ESTADIOS INICIALES Y LOCALMENTE AVANZADOS

Ana Blasco
Oncología Médica
HGUV

III PostAsco de Pulmón
Gido Valencia 2016
21 de Junio a las 16:00h
Hotel Primus (Valencia)
Organiza: GIDO
Avalado: SEOM

8542: Effect of time-to-treatment on survival in non-small cell lung cancer – Anggondowati T et al

- **Study objective**
  - To investigate the effect of time-to-treatment on OS in patients with NSCLC
- **Methods**
  - **Patients (n=693,554) diagnosed with NSCLC between 2003 and 2011 were identified from the National Cancer Data Base**
  - **Time-to-treatment was defined as the interval between diagnosis and treatment initiation and categorized as: 0 days; 0.1 to 4 weeks (*reference*); 4.1 to 6 weeks; and >6 weeks**
- **Key results**
  - Nearly 43% of patients started treatment >4 weeks after diagnosis and 25% waited >6 weeks
  - *In early stage patients (I/II) who survived at least 36 months, risk of death was higher among those who waited for 4.1−6.0 weeks (HR 1.06; 95%CI 1.03, 1.10), or >6 weeks (HR 1.18; 95%CI 1.15, 1.22) to start treatment, compared with those who waited 0.1−4.0 weeks*
  - A survival benefit of shorter time-to-treatment was not found in patients who survived <12 months and stage IV patients
- **Conclusion**
  - Survival benefit can be gained by expediting treatment for early stage NSCLC
  - Future research is needed to identify patients' characteristics that could predict the tolerable time-to-treatment for individual patients

Anggondowati et al. J Clin Oncol 2016; 34 (suppl): abstr 8542

8549: Optimal timing of lobectomy for clinical stage IA non-small cell lung cancer – Yang C-F et al

- Study objective
  - To investigate the impact on survival of increasing the time between diagnosis and lobectomy in patients with clinical stage IA NSCLC
- Methods
  - Retrospective analysis of 16,861 patients who underwent lobectomy as primary therapy for clinical stage IA NSCLC identified from the National Cancer Data Base (2006 to 2011)
  - **'Early' surgery was defined as within 1−36 days of diagnosis; 'late' surgery was ≥37 days**
- **Key results**
  - Patients with increased surgical waiting time were more likely to be older, black, have more comorbidities, uninsured, lower income and lower education status
  - *A delay in surgery was associated with worse 5-year OS (59.9% with late surgery vs. 65.5% with early; p<0.001)*
  - In a multivariable analysis, delaying surgery beyond 37 days led to an increased risk of death with a HR of 1.11
- **Conclusions**
  - Shorter time to surgery among patients with early stage NSCLC is associated with improved survival
  - If possible, surgical resection should be performed at least within five weeks of diagnosis

Yang et al. J Clin Oncol 2016; 34 (suppl): abstr 8549

8547: Non-examination of lymph nodes (LN) and overall survival (OS) in non-small cell lung cancer (NSCLC) patients – Jemal A et al

- **Study objective**
  - To investigate the survival impact of post-operative adjuvant therapy on patients without lymph node examination
- **Methods**
  - Retrospective analysis of 97,794 patients with stage I–IIIA NSCLC from the National Cancer Database
  - Analysed by pathological nodal status and survival
- **Key results**
  - 79.5% were node negative (pN0), 14.6% had node metastasis (pN1) and **5.9% did not have lymph node examination (pNx)**
  - 77% of pNX patients had sublobar resection, 87% of pN0 and 95% of pN1 patients had lobectomy or greater
  - **5-year OS rates were**: 65% (pN0) vs**. 47% (pNX)** vs. 44% (pN1) (log-rank p<0.0001)
  - Adjuvant chemotherapy and radiation therapy in pNX patients with tumour size ≤4 cm was associated with greater risk of all-cause mortality
- **Conclusions**
  - Patients with NSCLC without lymph node examination were more likely to have received sublobar resection
  - Survival of these patients was lower than those who had lymph node examination and this was not improved by adjuvant therapy

Jemal et al. J Clin Oncol 2016; 34 (suppl): abstr 8547

CONCLUSIONES

- En estadios iniciales (I/II), riesgo de muerte es mayor pacientes con retraso del tratamiento > 6 semanas desde el diagnóstico
- Este retraso no afecta a los pacientes en estadio IV
- Retraso de la cirugía > 37 días empeora la SG y aumenta el riesgo de muerte
- El retraso del inicio del tratamiento adyuvante > 35 días no se correlaciona con el tiempo libre de enfermedad

E1505: Adjuvant chemotherapy +/- bevacizumab for early stage NSCLC: Outcomes based on chemotherapy subsets

H.A. Wakelee[1], S.E. Dahlberg[2], S.M. Keller[3], W.J. Tester[4], D.R. Gandara[5], S.L. Graziano[6], A. Adjei[7], N. Leighl[8], S.C. Aisner[9], J.M. Rothman[10], J. Patel[11], M.D. Sborov[12], S.R. McDermott[13], R. Perez-Soler[14], A.M. Traynor[15], C. Butts[16], T. Evans[17], L. Horn[18], S.S. Ramalingam[19], J. Schiller[20] on behalf of ECOG-ACRIN

[1]Medicine (Oncology), Stanford Cancer Institute/Stanford University, Stanford, CA/USA, [2]Dana-Farber Cancer Institute/Harvard University, Boston, MA/USA, [3]Cardiovascular and Thoracic Surgery, Montefiore Medical Center, Bronx, NY/USA, [4]Albert Einstein Medical Center, Philadelphia, PA/USA, [5]UC Davis Comprehensive Cancer Center, Sacramento/USA, [6]Medical Oncology, SUNY Upstate Medical University, Syracuse, NY/USA, [7]Medicine, Roswell Park Cancer Institute, Buffalo, NY/USA, [8]Princess Margaret Cancer Centre, Toronto, ON/Canada, [9]Rutgers New Jersey Medical School, Newark, NJ/USA, [10]The Regional Cancer Center, Erie, PA/USA, [11]Northwestern University, Chicago, IL/USA, [12]Edina Clinic, Edina/USA, [13]Medical Oncology, The Adelaide and Meath Hospital, Dublin, Dublin/Ireland- Irish Cooperative Oncology Group, [14]Oncology, Montefiore Medical Center, Bronx, NY/USA, [15]University of Wisconsin, Madison, WI/USA, [16]Division of Oncology, University of Alberta, Edmonton, AB/Canada, [17]University of Pennsylvania, Philadelphia, PA/USA, [18]Vanderbilt University Medical Center, Nashville, TN/USA, [19]Winship Cancer Institute, Emory University, Atlanta, GA/USA, [20]Hematology/Oncology, UT Southwestern, Dallas/USA

