

Case # 6
Limited Stage SCLC:
What's New and What's Next?

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Case # 6: A 50-year-old manager, moderate smoker

- Referred to pulmonologist due to suspicious tumour mass on x-ray in the R hemithorax. Patient had flu 5 weeks ago when a dry cough started.
- CT scan of chest shows 4 cm right hilar mass with extensive ipsilateral mediastinal adenopathy and a small right pleural effusion.
- CT abdomen is normal. MRI brain is negative.
- Biopsies obtained by fiberoptic bronchoscopy show SCLC
- CBC: Hb 12.0; WBC 5,500; platelets 180,000; hepatic panel normal, normal renal function
- Performance status = 0

Case # 6: Would you perform a thoracentesis to evaluate the small right pleural effusion?

1. Yes
2. No
3. I don't know based on the case data

Case # 6: A small right pleural effusion in a patient with “thoracic only” SCLC

- Will the results have consequences?
See PART II
- Is thoracentesis feasible?

Case # 6: A small right pleural effusion in a patient with “thoracic only” SCLC

- **Pleural effusion: what is small?**
 - chest X-ray in standing position: detection if ≥ 150 ml
 - chest X-ray supine: detection if ≥ 500 ml
 - chest CT: detection if > 50 ml
 - ultrasound in standing or sitting position:

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 - chest X-ray in standing position: detection if ≥ 150 ml
 - chest X-ray supine: detection if ≥ 500 ml
 - chest CT: detection if ≥ 50 ml
 - ultrasound in standing or sitting position: if ≥ 5 ml
 - equals physiological quantities present in the pleura !
 - does not permit to conclude the presence of pleural disease

Collins et al, *Radiology* 105:51-53, 1972

Reuss, *Chest Sonography Textbook*, Springer 2008

Kocijancic et al, *Clin Radiol* 59:826-829, 2004

Case # 6: A small right pleural effusion in a patient with “thoracic only” SCLC

- YES [feasible]

Case # 6: A small right pleural effusion in a patient with “thoracic only” SCLC

- YES [feasible]
- Thoracentesis yielded pale yellow fluid, which was a transudate, contained no RBCs, and was negative for malignant cells by cytology.

Case # 6: How would these findings affect the patient's stage and treatment?

- 1. Would assume limited disease and treat accordingly**
- 2. Findings highly suspicious, would assume extensive disease and treat accordingly**
- 3. Not sure. Would consider thoracoscopy to better define stage**

Case # 6: How would these findings affect the patient's stage and treatment?

- What is the interpretation of the results?

Case # 6: How would the affect the patient's staging treatment?

- pale yellow fluid
- transudate
- no RBCs
- negative cytology

- **What is the interpretation of the results?**
 - **TNM guideline: most pleural effusions with lung cancer are due to tumour. In some patients there is ...**
 - **negative cytopathologic examination**
 - **non-bloody fluid**
 - **fluid which is not an exudate**
 - **where these elements are in place, and when clinical judgement dictates that the effusion is not related to the tumour, the effusion should be excluded as a staging element**

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 - TNM guideline: most pleural effusions with lung cancer are due to tumour. In some patients there is ...
 - negative cytopathologic examination
 - non-bloody fluid
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 - where these elements are in place, and when clinical judgement dictates that the effusion is not related to the tumour, the effusion should be excluded as a paraneoplastic element

