IASLC 2022 World Conference on Lung Cancer

AUGUST 6-9, 2022 | VIENNA, AUSTRIA

Best of WCLC
Early-Stage NSCLC Radiotherapy

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Disclosure

Research Funding: Genentech, EMD Serono, Merck

Consulting: Novocure, Boston Scientific, Astra Zeneca

Speakers' Bureau: Curio Science, Dava Oncology

I will discuss off label use of immune checkpoint inhibitors

Themes

Toxicity of SABR

MA 03.09: Real World Acute Toxicity in Patients with Stage I NSCLC Treated with SBRT

OA 14.04: Chest Wall Toxicity after Individualized Stereotactic Ablative Radiotherapy for Lung Tumors

Use of SABR and Disparities in Lung Cancer Treatment

EP 02.02-002: Increased Utilization of Stereotactic Body Radiotherapy in the United States has Decreased Treatment Disparities for Early-Stage Lung Cancer

Immunotherapy with SABR in Early-Stage NSCLC

P1.05-01: Phase II Study of ctDNA Directed Consolidation Durvalumab after Induction and Concurrent Durvalumab with SABR for Stage I NSCLC

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Real-world acute toxicity in patients with stage I NSCLC treated with SBRT

Peter S.N. van Rossum, **Nienke Wolfhagen**, Antoinet M. van der Wel, Liselotte W. van Bockel, Ida E.M. Coremans, André L.A.J. Dekker, Corine A. van Es, Katrien E.A. de Jaeger, Hans P. Knol, M. Willemijn Kolff, Friederike L.A. Koppe, Jacqueline Pomp, Dominic A.X. Schinagl, Femke O.B. Spoelstra, Caroline J.A. Tissing-Tan, J. Fred Ubbels, Ernest J.A. Vonk, Noëlle C.M.G. van der Voort van Zijp, Erwin M. Wiegman, A.M. van der Geest, Bart J.T. Reymen, Daphne van Kampen, Ronald A.M. Damhuis, José S.A. Belderbos.

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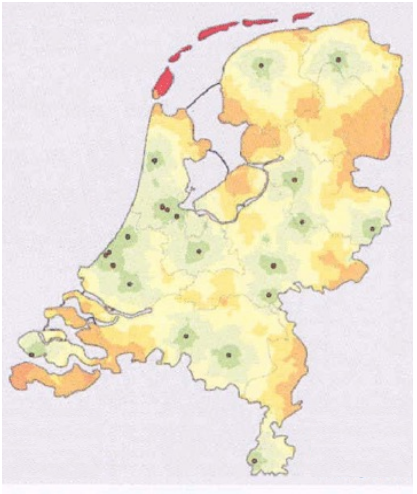
DUTCH LUNG CANCER AUDIT

METHODS

Nationwide population-based study:

- Data from DLCA-R (all 19 Rad Onc departments in The Netherlands)



Inclusion:

- Patients with primary cT1-2aN0M0 (stage I) NSCLC
- Either pathologic or clinical evidence
- SBRT with curative intent between 2017 and 2020

Outcome = Acute toxicity:

- Radiation-pneumonitis grade ≥2 ***or*** other non-hematologic toxicity grade ≥3
- <90 days after start of SBRT

Analysis:

- Multiple imputation of missing data
- Logistic regression prediction models

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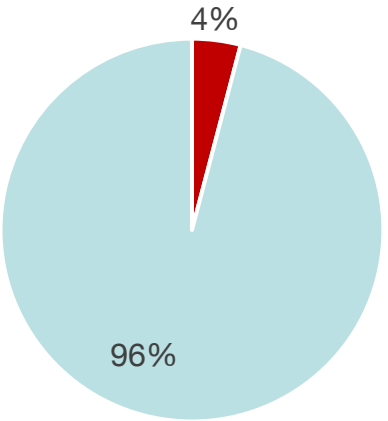
RESULTS

Total: n=5,285

- **Acute toxicity**: n=218 (**4.1%**)



Univariable analysis:

Associated with acute toxicity

- WHO performance status, pulmonary co-morbidity
- FEV1, DLCO
- Clinical (vs. histologic) evidence, middle/lower (vs. upper) lobe
- cT-stage, GTV, tumor BED, mean lung dose, lung V20Gy

Not associated with acute toxicity

- Age (linear or categorical)
- Gender, CCI, smoking, weight loss
- Tumor lateralization