ECOG-ACRIN cancer research group

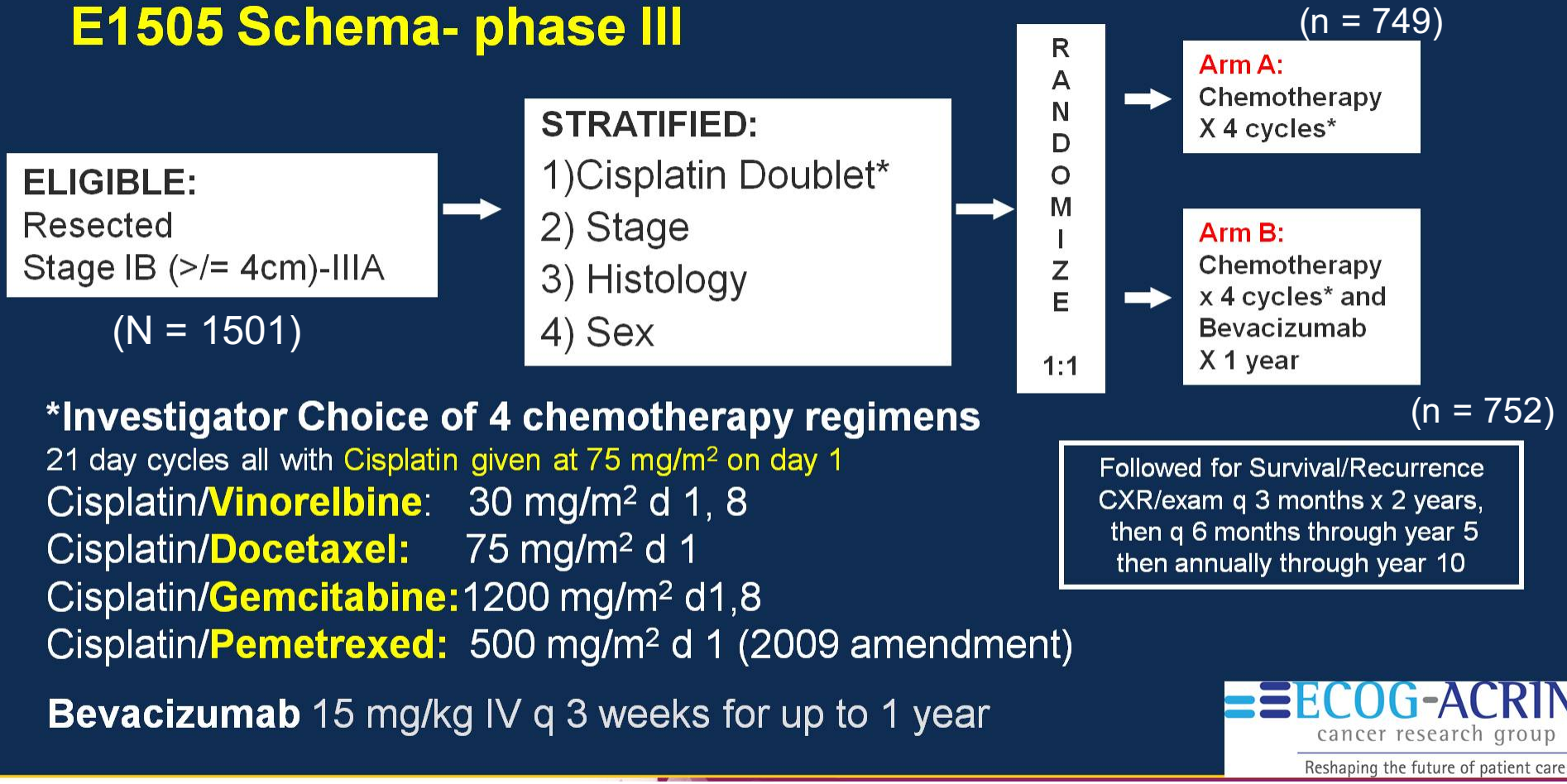
Reshaping the future of patient care

PRESENTED AT: ASCO ANNUAL MEETING '16

Abstr 8507: E1505 Chemotherapy subsets: Presented by: H. Wakelee

Presented By Heather Wakelee at 2016 ASCO Annual Meeting

E1505 Schema- phase III



- Primary endpoint: OS
- Secondary endpoint: DFS
- Study powered for primary endpoint only,not for the subset analyses

Presented By Heather Wakelee at 2016 ASCO Annual Meeting Abstract 8507.

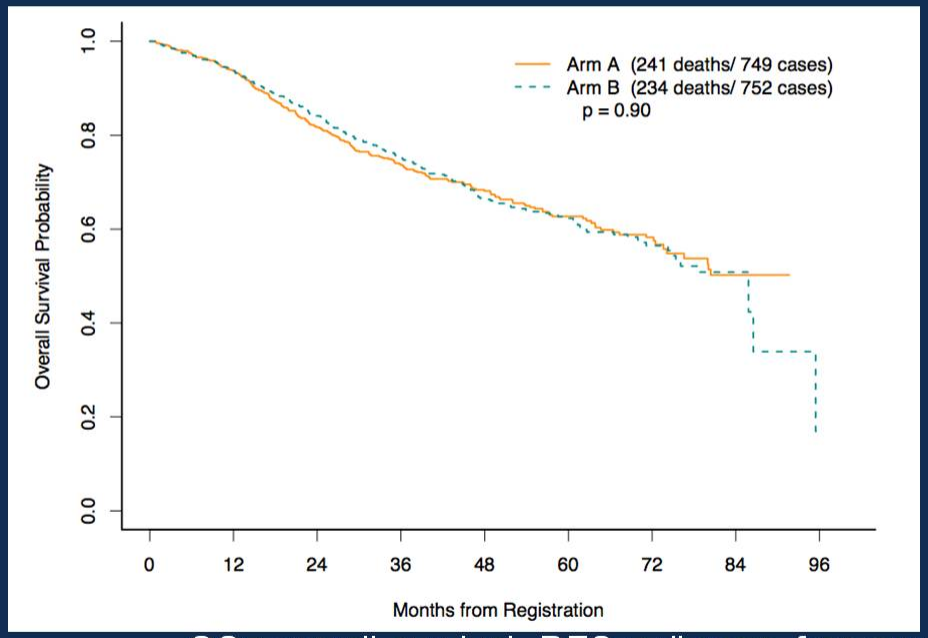
E1505 Chemotherapy Subset Analysis in Early-Stage, Resected NSCLC

- Adjuvant cisplatin-based chemotherapy provides only modest OS benefit (~ 5%) in pts with early-stage, resected NSCLC[1]
- E4599: addition of bevacizumab to platinum-based chemotherapy improved outcomes in pts with advanced nonsquamous NSCLC[2]
- E1505: randomized phase III study evaluated bevacizumab plus cisplatin-based doublet chemotherapy in early stage resected NSCLC
  - Cisplatin partners: vinorelbine, docetaxel, gemcitabine, pemetrexed
  - Bevacizumab addition failed to improve OS (HR: 0.99; 95% CI: 0.82-1.19; *P* = .90) or DFS (HR: 0.99; 95% CI: 0.86-1.15; *P* = .95)[3]
  - Trial stopped early for futility
- Post hoc analysis of pooled E1505 outcomes data by chemotherapy subset reported here[4]

1. Pignon JP, et al. J Clin Oncol. 2008;26:3552-3559. 2. Sandler A, et al. N Engl J Med. 2006; 355:2542-2550. 3. Wakelee HA, et al. WCLC 2015. Abstract 1608. 4. Wakelee HA, et al. ASCO 2016. Abstract 8507.

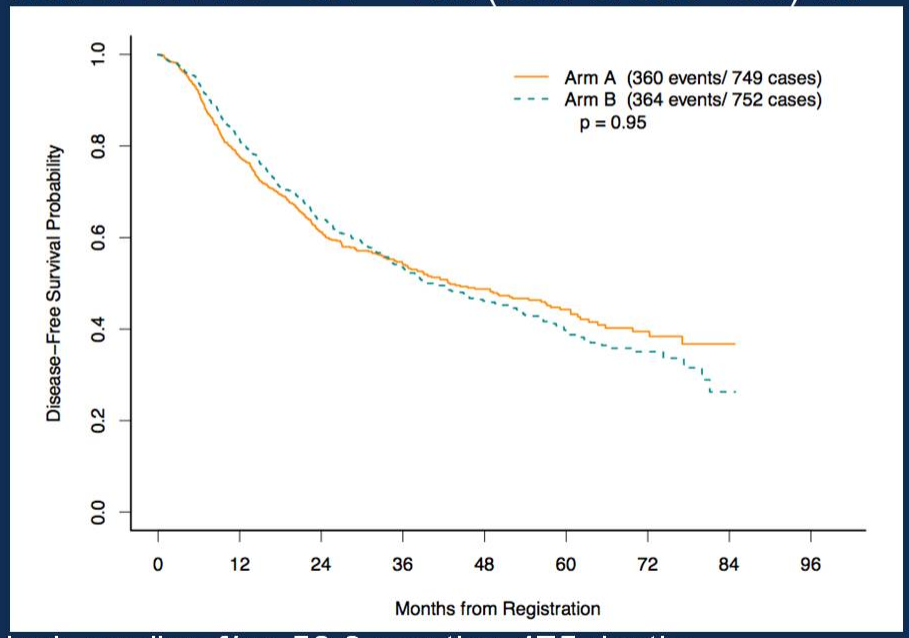
E1505 OS +/- Bevacizumab

OS hazard ratio (ChB:Ch): 0.99
95% CI: (0.82-1.19) ; p=0.90
Med OS ArmA Chemo NR
Med OS ArmB +Bev 85.8 (74.9-NA) mo



E1505 DFS+/- Bevacizumab

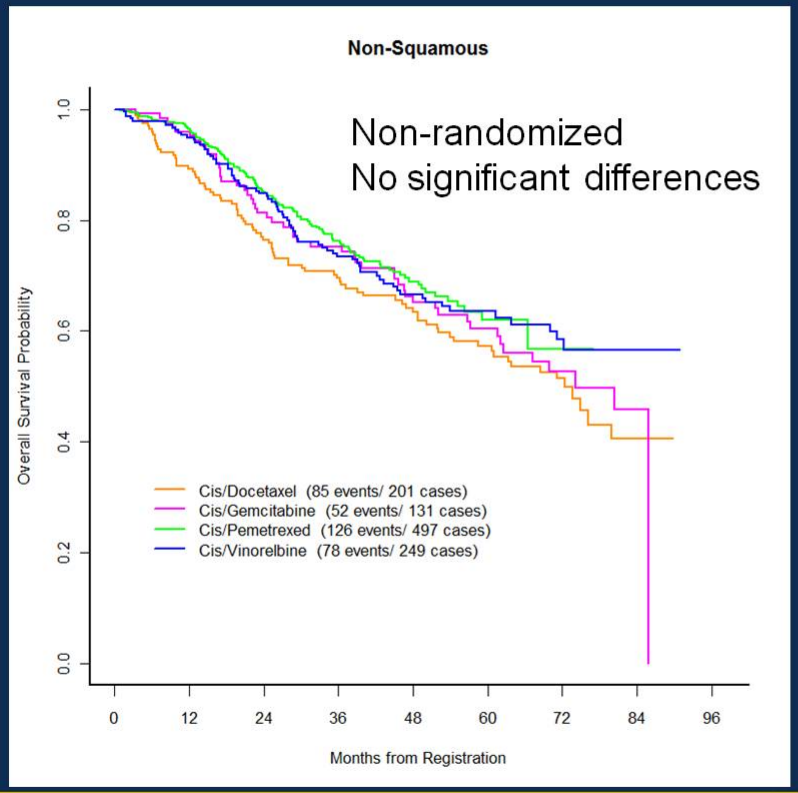
DFS hazard ratio (ChB:Ch): 0.99
95% CI: (0.86-1.15) ; p=0.95
Med DFS ArmA Chemo 42.9 (95% CI 36.7-57.0) mo
Med DFS ArmB +Bev 40.6 (95% CI 35.5-49.5) mo



