

Treatment Patterns, Overall Survival, and Disease-Free Survival in Early-Stage Non-Small Cell Lung Cancer Following Complete Resection

Howard (Jack) West¹, Xiaohan Hu², Thomas Burke², Mark S. Walker³, Yuexi Wang³, Ayman Samkari²

¹City of Hope Comprehensive Cancer Center, Duarte, CA, USA

²Merck & Co., Inc., Kenilworth, NJ, USA

³ConcertAI, Memphis, TN, USA

Background

- About 25% of the early-stage non-small cell lung cancer (NSCLC) patients receive surgical resection. However, high rate of recurrence is still observed after complete resection.¹ Approximately 45% of patients with stage IB, 62% with stage II, and 76% with stage III will still develop disease recurrence or die as a result of their disease within 5 years of resection, regardless of use of postoperative chemotherapy.²
- The survival post complete resection remains poor despite the advent of newer treatment.³ Based on National Cancer Institute data between 2011 to 2017, the 5-year survival rate is 59.8% for patients diagnosed with localized disease and 32.9% for patients with regional disease.⁴
- Adjuvant chemotherapy is currently recommended for patients with completely resected stage II to IIIA NSCLC, as well as stage IB patients considered high-risk.⁵
- For adjuvant chemotherapy, the National Comprehensive Cancer Network recommends a cisplatin-containing doublet regimen.⁶ Compared to best supportive care following complete resection, cisplatin-based chemotherapy is associated with improvement in disease-free survival (DFS) and overall survival (OS); however, improvement in OS translates to a mere absolute survival benefit of 5.4% at 5 years.²
- Real-world data is needed to understand treatment use in the adjuvant setting and long-term survival outcomes to inform unmet needs in patients with early-stage NSCLC following complete resection.

Objectives

- To examine the treatment pattern of adjuvant therapy, OS, and real-world disease-free survival (rwDFS) following complete resection in patients with early-stage (IB-IIIA) NSCLC.

Methods

- Study design
- Retrospective, non-interventional cohort study using electronic medical record (EMR) data.

- Data source
- The ConcertAI Patient360™ database consists of de-identified data including structured and unstructured data (text and image documents, e.g., physician notes) from selected patient cohorts according to specific disease specifications.
 - Data were drawn from geographically diverse practice locations within the USA and are primarily community oncology practices (80-90%) from both rural and urban centers.

