

Uluslararası Katılımlı

AKCİĞER SAĞLIĞI KONGRESİ

25-28 MART 2026

Sueno Deluxe Hotel, Belek/Antalya

Sizin Sesiniz, Sizin Kongreniz...



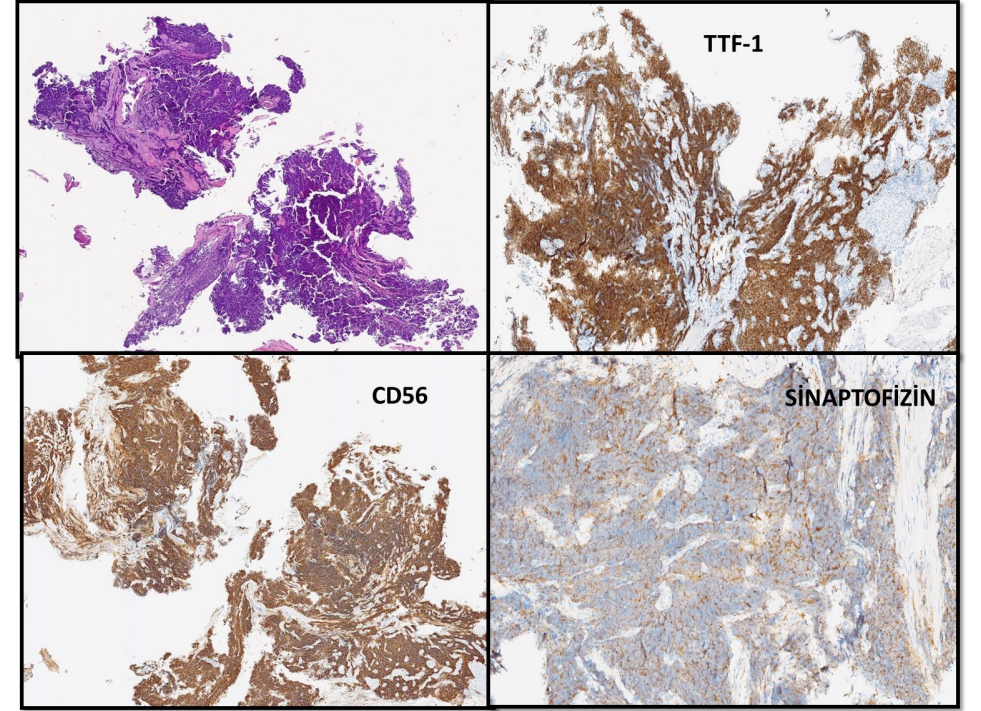
Yaygın Evre KHAK Olgusunda Tedavi

Dr. Ali Alkan

Muğla Sıtkı Koçman Üniversitesi Tıp Fakültesi

Tıbbi Onkoloji Bilim Dalı

- İ.K. 74 yaş erkek hasta
- 40 pktyıl sigara
- HT, DM, Hipotiroidi
- ECOG 2
- 02/2024 Öksürük nedeniyle yapılan tetkiklerde;



TANI

1-MALİGN NEOPLAZİ

1-Sağ akciğer üst lob girişinden bronkoskopik biyopsi

2-MALİGN SİTOLOJİ

2-Fırçalama sitolojisi

3-TANISAL OLMAYAN (NONDİAGNOSTİK) SİTOLOJİ

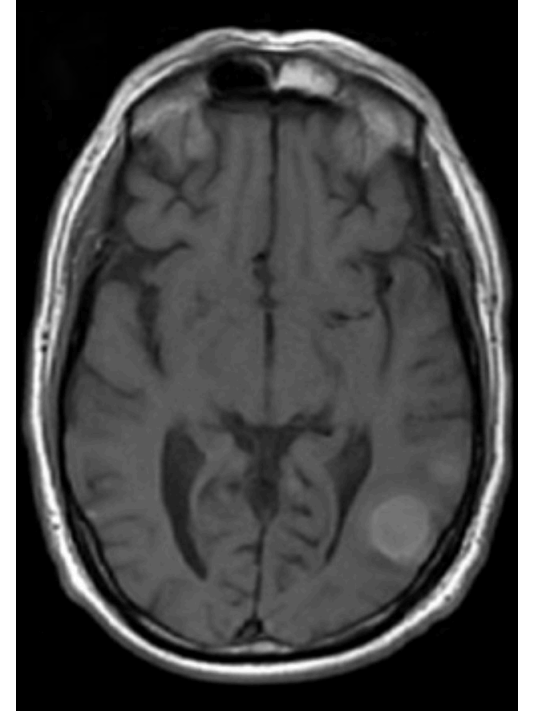
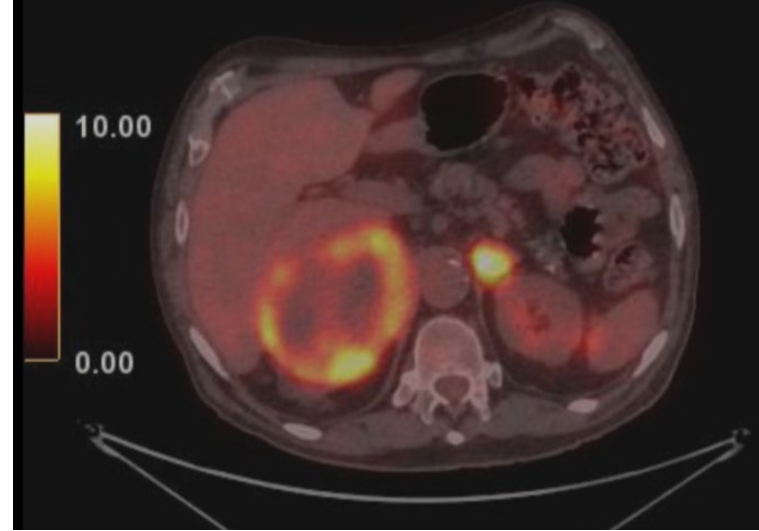
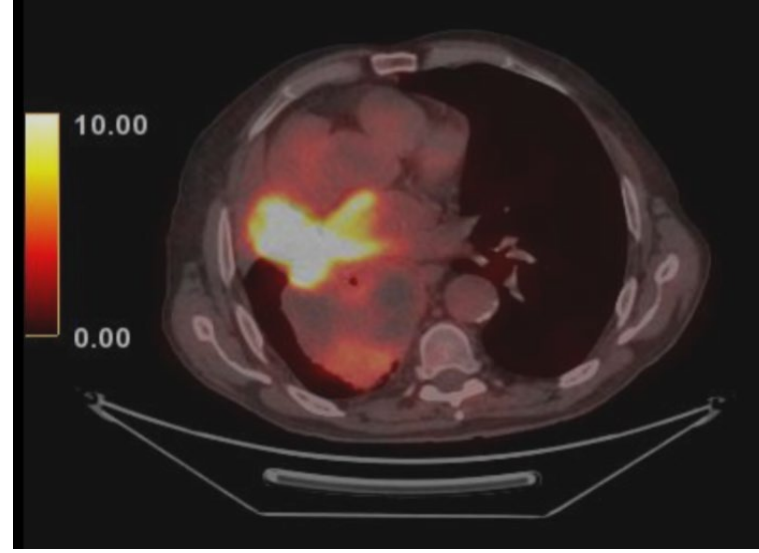
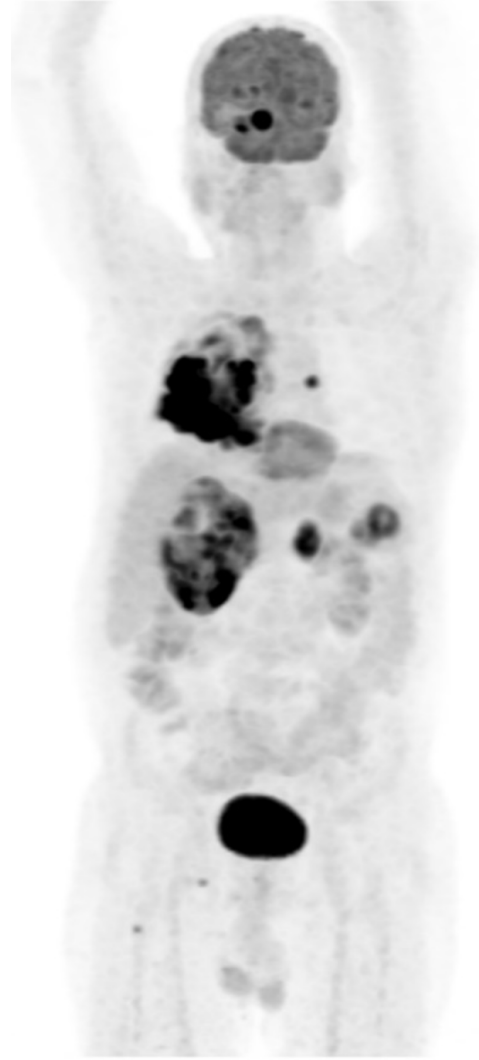
(Şekli kan elemanları)

3-Lavaj

Yorum

Tümör yaygın ve yoğun inflamasyon içerisinde çok dar alanlarda izlenmekte olup, 2 kere çalışılan TTF1, CD56, Sinaptofizin ile zayıf pozitif boyanmaktadır. CK7, p40, Napsin A, Kromogranin, CK5/6 negatif saptanmıştır. ki67 indeksi %80 civarındadır.

Mevcut bulgularla tümör öncelikle KÜÇÜK HÜCRELİ AKCİĞER KARSİNOMU lehine değerlendirilmiştir.



Toraks: Sağ akciğer üst lobun tamamını ve alt lob superior segmenti etkileyen geniş nekrotik alanlar ihtiva eden, önceki çalışmaya göre boyut ve FDG metabolizması artmış dev malign kitle (aksiyal uzun boyutu 14cm, SUVmaks: 24.4) izlenmiştir. Sağ alt paratrakeal ve hiler lenf nodlarının sınırları primer kitleden ayırt edilememiştir.

KHAK yaklaşım?

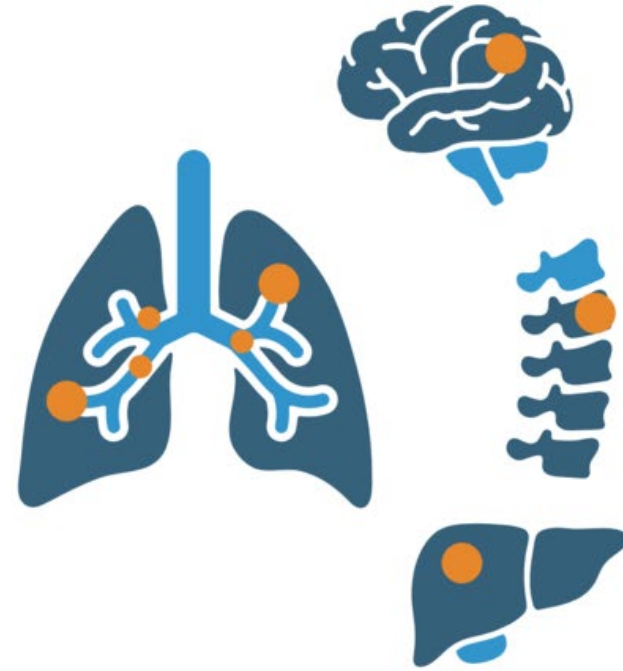
1. Basamak
seenekler?



Small Cell Lung Cancer



Limited Stage

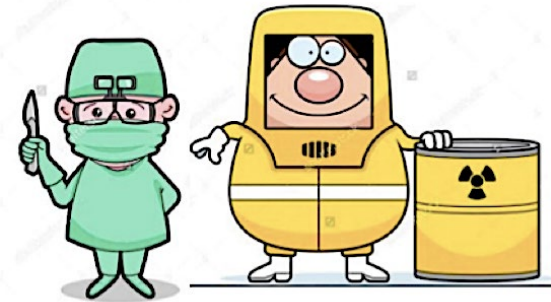
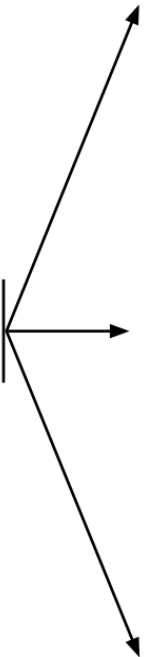


Extensive Stage



STAGE

Extensive stage
(see [ST-1](#) for TNM
Classification)^S





PRIMARY THERAPY FOR EXTENSIVE STAGE SCLC^c:

Four cycles of cytotoxic chemotherapy are recommended, but some patients may receive up to 6 cycles based on response and tolerability after 4 cycles.

Preferred

- Carboplatin AUC 5 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3 and Atezolizumab 1200 mg Day 1 every 21 Days x 4 cycles followed by maintenance Atezolizumab 1200 mg Day 1 every 21 Days x 4 cycles followed by maintenance
- Carboplatin AUC 5 Day 1 and Atezolizumab 1680 mg Day 1 and Lurbinectedin 3.2 mg/m² and Durvalumab 1500 mg Day 1 every 28 Days (category 1 for all)^{d,e,f,7} • Karbo+ Etoposid+ Atezolizumab → Atezo
- Carboplatin AUC 5 Day 1 and Lurbinectedin 3.2 mg/m² and Durvalumab 1500 mg Day 1 every 28 Days (category 1 for all)^{d,e,f,7} • Karbo+ Etoposid+ Atezolizumab → Atezo+ Lurbinektedin
- Carboplatin AUC 5–6 Day 1 and Durvalumab 1500 mg Day 1 every 28 Days (category 1 for all)^{d,e,f,7} • Karbo (Sisplatin)+ Etoposid+ Durvalumab → Durva
- Cisplatin 75–80 mg/m² Day 1 and Etoposide 80–100 mg/m² Days 1, 2, 3 and Durvalumab 1500 mg Day 1 every 21 Days x 4 cycles followed by maintenance

Other Recommended

- Carboplatin AUC 5–6 Day 1 and Etoposide 100 mg/m² Days 1, 2, 3⁸
- Cisplatin 75 mg/m² Day 1 and Etoposide 100 mg/m² Days 1, 2, 3⁹
- Cisplatin 80 mg/m² Day 1 and Etoposide 80 mg/m² Days 1, 2, 3¹⁰
- Cisplatin 25 mg/m² Days 1, 2, 3 and Etoposide 100 mg/m² Days 1, 2, 3¹¹

Useful in Certain Circumstances

- Carboplatin AUC 5 Day 1 and Irinotecan 50 mg/m² Days 1, 8, 15¹²
- Cisplatin 60 mg/m² Day 1 and Irinotecan 60 mg/m² Days 1, 8, 15¹³
- Cisplatin 30 mg/m² Days 1, 8 and Irinotecan 65 mg/m² Days 1, 8¹⁴

- Karbo+ Etoposid+ Atezolizumab → Atezo
- Karbo+ Etoposid+ Atezolizumab → Atezo+ Lurbinektedin
- Karbo (Sisplatin)+ Etoposid+ Durvalumab → Durva

- Karbo (Sisplatin)+ Etoposid

- Karbo (Sisplatin)+ Irinotekan

> [Cochrane Database Syst Rev. 2003;\(4\):CD001990. doi: 10.1002/14651858.CD001990.](#)

Chemotherapy versus best supportive care for extensive small cell lung cancer

Meta-Analysis

> [Cochrane Database Syst Rev. 2013 Nov 27;2013\(11\):CD001990. doi: 10.1002/14651858.CD001990.pub3.](#)

Chemotherapy versus best supportive care for extensive small cell lung cancer



BSC → ~3 ay
KT → ~10 ay
KT+IO → ~13 ay

1979

Clinical Trial > Cancer. 1979 Aug;44(2):406-13.