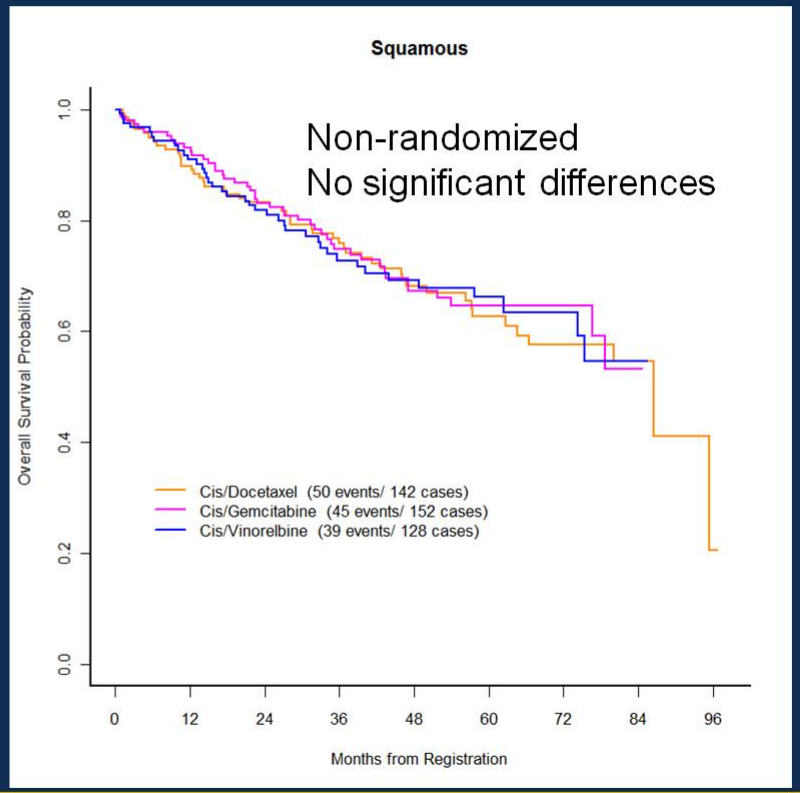
OS= overall survival, DFS = disease free survival: median f/up 50.3 months; 475 deaths

Pooled Chemo Analysis (all patients regardless of treatment arm)

OS by chemo group
Non-squamous : Logrank p=0.18



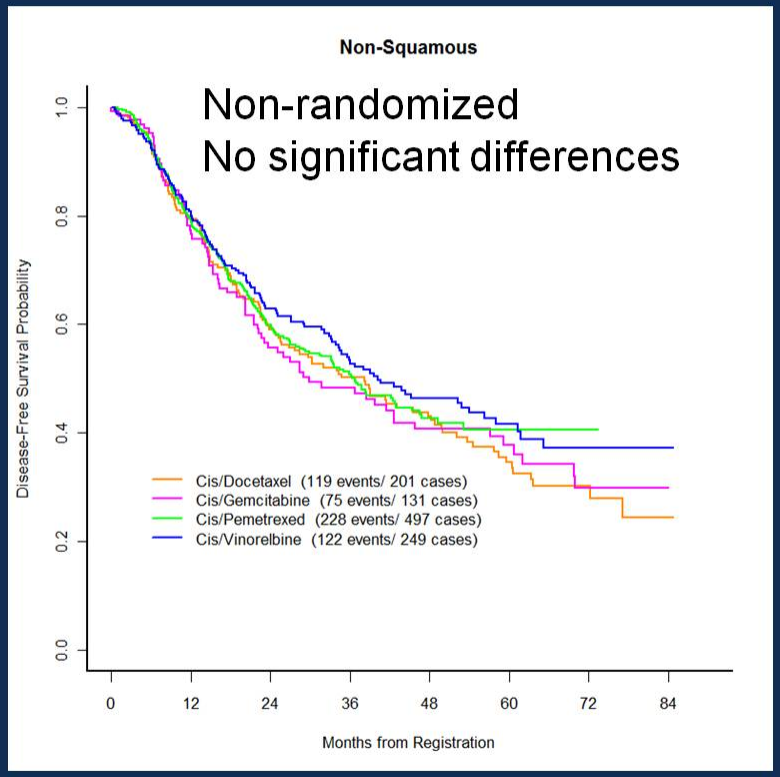
OS by chemo group
Squamous: Logrank p=0.99



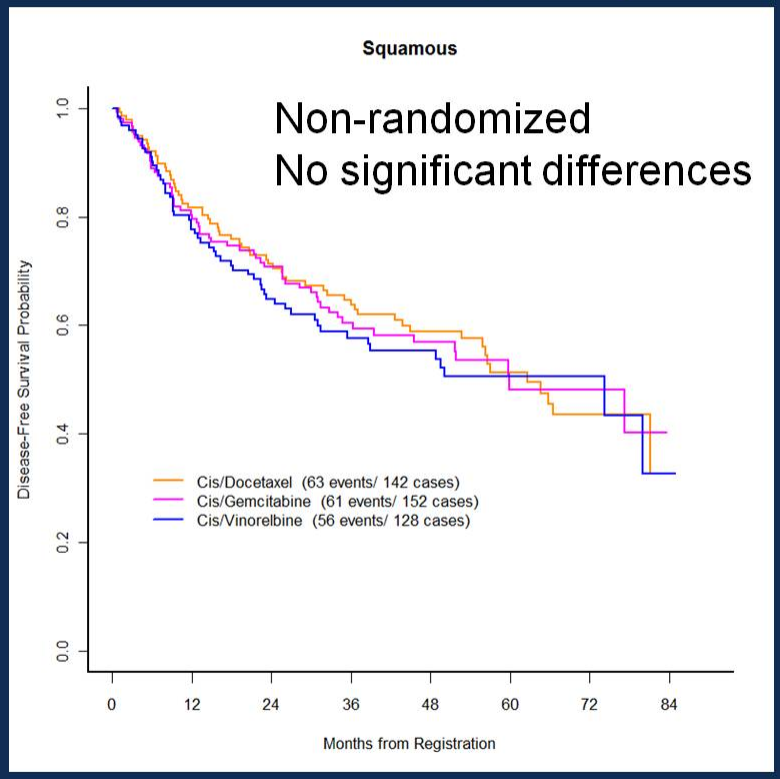
Presented By Heather Wakelee at 2016 ASCO Annual Meeting

Pooled Chemo Analysis (all patients regardless of treatment arm)

DFS by chemo group
Non-squamous : Logrank p=0.58



DFS by chemo group
Squamous : Logrank p=0.83



Toxicity

Toxicity Gr 3-5	Squamous (n=422)			Non-Squamous (n=1078)			
	V-127	D-140	G-149	V-241	D-199	G-132	P-485
	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Anemia	12	3	15	12	3	7	4
Febrile neutropenia	**9**	6	1	**15**	7	2	0
Neutrophil count decreased	**54**	39	41	**58**	40	44	12
Platelet count decreased	3	2	**23**	3	2	**12**	1
Fatigue	15	17	12	15	13	9	9
Diarrhea	6	9	1	5	10	2	1
Nausea	8	15	11	11	11	5	8
Vomiting	6	12	5	6	7	3	5
Dehydration	12	12	7	10	11	2	3
Hypertension	17	14	19	17	12	18	25
Thromboembolic event	6	2	5	6	4	9	3
WORST DEGREE	85	80	82	83	74	83	**64**

4% anaphylaxis in docetaxel arm

Reporting all attributions

With bevacizumab significantly increased:

- Neutropenia and Hypertension
- Overall worst grade 3-5, but no significant difference observed in grade 5 AEs

- For Chemotherapy Analysis:
- Known toxicity profiles of agents observed
- Vinorelbine > Neutropenia/ Febrile Neutropenia
- Gemcitabine > Thrombocytopenia

- Non-Squamous: Pemetrexed was associated with less total grade 3-5 toxicity than other chemotherapy groups ($p<0.001$)

E1505 Chemotherapy Subset Analysis: Conclusions

- No significant differences found in OS or DFS by chemotherapy subset in pts receiving adjuvant cisplatin-based chemotherapy for early stage resected NSCLC
- Toxicity profiles of chemotherapy agents similar to known profiles
  - Regardless of histology, neutropenia/febrile neutropenia occurred more frequently with vinorelbine and thrombocytopenia occurred more frequently with gemcitabine
  - Grade ≥ 3 toxicity lower in pemetrexed (nonsquamous) group than in other chemotherapy groups ($P < .001$)
  - Bevacizumab had most severe grade ≥ 3 toxicity, including significantly increased neutropenia and hypertension

Wakelee HA, et al. ASCO 2016. Abstract 8507.

