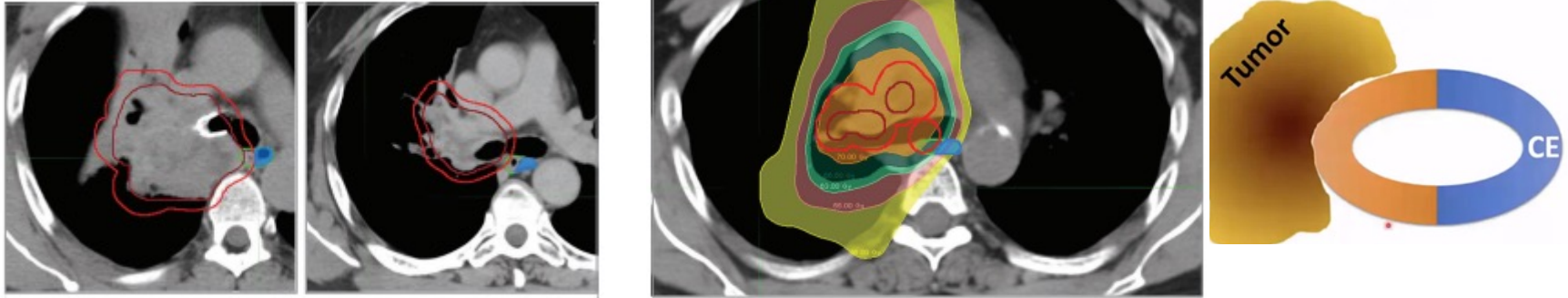
CE-sparing technique was associated with reduced risk of esophagitis among patients treated uniformly with chemo-radiotherapy (up to 70 Gy), with no grade 3 or higher esophagitis despite tumor within 1 cm

Kamran, JAMA 2021

Clinical practice

Treatment strategies for locally advanced non-small cell lung cancer in elderly patients: Translating scientific evidence into clinical practice

Laura Bonanno [a,*,1], Ilaria Attili [b,1], Alberto Pavan [a], Matteo Sepulcri [c], Giulia Pasello [a,d], Federico Rea [e], Valentina Guarneri [a,d], PierFranco Conte [a,d]
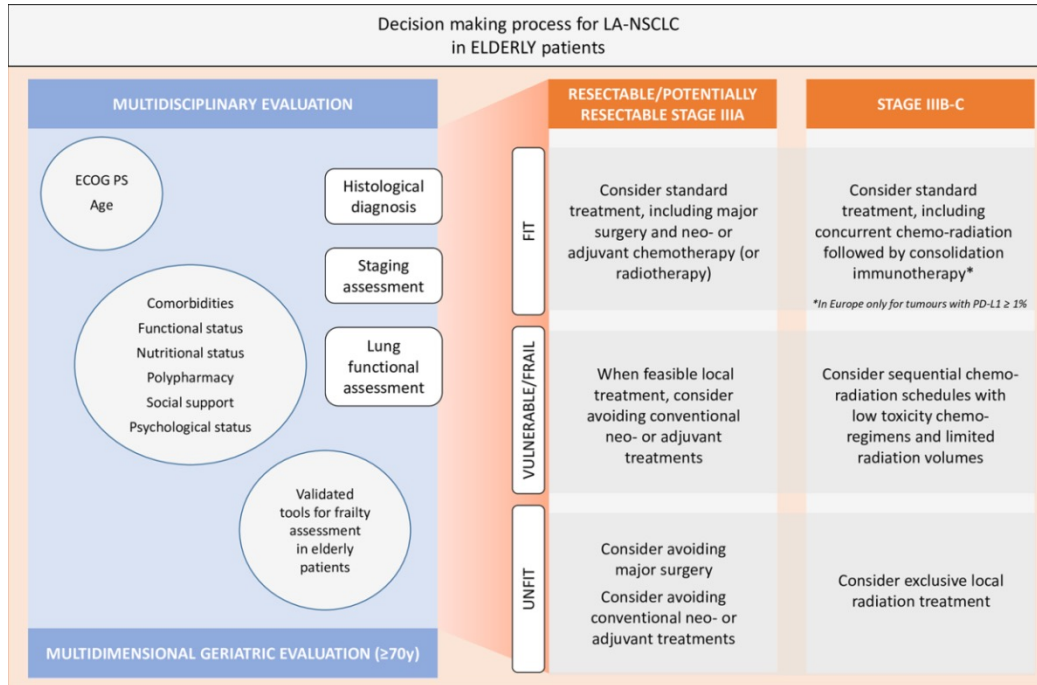
- Over 70 ys: Geriatric Assessment