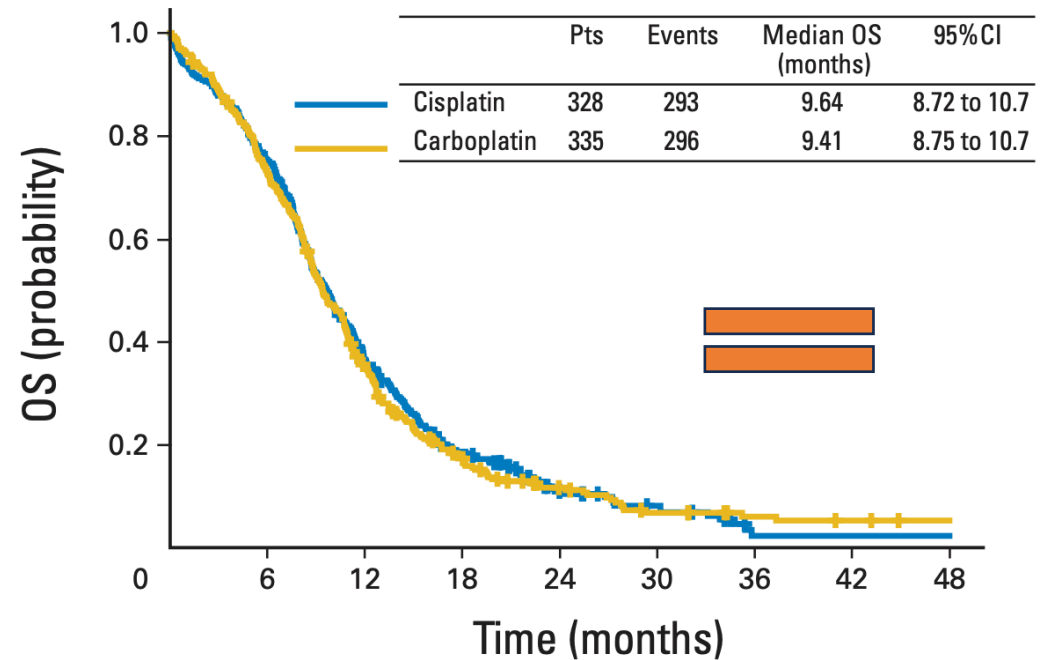
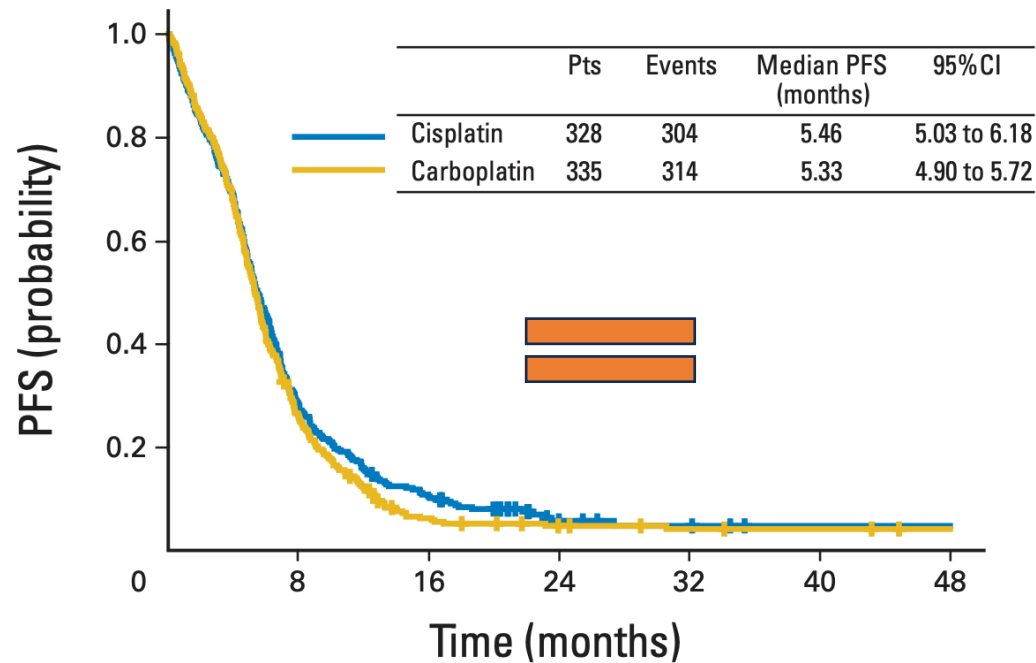
doi: 10.1002/1097-0142(197908)44:2<406::aid-cnrcr2820440206>3.0.co;2-1.

The superiority of combination chemotherapy over single agent chemotherapy in small cell lung carcinoma

- Platin bazlı 2'li rejimler etkin
- 3-4 ilaç kombinasyonu daha iyi değil

Sisplatin Vs Karboplatin

Carboplatin- or Cisplatin-Based Chemotherapy in First-Line Treatment of Small-Cell Lung Cancer: The COCIS Meta-Analysis of Individual Patient Data



Conclusion

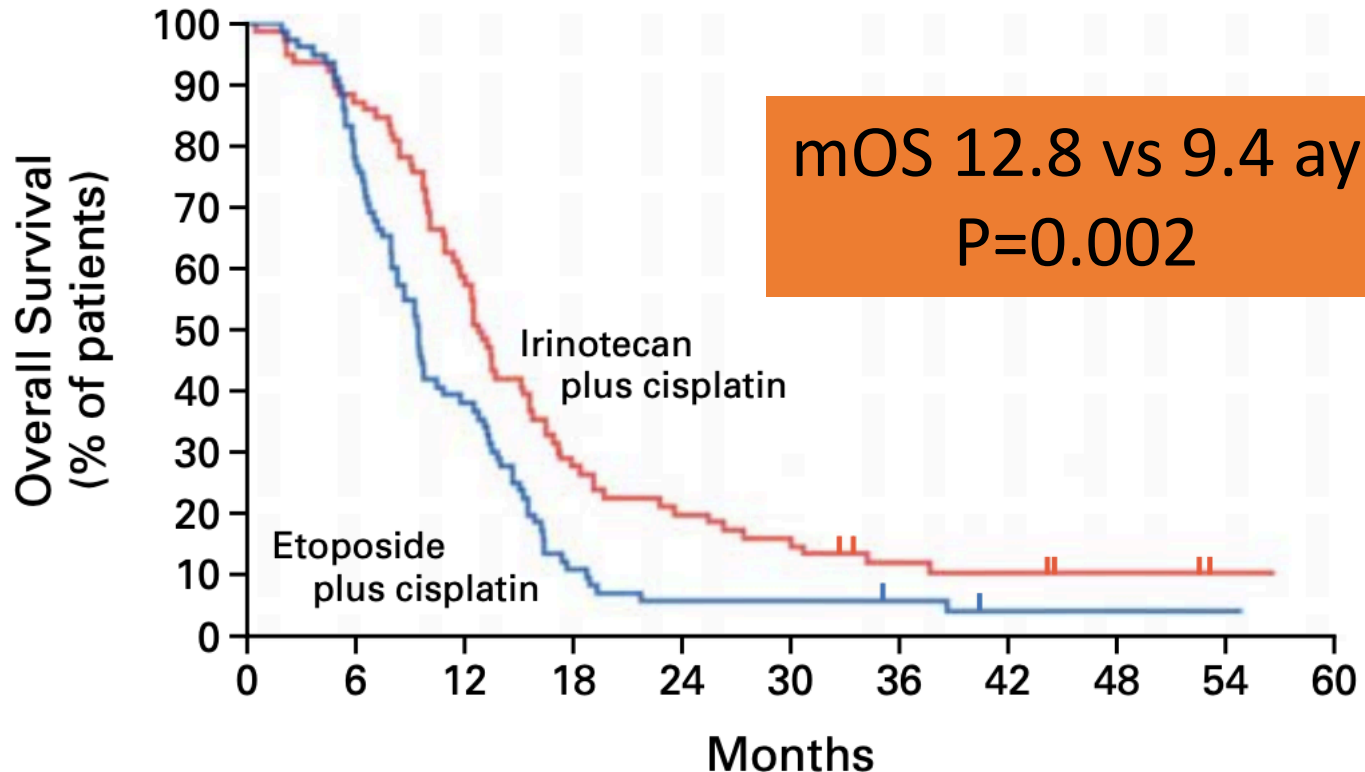
Our meta-analysis of individual patient data suggests no differences in efficacy between cisplatin and carboplatin in the first-line treatment of SCLC, but there are differences in the toxicity profile.

Toxicity	Patients With Toxicity Information	Any Grade					
		Cisplatin (%)	Carboplatin (%)	Exact OR	95% CI	<i>P</i> *	<i>P</i> † for Homogeneity
Leucopenia	655	74	77	1.22	0.81 to 1.88	.357	< .001
Neutropenia	458	86	90	1.53	0.81 to 2.92	.177	.397
Anemia	512	84	89	1.72	0.99 to 3.03	.049	.046
Platelets	512	39	71	3.36	2.83 to 6.34	< .001	< .001
Nausea/vomiting	655	72	63	0.66	0.47 to 0.93	.013	.012
Stomatitis	655	25	21	0.78	0.52 to 1.17	.239	.065
Diarrhea	458	19	22	1.23	0.76 to 2.00	.415	.999
Constipation	239	39	51	1.58	0.92 to 2.73	.091	.999
Neurotoxicity	416	19	7	0.29	0.14 to 0.58	< .001	.243
Renal toxicity	415	25	10	0.34	0.19 to 0.61	< .001	.787
Toxic deaths	655	—	—	—	—	—	—

Etoposid yerine Irinotekan?

JCOG
Japan Clinical Oncology Group
日本臨床腫瘍研究グループ

Irinotecan plus cisplatin compared with etoposide plus cisplatin for extensive small-cell lung cancer



Clinical Trial > J Clin Oncol. 2006 May 1;24(13):2038-43. doi: 10.1200/JCO.2005.04.8595.

Randomized phase III trial comparing irinotecan/cisplatin with etoposide/cisplatin in patients with previously untreated extensive-stage disease small-cell lung cancer

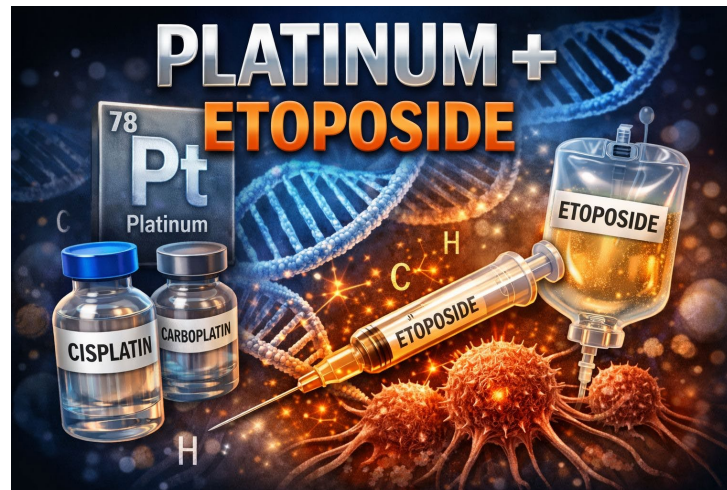
Clinical Trial > Ann Oncol. 2010 Sep;21(9):1810-1816. doi: 10.1093/annonc/mdq036.

Epub 2010 Mar 15.

A multicenter international randomized phase III study comparing cisplatin in combination with irinotecan or etoposide in previously untreated small-cell lung cancer patients with extensive disease

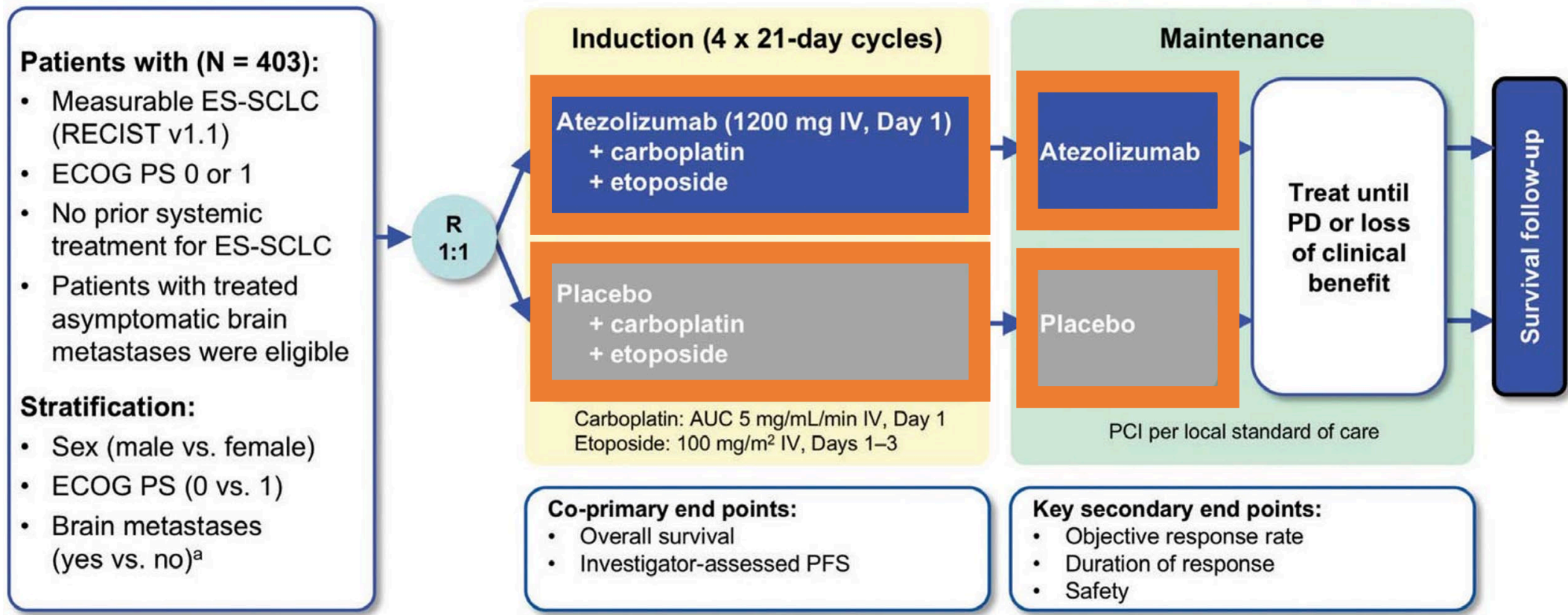
Daha iyi değil

Non-inferior

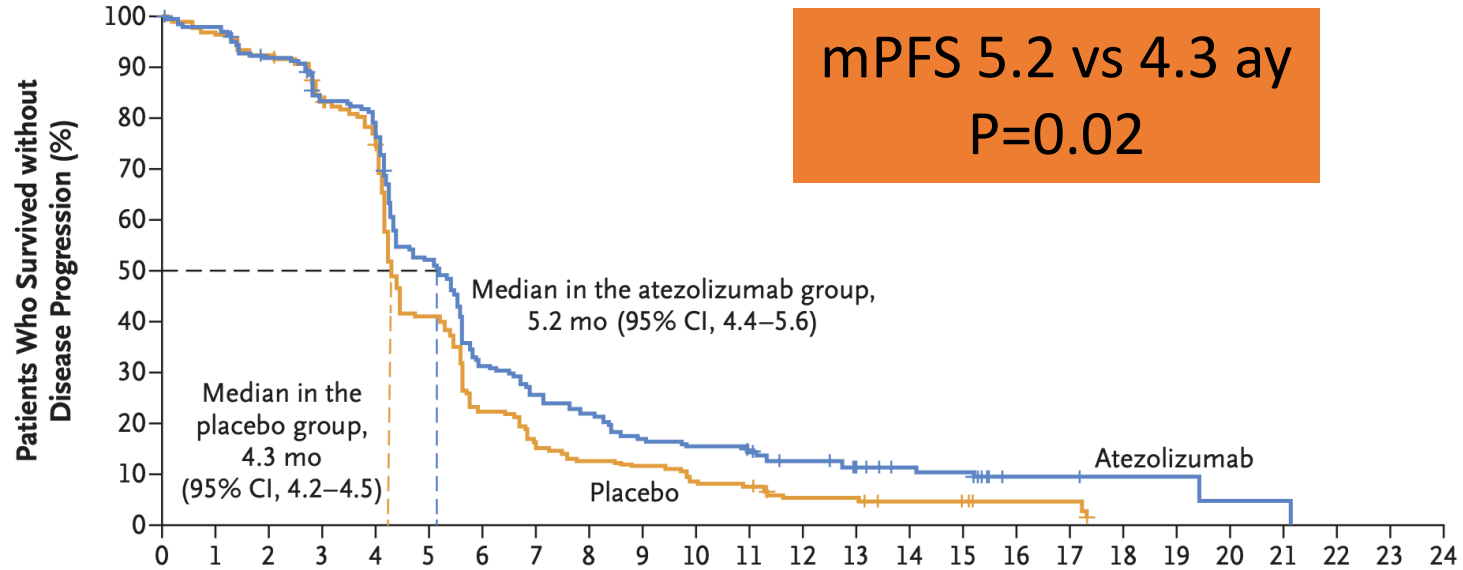


First-Line Atezolizumab plus Chemotherapy in Extensive-Stage Small-Cell Lung Cancer