Randomized phase III study of adjuvant chemotherapy with or without low-molecular weight heparin in completely resected non-small cell lung cancer patients: The NVALT-8 study

Harry J.M. Groen, Erik van der Heijden, Theo J Klinkenberg, Bonne Biesma, Joachim Aerts, Ad Verhagen, Corinne Kloosterziel, Hans J.M. Smit, Franz Schramel, Vincent van der Noort, Harm van Tinteren, Egbert F. Smit, Anne-Marie C. Dingemans
for the NVALT Study Group
The Netherlands

TrialNr: NTR1250

PRESENTED AT: ASCO ANNUAL MEETING '16

Presented by: Harry J.M. Groen

Rationale

- LMWH impairs the occurrence of metastases by inhibition of tumor cell growth by heparin-binding growth factors, tumor cell invasion by heparin-inhibition enzyme systems, tumor cell metastasis by heparin-binding cell surface selectins, tumor angiogenesis, and tumor matrix formation (1,2).
- Three studies have indicated that LMWH may be associated with survival benefit, not directly linked to a reduction in VTE.
  - MALT study: median survival 8.0 mo in nadroparin vs 6.6 mo in control, HR for death 0.75 (95% CI., 0.59 – 0.96) (3).
  - FAMOUS Study: median survival not different. However, a subgroup of patients who were alive at 17 months had improved 2- and 3-year survival (78% vs 55% and 60 vs 36%, resp; p=0.03). These effects were noticed long after LMWH were stopped (4).
  - CLOT Study: Survival benefit for LMWH in non-metastatic cancers (HR 0.50; 95% CI., 0.27 – 0.95; p=0.03), but not in advanced cancers (5).

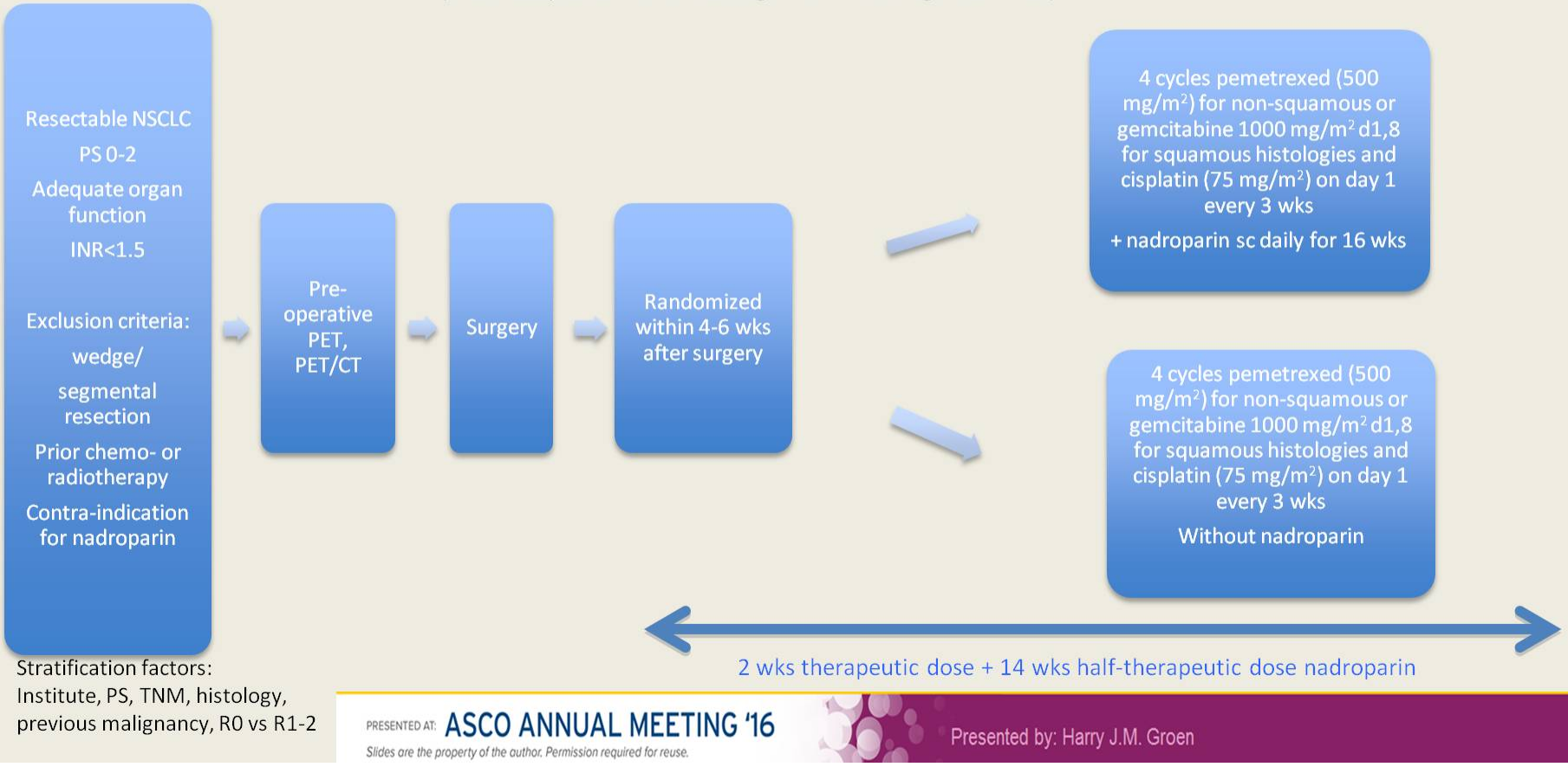
1. Amirkhosravi A, et al. J Thromb Haemost 2003; 1: 1972–1976
2. Mousa SH, Petersen LJ. Thromb Haemost 2009; 102: 258–267
3. Klerk CP, et al. J Clin Oncol. 2005; 23:2130-5.
4. Kakkar AK, et al. J Clin Oncol. 2004;; 22:1944-8.
5. Lee AY, et al.. J Clin Oncol. 2005;23:2123–2129.

Hypothesis

1. In patients with resected NSCLC adding nadroparin to adjuvant chemotherapy will improve recurrence-free survival.
2. The effect of chemotherapy may be different in high/low (SUVmax ≥ 10 vs < 10) FDG avidity NSCLC.
   - SUV max < 10: low probability on recurrence
   - SUVmax ≥ 10: high probability on recurrence

NVALT-8 Study Design

(after adaptation of the design from low/high SUVmax)



Stratification factors:
Institute, PS, TNM, histology, previous malignancy, R0 vs R1-2

Presented by: Harry J.M. Groen

Presented By Harry Groen at 2016 ASCO Annual Meeting

Endpoints

- Primary endpoint:
    - Recurrence-free survival (Follow up every 2 months first 2 years after surgery and thereafter every 3 months until 5 years after surgery)
- Secondary endpoints:
    - Overall survival
    - Dose intensity
    - Quality of life by EORTC QCQ-C30/LC13
    - Toxicity by CTCAE v3.0
    - Health economics by EuroQol questionnaire
- Explorative endpoint:
    - SUVmax