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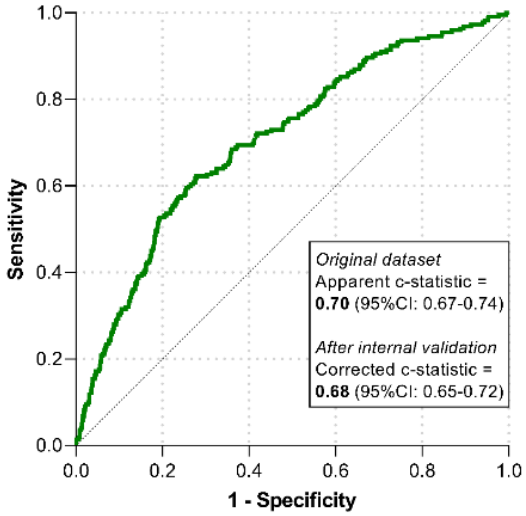
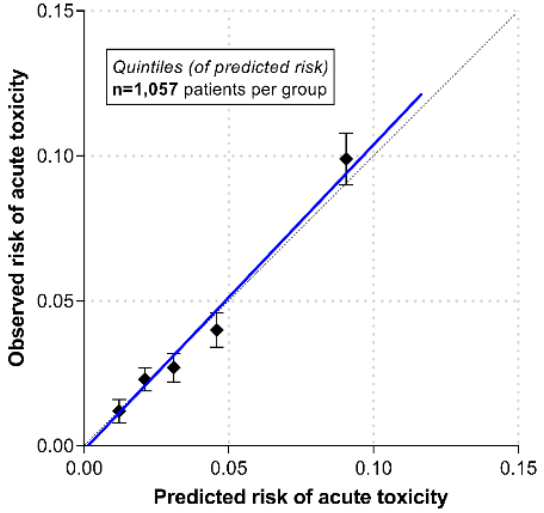
RESULTS: Prediction model

Predictor	OR (95% CI)
WHO performance status 0 1 ≥2	 *Ref* 1.13 (0.72-1.75) 1.88 (1.15-3.07)
Log(DLCO), % of predicted	0.30 (0.12-0.74)
Pathologic confirmation	0.62 (0.44-0.88)
Tumor location Upper lobe Middle/lower lobe	 *Ref* 1.54 (1.10-2.15)
Clinical T-stage cT1a cT1b cT1c cT2a	 *Ref* 1.59 (1.01-2.51) 2.15 (1.30-3.55) 2.21 (1.22-3.99)
Log(Mean Lung Dose), Gy	1.44 (0.86-2.42)





In Context

- 4.1% rate of acute toxicity in a large, real-world dataset is largely consistent with prior studies demonstrating low rates of acute and overall toxicity following lung SABR
- Many prospective SABR trials report acute and late toxicity in aggregate, thus direct comparison is challenging

Reported Toxicity in Prospective Trials

Trial	N=	Pneumonitis	All grade 3+ toxicity (acute+late)
RTOG 0236 (JAMA 2010)	55 evaluable	2 (3.6%) grade 3 No grade 4-5	15 (27%)
RTOG 0813 (JCO 2019)	92 evaluable for toxicity	2 (2%) grade 3 No grade 4-5	8 (9%)
RTOG 0618 (JAMA Onc 2018)	26 evaluable	No grade 3+ Grade 2 not reported	None
RTOG 0915 (IJROBP 2015)	84 evaluable	2 grade 3 pneumonitis Grade 2 not reported	10 (12%) (protocol specified AEs)
Baumann et al (JCO 2009)	57	10 (18%) grade 1-2 No grade 3+	16 (28%) first 18 months
Bral et al (JROBP 2011)	40	2 (12%)grade 3	5 (30%) grade 3 No grade 4-5
Current Report	5285	NR	4.1% acute toxicity

Age was **not** a predictor of acute toxicity

Consistent with prior studies, lung SBRT is safe in the elderly

Study	N	Median Age	Pneumonitis	Other Toxicity
Bei Y et al (J Radiat Res 2020) PMID 32383730	153	85 (range: 80-94)	8.5% grade 2 2.6% grade 3 0.6% grade 4	No grade 3+
Cassidy RJ et al (Clin Lung Cancer 2017) PMID 28373068	58	84.9 (range: 80.1-95.2)	31% grade 2 3.5% grade 3	5% grade 3
Sanndhu AP et al (Clin Lung Cancer 2014) PMID 24157245	24	85 (range:80-89)	No grade 3+	No grade 3+
Van der Voort van Zyp et al, Lung Cancer 2010 PMID 20060195	38	82 (range: 80-90)	2.6% grade 3	5% acute grade 3 16% late grade 3
Videtic GMM et al. PRO 2017. PMID 28867545	19	91.6 (range: 90-97)	No grade 3+	No grade 3+