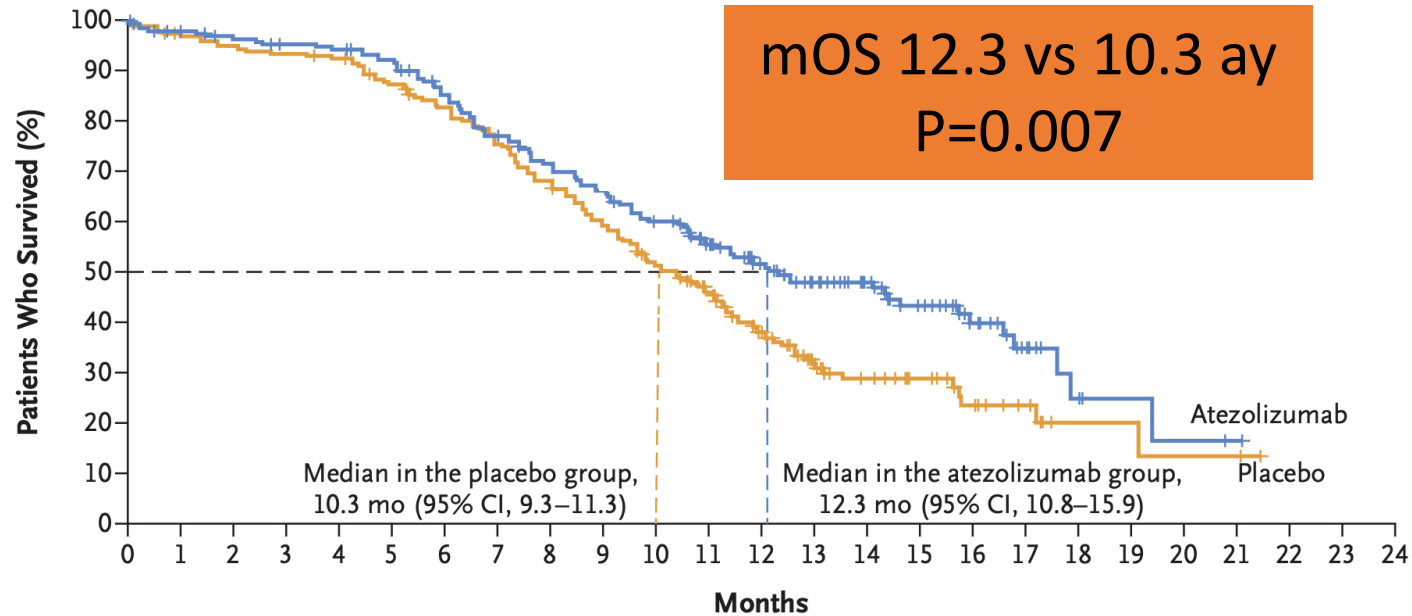
Study Design of IMpower133



Progression-free Survival



Overall Survival



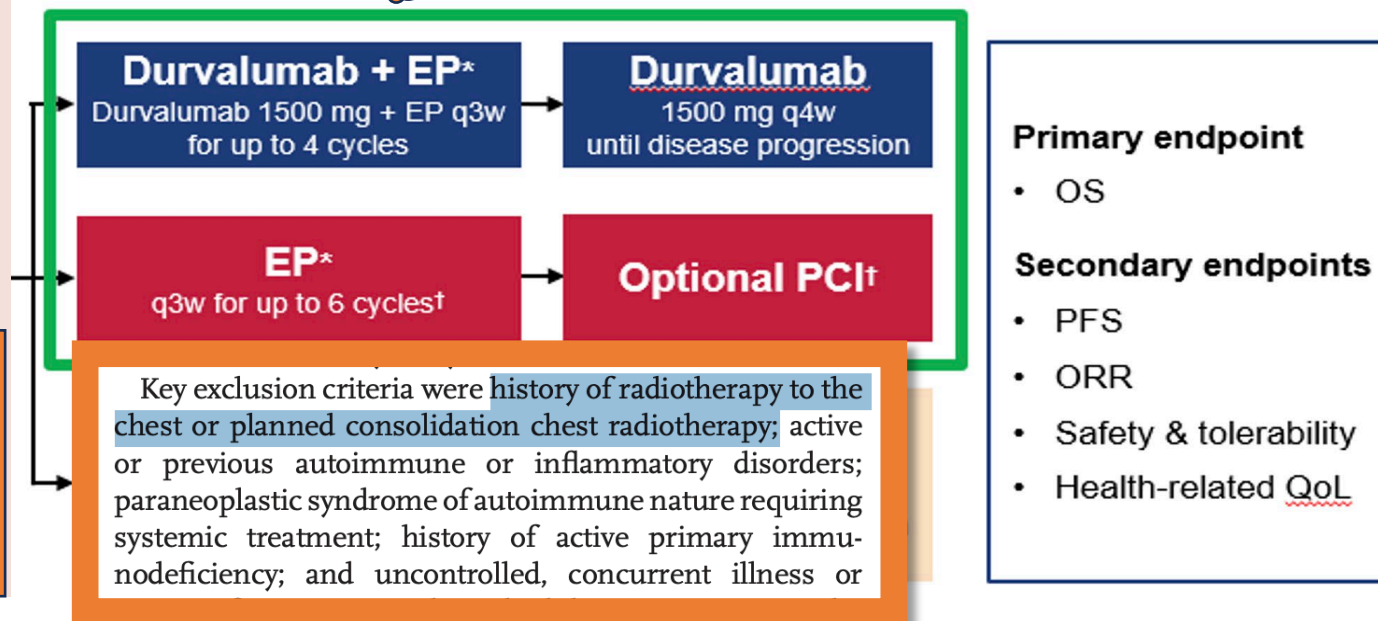
Durvalumab plus platinum–etoposide versus platinum–etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial

EP 6 küre tamamlayabilirsiniz

	Durvalumab plus platinum–etoposide (n=265)	Platinum–etoposide (n=266)
Median number of durvalumab doses	7 (6–11)	..
Patients receiving 12 or more durvalumab doses	64 (24%)	..
Median total duration of durvalumab, weeks	28.0 (20.0–43.1)	..
Platinum received*		
Carboplatin	208 (78%)	208 (78%)
Cisplatin	65 (25%)	67 (25%)
Median number of cycles of platinum–etoposide†	4 (4–4)	6 (4–6)
Patients receiving four or more cycles of platinum–etoposide†	230 (87%)	225 (85%)
Patients receiving five or more cycles of platinum–etoposide†	3 (1%)	167 (63%)
Patients receiving six cycles of platinum–etoposide†	1 (<1%)	151 (57%)

esign

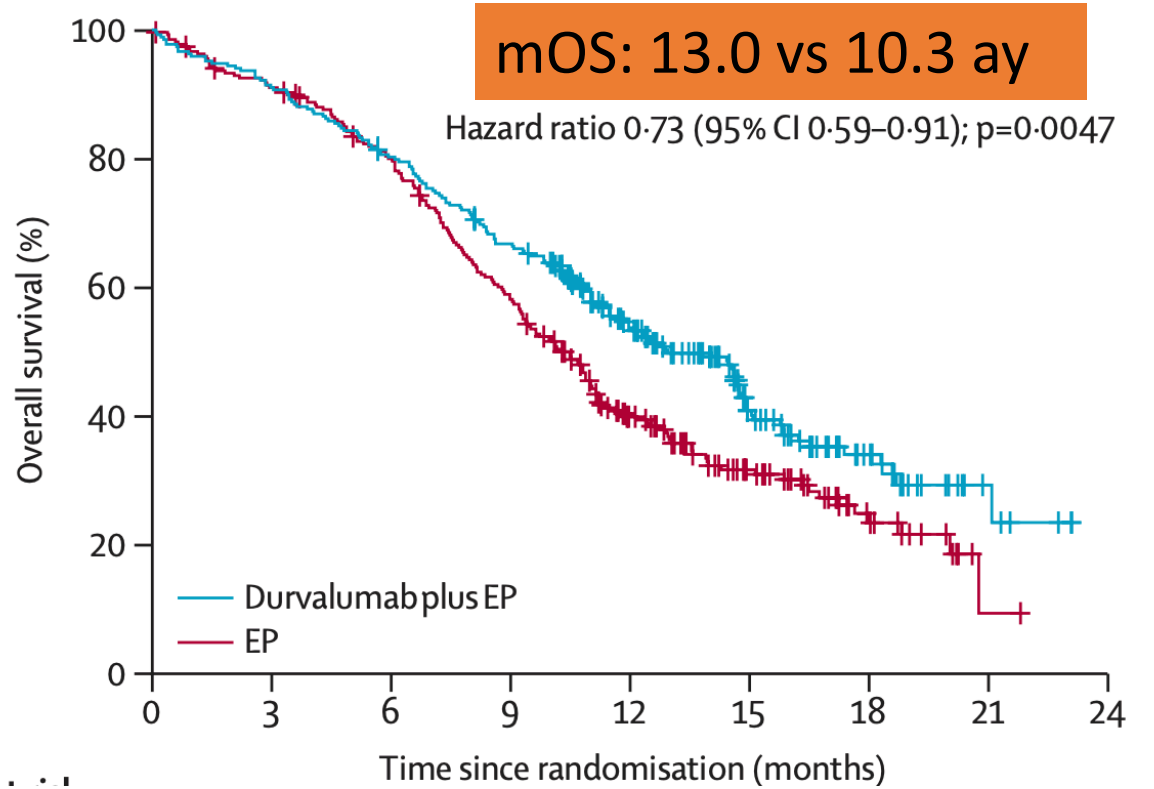
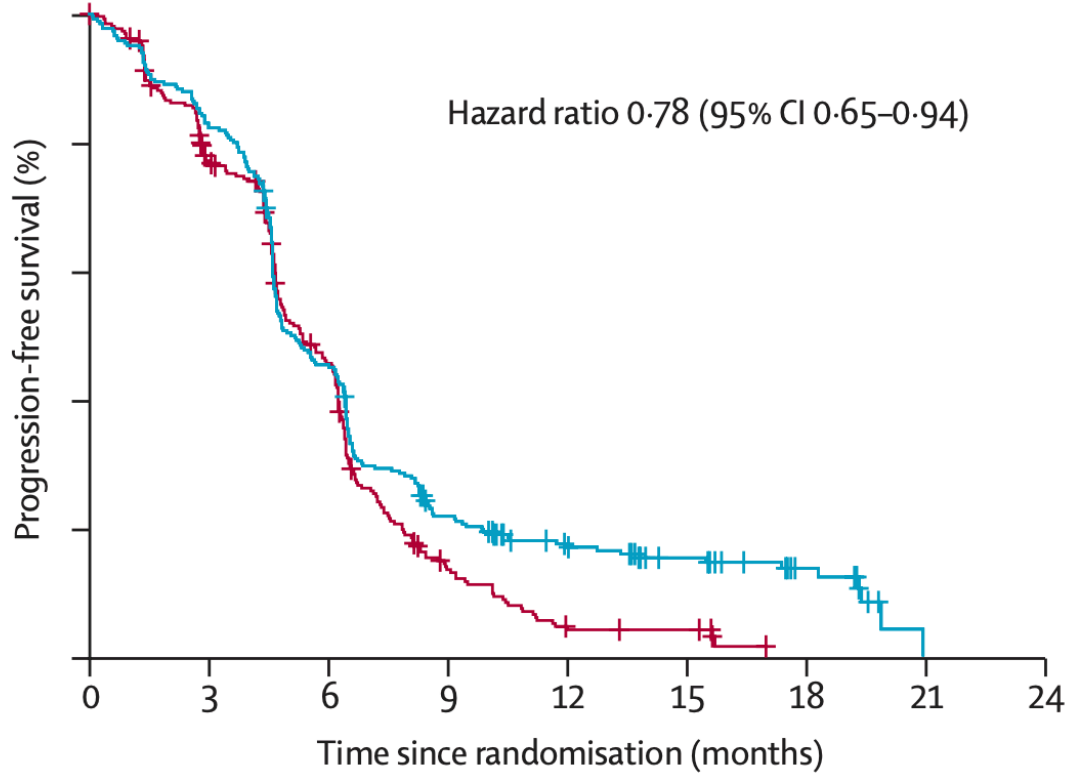
nised, open-label, sponsor-blind multicentre study



*EP consists of etoposide 80–100 mg/m² with either carboplatin AUC 5–6 or cisplatin 75–80 mg/m²

†Patients could receive an additional 2 cycles of EP (up to 6 cycles total) and PCI at the investigator's discretion

Lancet 2019; 394: 1929–39





- Atezolizumab

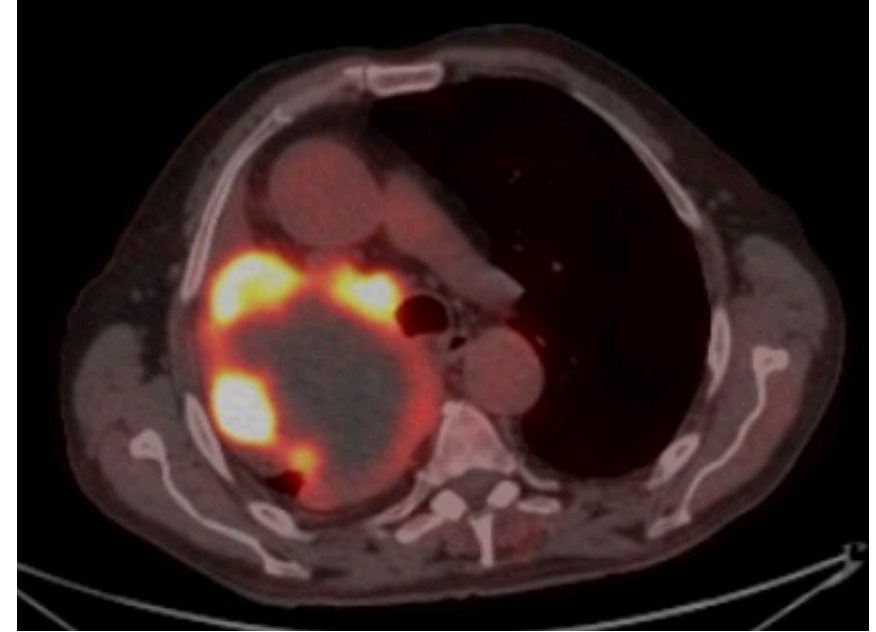
- Ruhsat+ Geri ödeme mevcut
- Karboplatin+ Etoposid ile



- Durvalumab

- Ruhsat+ Geri ödeme yok
- 4 kür karboplatin ya da sisplatin ile

- Bař ađrısı ve bulantı nedeniyle kraniyet Steroid+ Radyoterapi
- Akciđer kitle+ sűrrenal ve beyin metastatik
- Karboplatin+ Etoposid+ Atezolizumab 4 kűr (03/2024-06/2024)



2. Basamak
seenekler?



Recurrent SCLC (i.e. second-line therapy and beyond)

Platinum-resistant relapse
(<3 months TFI)

Platinum-sensitive relapse
(≥ 3 months TFI)



SCLC SUBSEQUENT SYSTEMIC THERAPY (PS 0–2)⁹ Consider dose reduction or growth factor support for patients with PS 2

Preferred

Tarlatamab-dlle^{i,27} (category 1)

- Clinical trial enrollment
- Irinotecan^{i,25,26}
- Lurbinectedin (if not previously used)^{20,21}
- If prolonged disease free time, re-treatment with platinum-based doublet with or without immunotherapy¹⁵⁻¹⁹
- Topotecan Oral (PO) or Intravenous (IV)^{17,22-25}