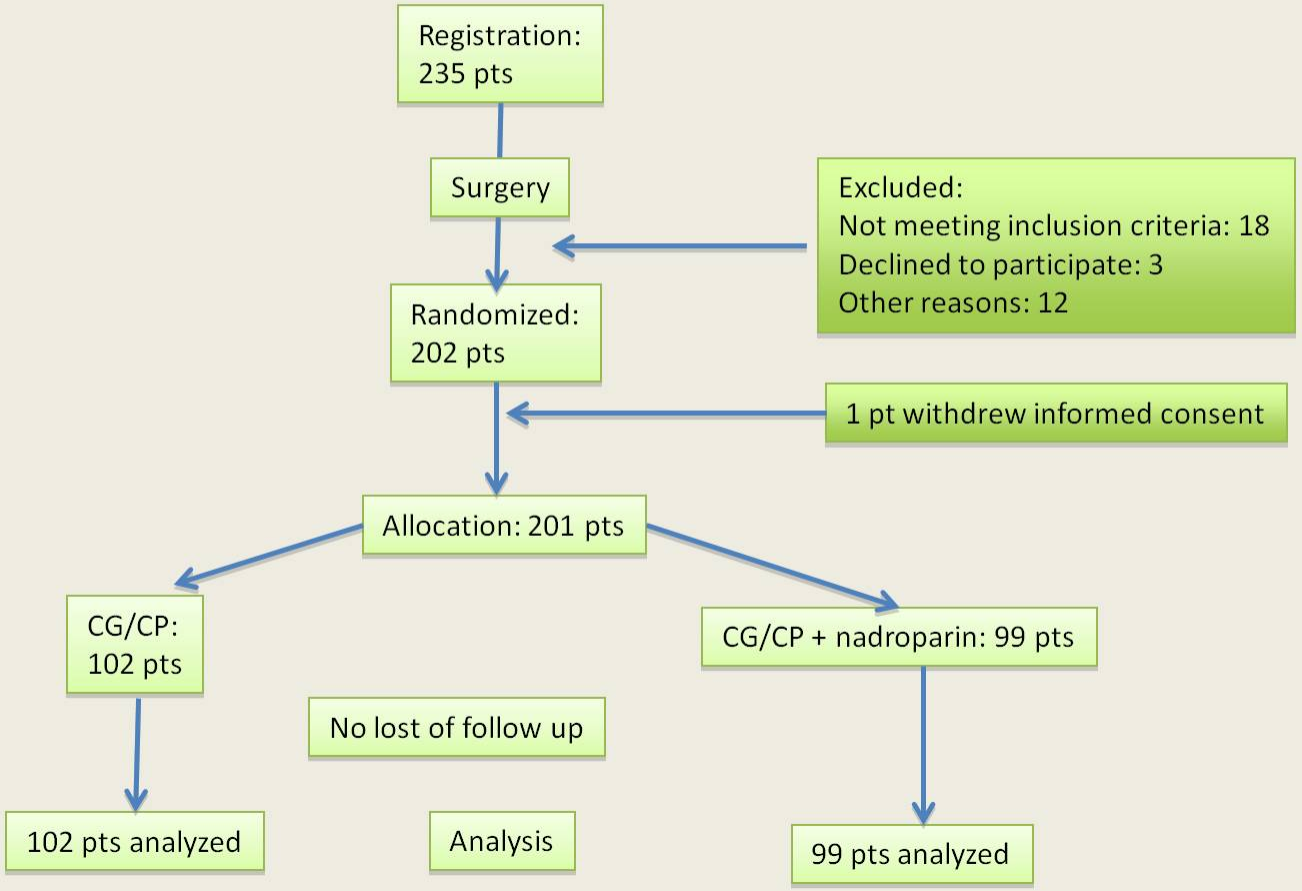
Statistics

- All statistical analyses were performed in all eligible patients according to intention-to-treat principle.
- Estimated RFS at 3 yrs of surgery + adj chemo 60%, with adj chemo + nadroparin 75%.
- Cox proportional hazard models was used to evaluate whether nadroparin is an independent factor for survival, both in pts with high/low FDG avidity NSCLC and adjusted for age, PS and stage.

- In Januari 2010 the protocol was adapted due to slow accrual. SUVmax was not a selection criterium anymore. After 60 pts we continued the study as NVALT-8 study (NTR1250).
- Decreasing the number of pts from 600 to 202, provided 80% power to compare RFS at 94 events ($\alpha = 0.05$; 2-sided log-rank test) in both arms at 3 yrs from 60 to 75%, assuming exponential survival (+ 4 years follow up).
- Updated results will be presented.

Consort Diagram

Registered in 15 hospitals between December 2007 and July 2013



Presented By Harry Groen at 2016 ASCO Annual Meeting

Patient characteristics

	CP/CG	CP/CG + nadroparine	Total
No of patients	102	99	201
Male/Female	63/39	56/43	119 (59%)/82 (41%)
Age (median + range)	63 (56 – 69)	61 (54 – 67)	62 (54 – 69)
Performance score:			
0-1	99	98	197 (98%)
2	3	1	4 (2%)
Histology:			
Squamous	40 (39%)	36 (36%)	76 (38%)
Non-squamous	62 (61%)	63 (64%)	125 (62%)
TNM stage:			
pT1N1	32 (31%)	27 (27%)	59 (29%)
pT2N0	6 (6%)	3 (3%)	9 (4%)
pT2N1	24 (24%)	27 (27%)	51 (25%)
pT3N0	17 (17%)	22 (22%)	39 (19%)
pT1-4N0-2 (stage IIIA)	21 (21%)	18 (18%)	39 (19%)
pT1-4N1-3 (stage IIIB)	2 (2%)	2 (2%)	4 (2%)

	CP/CG	CP/CG + nadroparine	Total
Median SUVmax	13.7	13.4	13.7
SUVmax < 10, n	16	30	46 (23%)
SUVmax ≥ 10, n	70	53	123 (61%)
NEDPAS or EARL not fullfilled*, n	16	16	32 (16%)
Surgery: (Bi)lobectomy Pneumonectomy Other R0 R1	 81 (79%) 20 (20%) 1 (1%) 93 (95%) 5 (5%)	 77 (78%) 22 (22%) 0 (0%) 91 (96%) 4 (4%)	 158 (79%) 42 (21%) 1 (<1%) 184 (95%) 9 (5%)
Median time from surgery to start chemo (wk)	5 (5-6)	5 (5-6)	5 (5-6)
Patients with: Platinum + gem < 4 cy Platinum + gem = 4 cy Platinum + pem < 4 cy Platinum + pem = 4 cy	 13 27 15 47	 21 15 15 48	 34 42 30 95

* 15 scans did not fulfill NEDPAS criteria, 7 scans were not EARL accredited, 3 were not on calibrated scans, 7 pts no data.

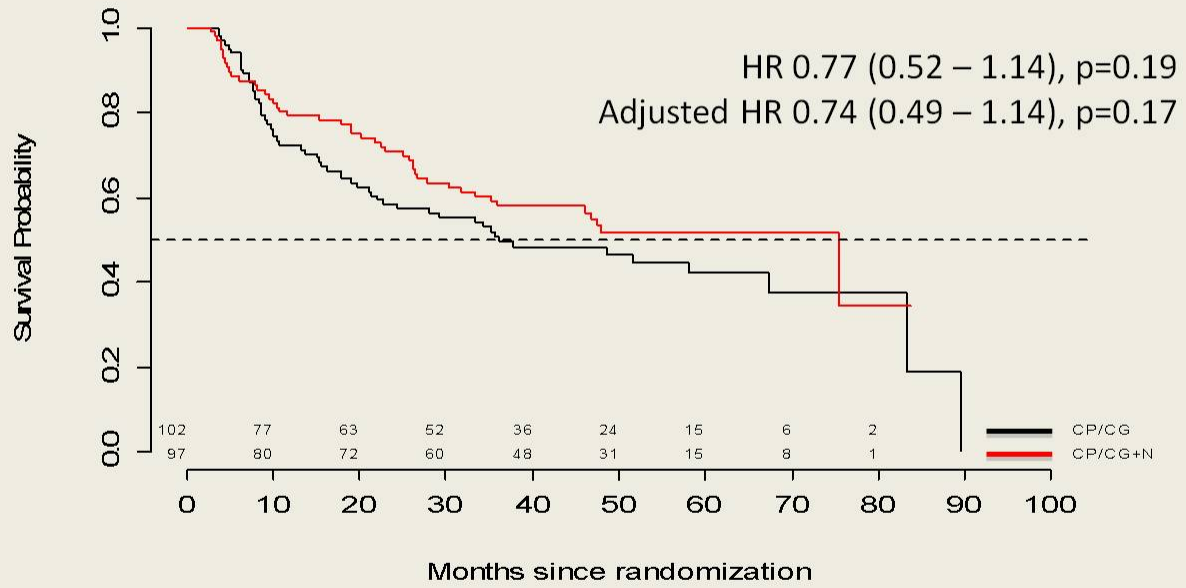
Adverse events CTC grade 3-4

Toxicity	CP/CG (n=102)	CP/CG + nadroparine (n=99)	Total (n=201)
Fatigue	4	8	12 (5.9%)
Nausea	11	16	27 (13.4%)
Neutropenia	20	26	46 (22.8%)
Febrile neutropenia Infection	4 4	6 10	12 (5.9%) 14 (6.9%)
Thrombopenia	1	3	4 (1.9%)
Thrombosis	2	0	2 (0.9%)
Vomiting	2	6	8 (3.9%)
Renal dysfunction	6	8	14 (6.9%)
Dyspnoe Bronchopleural fistula Wound infection	4 0 1	5 1 1	9 (4.4%) 1 (0.5%) 2 (0.9%)

Toxicity

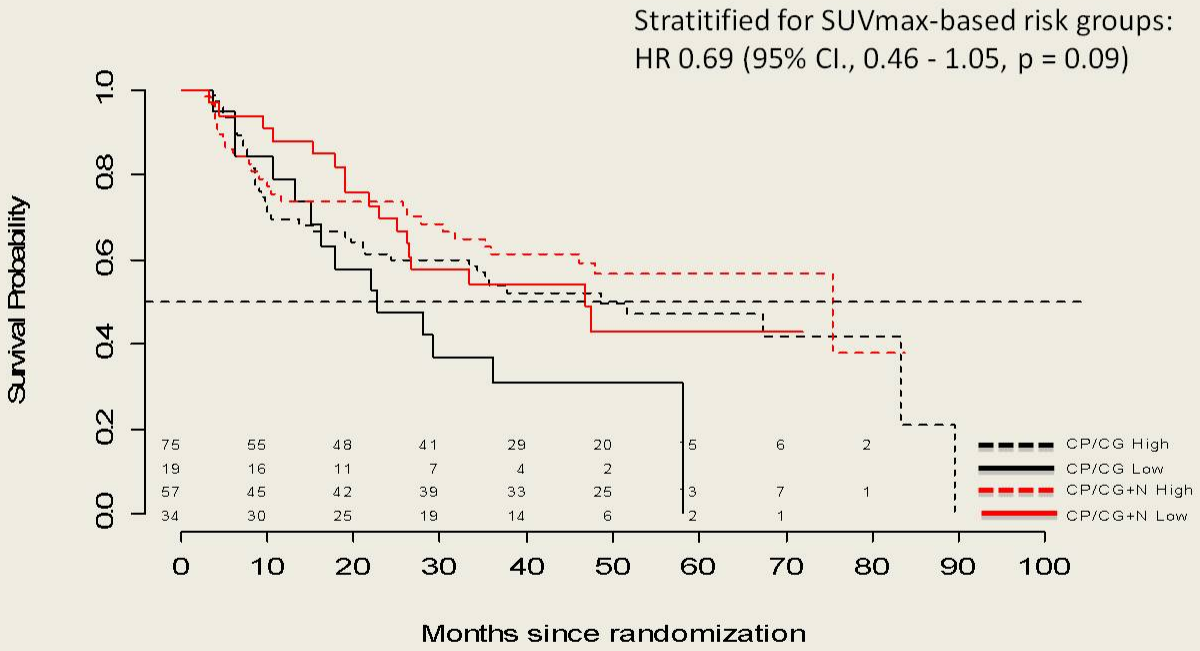
- No major surgical complications reported.
- Most common toxicity: fatigue, nausea and pain.
- No differences in bleeding events occurred.