Limitations

- Authors define acute toxicity as grade 2+ pneumonitis or grade 3+ non-hematologic toxicity within 90 days of SBRT
- Window for development of pneumonitis extends to ~6 months in many studies and risk of pneumonitis may be underestimated by this window
- Majority of serious toxicity following lung SABR is late, not acute
  - Hemoptysis, strictures, fibrosis
- Nonetheless, these data provide an excellent real-world estimate of acute toxicity following lung SABR

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Chest wall toxicity after individualized stereotactic ablative radiotherapy for lung tumors

Brianna Lau, Yufan (Fred) Wu, Jie Fu, Sunan Cui, Daniel Pham, Lawrie Skinner, Hiroki Shirato, Hiroshi Taguchi, Michael Gensheimer, Harriet Gee, Alexander Chin, Maximillian Diehn, Billy Loo, Lucas Vitzthum

Stanford University, School of Medicine
Palo Alto, CA, USA

iSABR (individualized SABR) trial (NCT01463423)

Diagnosis of limited primary or metastatic lung tumors with no evidence of uncontrolled extrathoracic metastases

174

A Phase II Trial of Individualized Stereotactic Ablative Radiotherapy for Lung Tumors (iSABR)

M.F. Gensheimer,[1] H.E. Gee,[2,3] R. Von Eyben,[4] H. Shirato,[5] H. Taguchi,[5] S. Wong,[4] E. Brown,[4] N. Nguyen,[4] R. Liang,[4] P.G. Maxim,[6] Diehn[4];
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Individualized SABR to lung cancer results in excellent local control and favorable toxicity profiles

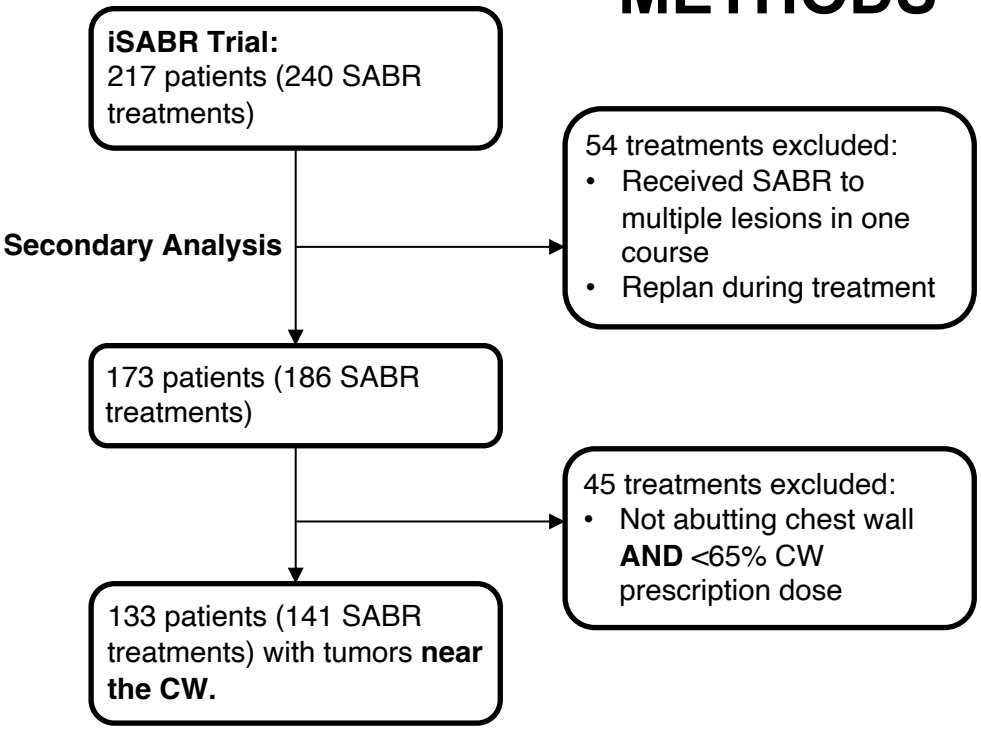
P

Small (<=10cc) 25 Gy/1fxn
Medium (>10 & <=30cc)
50 Gy/4 fxns
Large (>=30cc)
54 Gy/3 fxns