- Evaluate FEV1 and DLCO

- Chemo: weekly carbo-paclitaxel

- RT dose: 60 Gy in 30 fractions (VMAT/IMRT)

- Rapid recognition and management of acute esophagitis

- Pay attention to pneumonitis

Future perspectives
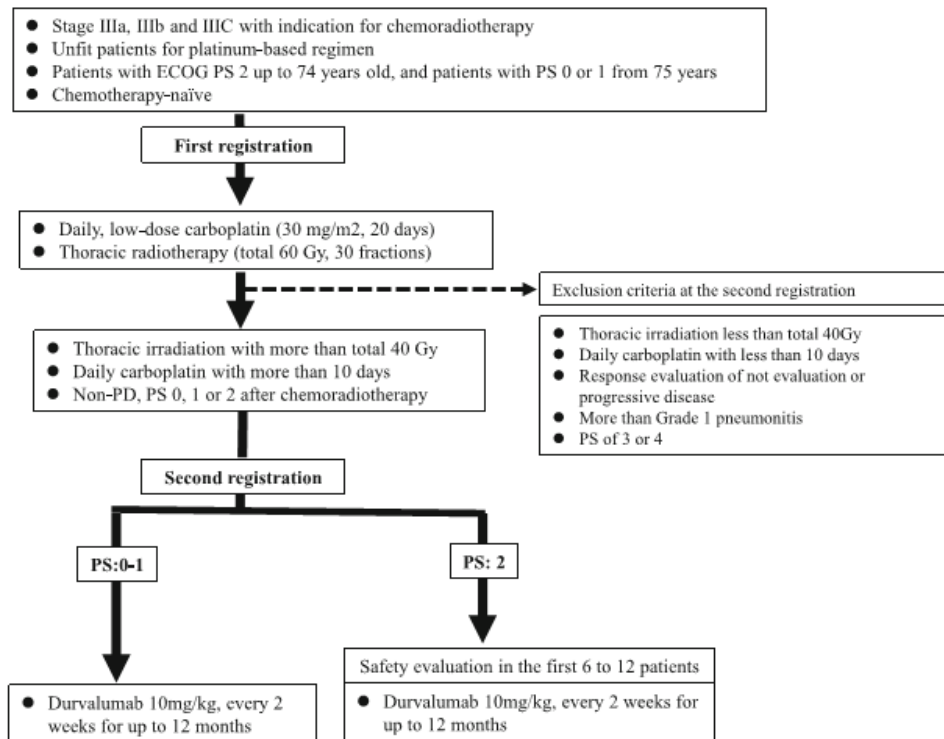
A phase II study of daily carboplatin plus irradiation followed by durvalumab for stage III non-small cell lung cancer patients with PS 2 up to 74 years old and patients with PS 0 or 1 from 75 years: NEJ039A