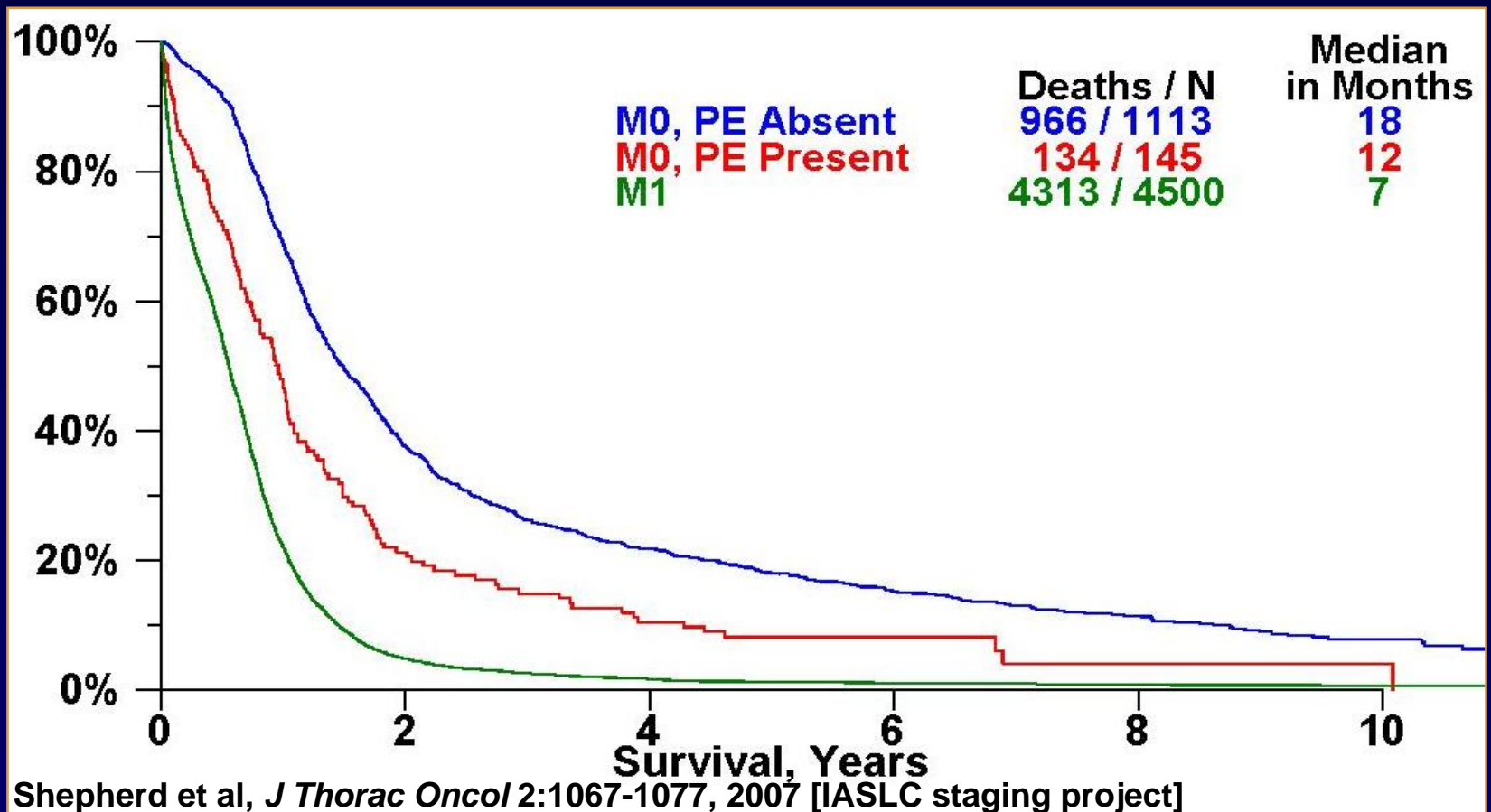
- extensive ipsilateral mediastinal adenopathy

Case # 6: How would these findings affect the patient's stage and treatment?

- What is the meaning of a pleural effusion for stage and choice of treatment? → IASLC consensus definition of limited disease (1989)
 - primary tumour in one hemithorax
 - ipsi- & contralateral hilar, mediastinal, supraclavicular LNs
 - ipsilateral pleural effusion, *both cytology positive and negative*
- Controversy: pleural effusion