Other Recommended

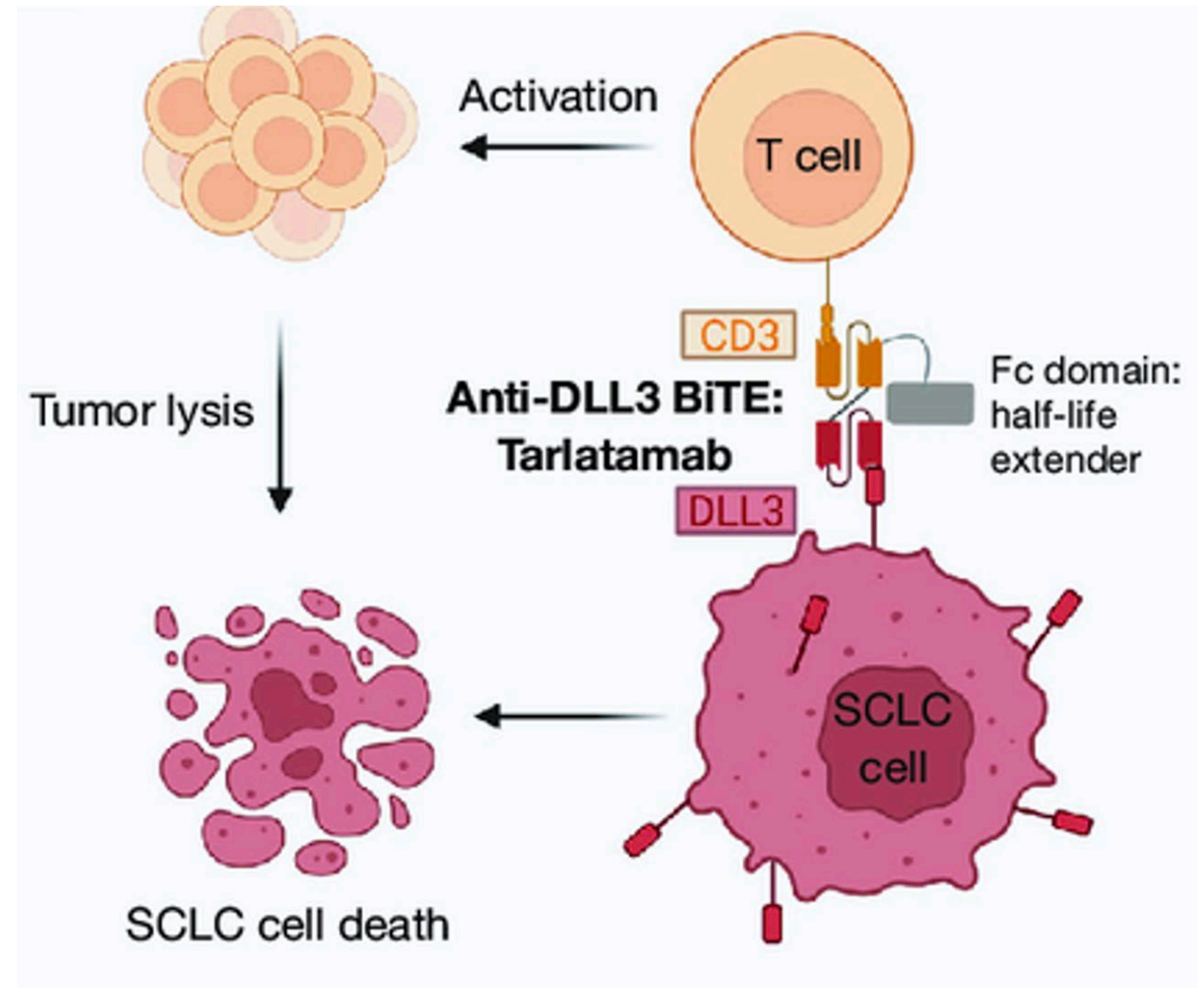
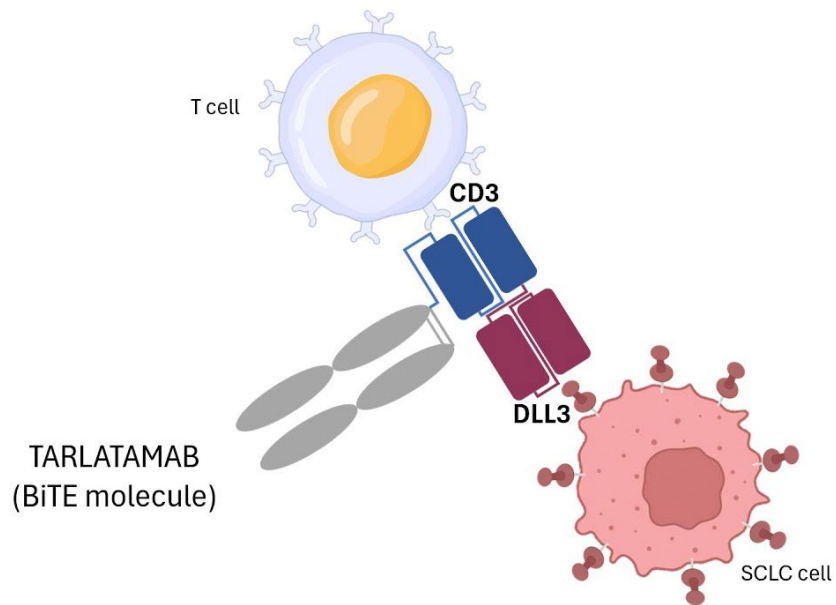
- CAV (Cyclophosphamide/Doxorubicin/Vincristine)²²
- Docetaxel³⁶
- Gemcitabine^{37,38,39}
- Nivolumabⁿ or Pembrolizumab (if not previously treated with an ICI)^{d,28-31}
- Oral Etoposide^{40,41}
- Paclitaxel^{32,33}
- Temozolomide^{34,35}

Rechallenge with platinum–
etoposide [II, B]
Oral or i.v. topotecan [I, A]
Cyclofosfamide–doxorubicin–
vincristine [II, B]

+ Atezo?
+ Durva?

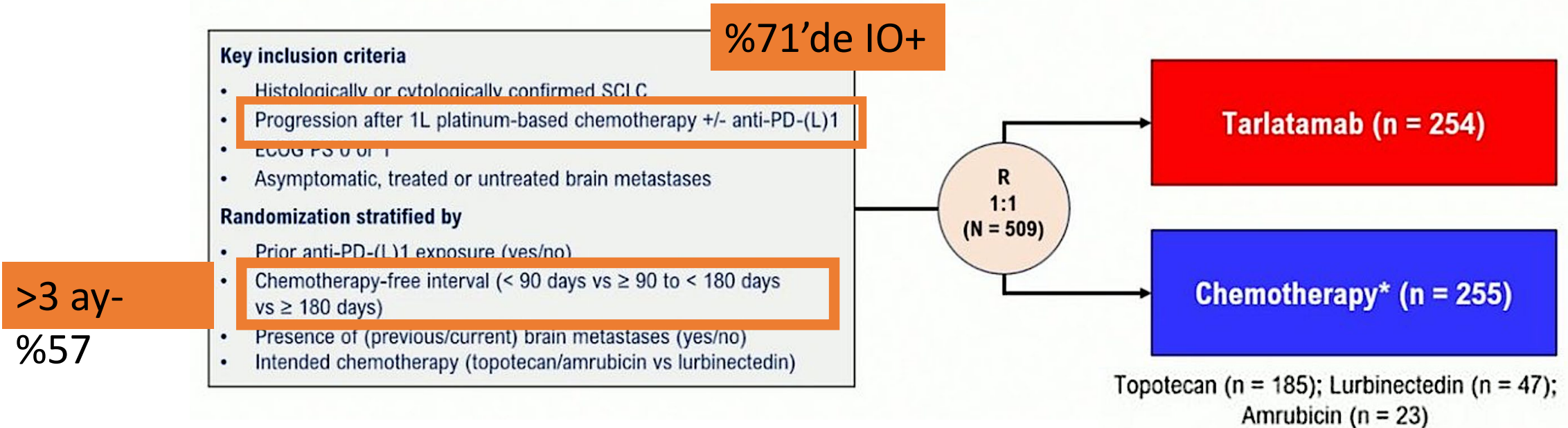
Bispecific T-cell engager

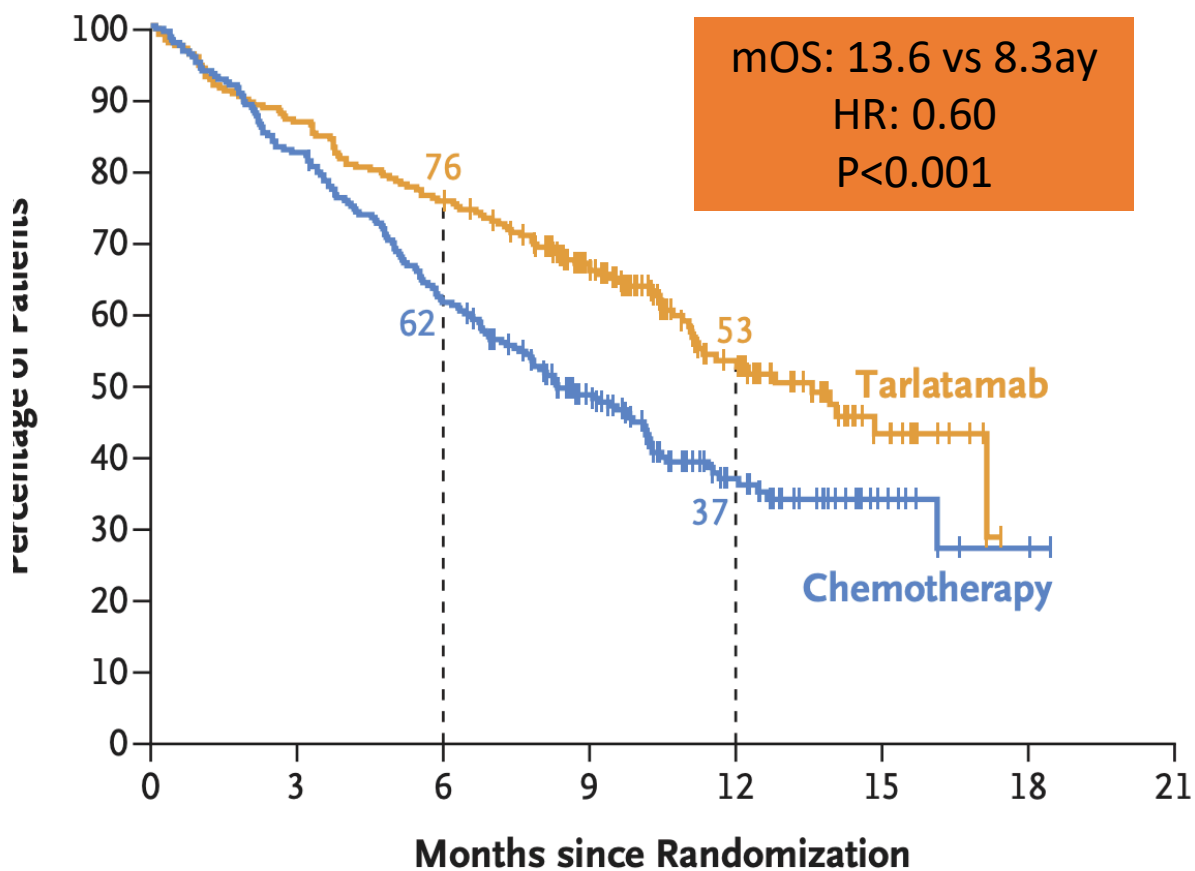
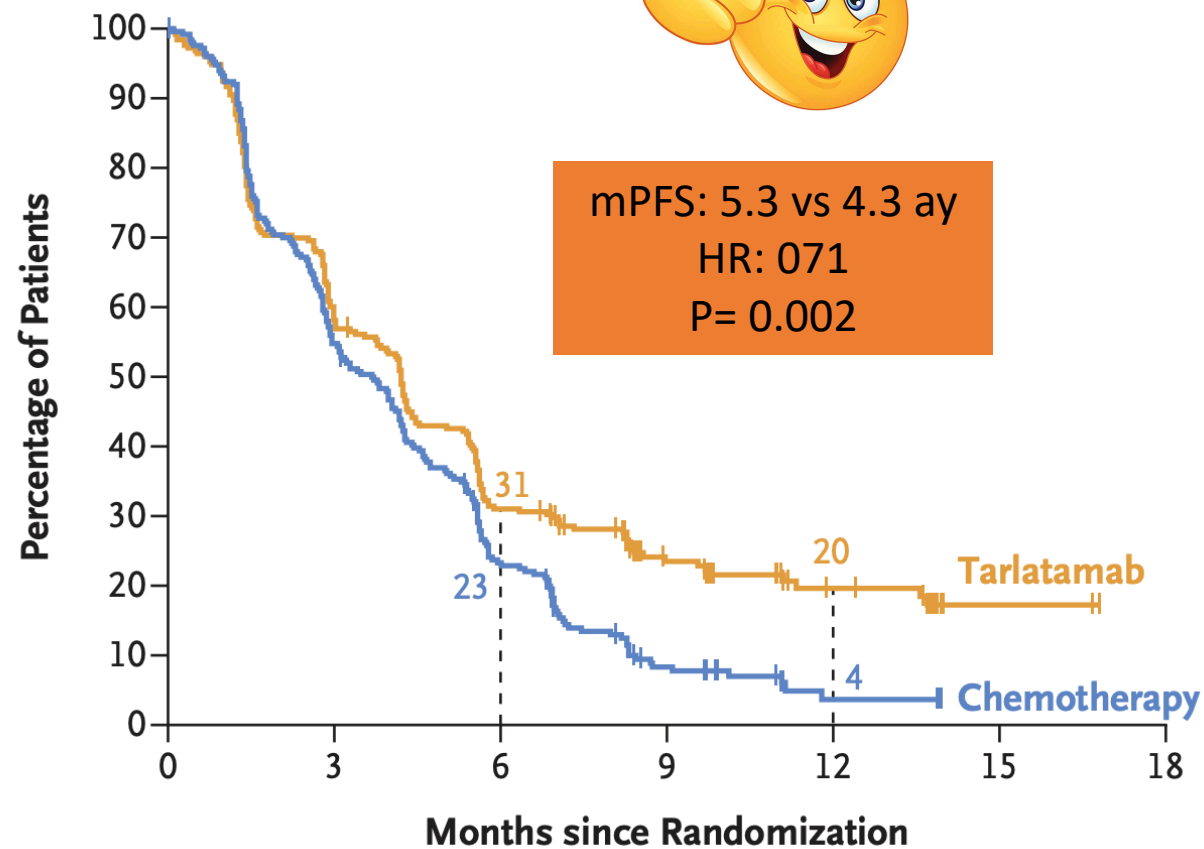
- Delta-like ligand 3 (DLL3)
- CD3



Tarlatamab in Small-Cell Lung Cancer after Platinum-Based Chemotherapy

Randomized, controlled, phase 3 DeLLphi-304 study (NCT05740566)





SCLC SUBSEQUENT SYSTEMIC THERAPY (PS 0–2)⁹
Consider dose reduction or growth factor support for patients with PS 2

Preferred

- Tarlatamab-dlle^{j,27} (category 1)
- Clinical trial enrollment
- Irinotecan^{1,20,20}
- Lurbinectedin (if not previously used)^{20,21}
- If prolonged disease free time, re-treatment with platinum-based doublet with or without immunotherapy¹⁵⁻¹⁹
- Topotecan Oral (PO) or Intravenous (IV)^{17,22-25}