Chemo: Daily, low-dose carboplatin (30 mg/m2 in a 30-min infusion) 1 h before RT for the first 20 fractions.
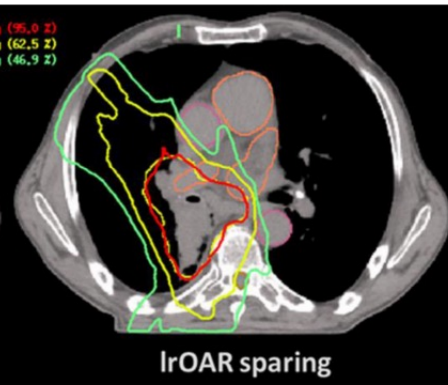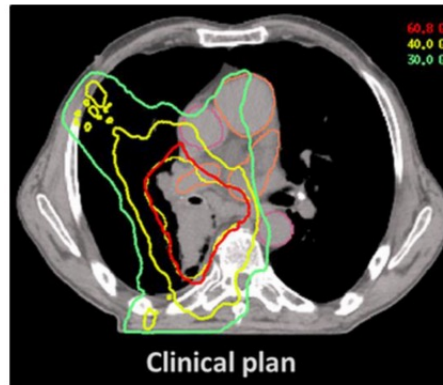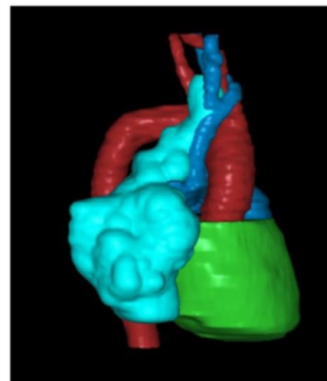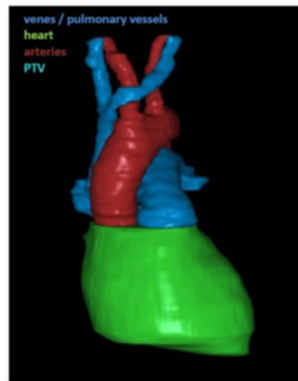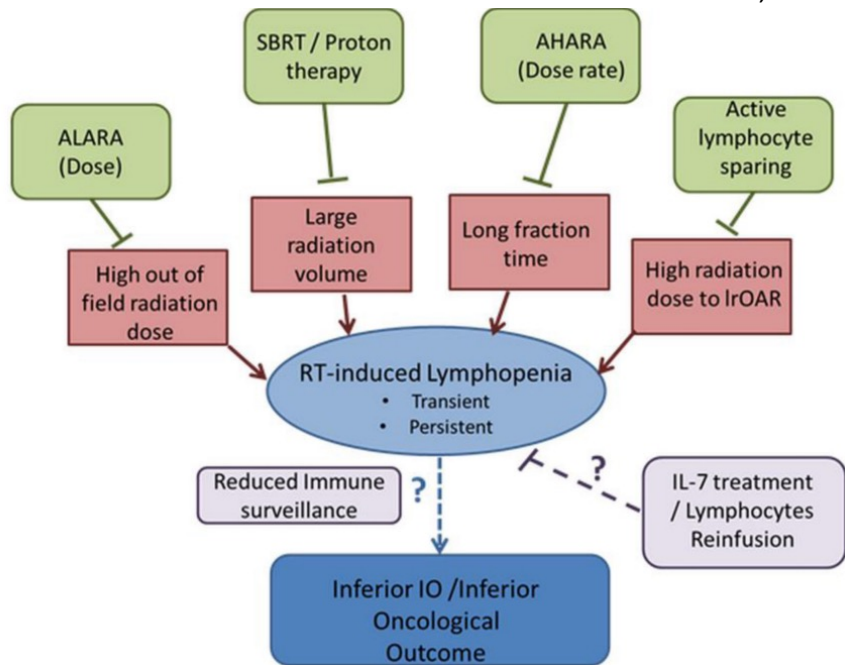
Radiotherapy: 60 Gy in 30 daily fractions.

Durvalumab at a dose of 10 mg/kg/body intravenously every 2 weeks for up to 12 months after CT-RT.

Kaira K et al. BMC Cancer (2020) 20:961
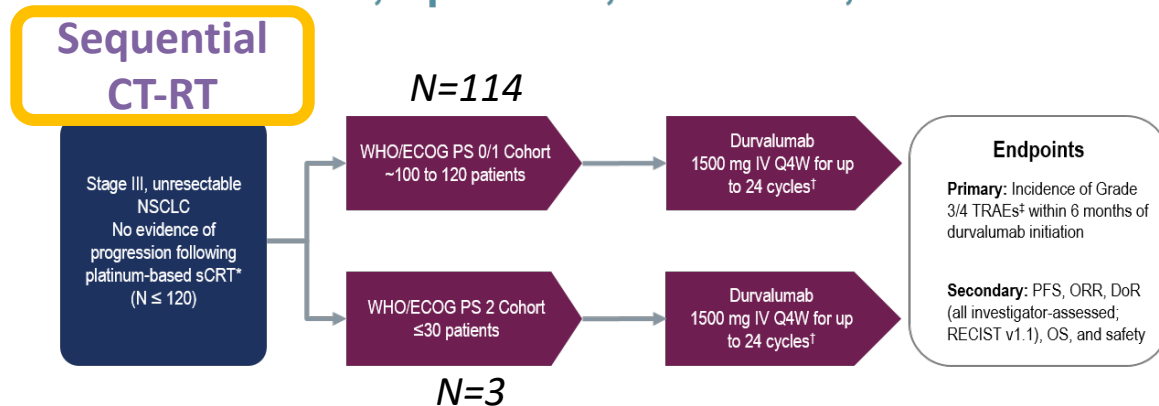
Future perspectives

Lymphocyte-Sparing Radiotherapy: the rationale for protecting lymphocyte-rich organs when combining radiotherapy with immunotherapy

Lambin, P. Semin Rad Onc 2020

New data: PACIFIC-6

PACIFIC-6: Phase 2, Open-label, Multicentre, International Trial

- Median treatment duration: 41 weeks (4-108)
- Tox G3/4 (<6 m): 4.3%
- Pneumonitis (17% any grade, 1.7% G3/4
- Median OS: 39 m (30.6-x)
- 3-yr OS: 56.5%
- Median PFS: 13.1 m (7.4-19.9)