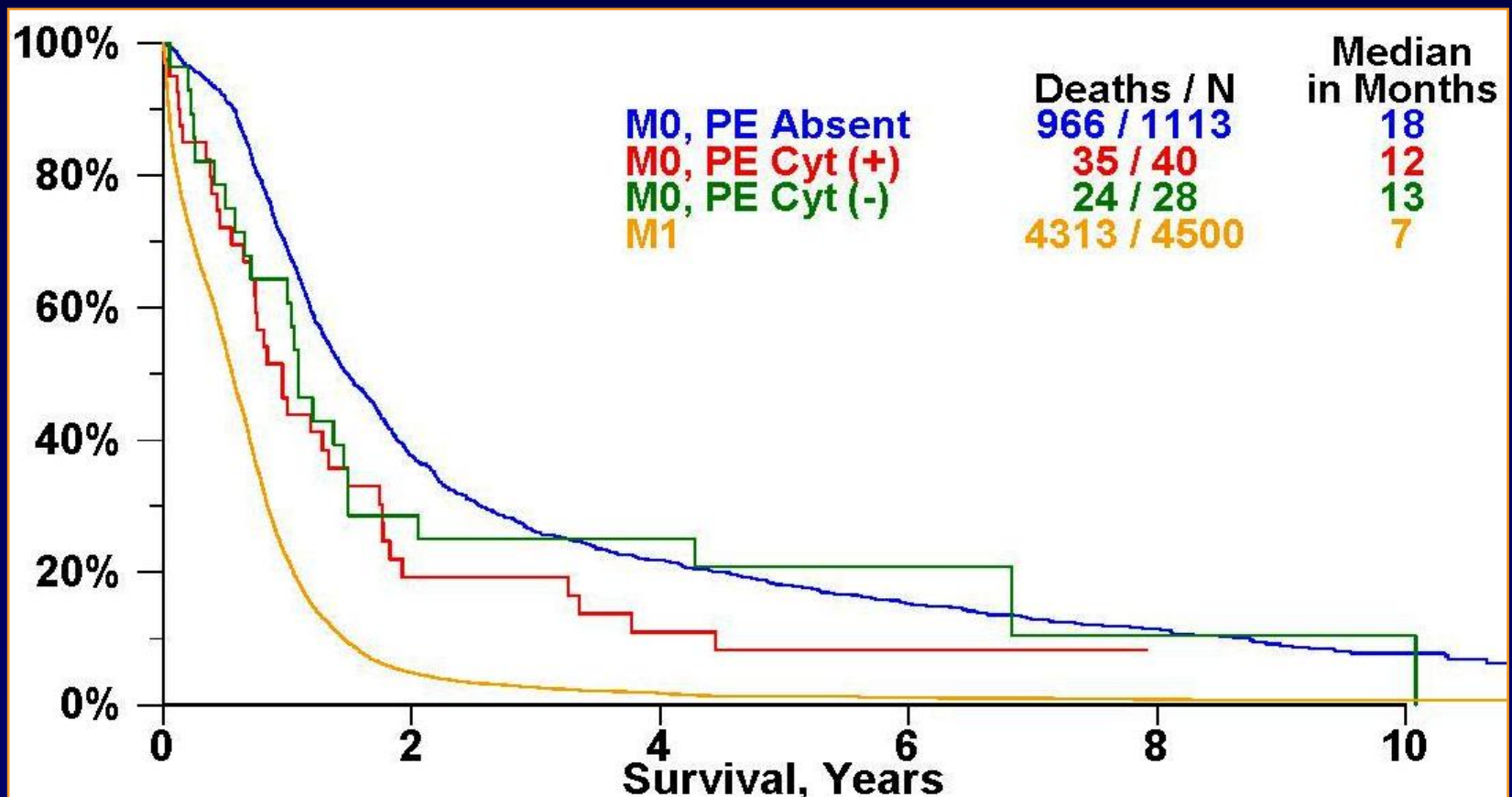
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Shepherd et al, *J Thorac Oncol* 2:1067-1077, 2007 [IASLC staging project]

Case # 6: How would these findings affect the patient's stage and treatment?

- What is the meaning of a pleural effusion for stage and choice of treatment? → IASLC staging project
 - patients with pleural effusion (positive or negative) have an intermediate prognosis between LD and ED
 - further data are needed to determine if there is a difference in prognosis for patients with cytology +ve or -ve pleural effusions

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Case # 6: A 50 year old manager with limited disease SCLC

- **Patient was treated with cisplatin-etoposide with concurrent chest radiotherapy and CR was achieved.**
- **25 Gy prophylactic cranial irradiation (PCI) was given.**
- **Patient did well for 14 months when he developed a cough, fatigue and weight loss.**
- **With further investigation, PD was confirmed in lung and liver. AST and ALT were 10% above the ULN, bilirubin and renal function tests were normal.**
- **Performance status = 1.**

Case # 6: Relapsed SCLC - which chemotherapy would you suggest at this time?

1. Rechallenge with cisplatin-etoposide
2. Cyclophosphamide-doxorubicin-vincristine (CAV)
3. Cisplatin-topotecan
4. Oral topotecan
5. Oral etoposide
6. Phase II clinical trial with tyrosine kinase inhibitor

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- **Why choose CAV? → Concept that platinum-etoposide and CAV are non-cross-resistant**
 - 1980s: alternation of both regimens to improve prognosis
 - Large RCT: not beneficial (MST 8.6m for PE, 8.3m for CAV, 8.1m for CAV/PE) *
 - Other RCT: 23% reponse with PE after failure of CAV, while only 8% response with CAV after failure of PE °

* Roth et al, *J Clin Oncol* 10:281-292, 1992

° Fukuoka et al, *J Natl Cancer Inst* 83:855-861, 1991

Case # 6: Relapsed SCLC - which chemotherapy would you suggest at this time?