Other Recommended

- CAV (Cyclophosphamide/Doxorubicin/Vincristine)²²
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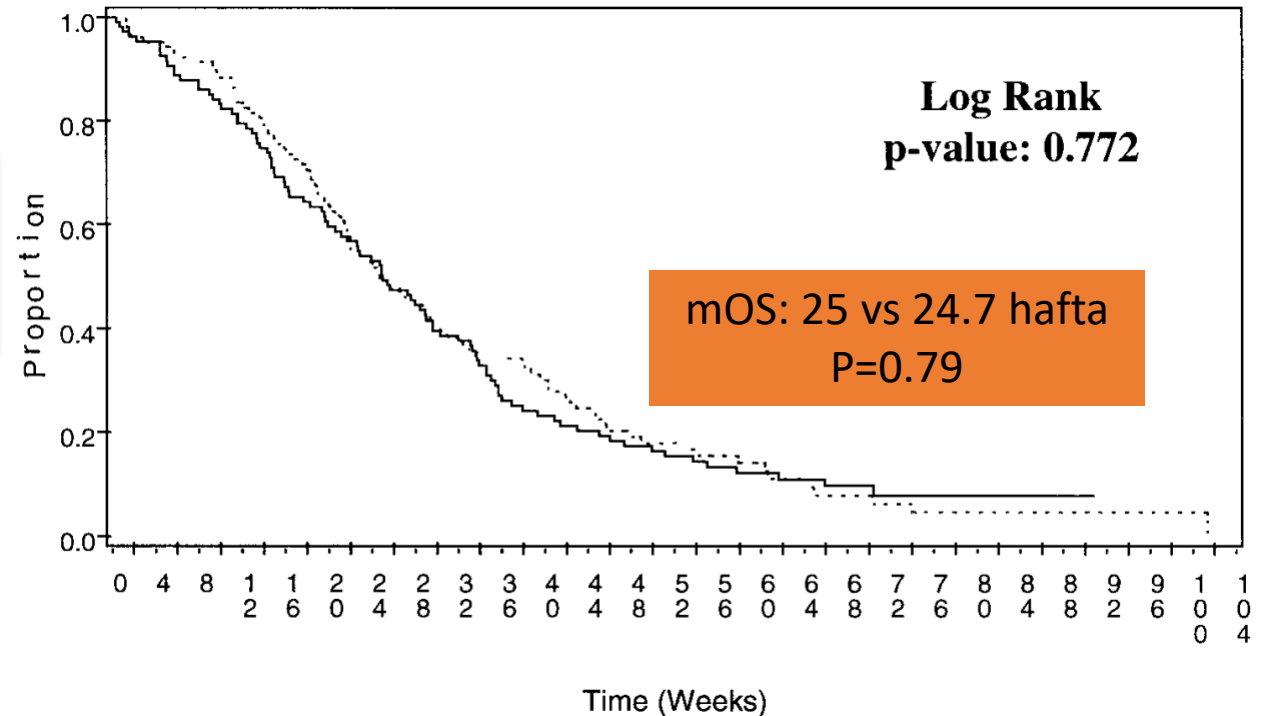
Phase III Trial Comparing Supportive Care Alone With Supportive Care With Oral Topotecan in Patients With Relapsed Small-Cell Lung Cancer

J Clin Oncol. 2006;24(34):5441.

Topotekan > BSC
mOS: 25 vs 13 hafta
P=0.01

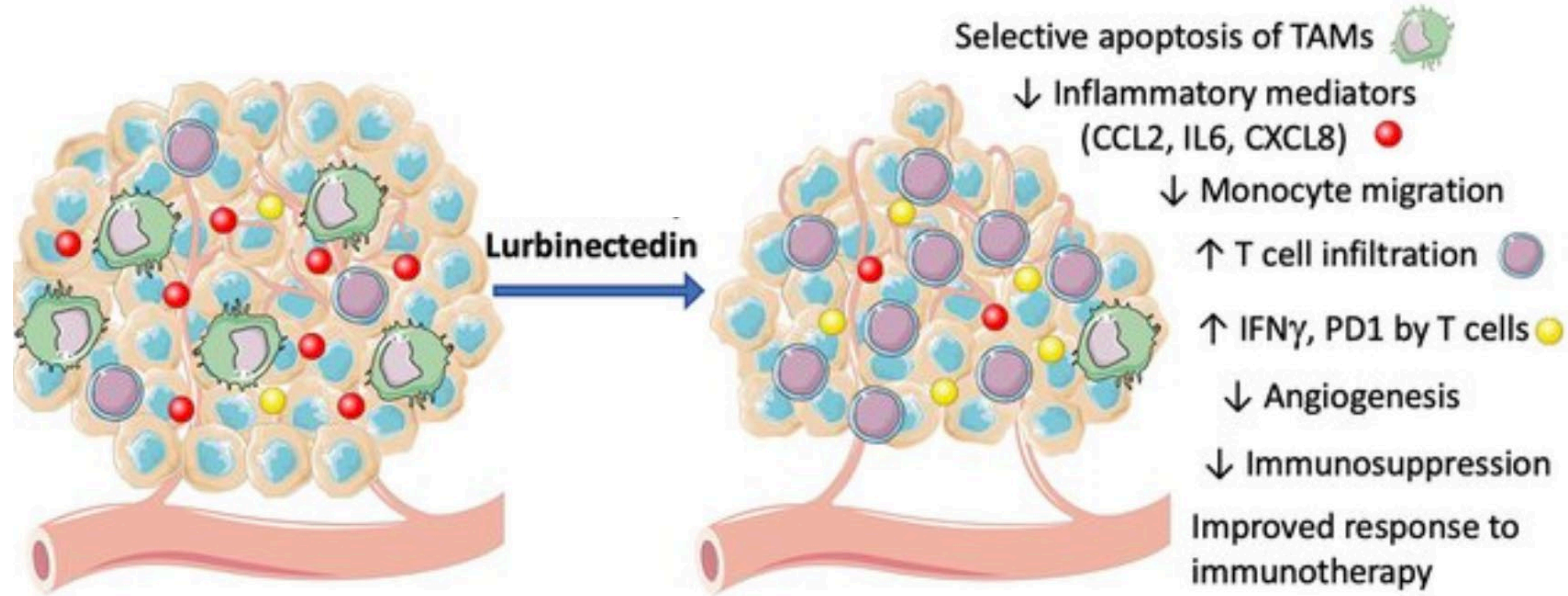
Topotecan Versus Cyclophosphamide, Doxorubicin, and Vincristine for the Treatment of Recurrent Small-Cell Lung Cancer

J Clin Oncol. 1999;17(2):658



Lurbinectedin

- Sentetik alkilleyici ajan
- DNA'nın minor groove'una bağlanır → RNA polimeraz II'yi inhibe eder → transkripsiyon durur



All treated patients (n=105)	
Disease stage at diagnosis	
Limited	32 (30%)
Extensive	73 (70%)
Median number of previous therapy lines	
1 line	98 (93%)
2 lines	7 (7%)§
Previous therapies	
Platinum compounds	105 (100%)
Etoposide	104 (99%)¶
Immunotherapy	8 (8%)
Poly(ADP-ribose) polymerase inhibitor	2 (2%)
Best response to previous platinum therapy	
Complete response	9 (9%)
Partial response	70 (67%)
Stable disease	19 (18%)
Disease progression	4 (4%)
Unknown	3 (3%)
Median chemotherapy-free interval, months	
<90 days	45 (43%)
≥90 days	60 (57%)

Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial

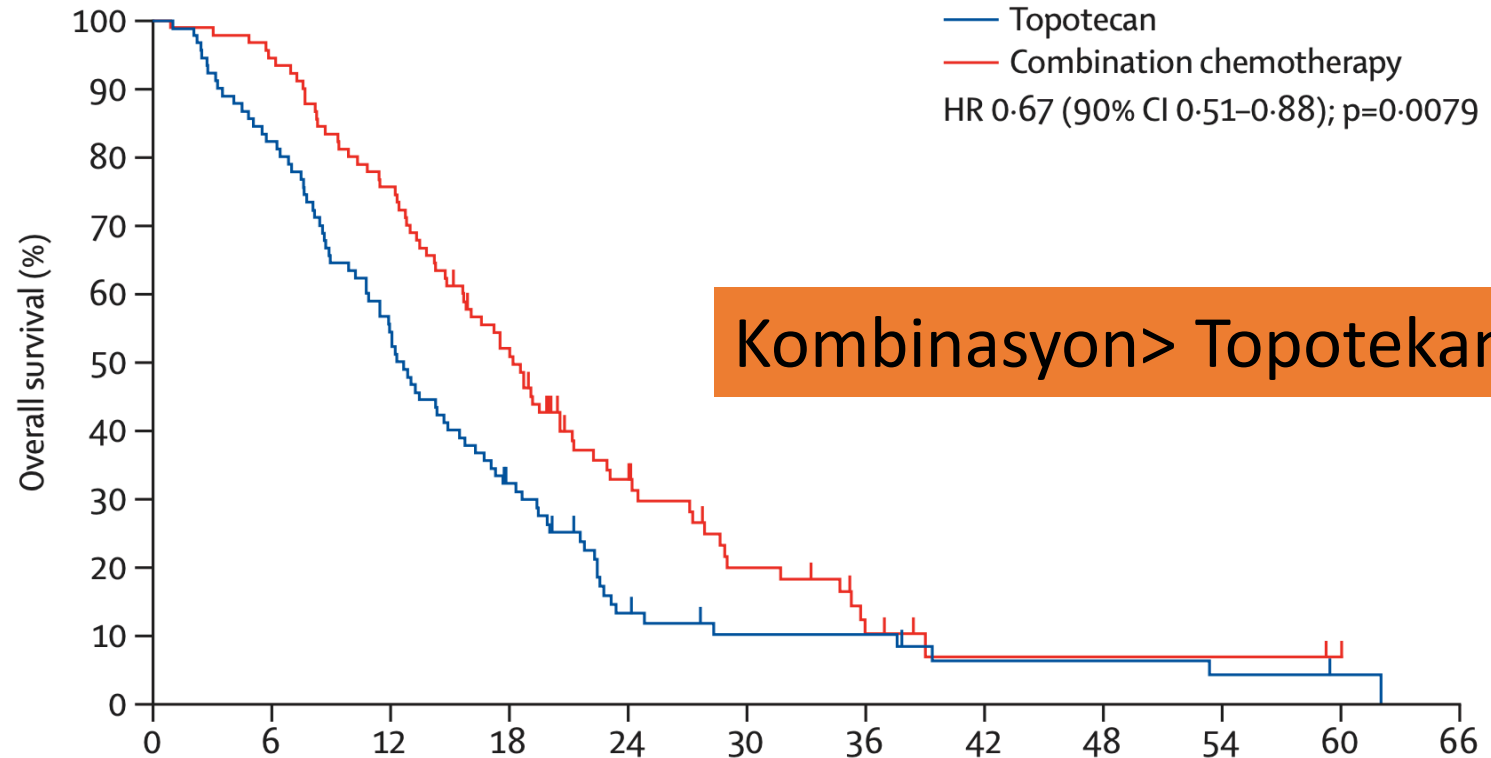
	All patients (n=105)	Chemotherapy-free interval <90 days (n=45)	Chemotherapy-free interval ≥90 days (n=60)
Overall survival			
Deaths	66 (63%)	37 (82%)	29 (48%)
Median overall survival, months (95% CI)	9.3 ay	5.0 ay	11.9 ay
6-month overall survival (95%CI)	67.1% (57.6-76.7)	45.8% (30.4-61.3)	83.6% (73.7-93.5)
12-month overall survival (95% CI)	34.2% (23.2-45.1)	15.9% (3.6-28.2)	48.3% (32.5-64.1)



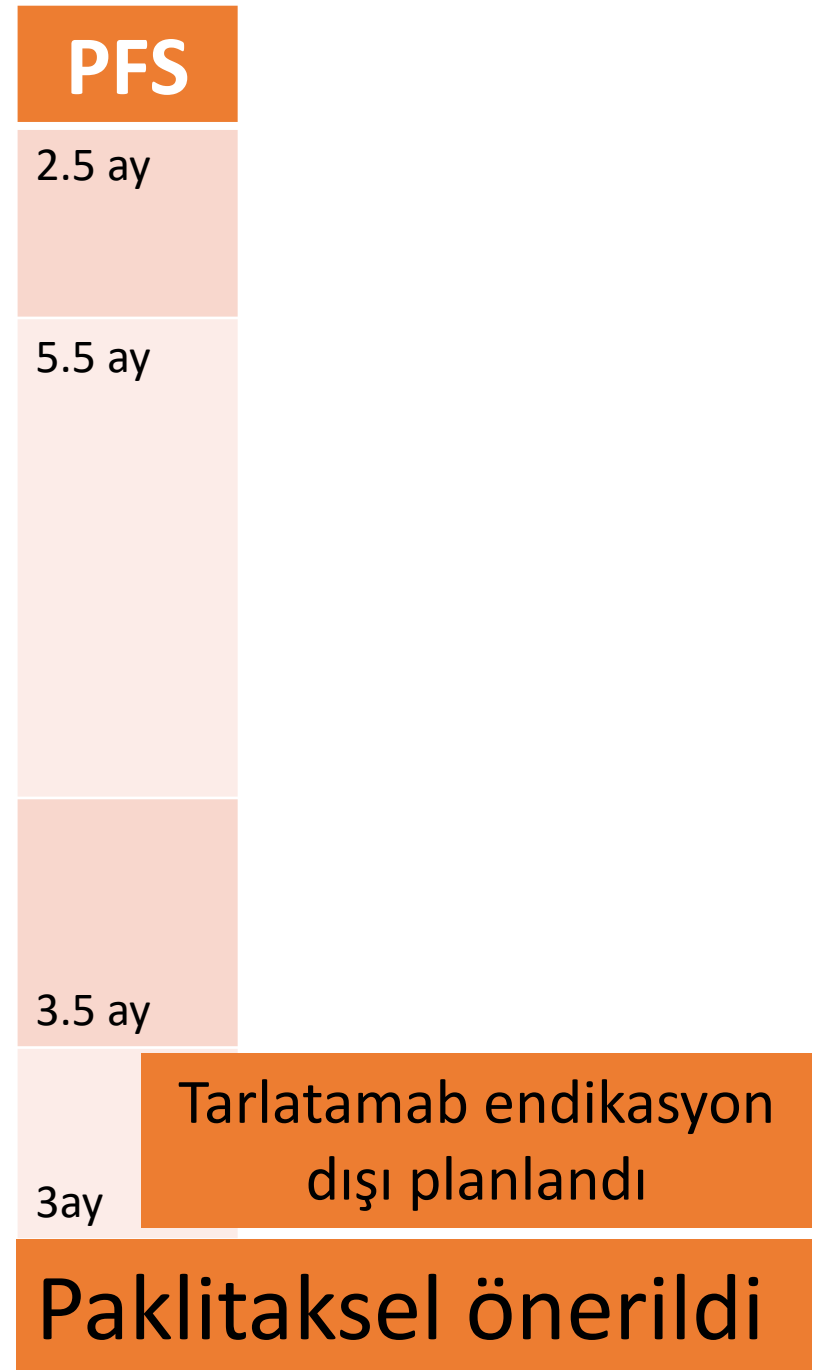
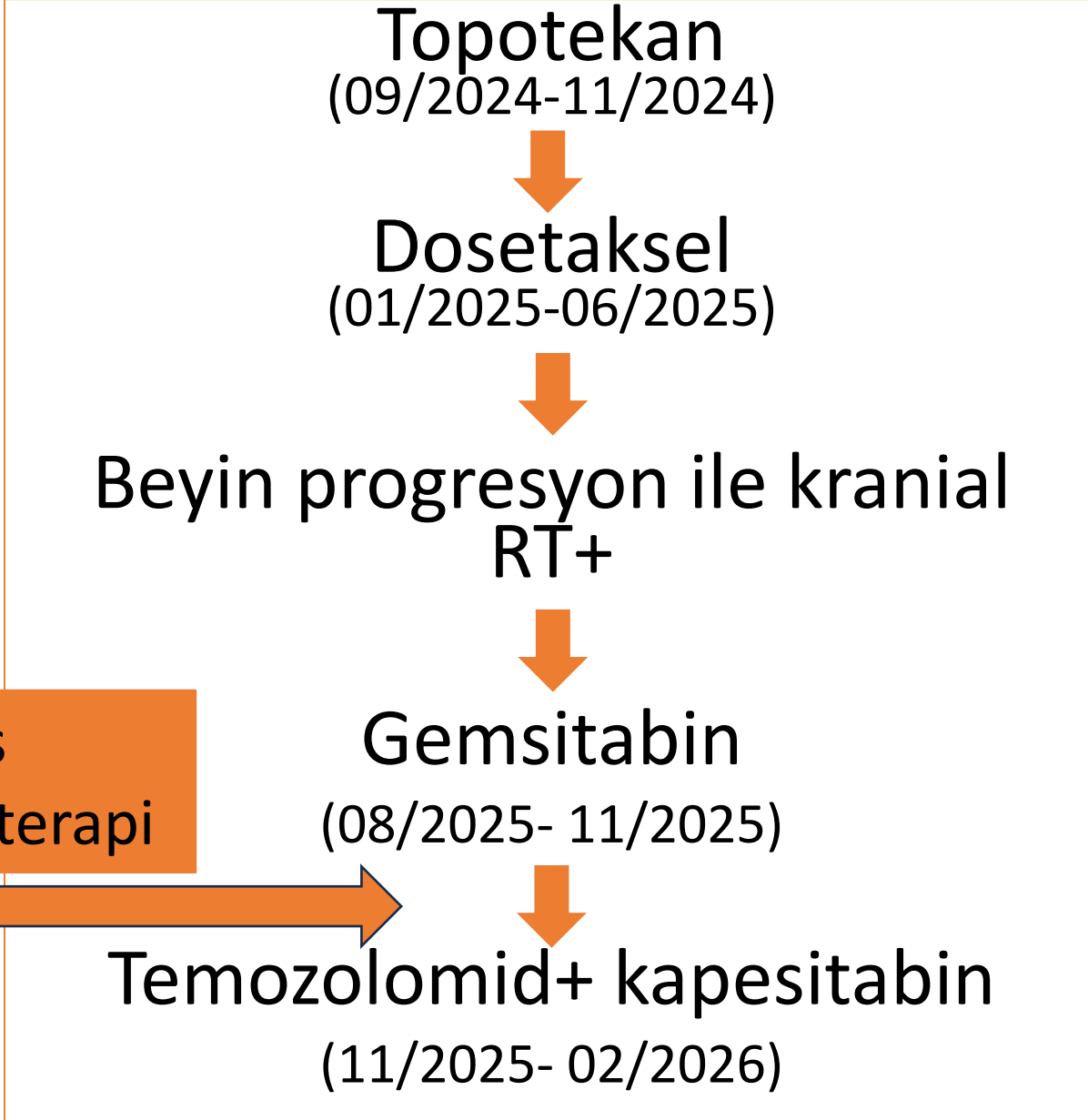
Combined chemotherapy with cisplatin, etoposide, and irinotecan versus topotecan alone as second-line treatment for patients with sensitive relapsed small-cell lung cancer (JCOG0605): a multicentre, open-label, randomised phase 3 trial