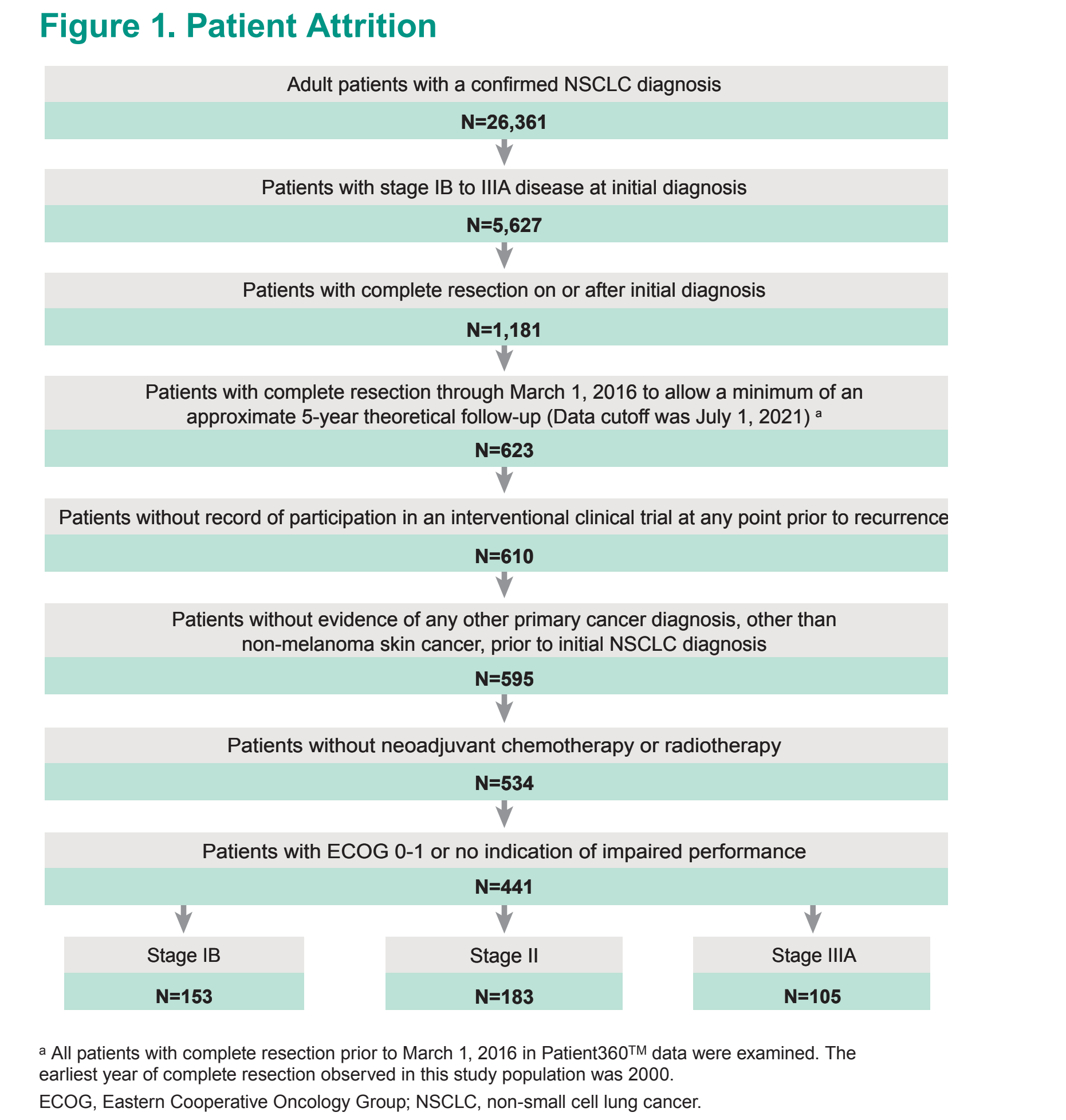
- Eligibility
- Patients with a primary diagnosis of stage IB-IIIA NSCLC were eligible if they had undergone complete resection prior to March 1, 2016, to allow a minimum of an approximate 5-year theoretical follow-up. Patients with prior neoadjuvant chemotherapy or radiotherapy were excluded (Figure 1 for complete eligibility criteria). The earliest year of complete resection observed in this study population was 2000.

- Study variables
- Patient demographic characteristics, including age, gender, race, and USA region.
 - Patient clinical characteristics, including comorbidities, stage, histology, performance status, and type of surgery.
 - Treatment patterns for systemic anticancer treatment in the adjuvant setting, including the treatment distribution and treatment duration.
 - OS was defined as time from date of complete resection to date of death. Patients were censored at the date of the last medical record if there was no evidence of death.
 - rwDFS was defined as time from date of complete resection to date of first recurrence event (locoregional recurrence or distant recurrence, based on provider documentation), new diagnosis of other primary cancer other than non-melanoma skin cancer, or date of death, whichever occurred first. Patients were censored at the date of last medical record if there was no evidence of recurrence or death.

- Statistical methods
- Descriptive statistics were used to summarize patient characteristics and treatment pattern in the adjuvant setting.
 - Kaplan-Meier analyses were conducted for OS and rwDFS by stage at initial diagnosis.

Results

- Patient Attrition (Figure 1)
- After applying all eligibility criteria, a total of 441 patients were included in this study.