RFS by treatment arm



Median RFS **36.1** mo (95% CI., 22.7 – NA) in control vs **75.5** mo (95% CI., 36 – NA) in nadroparin arm.
Primary endpoint; 3-yrs RFS **51%** (95%CI 42 – 62%) in control vs **59%** (95% CI., 50 – 70%) in nadroparin arm.

RFS stratified for SUVmax risk groups



Conclusions

- Adjuvant nadroparin in patients with resected NSCLC added to adjuvant chemotherapy does not improve RFS.
- SUVmax does not predict for recurrence-free survival in resectable NSCLC.

CONCLUSIONES

- No se obtienen beneficios en SG ni con Bevacizumab ni con HBPM
- Todos los esquemas de quimioterapia muestran resultados similares, con diferente perfil toxico
- Posicionamiento de Pemetrexed en adyuvancia
- Van apareciendo estudios con Inmunoterpia en adyuvancia

8508: A pooled analysis of concurrent chemoradiotherapy (CCRT) for patients with stage III non-small cell lung cancer (NSCLC) who participated in U.S. cooperative group trials: Comparing the outcomes of elderly to younger patients (pts) – Stinchcombe T et al

- **Study objective**
  - To analyse the outcomes of CCRT in elderly patients with stage III NSCLC compared with younger patients
- **Methods**
  - **Analysis of 3,070 stage IIIA/B patients from 15 clinical trials in the US Cooperative Group**
  - Compared OS, PFS and AEs for patients aged ≥70 years (n=733) and <70 years (n=2,337)
- **Key results**
  - OS was significantly worse in elderly patients (HR 1.18 [95%CI 1.08, 1.29]; p=0.0006)
  - PFS did not differ by age (HR 1.05 [95%CI 0.96, 1.14]; p=0.41)
  - There was a higher rate of grade ≥3 AEs in elderly compared with younger patients (OR 1.23 [95%CI 0.97, 1.56])
  - Grade 5 AEs were more common in elderly patients (7.6% vs. 3.8% in younger patients; p<0.05), but treatment-related deaths were not different
- **Conclusions**
  - **Elderly patients showed significantly worse OS and similar PFS to younger patients**
  - Grade 3 and 5 AEs were more frequent in elderly patients, but rate of death attributed to treatment was similar

Stinchcombe et al. J Clin Oncol 2016; 34 (suppl): abstr 8508

Abstract

Background: Concurrent chemoradiotherapy (cCRT) has proven to increase survival in elderly patients with unresectable stage III NSCLC, but it is not yet accepted as standard of care. The geriatric assessment (GA) might help to characterize patients who benefit from cCRT.

Methods: Elderly patients (≥ 74 years) with stage II-III NSCLC underwent GA and were classified according to the GA into fit and medium fit who were deemed candidates for antitumoral treatment and unfit patients received best supportive care. Clinical, GA and follow-up data were prospectively collected.

Results: From 04/2008 to 11/2015, 85 elderly patients with unresectable stage II-III NSCLC were identified. Median age: 79.5 (74-87); gender (M/F): 89%/11%; histology (SCC/AD/NOS): 54%/25%/21%; stage (IIA/IIB/IIIA/IIIB): 3.5%/9%/56.5%/31%; ECOG PS (0-1/≥2): 78%/22%; GA groups (fit/medium fit/unfit): 37%/48%/15%; VES-13 (≥ 3/<3): 43.5%/56.5%. Fit and medium fit patients had significantly better mOS (20.6 and 17.5 m, respectively) as compared with unfit patients (10.1 m, p=0.009). Vulnerable patients (VES-13 ≥ 3) had significantly shorter mOS (11.6 m) as compared to other patients (19.1 m, p=0.008). In the multivariate Cox analysis, GA groups and VES-13 had prognostic value independently of age, gender, stage and weight loss. Most fit and medium fit patients received CRT (69%) and had a mOS of 22.4 m (95% CI 17.5 – 27.4). Vulnerable patients (VES-13≥3) had significantly shorter mOS (p=0.018) and higher risk of G3-4 toxicity (p=0.006).

Conclusions: GA and VES-13 may help in the selection of elderly patients for cCRT to avoid undertreatment of those patients. VES-13 had independent prognostic value and was significantly associated with higher risk of toxicity.

Background

- The number of elderly patients with lung cancer who requires appropriated treatment is increasing (1).
- Elderly lung cancer patients represent a heterogeneous group and their functional status cannot be predicted on the basis of chronological age. Geriatric Assessment (GA) is a valuable tool able to predict severe treatment-related toxicity and OS in a variety of tumors (2).
- There is a lack of consensus on the treatment of elderly patients with unresectable stage III NSCLC. Adapted concurrent chemoradiotherapy is considered an acceptable option for elderly patients not fit enough for a standard chemoradiotherapy protocol (3,4).
- Surveys indicate that elderly patients in this setting are currently undertreated, and research in this area is needed.

References
(1) Vincent GK, Velkoff VA: http://www.census.gov/prod/2010pubs/p25-1138.pdf;
(2) Wildiers et al. J Clin Oncol 2014
(3) Cardenal F et al. Ann Oncol 2014
(4) Atagi et al. Lancet Oncol 2012.

Hypothesis and Aims

- We hypothesized that GA may help to identify elderly patients with locally advanced NSCLC who might benefit from adapted concurrent chemoradiotherapy.

Aims:

1) To classify patients in geriatric groups (fit, medium fit and unfit) in order to select patients fit enough to be treated.
2) To correlate geriatric groups with survival and toxicity.
3) To study the potential of the vulnerability screening tool Vulnerable Elders Survey (VES-13) for identifying fit patients.

Materials and methods

- Elderly patients (≥ 75y) with unresectable stage II-III NSCLC underwent a geriatric assessment (GA) including comorbidity, functional and nutritional status, geriatric syndromes, mood, social support, cognition and Vulnerable Elders Survey (VES-13).
- Clinical data and GA data were prospectively collected. From April 2008 to November 2015, 85 patients with unresectable stage II-III NSCLC were identified.
- Overall survival (OS) was calculated using the Kaplan-Meier method and a multivariate analysis was performed using Cox regression. A logistic regression was used to test the ability of some variables to predict toxicity.
- This pilot study was approved by the Institutional Review Board.
- Patients were classified according to GA into 3 groups (adapted from Balducci and Extermann):

	Fit	Medium fit	Unfit
Disabilities	Independent	<3 IADL No ADL disability	>3 IADL Any ADL disability
Comorbidities	<3	<3	≥3
Geriatric syndrome	No	No	Yes

Adapted concurrent chemoradiotherapy (CRT)

Best supportive care or palliative RT

3D Thoracic Radiotherapy (2 Gy/fraction). Total dose: 60 Gy. Chemotherapy started on d1 of radiotherapy. Chemotherapy schedules:
1) CBDCA AUC 2.5 + iv vinorelbine 15mg/m2 d1, d8, d21 and d29
2) CBDCA AUC 2 + paclitaxel 45mg/m2 weekly x 6 weeks
3) CBDCA AUC 2 weekly x 6 weeks

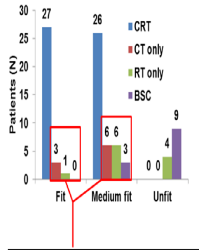
Results

1. Patient's characteristics.

	Fit (n=31)	Medium fit (n=41)	Unfit (n=13)	All (n=85)
Age, median (range)	79.7 (75 - 84)	78.9 (74 - 87)	80.7 (75 - 87)	79.5 (74 – 87)
Gender, N (%)				
Male	26 (84%)	39 (95%)	11 (85%)	76 (89%)
Female	5 (16%)	2 (5%)	2 (15%)	9 (11%)
Smoking history, N (%)				
Current	4 (13%)	9 (23%)	3 (23%)	16 (19%)
Former	22 (71%)	28 (72%)	9 (69%)	59 (71%)
Never	5 (16%)	2 (5%)	1 (8%)	8 (10%)
Histology, N (%)				
Squamous cell	11 (35.5%)	25 (61%)	10 (77%)	46 (54%)
Adenocarcinoma	11 (35.5%)	8 (20.5%)	2 (15%)	21 (25%)
NOS	9 (29%)	8 (20.5%)	1 (8%)	18 (21%)
Stage, N (%)				
IIA	1 (3%)	2 (5%)	0 (0%)	3 (3.5%)
IIB	3 (10%)	4 (10%)	1 (8%)	8 (9%)
IIIA	20 (64%)	22 (54%)	6 (46%)	48 (56.5%)
IIIB	7 (23%)	13 (31%)	6 (46%)	26 (31%)
ECOG PS, N (%)				
0-1	30 (97%)	32 (78%)	4 (31%)	66 (78%)
≥2	1 (3%)	9 (22%)	9 (69%)	19 (22%)
VES-13, N (%)				
<3	24 (77%)	13 (32%)	0 (0%)	37 (43.5%)
≥3	7 (23%)	28 (68%)	13 (100%)	48 (56.5%)

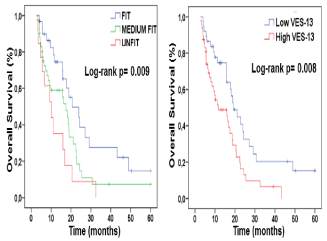
2. Treatment according to GA groups (n=85):

- 74% of patients (53/72) classified as fit or medium fit were treated with chemoradiotherapy (CRT):
  - 50 concurrent CRT.
  - 3 sequential CRT.