- Incidence of AEs (CTCAE v4.03), and the ORR, were summarised with descriptive statistics

- PFS and OS were analysed by Kaplan–Meier method (to estimate medians, 12-month rates and associated 95% CIs)

New data: DUART

New data: DUART

Patients characteristics (N 102)

Median Age:
Cohort A: 78 years (43-87)
Cohort B: 80 years (56-87)

ECOG PS 1: 73.3%
A: 70.7%
B: 76.7%

AEs Summary

- Grade 3/4 PRAEs* within 6 months (primary endpoint): 9.8% (95% CI: 4.8–17.3)†
  - Cohort A: 11.9% (95% CI: 4.9–22.9)†
  - Cohort B: 7.0% (95% CI:1.5–19.1)†
- 9.8% had PRAEs leading to discontinuation, most commonly pneumonitis (3.9% of all patients)

	All-cause AEs			PRAEs*		
	Cohort A (standard RT; n=59)	Cohort B (palliative RT; n=43)	Total (N=102)	Cohort A (standard RT; n=59)	Cohort B (palliative RT; n=43)	Total (N=102)
Any AE, n (%)	56 (94.9)	43 (100)	99 (97.1)	40 (67.8)	21 (48.8)	61 (59.8)
Grade 3/4	25 (42.4)	15 (34.9)	40 (39.2)	9 (15.3)	3 (7.0)	12 (11.8)
Within 6 months	—	—	—	7 (11.9)	3 (7.0)	10 (9.8)
SAE	25 (42.4)	13 (30.2)	38 (37.3)	7 (11.9)	2 (4.7)	9 (8.8)
Outcome of death‡	5 (8.5)	2 (4.7)	7 (6.9)	1 (1.7)	0	1 (1.0)
Leading to Tx discontinuation	11 (18.6)	7 (16.3)	18 (17.6)	7 (11.9)	3 (7.0)	10 (9.8)
Leading to Tx interruption	31 (52.5)	17 (39.5)	48 (47.1)	8 (13.6)	5 (11.6)	13 (12.7)
AESI	26 (44.1)	15 (34.9)	41 (40.2)	21 (35.6)	9 (20.9)	30 (29.4)
imAE	23 (39.0)	13 (30.2)	36 (35.3)	22 (37.3)	12 (27.9)	34 (33.3)

AE, adverse event; AESI, adverse event of special interest; CI, confidence interval; imAE, immune-mediated adverse event; PRAE, adverse event possibly related to treatment; SAE, serious adverse event; Tx, treatment.

*PRAE is alternative nomenclature for a treatment-related AE and is used here to align with the case report form used to collect investigators' responses.
†CI calculated using the Clopper-Pearson method.
‡PRAE with outcome of death was pneumonitis (n=1) in Cohort A.

MADRID 2023 ESMO congress

New data: DUART

Efficacy
Objective Response Rate

Endpoint	Cohort A (standard RT; n=59)	Cohort B (palliative RT; n=43)	Total (N=102)
Confirmed ORR*, % (95% CI)†	28.8 (17.8–42.1)	23.3 (11.8–38.6)	26.5 (18.2–36.1)
Response status, n (%)			
Complete response	0	0	0
Partial response	17 (28.8)	10 (23.3)	**27 (26.5)**
Stable disease	25 (42.4)	22 (51.2)	**47 (46.1)**
Progression	10 (16.9)	6 (14.0)	16 (15.7)
RECIST v1.1 progression	6 (10.2)	5 (11.6)	11 (10.8)
Death	4 (6.8)	1 (2.3)	5 (4.9)
Not evaluable	7 (11.9)	5 (11.6)	12 (11.8)

- The confirmed ORR was 26.5% and 46.1% of patients had stable disease

CI, confidence interval; ORR, objective response rate; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1

*An additional 7 patients (6.9%) had unconfirmed responses (3 [5.1%] in Cohort A and 4 [9.3%] in Cohort B).
†CI calculated using the Clopper-Pearson method.

Median OS: 15.9 m (better than historical data of RT alone.
RT plus consolidation IT a novel option for this common subset of elderly and frailty patients

Take home messages

- Patient clinical evaluation (carefully!)

- Identify frail patients

- Management of toxicities

- Radical modern RT improves outcomes

- Immunotherapy feasible and effective even in elderly/frailty patients

- Personalize the treatment in order to maximise the risk/benefit ratio

Associazione Italiana
Radioterapia e Oncologia clinica

Thank you for your attention

matteo.sepulcri@iov.veneto.it

Radioterapia Oncologica: l'evoluzione al servizio dei pazienti