Small (<=10cc) 40 Gy/4 fxn
Medium (>10 & <=30cc)
50 Gy/4 fxns
Large (>=30cc)
60 Gy/8 fxns

NOTE: Lung metastases from colorectal cancer:
Peripheral: <= 30 mL 50Gy in 4 fxns; >30 mL 54 Gy in 3 fxns
Central: <=30mL 50 Gy in 4 fxns; >30 mL 60 Gy in 8 fxs

METHODS



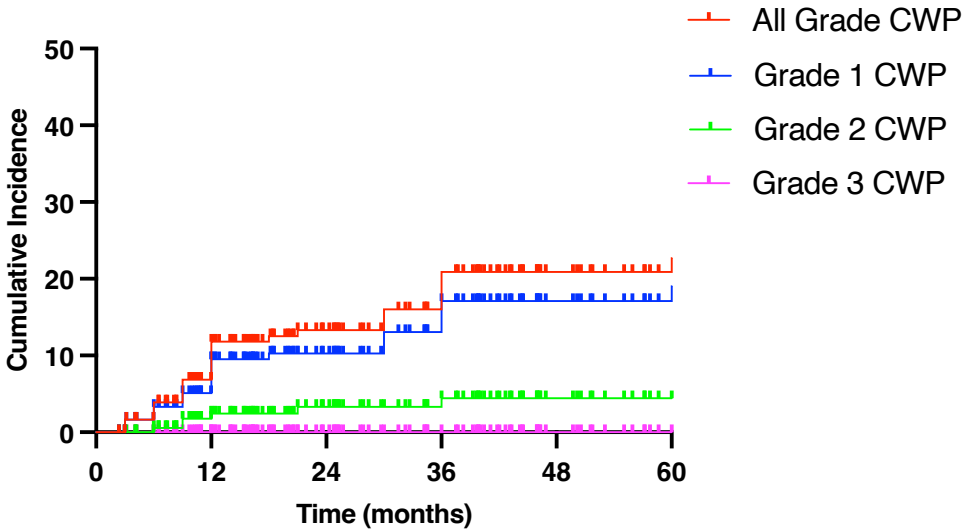
- Tumor location relative to the chest wall (i.e abutting vs. not abutting), treatment plan parameters and toxicity profiles were collected.
- Toxicity was graded per the National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) Version 4.
- Evaluated the potential association using Log-rank analysis.

BASELINE CHARACTERISTICS

Total (n)	186
Peripheral Central	71% 29%
Primary Metastatic	76% 24%
Adenocarcinoma Squamous cell Other	60% 17% 21%
≤10 cc **10-30 cc** **>30 cc**	74% 20% 7%
Abutting CW Not Abutting/Close Not Close	46% 30% 24%

RESULTS

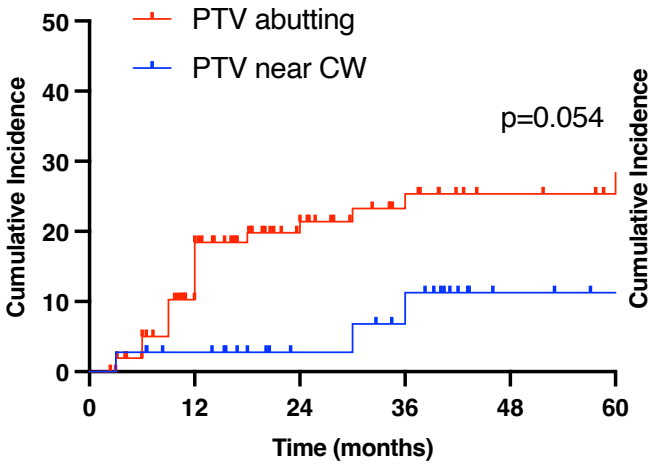
Thirty-one patients (16.8%) developed chest wall pain. **There was no Grade 3+ toxicity.**