Reasons for not being treated with CRT	Fit (n=4)	Medium fit (n=15)	All (n=19)
Tumor extension	2 (50%)	4 (27%)	6 (31%)
Poor respiratory function	1 (25%)	2 (13%)	3 (16%)
Death before treatment	0 (0%)	1 (7%)	1 (5%)
Physician decision	1 (25%)	6 (36%)	7 (37%)
Patient preferences	0 (0%)	2 (13%)	2 (11%)

3. Overall Survival according to GA groups and VES-13 (n=85).



	Median OS (CI 95%)
Fit (n=31)	20.6 (10.9 – 30.4)
Medium fit (n=41)	17.5 (13.8 – 21.1)
Unfit (n=13)	10.1 (4.5 – 15.7)

	Median OS (CI 95%)
Low VES-13 (n=37)	19.1 (14.4 – 23.8)
High VES-13 (n=48)	11.6 (4.8 – 18.4)

4. Univariate analysis of Overall Survival (n=85).

	HR (CI 95%)	*P*-value
Age, continuous	0.98 (0.90-1.07)	0.662
Gender (M vs. F)	1.45 (0.52-4.03)	0.472
Histology (SCC vs. non-SCC)	1.24 (0.74-2.06)	0.418
Smoking status (smoker vs never smoker)	1.15 (0.42-3.20)	0.783
Stage (III vs. II)	1.39 (0.59-3.24)	0.449
Weight loss (≥5% vs. <5%)	2.34 (1.24-4.41)	**0.009**
ECOG PS, continuous	2.47 (1.53-3.97)	**<0.001**
Comorbidities (≥4 vs. <4)	1.85 (1.06-3.24)	**0.031**
VES-13 (≥3 vs. <3)	2.02 (1.19-3.43)	**0.009**
GA group (type 1 vs. type 2)	1.85 (1.02-3.35)	**0.042**
GA group (type 1 vs. type 3)	3.01 (1.43-6.34)	**0.004**

5. Multivariate analysis of Overall Survival (n=85).

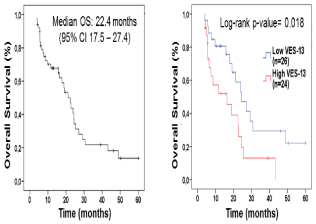
- GA group and VES-13 status were prognostic factors independent of age, gender, stage and weight loss.

	HR (CI 95%)	*P*-value
Age, continuous	0.98 (0.90-1.07)	0.696
Gender (M vs. F)	1.62 (0.56-4.66)	0.372
Stage (III vs. II)	1.20 (0.46-3.14)	0.708
Weight loss (≥5% vs. <5%)	2.39 (1.16-4.32)	0.017
GA group (type 1 vs. type 2)	1.77 (0.97-3.23)	0.065
GA group (type 1 vs. type 3)	**2.45 (1.14-5.44)**	**0.022**

	HR (CI 95%)	*P*-value
Age, continuous	0.99 (0.91-1.08)	0.994
Gender (M vs. F)	1.71 (0.60-4.84)	0.316
Stage (III vs. II)	1.50 (0.57-3.94)	0.407
Weight loss (≥5% vs. <5%)	2.38 (1.23-4.59)	0.010
VES-13 (≥3 vs. <3)	**2.01 (1.17- 3.45)**	**0.012**

6. Overall Survival of patients treated with concurrent CRT (n=50).

- Twenty-three (46%) patients were ≥80y
- 92% male; SCC/AD/NOS:50%/30%/20%; stage II/III: 16%/84%; GA risk groups: fit/medium fit: 48%/52%; VES-13: low/high 52%/48%.
- High VES-13 showed a significantly shorter median OS compared to low VES-13 (24.3 vs 16.3 months, respectively).



7. Toxicity of patients treated with concurrent CRT (n=50).

	G1-G2	G3-4	G5
Neutropenia	14 (27.5%)	11 (22%)	0
Febrile neutropenia	0	4 (8%)	0
Anemia	25 (49%)	2 (4%)	0
Thrombocytopenia	8 (16%)	3 (6%)	0
Fatigue	41 (80%)	6 (12%)	0
Anorexia	27 (53%)	1 (2%)	0
Diarrhea	7 (14%)	1 (2%)	0
Esophagitis	33 (65%)	1 (2%)	0
Respiratory infection	3 (6%)	13 (24.5%)	2 (4%)
Radiation pneumonitis	1 (2%)	7 (14%)	6 (12%)

- Vulnerable patients defined as VES-13 ≥3 had a significantly higher risk of developing G3-4 toxicity (OR=5.46; 95%CI 1.63 – 18.3; p=0.006).
- However, age, ECOG/PS, comorbidities, weight loss ≥5% or GA risk groups were not predictive of G3-4 toxicity.

Conclusions

- GA was useful for selecting elderly patients with locally advanced NSCLC that might benefit from adapted concurrent CRT and seems to avoid undertreatment for those patients.
- The survival of elderly fit patients treated with concurrent CRT was similar to that expected for younger patients in this clinical setting.
- VES-13 had independent prognostic value and in patients receiving concurrent CRT was significantly associated with higher risk of G3-4 toxicity. The value of VES-13 to predict toxicity and to assess prognosis should be further studied.

Contact e-mails: ernestnadal@gmail.com; mantonio@iconcologia.net

8538: Randomized phase II trial (RENO): efficacy results of oral vinorelbine or etoposide combined with cisplatin in chemo-radiotherapy treatment of locally advanced NSCLC (LA-NSCLC). SLCG 10/02 – Provencio M et al

- **Study objective**
  - To assess the efficacy and safety of oral vinorelbine or etoposide combined with cisplatin in chemoradiotherapy treatment of locally advanced NSCLC
- **Methods**
  - Open-label, 2-arm, randomized, phase 2 study of patients with locally advanced NSCLC
    - Arm A: Cisplatin 80 mg/m^2 D1 + vinorelbine 80 mg/m^2 D1, 8 (2 cycles) followed by cisplatin 80 mg/m^2 D1 + vinorelbine 40 mg/m^2 D1, D8 + radiotherapy (2 cycles)
    - Arm B: Cisplatin 50 mg/m^2 D1, 8, 29, 36 + etoposide 50 mg/m^2 D1−5, 29−33 + radiotherapy
  - Primary endpoint was PFS; secondary endpoint was ORR and OS
- **Key results**
  - Median PFS was similar between treatment arms (11.4 months in Arm A and 11.8 months in Arm B, p=0.37)
  - Grade 3/4 AEs were more frequent in Arm B than Arm A, including esophagitis, anaemia, neutropenia, thrombocytopenia, pneumonia and sepsis
- **Conclusions**
  - Oral vinorelbine in combination with cisplatin had a better safety profile than etoposide
  - No difference in efficacy was observed between the treatment arms

Provencio et al. J Clin Oncol 2016; 34 (suppl): abstr 8538

8510: Randomized phase II study of preoperative chemoradiotherapy (CRT)+/- Panitumumab (P) followed by consolidation chemotherapy (C) in potentially operable locally advanced (stage IIIa, N2+) non-small cell lung cancer (LANSCLC): Nrg oncology/RTOG 0839 – Edelman M et al

- **Study objective**
  - To investigate the efficacy and safety of adding panitumumab to induction chemoradiation followed by surgery (if resectable) and consolidation chemotherapy in locally advanced NSCLC
- **Methods**
  - Patients were randomized to induction chemotherapy (paclitaxel + carboplatin) + concurrent radiotherapy (total 60 Gy) with or without panitumumab 2.5 mg/kg/week for 6 weeks
  - Mediastinum was pathologically reassessed prior to or at the time of resection followed by treatment with consolidation chemotherapy (paclitaxel + carboplatin)
- **Key results**
  - 61 patients were eligible for analysis
  - Grade 4 and 5 AEs occurred in 13.6% and 0% of patients on chemoradiotherapy alone vs. 15.4% and 7.7% of those on additional panitumumab, respectively
  - Rates of mediastinal nodal sterilization were 68.2% for chemoradiotherapy and 48.7% for chemoradiotherapy + panitumumab (p=0.96)
- **Conclusions**
  - The addition of panitumumab to chemoradiotherapy did not improve rates of mediastinal nodal sterilization
  - There was an unexpectedly high mortality rate in the panitumumab arm, although the relationship to panitumumab is unclear