180 enrolled and randomised

Topotekan monoterapi



Kombinasyon > Topotekan



SCLC SUBSEQUENT SYSTEMIC THERAPY (PS 0-2)⁹

Consider dose reduction or growth factor support for patients with PS 2

Preferred

- **Tarlatamab-dlle^{j,27}** (category 1)

- Clinical trial enrollment

- Irinotecan^{25,26}

- **Lurbinectedin** (if not previously used)^{20,21}

- If prolonged disease free time, re-treatment with platinum-based doublet with or without irinotecan

- Topotecan Oral (PO) or Intravenous (IV)^{17,22-25}

Other Recommended

- CAV (Cyclophosphamide/Doxorubicin/Vincristine)²²

- Docetaxel³⁶

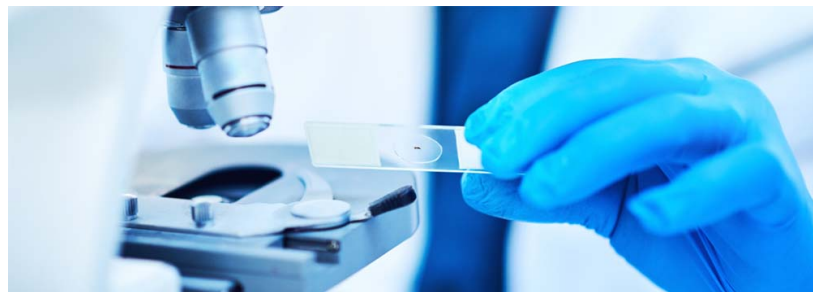
- Gemcitabine^{37,38,39}

- **Nivolumabⁿ** or Pembrolizumab (if not previously treated with an ICI)^{d,28-31}

- Oral Etoposide^{40,41}

- Paclitaxel^{32,33}

- Temozolomide^{34,35}



Patoloji konsultasyonu



NGS hedef yok

- B.C.
- 63 yaş erkek hasta
- 50pktyıl sigara
- BPH
- ECOG 1
- Öksürük/ balgam nedeniyle tekiklerde;

Sürrenal+ kemik metastazları

Toraks: Sağ akciğer santral parahiler alanda bronşları çevreleyen, orta lob bronşunu oblitere edip periferde atelektaziye sebep olan, nekrotik alanlar ihtiva eden kitle/konglomere lenf nodu (yaklaşık 6 cm, SUVmaks: 10.6) görülmüştür.

TANI

1-2-MALİGN NEOPLAZİ

1-Sağ akciğer orta-alt lob ayrımından bronkoskopik biyopsi-1

2-Sağ akciğer orta-alt lob ayrımından bronkoskopik biyopsi-2

3-4-MALİGN SİTOLOJİ

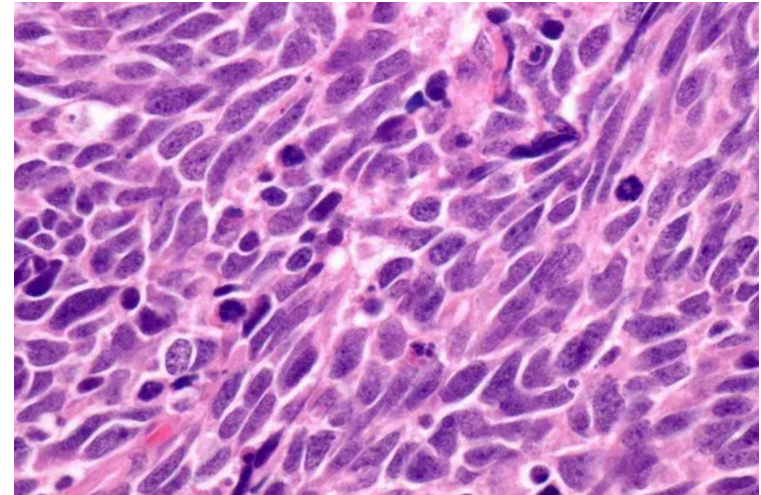
3-Fırçalama sitolojisi

4-Bronş lavajı

Yorum

Her 2 şişede gönderilen biyopsilerdeki tümörler aynı morfolojide olup, tümörde TTF1, CD56, Sinaptofizin pozitif, CK5/6 negatif saptanmıştır. ki67 indeksi % 90 civarındadır.

Mevcut bulgularla tümör KÜÇÜK HÜCRELİ AKCİĞER KARSİNOMU ile uyumludur.



Karboplatin+ Etoposid+ Atezolizumab (4 kür)
(Parsiyel yanıt)



+Zoledronik asit

Atezolizumab idame (04/2024- 12/2025) **(20 ay)**



RESPONSE ASSESSMENT FOLLOWING PRIMARY TREATMENT

- See Treatment Response Assessment in Principles of Imaging ([SCL-G](#))
- CBC
- Electrolytes, LFTs, BUN, creatinine

Complete response or partial response

Limited stage

- Durvalumab^{m,y,z} (category 1)
- Prophylactic cranial irradiation (PCI)^{c,n,v,w} or consider MRI brain surveillance^{e,v}

Extensive stage

- MRI brain surveillance^{e,v} ±
- Consider PCI^{n,v}
- Consider thoracic RT^{n,x}

Stable disease

Limited stage

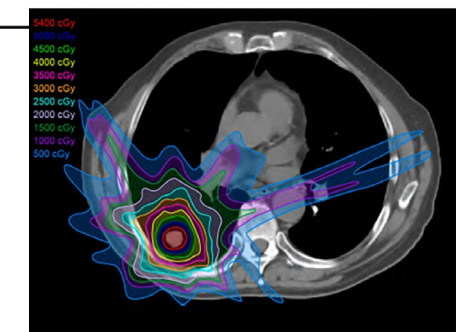
Durvalumab^{m,z} (category 1)

Extensive stage

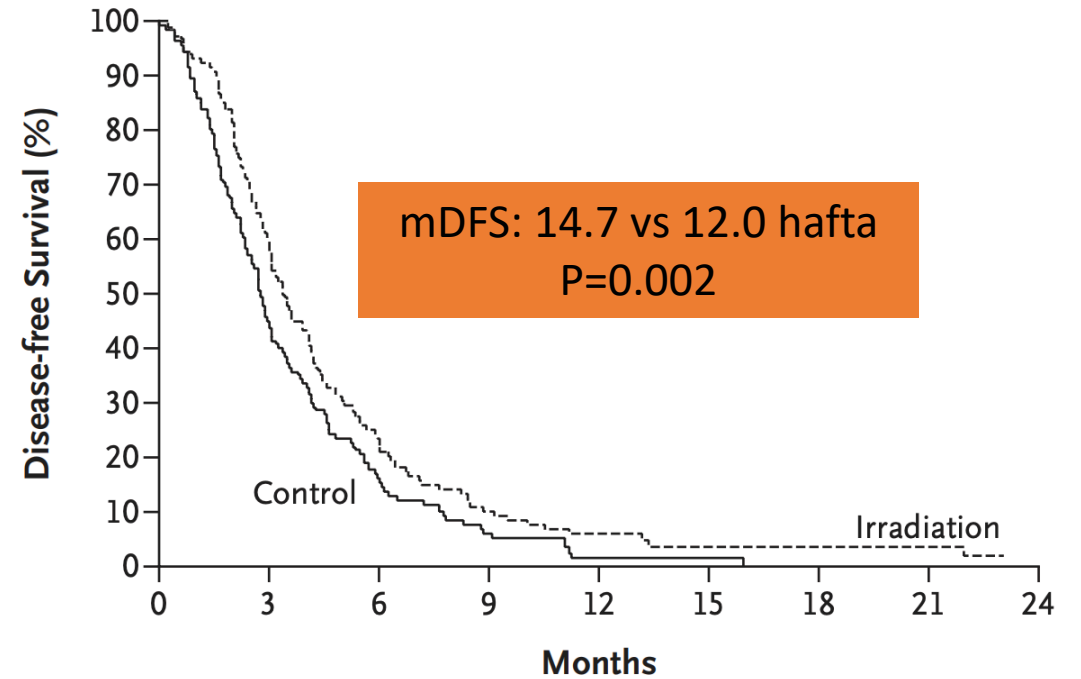
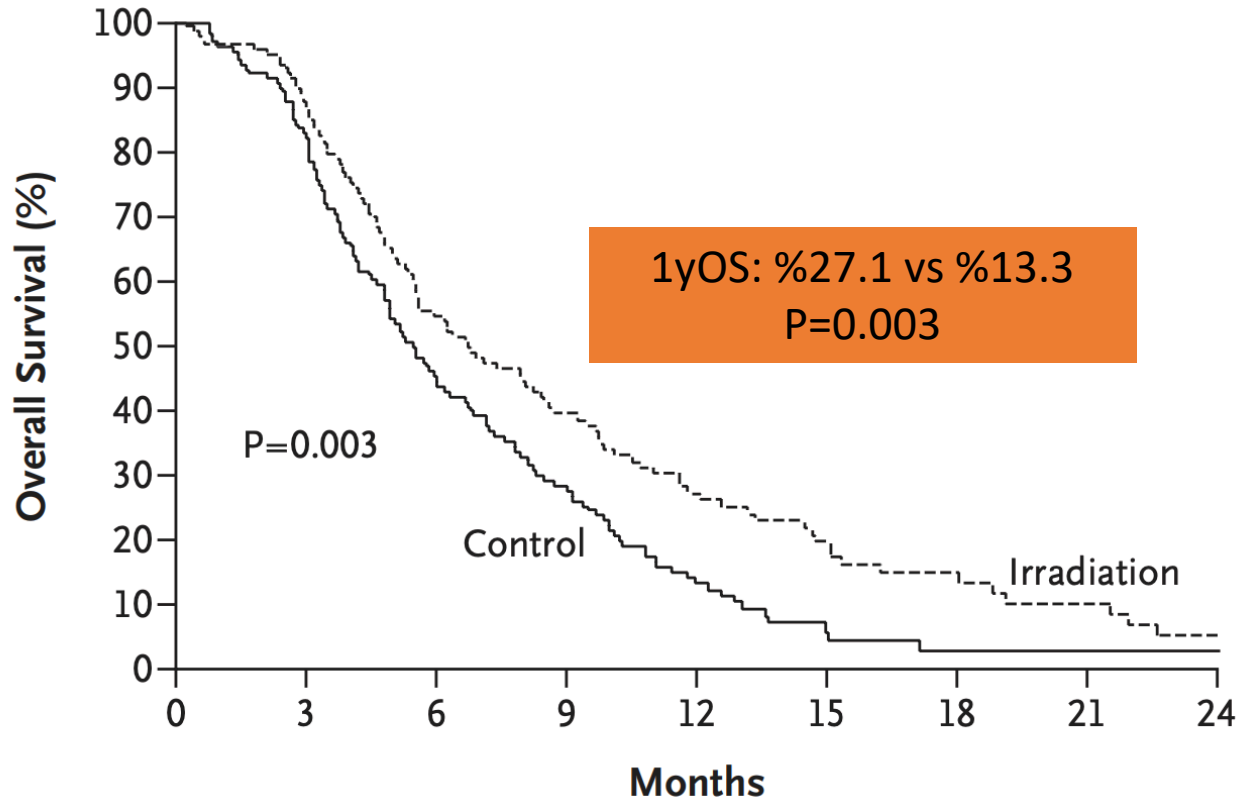
Primary progressive disease

[Subsequent Therapy/Palliative Therapy \(SCL-8\)](#)

