

Immunotherapy in ES-SCLC: Real-world impact of atezolizumab/durvalumab, radiotherapy, and metastatic burden across ECOG 0-2 patients

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Background

- Extensive-stage SCLC (ES-SCLC) progresses rapidly and is often diagnosed with brain, liver, or bone metastases upfront.
- Immune checkpoint inhibitors (ICIs) such as atezolizumab (Atezo) or durvalumab (Durva) with platinum-etoposide improve survival in trials, but real-world effectiveness across ECOG 0-2, metastatic subgroups, or with radiotherapy (RTx) remains unclear.
- This study evaluates population-based data from the Baden-Württemberg Cancer Registry (BWCR), Germany.

Methods

- Retrospective, registry-based cohort study used data from the BWCR
- Patients aged ≥ 18 years with ES-SCLC diagnosed 2018-2024
- First-line regimens:
 - Carboplatin-etoposide (Carbo+Eto),
 - Carbo+Eto+Atezo
 - Carbo+Eto+Durva, Cisplatin+Eto+Durva
- Subgroup analyses: ECOG 0-2, metastatic sites, and thoracic/cranial RTx
- Primary endpoint: overall survival (OS)
 - Analysed with Kaplan-Meier estimates and Cox models, adjusted for key clinical parameters (age, sex, ECOG, metastatic burden)

Results

Study Cohort: Baseline Characteristics

Table. Patient Demographics and Clinical Baseline Characteristics				
Characteristic	overall	CTx	ICI + CTx	p-value
n	1632	573 (35.1)	1059 (64.9)	
Age - median	67.0	68.0	67.0	0.001
Sex				
m	965 (59.1)	343 (59.9)	622 (58.7)	0.697
w	667 (40.9)	230 (40.1)	437 (41.3)	
ECOG				
0	524 (32.1)	145 (25.3)	379 (35.8)	<0.001
1	803 (49.2)	286 (49.9)	517 (48.8)	
2	305 (18.7)	142 (24.8)	163 (15.4)	
Metastasis sites				
1	690 (42.3)	261 (45.5)	429 (40.5)	0.100
2	449 (27.5)	155 (27.1)	294 (27.8)	
3+	493 (30.2)	157 (27.4)	336 (31.7)	
metastasis location				
brain	468 (28.7)	171 (29.8)	297 (28.0)	0.478
liver	759 (46.5)	245 (42.8)	514 (48.5)	0.029
bone	501 (30.7)	169 (29.5)	332 (31.4)	0.472
Thoracic radiatio	254 (15.6)	87 (15.2)	167 (15.8)	0.81

The cohort comprised 1632 patients:

- CTx: 35.1%;
- ICI+CTx: 64.9%

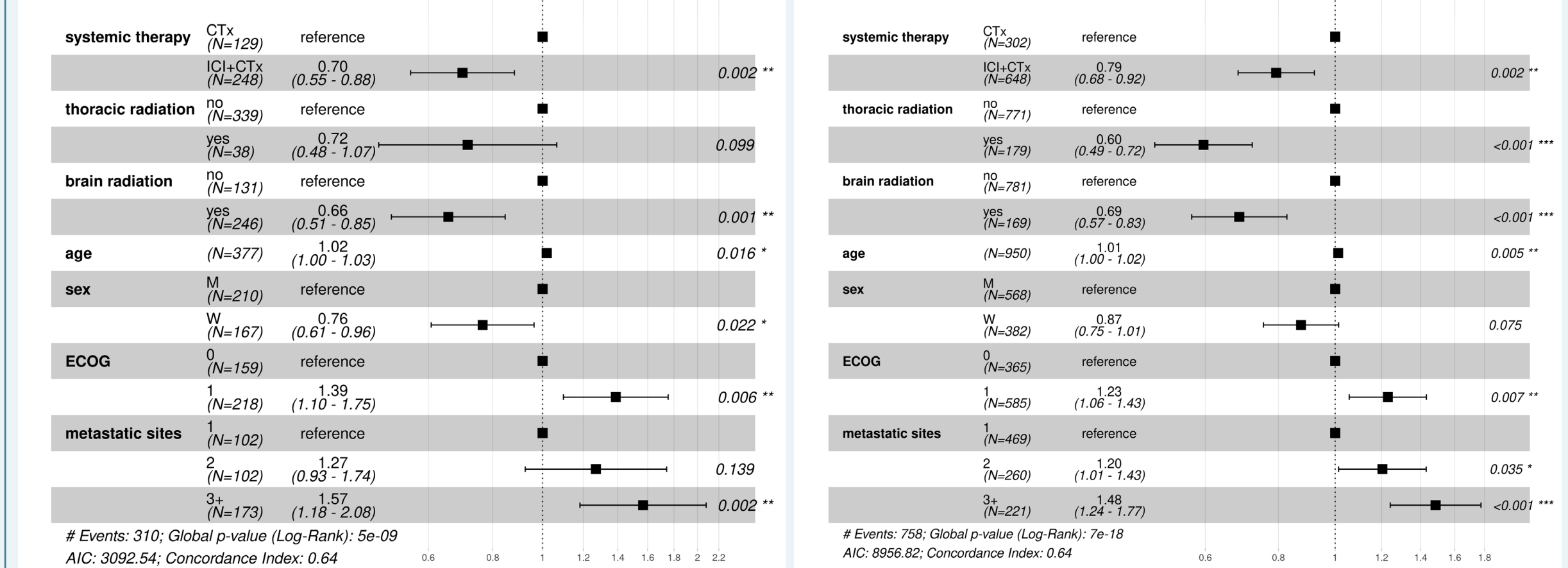
- Sex: balanced between groups
- Age: slightly younger in ICI+CTx (p = 0.001)
- ECOG: better in ICI+CTx
- Metastases:
 - Liver less frequent in ICI+CTx
 - Brain and bone: comparable