- **Rechallenge with the same regimen?**
 - reasonable option if previous response and relapse-free interval >3 m
 - this patient had a good response and was well for 14 m

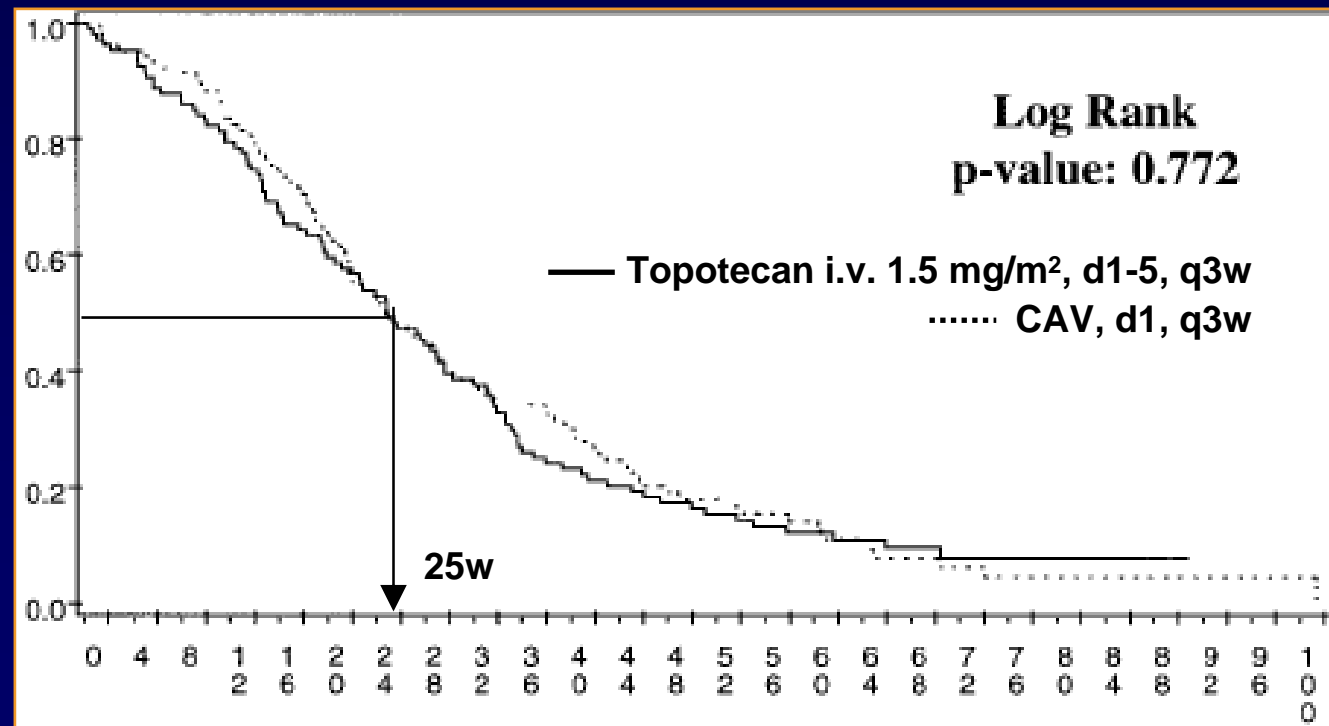
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Case # 6: Relapsed SCLC - which chemotherapy would you suggest at this time?