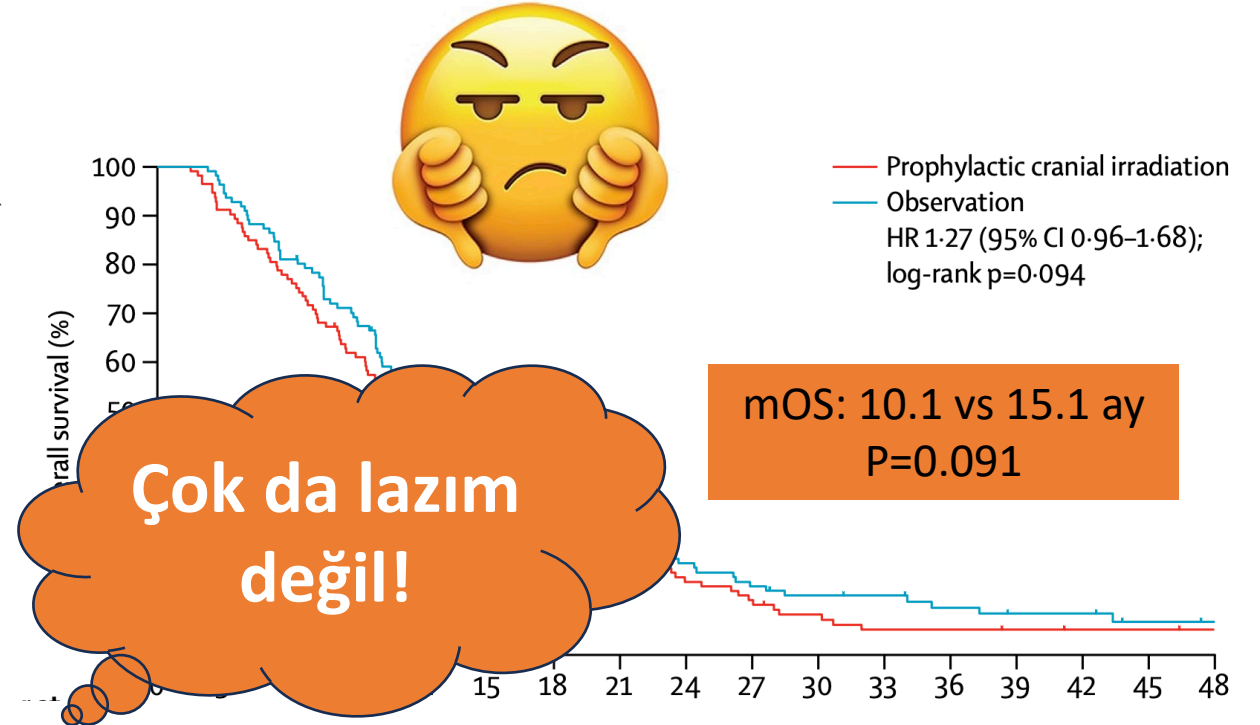
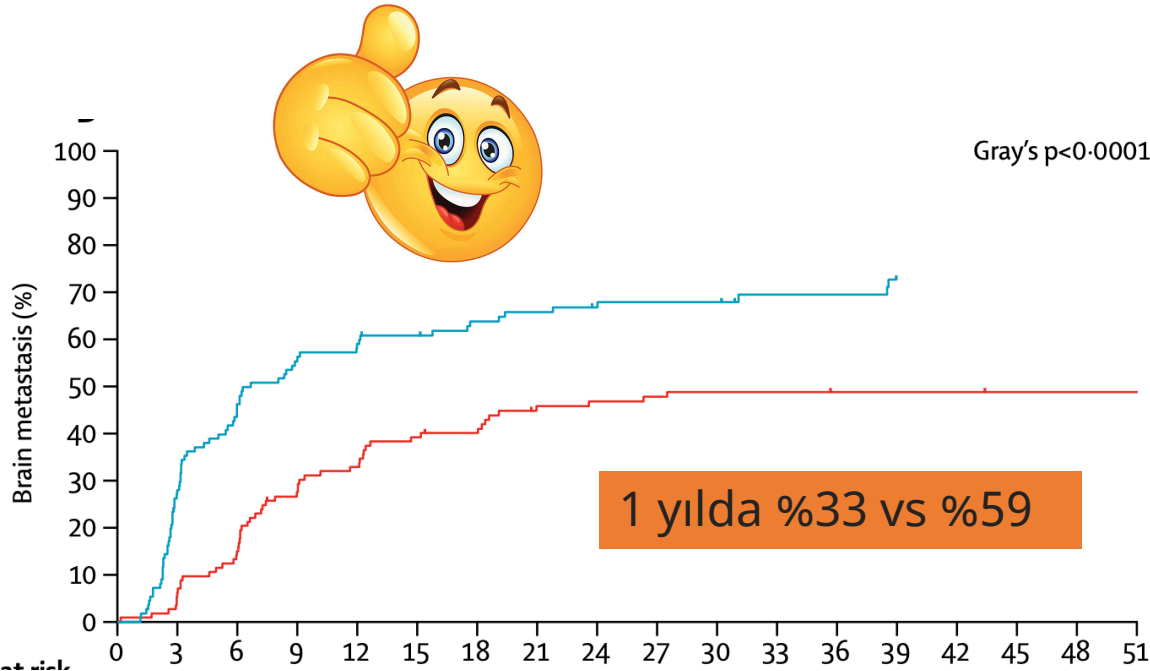
ADJUVANT THERAPY



Prophylactic Cranial Irradiation in Extensive Small-Cell Lung Cancer

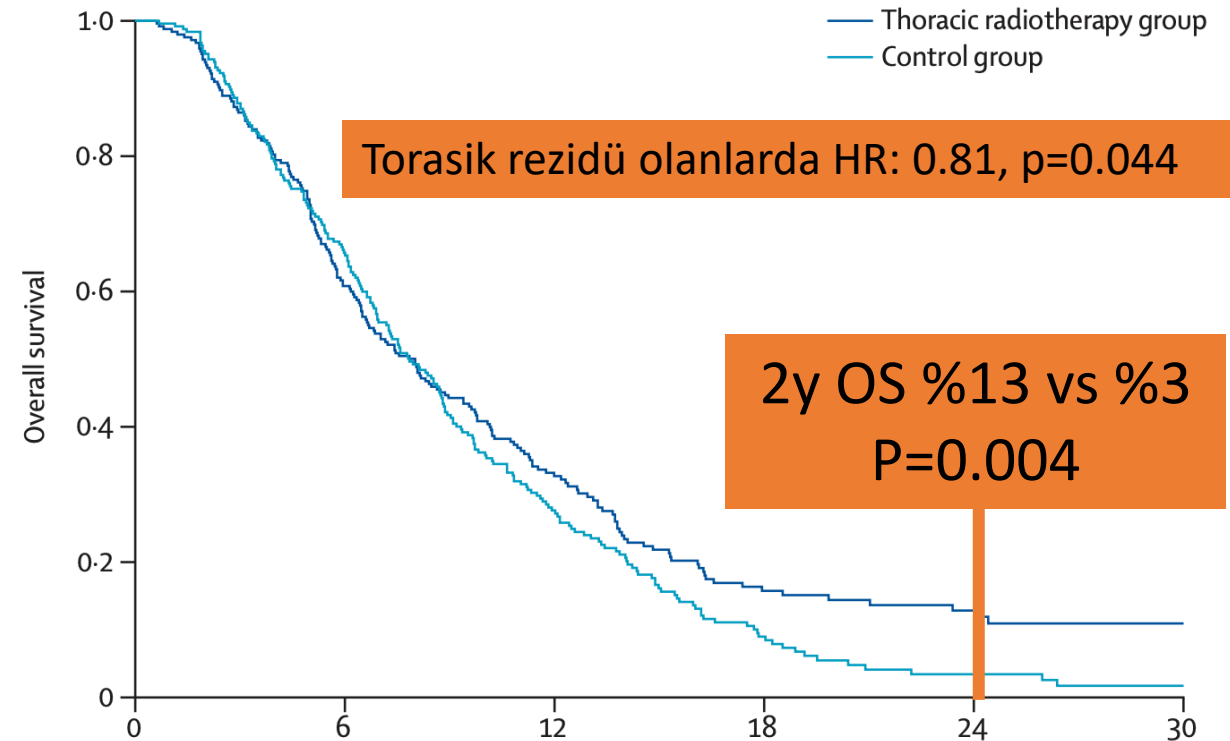
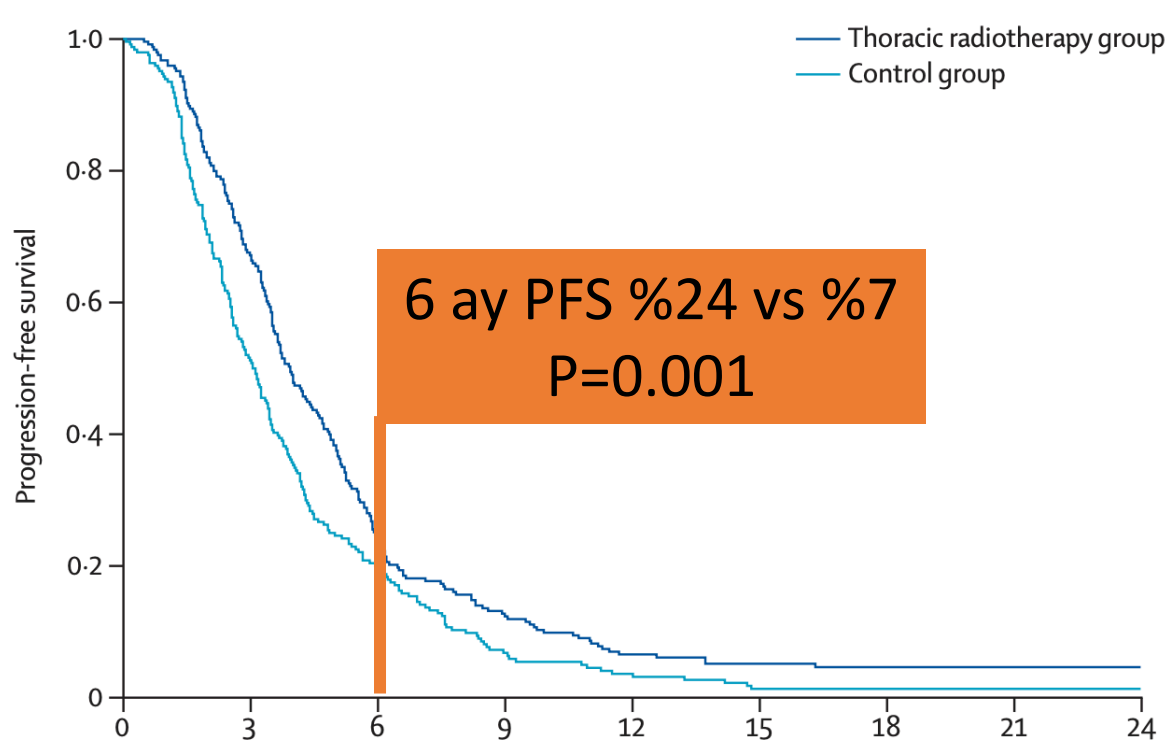


Prophylactic cranial irradiation versus observation in patients with extensive-disease small-cell lung cancer: a multicentre, randomised, open-label, phase 3 trial



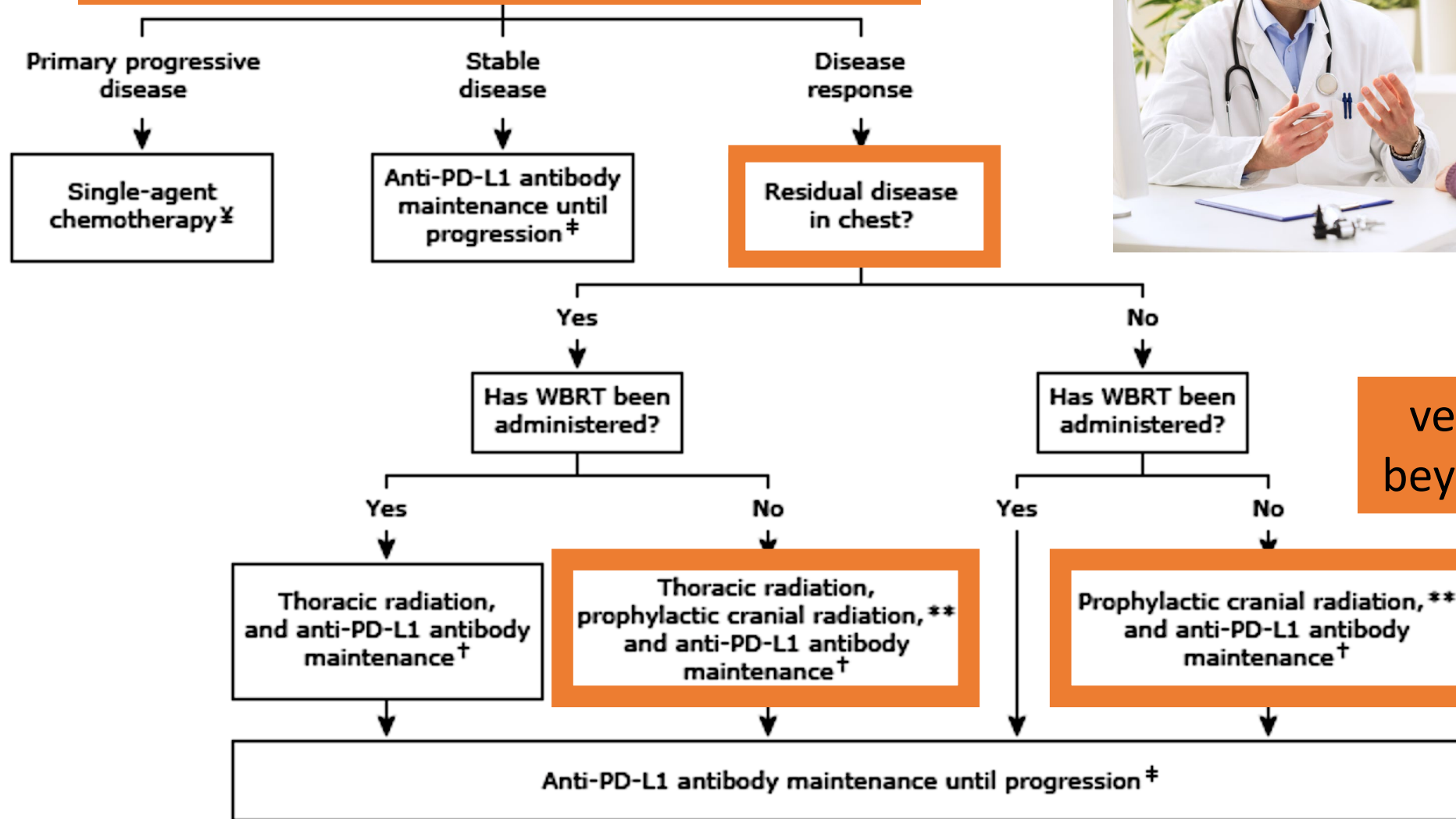
Interpretation In this Japanese trial, prophylactic cranial irradiation did not result in longer overall survival compared with observation in patients with extensive-disease small-cell lung cancer. Prophylactic cranial irradiation is therefore not essential for patients with extensive-disease small-cell lung cancer with any response to initial chemotherapy and a confirmed absence of brain metastases when patients receive periodic MRI examination during follow-up.

Use of thoracic radiotherapy for extensive stage small-cell lung cancer: a phase 3 randomised controlled trial



Interpretation Thoracic radiotherapy in addition to prophylactic cranial irradiation should be considered for all patients with ES-SCLC who respond to chemotherapy.