- Metastatic burden & thoracic radiation: similar between groups

ECOG 0-1: Treatment Effects by Brain Metastasis Status

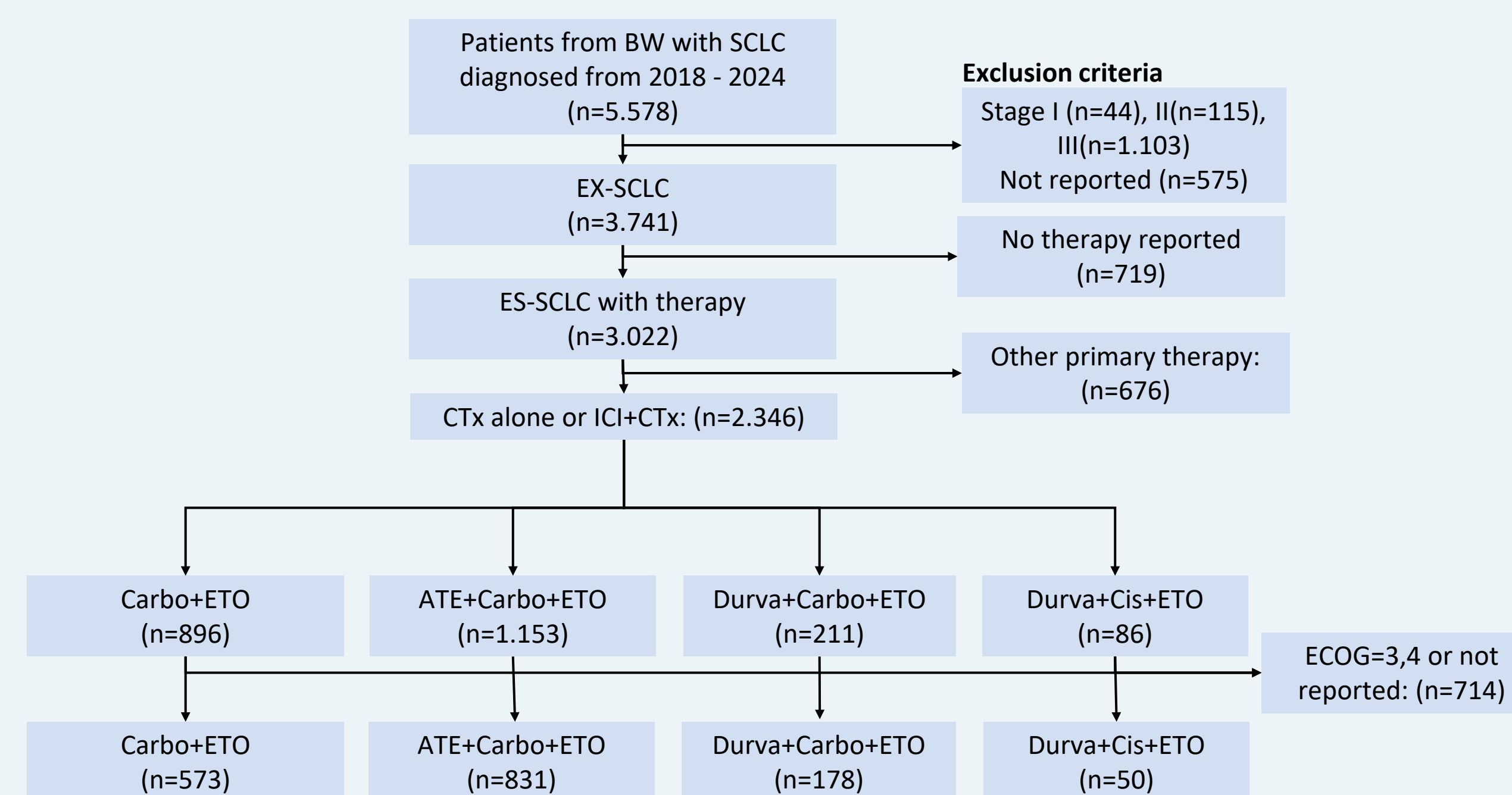
Fig. Multivariate Cox Models by brain metastasis status