- **Topotecan?**

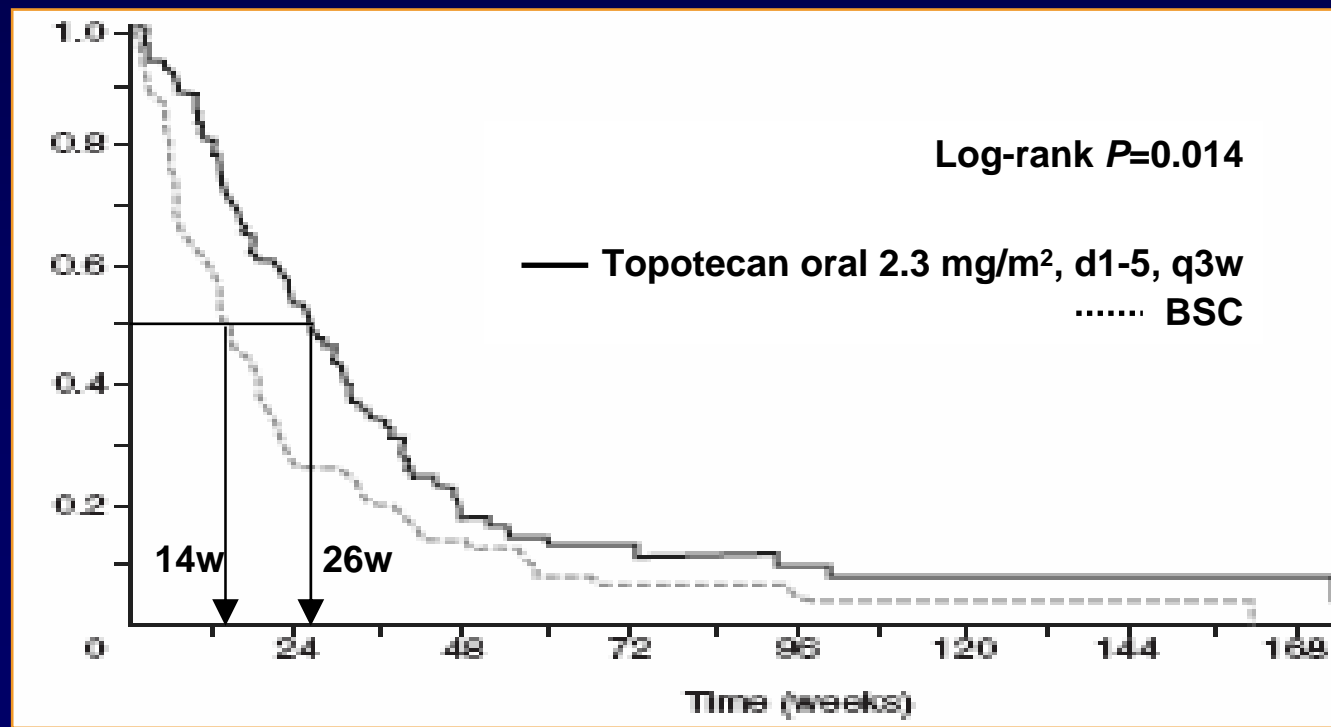
- SCLC relapsed ≥ 60 d after 1st line therapy (n=211)
- similar response (24 vs. 18%), median TTP (13.3w vs. 12.3w)
- better symptom improvement with Topotecan ($P=0.043$).



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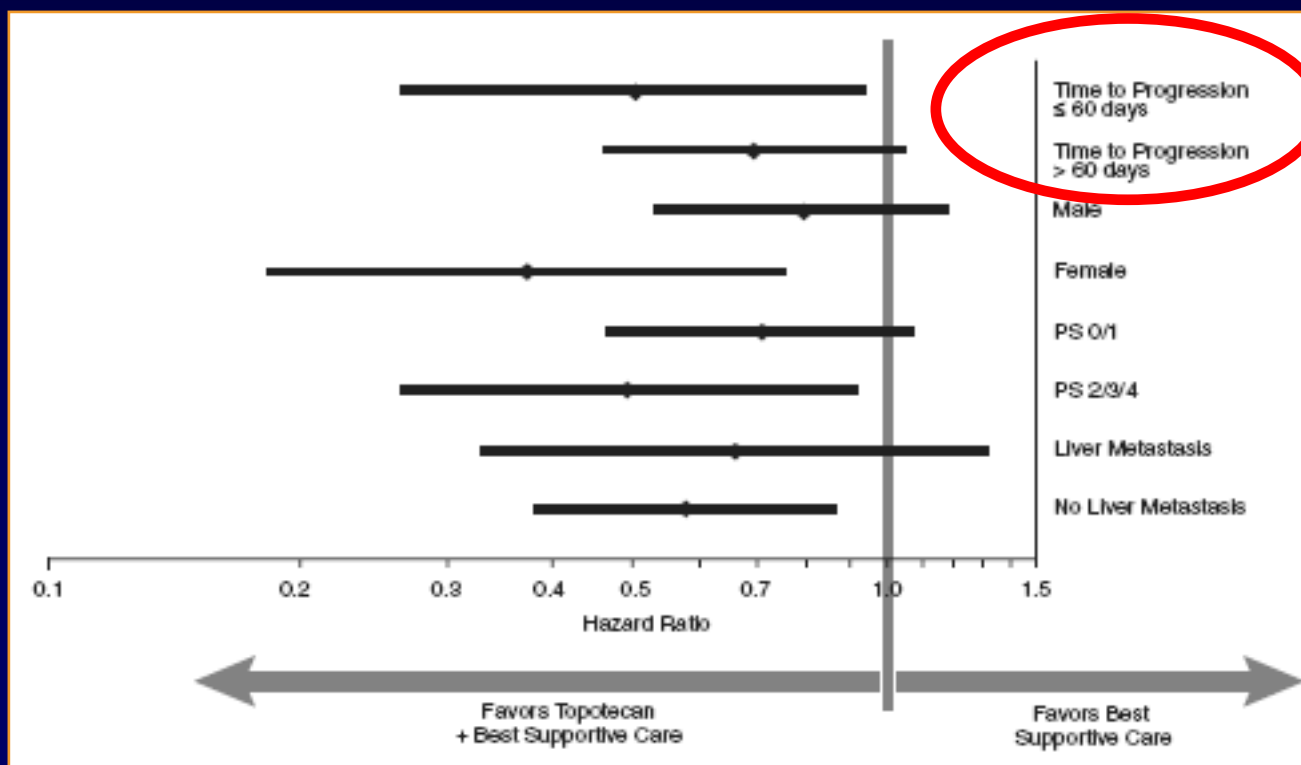
- **Topotecan?**