1. Basamak EP+ Atezo/ Durva



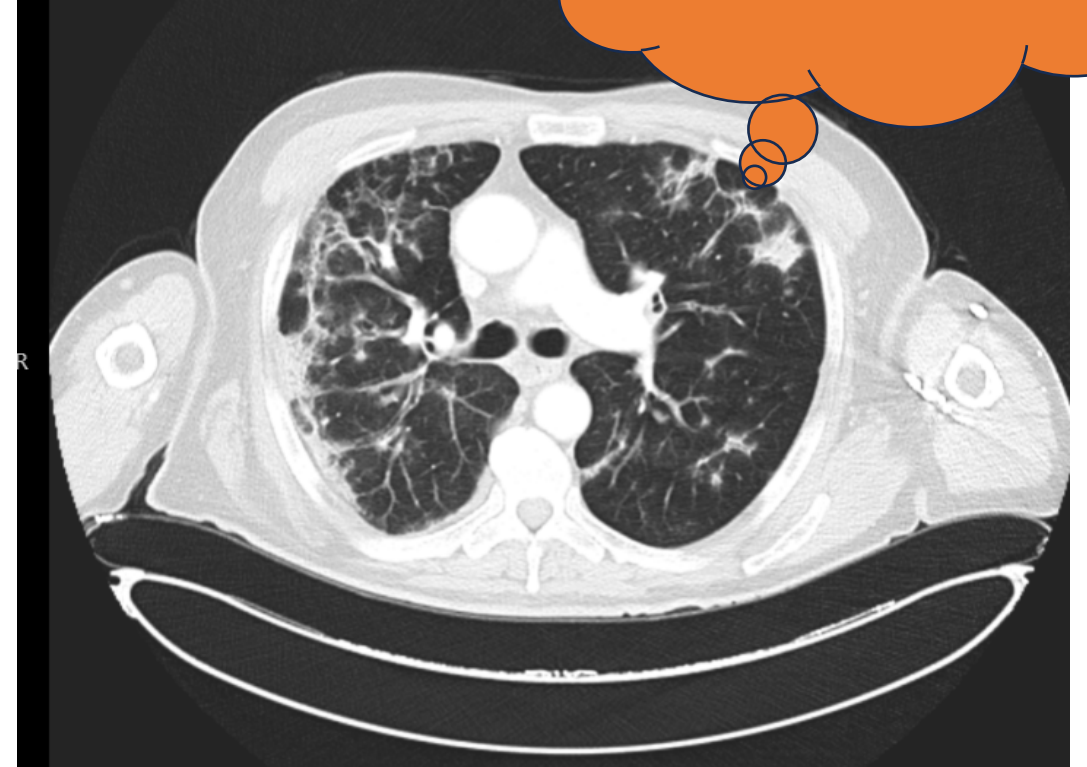
veya düzenli beyin MR takip

İdame Atezolizumab altında
01/2026 öksürük+ dispne+ hipoksemi

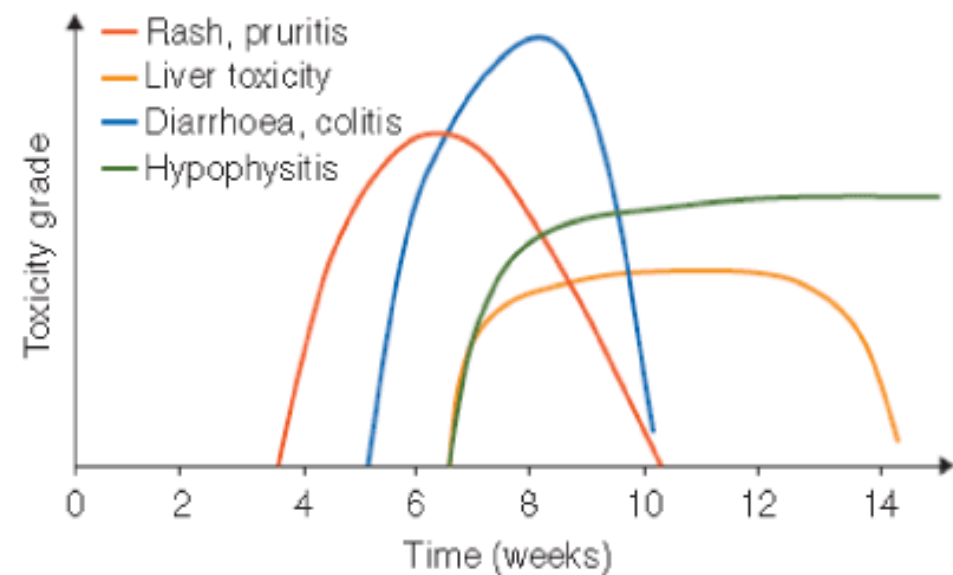
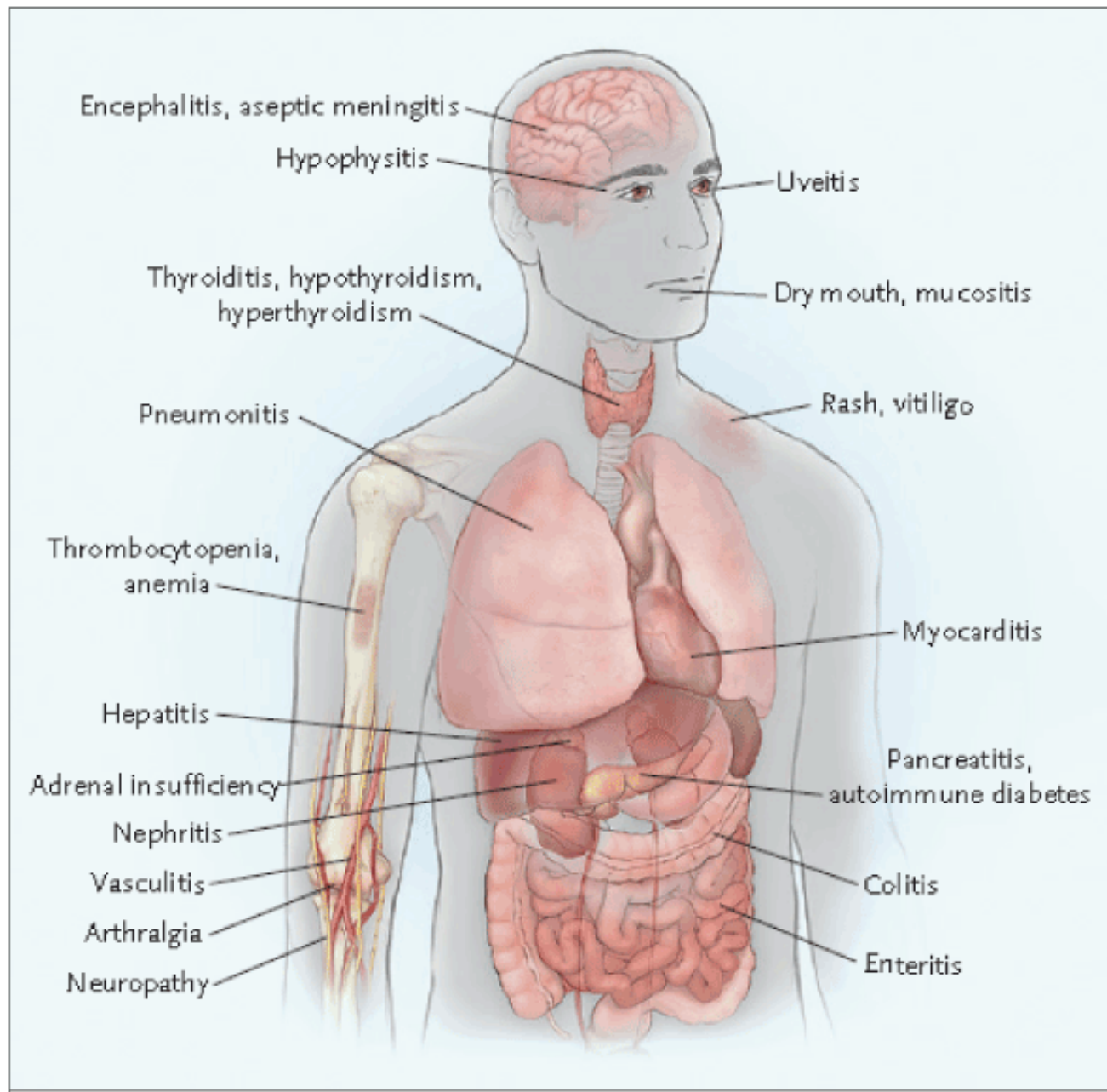
Atezo ilişkili
Pnömonit?



**Perihiler ve alt zonlarda belirgin
yama tarzında alveoler opasiteler**



**Periferik ve peribronkovasküler alanlarda yama
tarzında buzlu cam opasiteler ve konsolidasyon alanları**



79(%39.9)

48(%24.5)

Table S10. Immune-Related Adverse Events.

Patients — no. (%)	Atezolizumab Group (N=198)	Placebo Group (N=196)
Rash		
All grades	37 (18.7)	20 (10.2)
Grade 3–4	4 (2.0)	0
Hypothyroidism		
All grades	25 (12.6)	1 (0.5)
Grade 3–4	0	0
Hepatitis (diagnosis)		
All grades	14 (7.1)	9 (4.6)
Grade 3–4	3 (1.5)	0
Hepatitis (laboratory abnormalities)		
All grades	14 (7.1)	9 (4.6)
Grade 3–4	3 (1.5)	0
Infusion-related reaction		
All grades	11 (5.6)	10 (5.1)
Grade 3–4	4 (2.0)	1 (0.5)
Hyperthyroidism		
All grades	11 (5.6)	5 (2.6)
Grade 3–4	0	0
Pneumonitis		
All grades	4 (2.0)	5 (2.6)
Grade 3–4	1 (0.5)	2 (1.0)
Colitis		
All grades	3 (1.5)	0
Grade 3–4	2 (1.0)	0
Pancreatitis		
All grades	1 (0.5)	2 (1.0)
Grade 3–4	1 (0.5)	2 (1.0)
Severe cutaneous reaction		
All grades	2 (1.0)	0
Grade 3–4	0	0
Adrenal insufficiency		
All grades	0	2 (1.0)
Grade 3–4	0	0

	Durvalumab + EP (n=265)		EP (n=266)	
	Any grade*	Grade 3 or 4	Any grade*	Grade 3 or 4
Any immune-mediated adverse event (grouped term), n (%) ^{†,‡}	52 (20%)	12 (5%)	7 (3%)	1 (<1%)
Hypothyroid events	24 (9%)	0	2 (1%)	0
Hyperthyroid events	14 (5%)	0	0	0
Pneumonitis	7 (3%)	2 (1%)	2 (1%)	1 (<1%)
Hepatic events	7 (3%)	5 (2%)	0	0
Dermatitis/rash	4 (2%)	0	2 (1%)	0
Diarrhoea/colitis	4 (2%)	1 (<1%)	1 (<1%)	0
Thyroiditis	4 (2%)	0	0	0
Type 1 diabetes mellitus	4 (2%)	4 (2%)	0	0
Adrenal insufficiency	1 (<1%)	0	0	0
Pancreatic events	1 (<1%)	1 (<1%)	0	0
Other rare/miscellaneous [§]	2 (1%)	0	0	0

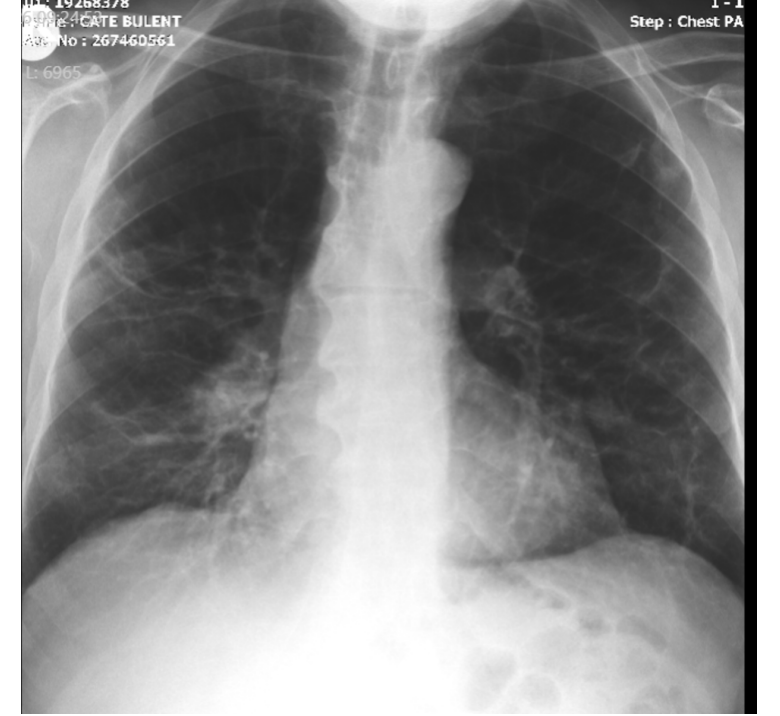
Hospitalizasyon ile 1mg/kg Metilprednizolon
Sonrasında oral devam



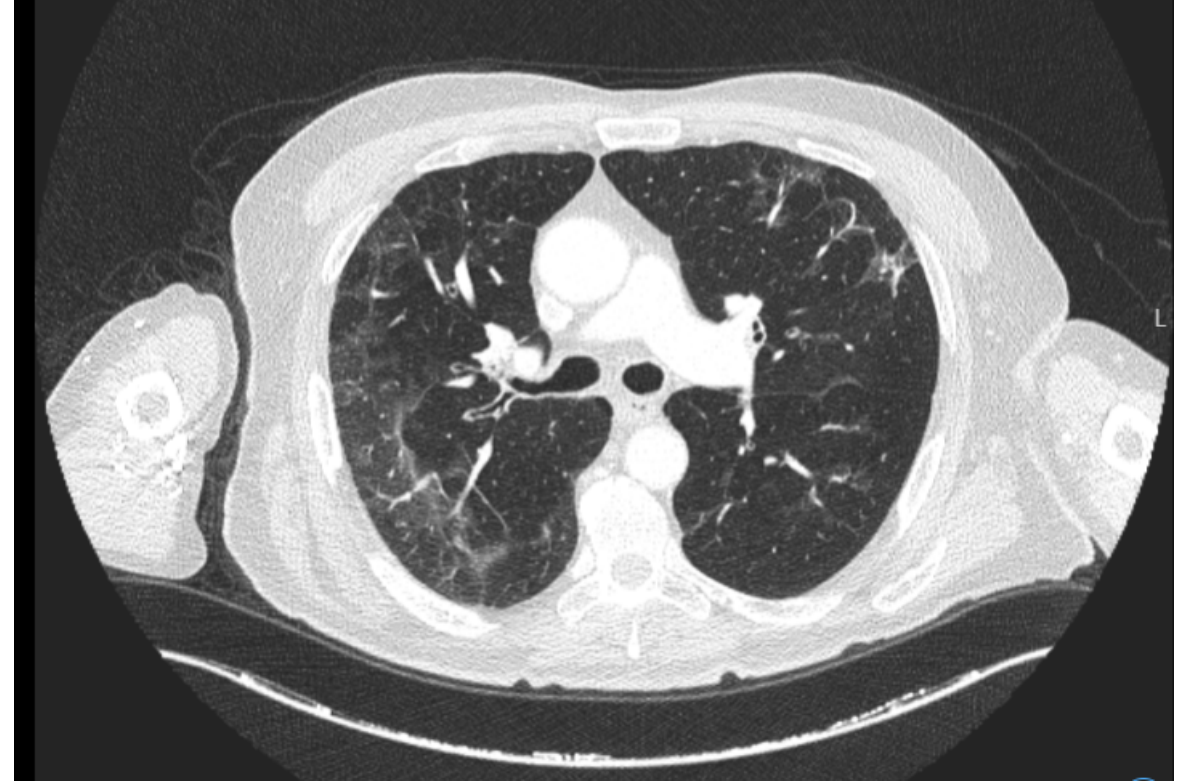
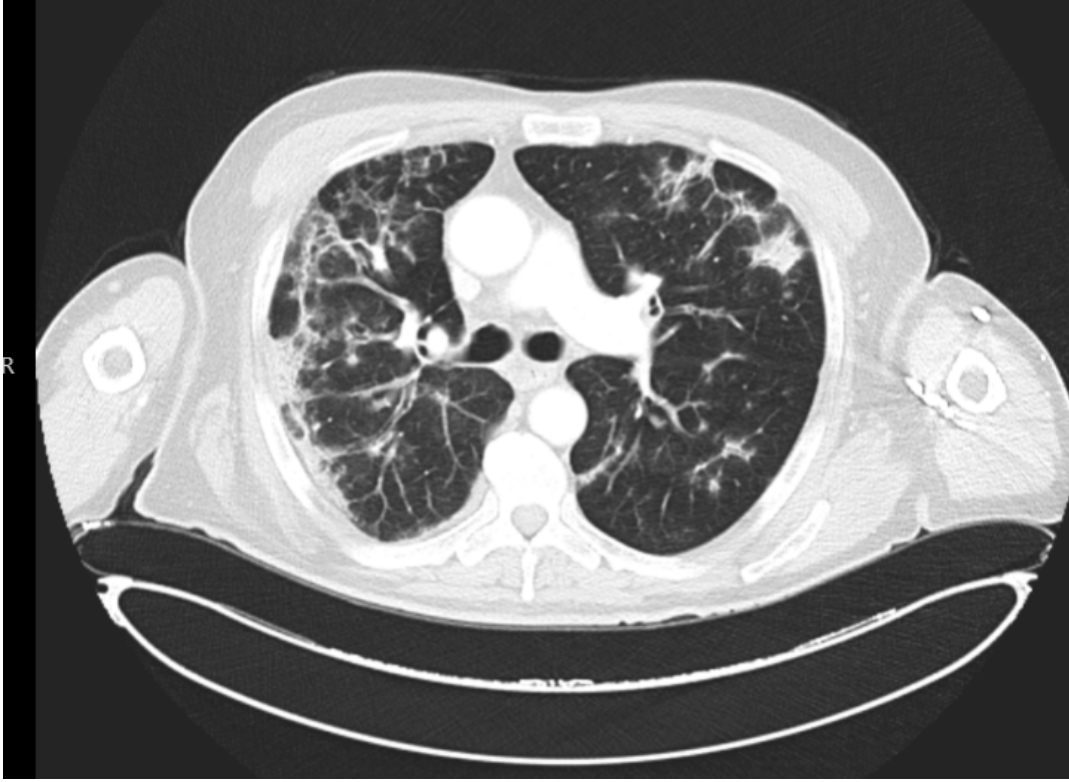
Tanıda



2. hafta



6. hafta



- Atezolizumab rechellange planlanmadı
- **Hiler kitlede progresyon** ile yeniden evreleme planlandı

Sorular

1. Birinci basamakta kime Atezolizumab kime Durvalumab?
2. İkinci basamak ve sonrasında en uygun tedavi sıralaması nasıl olmalı?
(Hayaller vs gerçekler)
3. Geç relapslarda IO rechellange yapalım mı?
4. Moleküler analiz kime, ne zaman?
5. Patolojik tanıdan şüphe duymalı mıyız? Takipte rebiyopsisinin rasyoneli var mı?

Teşekkürler...