A. Patients with brain metastases B. Patients without brain metastases



- ICI + CTx improved survival irrespective of brain metastasis status.
- Brain-directed radiation (RT/PCI) was associated with better outcomes.
- Thoracic radiation benefited patients without, but not with, brain metastases.
- Poor ECOG and ≥ 3 metastatic sites predicted worse survival.

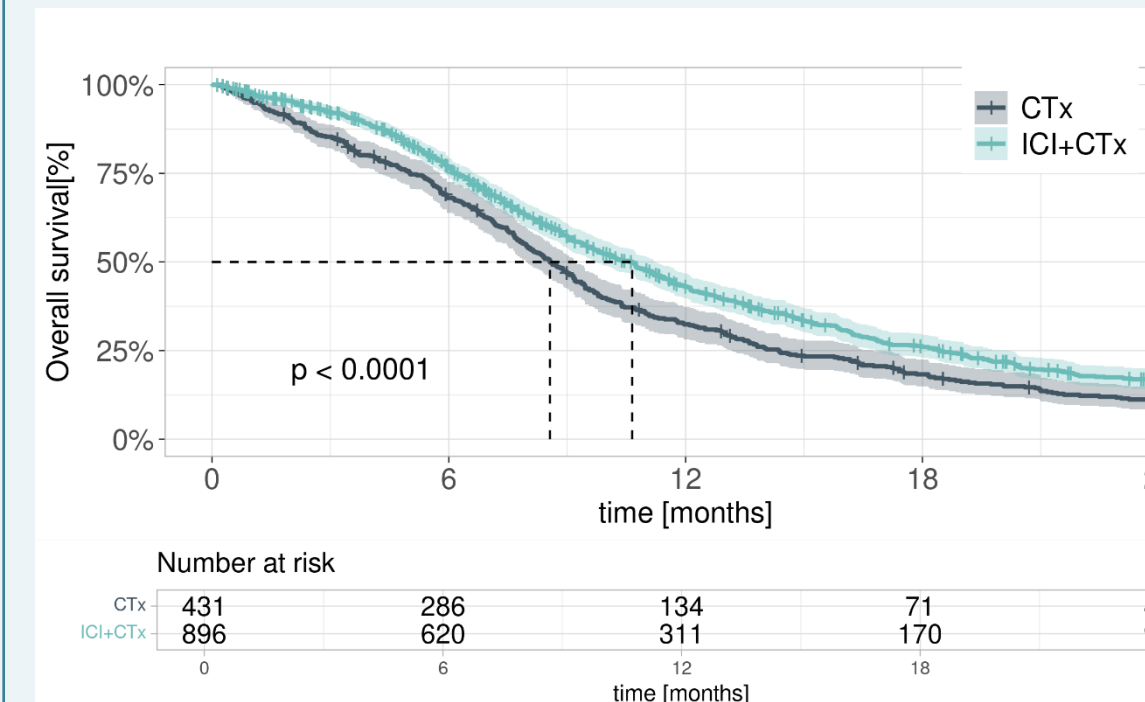
Consort diagram and cohort definition



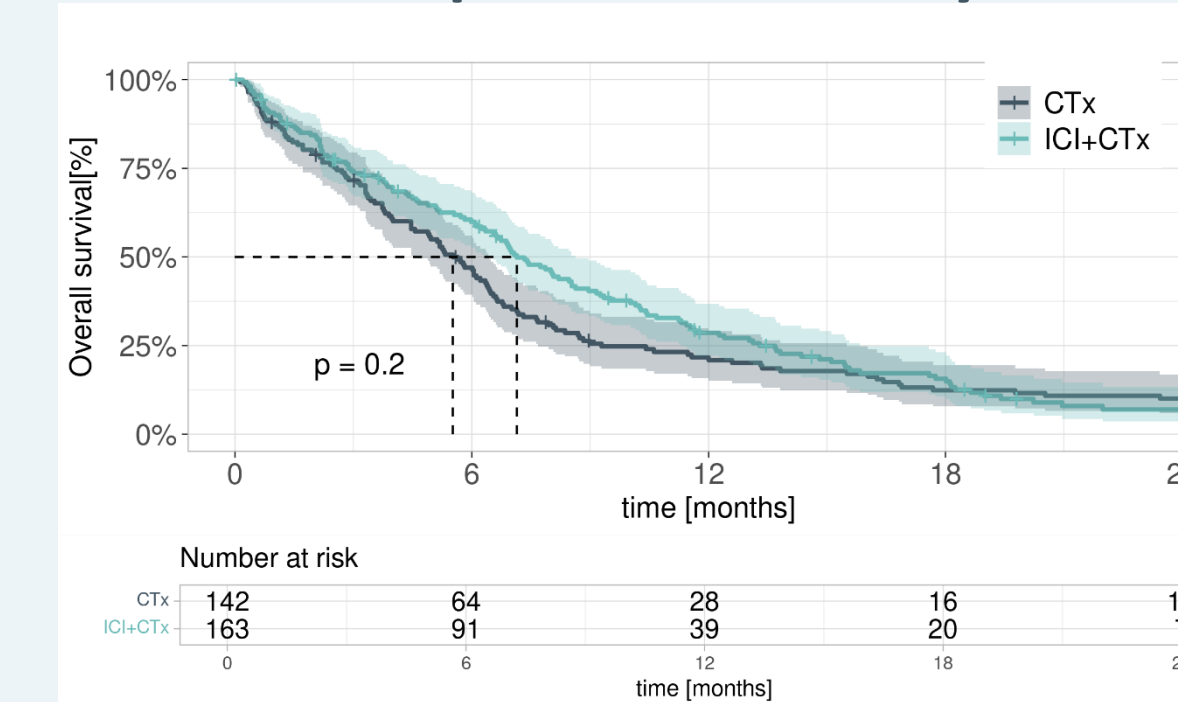
- Among 1632 patients with ECOG 0-2, Carbo+Eto showed the poorest OS
- Atezolizumab- and durvalumab-based regimens demonstrated comparable outcomes
- Therefore, all ICI+CTx regimens were pooled for subsequent analyses.