- relapsed SCLC not considered for i.v. therapy (n=141)
- 7% response and 44% stable disease with topotecan
- Topotecan group had slower QoL deterioration / greater symptom control



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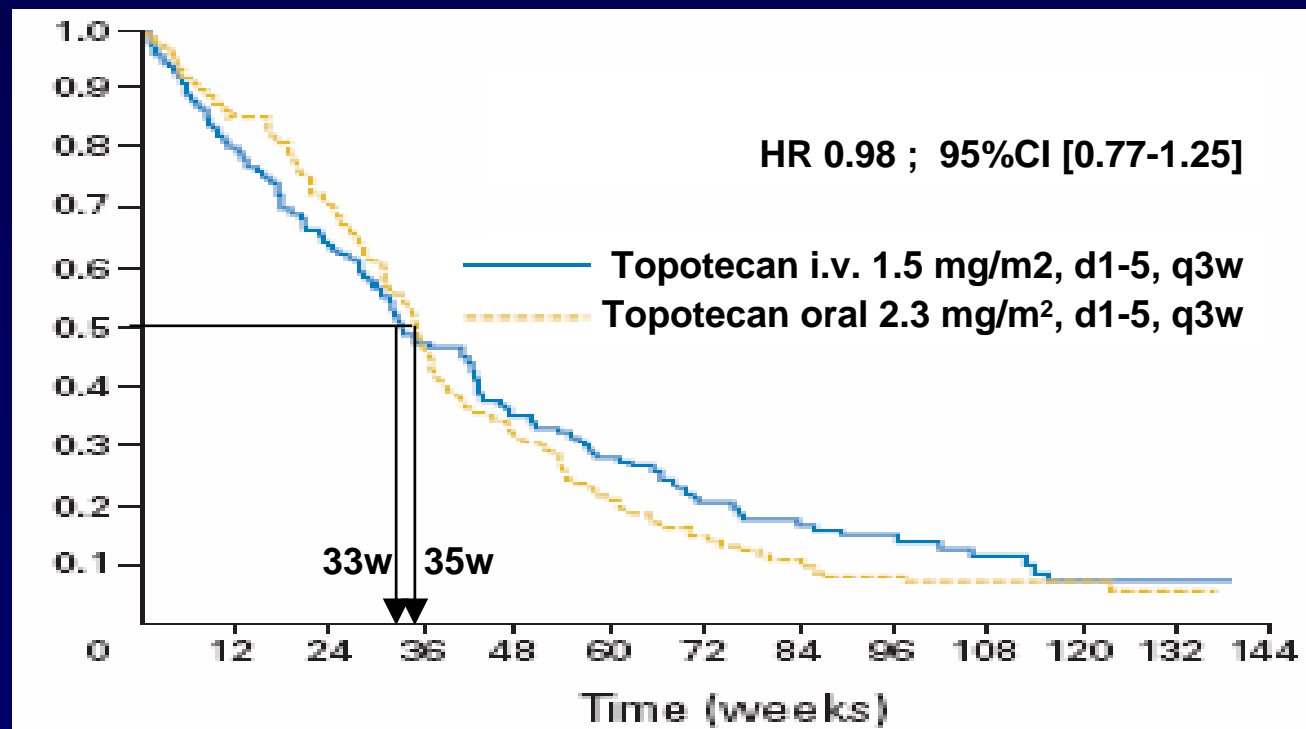
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Case # 6: Relapsed SCLC - which chemotherapy would you suggest at this time?