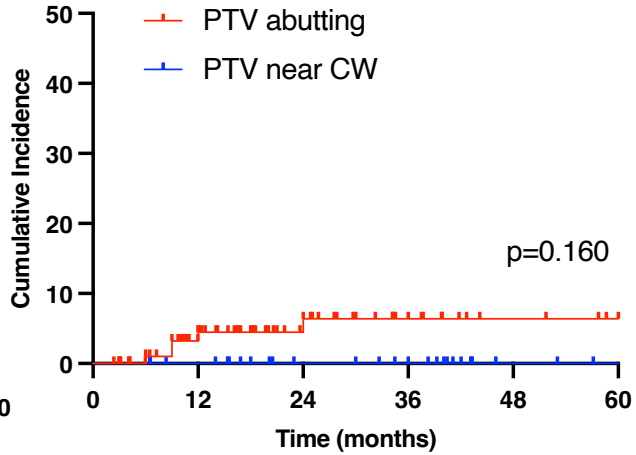
RESULTS

Cumulative Incidence of Chest Wall Pain **by location**

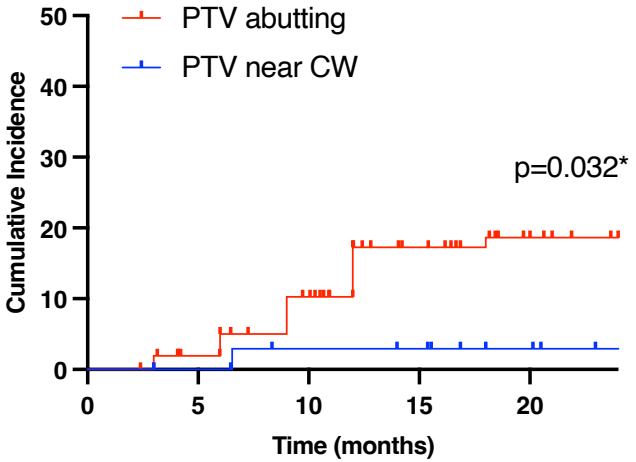
All Grade Chest Wall Pain



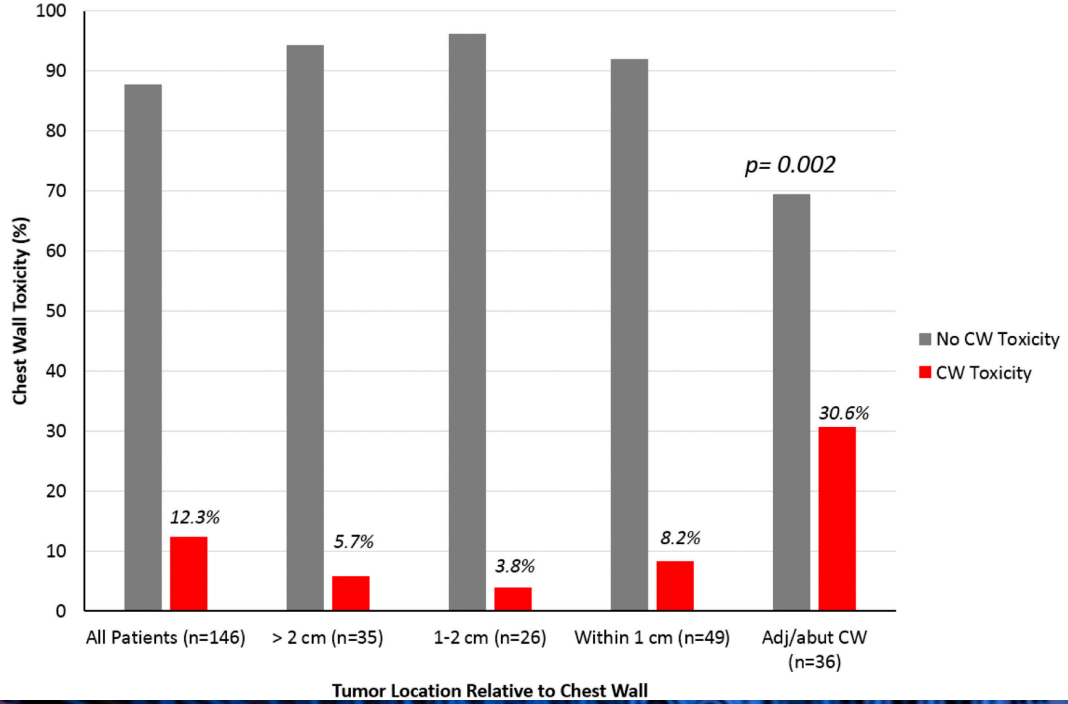
Grade 2 Chest Wall Pain

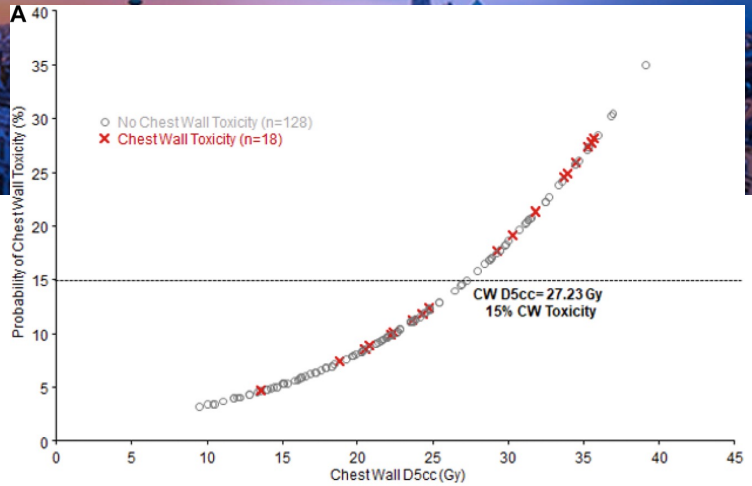


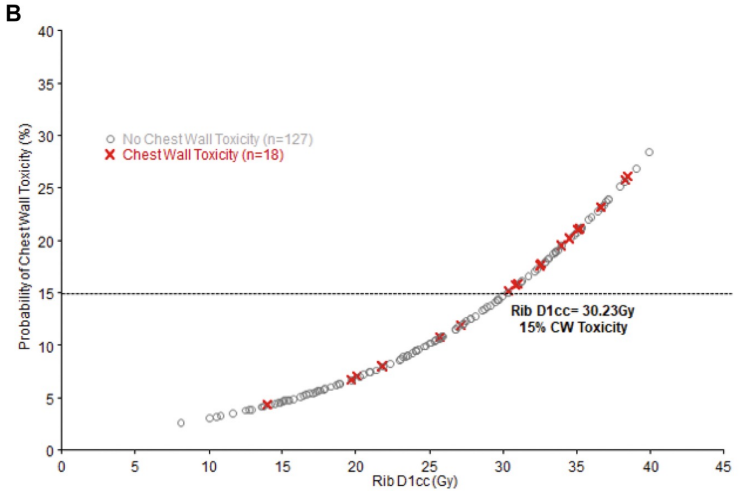
Sub-acute Chest Wall Pain (2 years)



Single Fraction SABR and Chest Wall Toxicity







Manyam BV et al. Effect of Tumor Location and Dosimetric Predictors for Chest Wall Toxicity in Single-Fraction Stereotactic Body Radiation Therapy for Stage I Non-Small Cell Lung Cancer. PRO 2019

Increased Utilization of Stereotactic Body Radiotherapy in the United States has Decreased Treatment Disparities for Early-Stage Lung Cancer

Ashwin Ganesh, BS, Mark Korpics, MD, Mary Pasquinelli, DNP, Lawrence Feldman, MD, Matthew Koshy, MD
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CHICAGO PEORIA ROCKFORD URBANA

- The National Cancer Database (NCDB) was utilized to determine the proportion of patients with NSCLC receiving surgical treatment, SBRT, or no definitive treatment (observation) for clinical stage I-IIA N0M0 NSCLC from 2004-2017 (n=337794).
- The receipt of treatment for NSCLC was evaluated in terms of the overall population and by race.
- Univariable and multivariable logistic regressions were used to determine factors associated with the likelihood of receiving definitive treatment.
- Subsequently, we evaluated changes in age-adjusted mortality using the Surveillance, Epidemiology, and End Result (SEER) database.