Edelman et al. J Clin Oncol 2016; 34 (suppl): abstr 8510

8550: Multimodality therapy in IIIA-N2 NSCLC: Factors associated with treatment selection and survival – Brandmaier A et al

- **Study objective**
  - To examine patterns of care, outcomes of different treatment regimens and associated socioeconomic and clinicopathological factors in patients with stage IIIA−N2 NSCLC
- **Methods**
  - Retrospective analysis of 28,147 patients with stage IIIA−N2 NSCLC identified in the National Cancer Data Base between 2004 and 2013
  - Four treatment cohorts were evaluated: definitive chemoradiation (CR), neoadjuvant chemoradiation followed by surgery (CRS), neoadjuvant chemotherapy followed by surgery (CS), and surgery +/- adjuvant therapy (SA)
  - Data were analysed for the impact of clinicopathological factors and treatment sequencing on OS
- **Key results**
  - The frequency of treatment courses was: 70.8% CR, 8.8% CRS, 3.9% CS and 16.5% SA
  - Improved OS was observed in patients who received CRS or CS (HR 0.8; $p<0.0001$)
- **Conclusions**
  - The majority of patients with stage IIIA−N2 NSCLC were treated with CR
  - Patients who received neoadjuvant therapy followed by surgery had improved OS including when controlling for age and comorbidity index

Brandmaier et al. J Clin Oncol 2016; 34 (suppl): abstr 8550

8531: Utility of surveillance imaging in stage III non-small cell lung cancer (NSCLC) patients: A SEER-Medicare analysis. Manish K. Thakur

- **Study objective**
  - NCCN guidelines recommend surveillance imaging every 6-12 months, we conducted a retrospective analysis of stage III NSCLC patients to assess the rate of surveillance imaging and its association with survival.
- **Methods**
  - Stage III NSCLC patients diagnosed from 2007 through 2011 from the SEER-Medicare database who survived at least 4 months after receiving treatment with curative intent were eligible for inclusion in the study. Surveillance was defined as receipt of chest CT and/or PET scans between 4 to 6 months after the completion of treatment.
- **Key results**
  - Of the 14,965 stage III NSCLC patients diagnosed during the study period, 2,358 patients received treatment with curative intent. Of these patients, only 34% received surveillance scans. Overall survival was significantly higher for those who received a surveillance scan (31 months) compared to those who did not (26 months, $p = 0.0011$). When adjusted for clinical and demographic variables significantly associated with overall survival, the survival benefit persisted (HR 0.79, 95% CI 0.71-0.87).
- **Conclusions**
  - Surveillance imaging after definitive treatment in stage III NSCLC patients was associated with improved survival.

Manish K. Thakur, J Clin Oncol 34, 2016 (suppl; abstr 8531)

Outcomes of Patients (pts) with Disease Recurrence After Treatment for Locally Advanced Non-Small Cell Lung Cancer (LANSCLC) Detected by Routine Follow-up (f/u) CT Scans vs. Symptom (sx) Driven Evaluation

Abstract ID: 8515

J. Nicholas Bodor, Josephine L. Feliciano, Soren Bentzen, Martin J. Edelman

UM Marlene and Stewart Greenebaum Cancer Center, University of Maryland Medical Center, Baltimore, MD

Abstract

Background: At least 75% of pts with LANSCLC relapse despite treatment with curative intent. Pts with recurrent NSCLC may benefit from further treatment. An optimal follow-up strategy, particularly in terms of the timing of CT chest scanning, has not yet been defined.

Methods: A retrospective review was performed on pts who had undergone definitive treatment (chemotherapy + radiotherapy +/- surgery) for LANSCLC (stage IIIa,b 7th ed). Standard f/u was q 3mo CT chest x 1 y, q 4mo x 2 y, q 6 mo x 1 y and then annually. We evaluated whether outcome was dependent upon how progression was diagnosed (f/u or sx) as well as the pattern of recurrence: local relapse (LR) or systemic. If systemic, we evaluated whether there were single (SM) or multiple sites (MM) of metastasis. Survival was determined with Kaplan-Meier curves and compared by log rank.

Results: 311 patients with LANSCLC were treated between 01/01/2000 and 2/28/2015, of which 167 pts relapsed and there were adequate records. 99 progressions were detected by f/u and 68 by sx. The median time to progression was 11.5 mo vs. 9.6 mo (p=0.186); OS for f/u vs. sx was 7.5 mo vs. 6.4 mo (p =0.843). When evaluating pts with LR or MM, f/u pts had a trend towards better OS than sx pts (10.3 mo vs. 4.7 mo, p=0.141; 5.0 mo vs. 2.9 mo, p=0.135, respectively). SM pts had longer OS than those with LR or MM (12.7 mo vs. 8.5 mo vs. 3.7 mo, p < 0.001).

Conclusions: Our findings suggest that, in the case of CT chest scans, symptom-driven evaluation may not adversely affect survival.

Background

- Approximately 75% of pts with LANSCLC relapse even after receiving definitive chemoradiotherapy or chemoradiotherapy + surgery. Early detection of recurrence before symptoms develop potentially could allow more salvage treatments with curative intent for local recurrence/solitary metastases, or earlier institution of systemic therapy. An optimal follow-up strategy to detect recurrence, has yet to be determined.
- This study examined whether outcome was dependent upon how progression was diagnosed (routine CT f/u vs. sx evaluation) and whether recurrence pattern (i.e. LR - local relapse, SM – single metastatic site, MM - multiple metastatic sites) modified results.

Methods

- 311 pts with LANSCLC (stage IIIa,b, 7th ed) were treated with definitive treatment (chemotherapy + radiotherapy +/- surgery) between 1/1/2000 and 2/28/2015, of which 167 pts relapsed and there were adequate records.
- Standard routine f/u was q 3 month CT chest scanning for 1 year, q 4 months for 2 years, q 6 months for 1 year, and then annually.
- Outcomes analyzed included median time to progression (TTP) and overall survival (OS).
- Survival was calculated using Kaplan-Meier curves. Comparisons between f/u and sx cases, and patterns of recurrence were assessed using the log-rank test.

Results

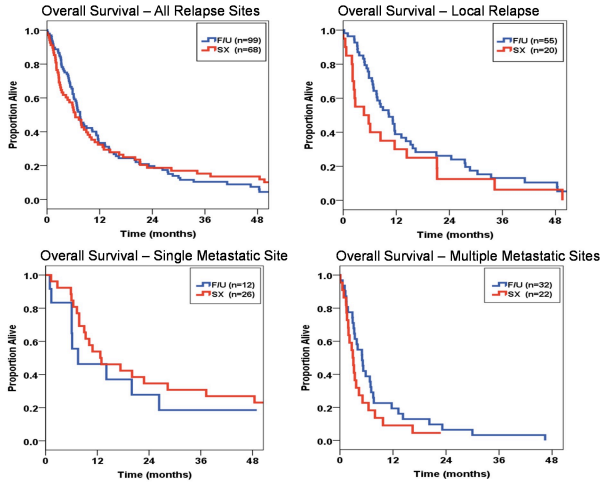
	F/U (n = 99)	SX (n = 68)	p-value
	n (%)		
Gender			0.99
Male	48 (48%)	33 (49%)	
Female	51 (52%)	35 (51%)	
Race			0.14
White	51 (52%)	41 (63%)	
Black	48 (48%)	24 (37%)	
Stage			0.77
IIIa	46 (46%)	30 (44%)	
IIIb	53 (54%)	38 (56%)	
Recurrence			0.001
LR	55 (56%)	20 (29%)	
SM	12 (12%)	26 (38%)	
MM	32 (32%)	22 (32%)	
Median Age at Diagnosis	61 yr	57 yr	0.24

	F/U (n = 99)	SX (n = 68)	p-value
	Median in months (min, max)		
TTP			
All sites	11.5 (2.4, 163.5)	9.6 (1.6, 81.1)	0.19
LR	12.3 (2.9, 163.5)	11.1 (3.3, 81.1)	0.91
SM	5.4 (2.4, 38.6)	8.0 (2.9, 27.0)	0.39
MM	11.9 (3.0, 68.4)	8.1 (1.6, 26.8)	0.32
OS			
All sites	7.5 (0.1, 71.5)	6.4 (0.0, 169.3)	0.84
LR	10.3 (0.2, 71.5)	4.7 (0.0, 49.6)	0.14
SM	7.5 (1.0, 49.0)	12.7 (1.3, 169.3)	0.41
MM	5.0 (0.1, 46.4)	2.9 (0.1, 22.8)	0.14

Sources of funding: PJ Aldridge Foundation, P30 CA134274

Corresponding author: jbodor@umm.edu (JN Bodor)

Results



Conclusions

- Overall survival did not significantly differ between follow-up and symptomatic patients (7.5 months vs. 6.4 months, p=0.84)
- Among patients with LR or MM, those diagnosed by follow-up scans had a trend towards better survival than symptomatic patients, though not statistically significant.
- This study suggests that, in case of CT chest scans, symptom-driven evaluation may not significantly affect survival.

CONCLUSIÓN

- Muchos estudios presentados con poca relevancia en la práctica clínica habitual.
- Muchos análisis de las bases de datos de pacientes
- Incorporación paulatina de la inmunoterapia a los estadios precoces