- **Topotecan?**

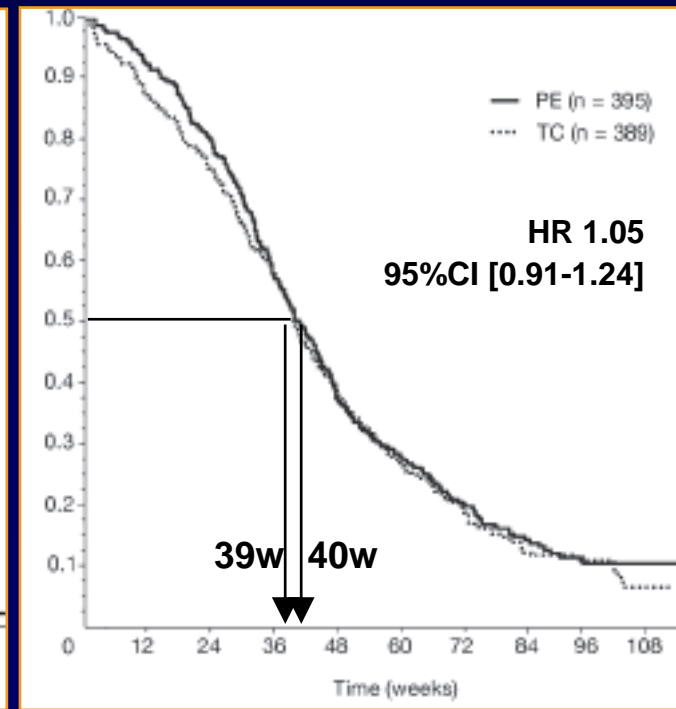
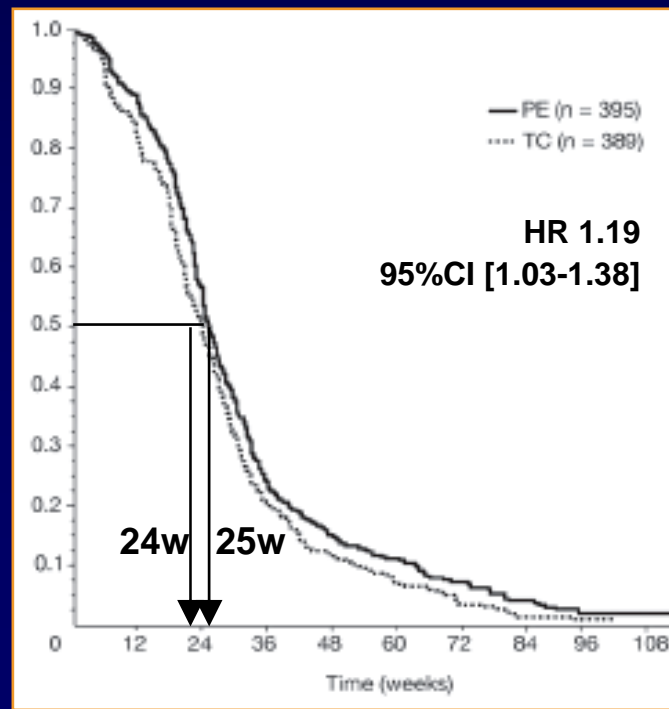
- SCLC sensitive relapse (≥ 90 d after 1st line therapy) (n=309)
- similar response (22 vs. 18%), median TTP (14.6w vs. 11.9w)
- more grade 4 neutropenia with i.v. (64 vs. 47%)



Case # 6: Relapsed SCLC - which chemotherapy would you suggest at this time?