Impact of ICI+CTx on Overall Survival Across Subgroups

ECOG 0-1. Kaplan-Meier Analysis



ECOG 2. Kaplan-Meier Analysis

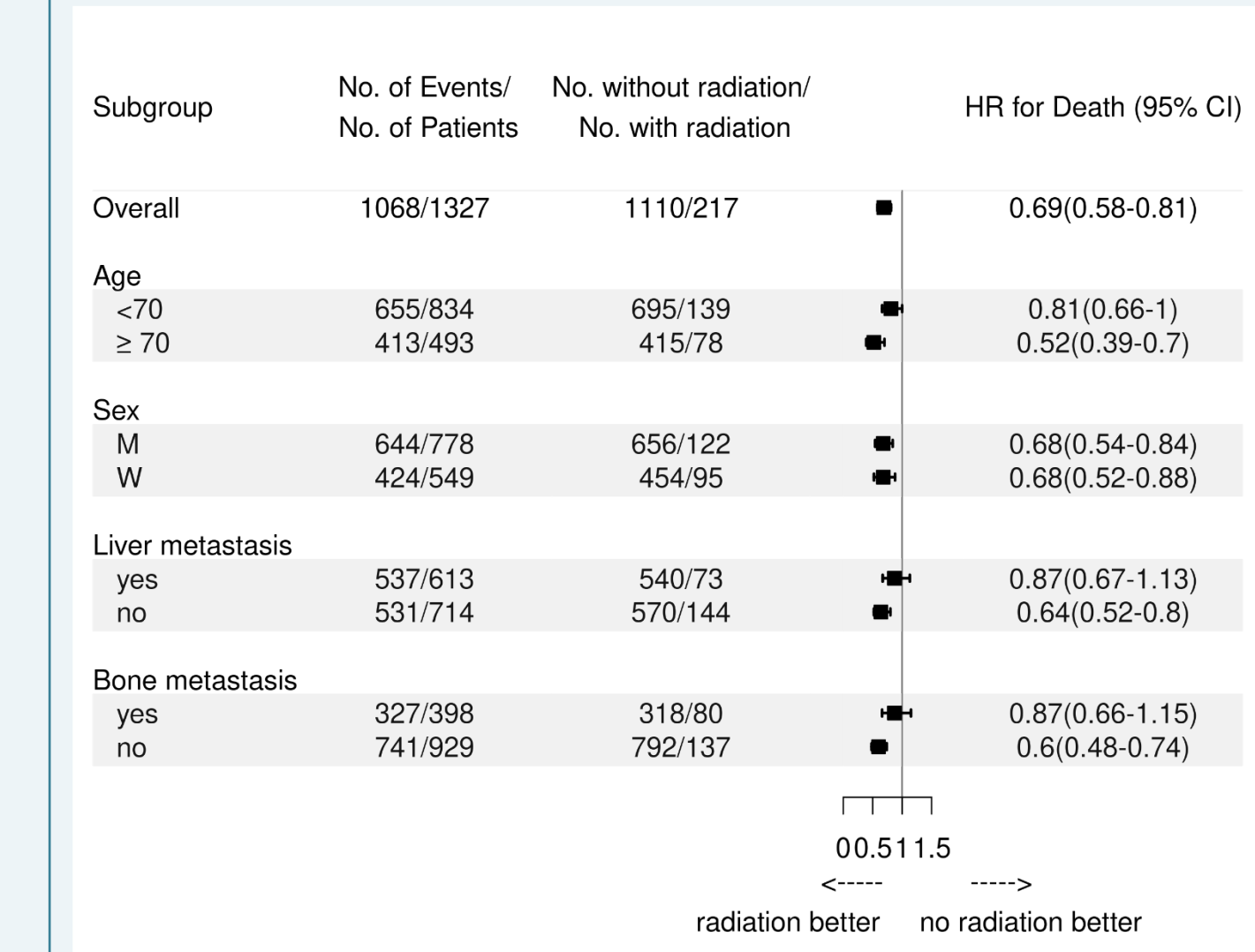


- ECOG 0-1: ICI+CTx significantly improved OS vs. CTx (mOS 10.6 vs. 8.6 months)
- ECOG 2: Early OS benefit with ICI+CTx vs. CTx (≤ 12 mo), with later convergence

Subgroup	No. of Events/ No. of Patients	No. CTx/ No. ICI+CTx	HR for Death (95% CI)
Overall	1068/1327	431/896	0.78(0.69-0.88)
Age			
<70	655/834	251/583	0.81(0.69-0.95)
≥ 70	413/493	180/313	0.74(0.61-0.91)
Sex			
M	644/778	254/524	0.82(0.7-0.97)
W	424/549	177/372	0.7(0.57-0.85)
Liver metastasis			
yes	537/613	186/427	0.85(0.7-1.02)
no	531/714	245/469	0.7(0.59-0.83)
Bone metastasis			
yes	327/398	130/268	0.83(0.66-1.04)
no	741/929	301/628	0.74(0.64-0.86)

- Subgroup analysis: Cox models adjusted for key clinical factors and use of thoracic radiation
- ICI+CTx showed a consistent OS benefit vs. CTx across almost all subgroups
- No significant OS benefit from ICI was seen in pts with liver metastases or bone metastases

Impact of thoracic radiation on Overall Survival Across Subgroups



- Subgroup analysis: Cox models adjusted for key clinical factors and use of systemic therapy
- Thoracic radiotherapy showed a consistent OS benefit across key subgroups (HR $\sim 0.52-0.81$)
- Stronger effects in patients without bone and liver metastasis

Conclusion

- ICI+CTx confers a significant and clinically meaningful OS benefit over CTx, particularly in ECOG 0-1 patients.
- An early survival advantage with ICI+CTx is also evident in ECOG 2 patients (up to ~ 12 months), supporting its use beyond fit populations.
- The OS benefit of ICI+CTx is consistent across key subgroups
- Thoracic and brain-directed radiotherapy are associated with improved outcomes, highlighting the importance of multimodal treatment strategies