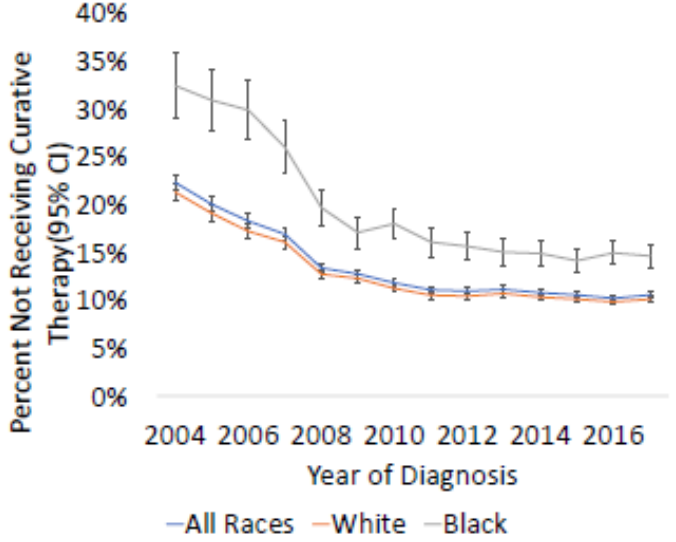


Figure 1. Percent of Patients Receiving Observation for Early-Stage NSCLC over Time