- **Topotecan?**

- SCLC 1st line setting: cisplatin+oral topotecan vs. PE i.v. (n=784)
- similar response (63 vs. 69%), median TTP better with PE
- Lung Cancer Symptom Scale scores statistically better with PE
- more grade 4 neutropenia with PE (58 vs. 26%), but less sepsis (2 vs. 4%)



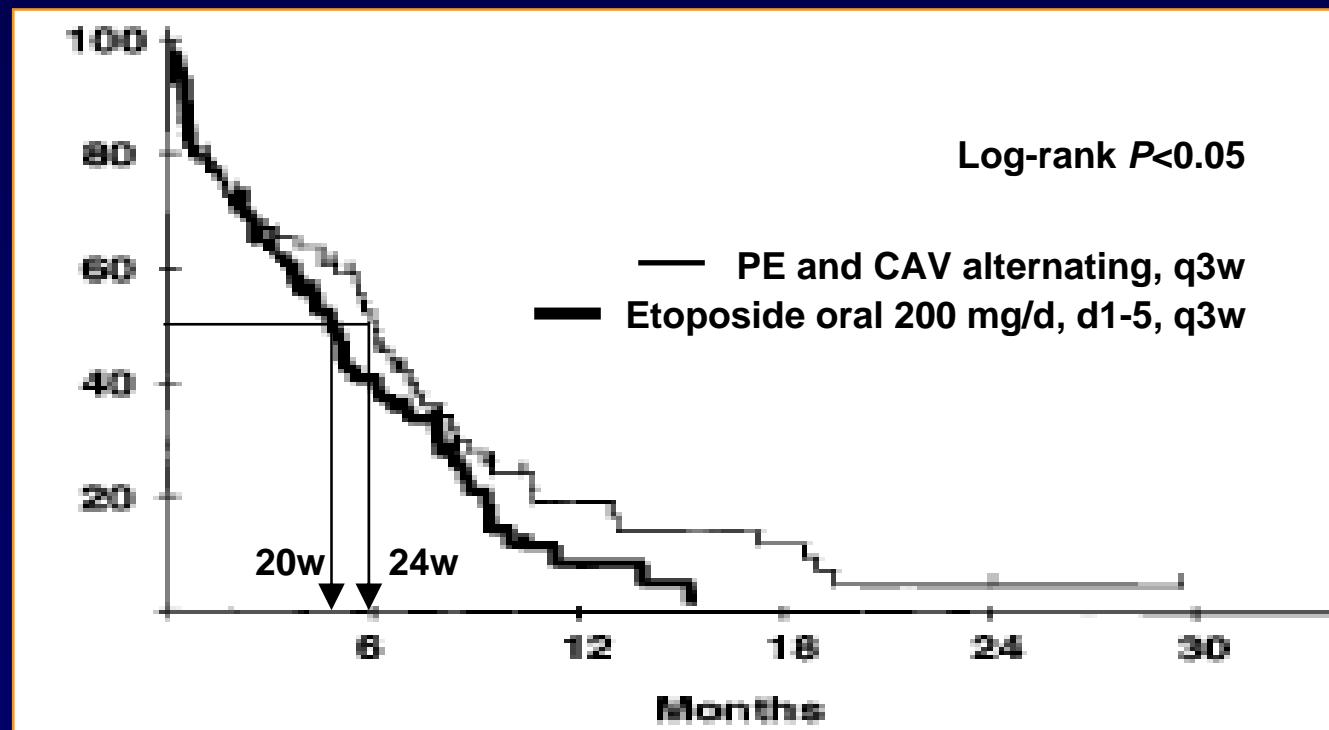
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- 4. Oral topotecan**
- 5. Oral etoposide**
- 6. Phase II clinical trial with tyrosine kinase inhibitor**

Case # 6: Relapsed SCLC - which chemotherapy would you suggest at this time?

- **Oral etoposide?**

- response (33 vs. 46%) and median PFS (3.6 vs. 5.6 m) significantly worse with oral etoposide
- almost all aspects of symptom control and QoL either same or worse with oral etoposide



Case # 6: Relapsed SCLC - which chemotherapy would you suggest at this time?

- **Phase II clinical trial with TKI?**
 - **EGFR-TKI: phase II study with Gefitinib: negative ***
 - **VEGF-TKI: Sunitinib under investigation**
 - **multiple-target TKI: Vandetanib maintenance study negative °**
- **Not a choice in this patient with standard options**

* Moore et al, *Lung Cancer* 52:93-97, 2006

° Arnold et al, *J Clin Oncol* 25:4278-4284, 2007

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1. Rechallenge with cisplatin-etoposide
2. Cyclophosphamide-doxorubicin-vincristine (CAV)
3. Cisplatin-topotecan
4. Oral topotecan [future option]
5. Oral etoposide
6. Phase II clinical trial with tyrosine kinase inhibitor



**Thank you for
your kind
attention**

Leuven, Gothic Town Hall (1448)