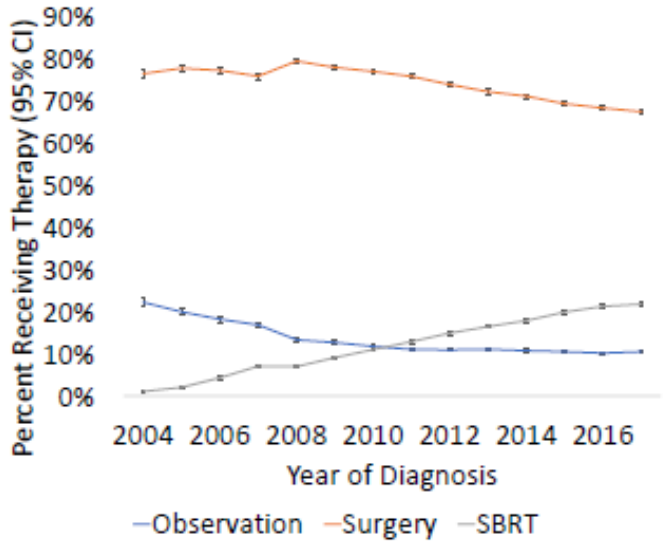


Figure 2. Trends in Curative Therapy for Stage I Lung Cancer over Time

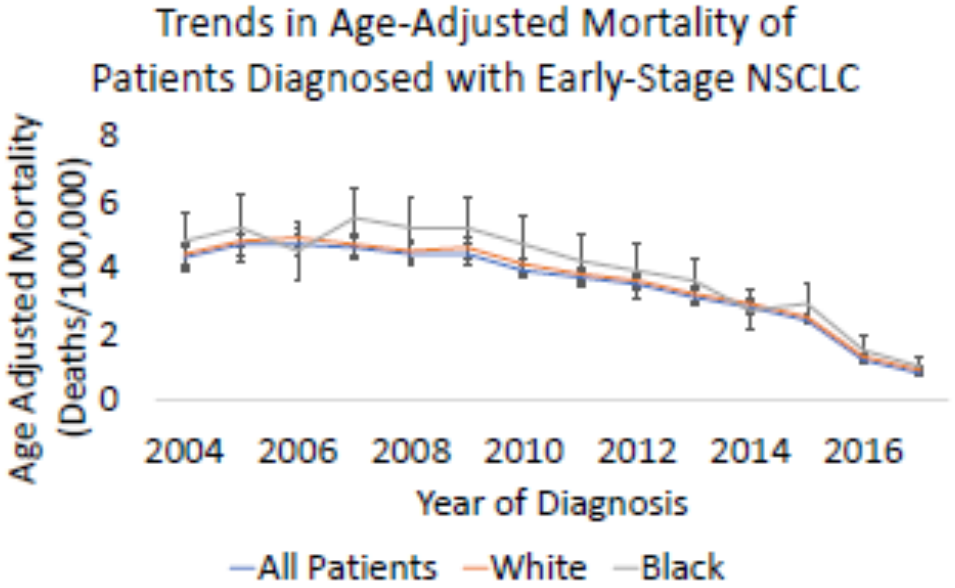


Figure 3. Changes in Age-Adjusted Mortality of Early-Stage NSCLC over Time

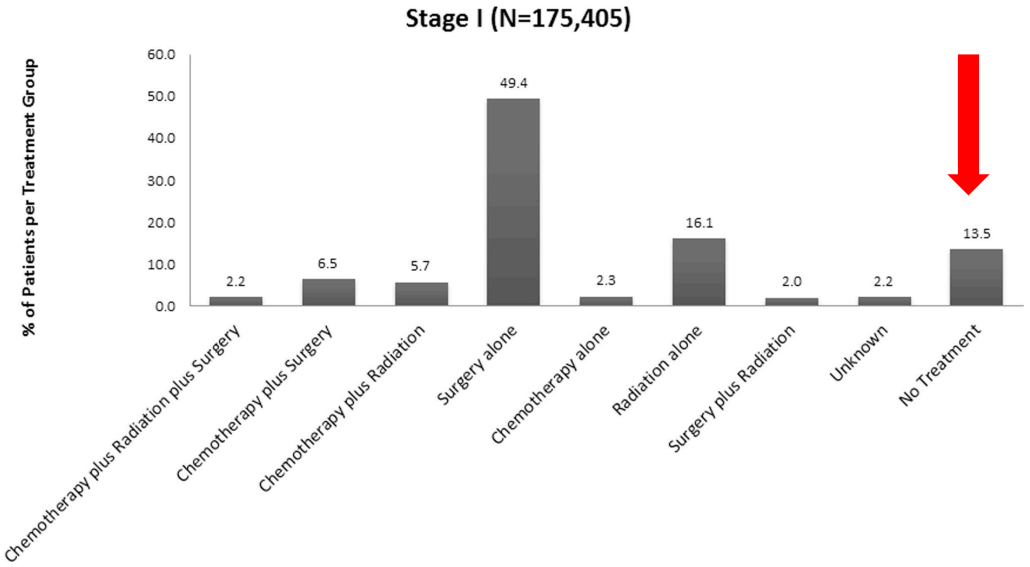
No treatment is common in NSCLC

Prior NCDB study evaluating era from 1998-2012 found a **13.5%** rate of no treatment for Stage I NSCLC

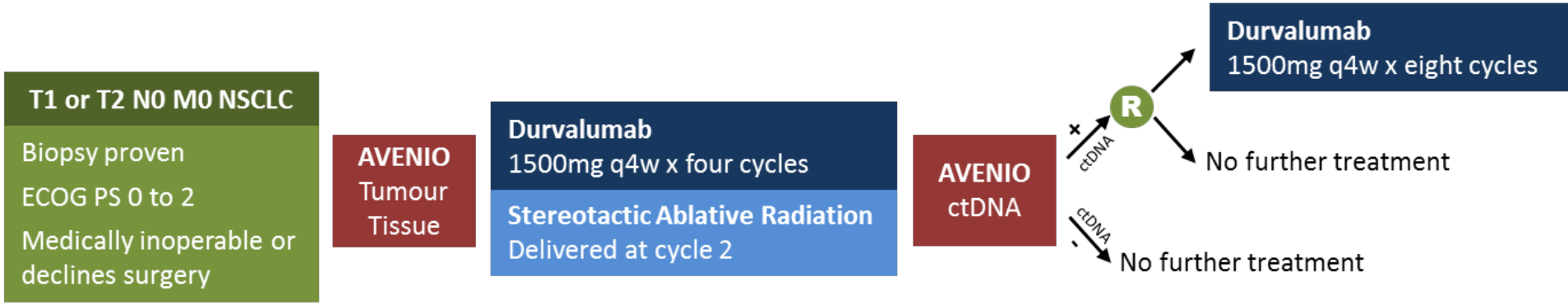
Regardless of stage, untreated patients had significantly shorter overall survival (OS) ($p < 0.0001$).

WCLC 2022 study highlights how SABR has changed these patterns and improved survival in early-stage NSCLC

Supplementary Figure 1.



Trial in Progress: IO in Early Stage, Medically Inoperable NSCLC



Ongoing Randomized Trials with SABR + ICI for Early-Stage NSCLC

Study	Drug	Timing	Duration Checkpoint Inhibitor	Primary Endpoint	N
PACIFIC 4	Durvalumab	Adjuvant	Up to 24 months	PFS	630
SWOG/NRG S1914	Atezolizumab	Neoadjuvant, concurrent and adjuvant	Up to 6 months	OS	480
KEYNOTE 867	Pembrolizumab	Concurrent and Adjuvant	Up to 12 months	OS and EFS	530

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Thank you!