- Demographic and Clinical Characteristics (Table 1)
- Patients had a median age of 67 years at initial diagnosis, and 50.3% were male.
 - Most patients were White (83.9%) and were located in the Midwest (41.3%) or South (34.7%) regions of the USA.
 - The most common disease histology at initial diagnosis was adenocarcinoma, not otherwise specified (NOS) (38.5%), followed by squamous cell carcinoma NOS (20.2%), and adenocarcinoma with mixed subtypes (5.4%).
 - With regards to performance status closest to initial diagnosis, 17% of patients had an Eastern Cooperative Oncology Group (ECOG) score of 0, 12% had an ECOG score of 1, and there was no indication of impaired performance for the remaining 71% of patients.
 - Chronic obstructive pulmonary disease and diabetes were the most common comorbid conditions in this sample of patients (25.9% and 11.8%, respectively).

- Treatment Pattern in the Adjuvant Setting (Table 2 & Figure 2)
- Patients diagnosed with stage IIIA disease had the highest proportion of patients with adjuvant therapy (50.5%), followed by stage II disease (42.1%) and stage IB disease (15.7%).
 - Among the total 441 patients, 26 patients received a second adjuvant therapy (5.9%), and 9 patients received a third adjuvant therapy (2.0%).
 - The most commonly used first adjuvant regimens were docetaxel + cisplatin (23.4%, 36 out of 154 patients with adjuvant therapy) and pemetrexed + cisplatin (20.8%, 32 out of 154 patients) across all stages.
 - The median duration of first adjuvant therapy regimen was 2.1 months (Q1-Q3: 2.1-2.3 months).

Table 1. Demographic and Clinical Patient Characteristics of Completely Resected Stage IB-IIIA NSCLC Patients

Patient Characteristics	Early-Stage NSCLC (N=441)
Age at Initial Diagnosis, median (Q1-Q3), years	67.0 (59.0, 73.0)
Male, n (%)	222 (50.3%)
White, n (%)	370 (83.9%)
Geographical Region of USA, n (%)	
Midwest	182 (41.3%)
Northeast	53 (12.0%)
South	153 (34.7%)
West	48 (10.9%)
Unknown/undocumented	5 (1.1%)
Stage of Disease at Initial Diagnosis, n (%) ^a	
IB	153 (34.7%)
II	183 (41.5%)
IIIA	105 (23.8%)
Disease Histology, n (%)	
Adenocarcinoma, NOS	170 (38.5%)
Squamous cell carcinoma, NOS	89 (20.2%)
Adenocarcinoma with mixed subtypes	24 (5.4%)
Other	82 (18.6%)
Undocumented	106 (24.0%)
Performance Status at Initial Diagnosis, n (%)	
ECOG score - 0	75 (17.0%)
ECOG score - 1	53 (12.0%)
No indication of impaired performance ^b	313 (71.0%)
Comorbidities at Initial Diagnosis, n (%) ^c	
Chronic obstructive pulmonary disease	114 (25.9%)
Diabetes	52 (11.8%)
Cerebrovascular disease	22 (5.0%)
Type of Surgery Performed for Complete Resection, n (%)	
Lobectomy of lung	243 (55.1%)
Thoracoscopic lobectomy of lung	100 (22.7%)
Total pneumonectomy	23 (5.2%)
Wedge resection	29 (6.6%)
Thoracoscopic wedge resection of lung	18 (4.1%)
Other	28 (6.3%)

^a Staging of disease at initial diagnosis could be based on American Joint Committee (AJCC) 6th or 7th edition, based on the time of initial diagnosis. Exact mapping from AJCC 6 to AJCC 7 was not possible due to limited information of tumor size recorded in the database.
^b Include patients without a documentation of ECOG score at initial NSCLC diagnosis but had no indication of impaired performance.
^c Comorbidities examined in this study include myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, Alzheimer's or other dementia, chronic obstructive pulmonary disease, connective tissue disease, ulcer disease, diabetes, renal disease, leukemia, lymphoma, cirrhosis or other serious liver disease, HIV/AIDS, and autoimmune disease. Comorbid conditions with <5% prevalence are not shown in this table.
AIDS, acquired immune deficiency syndrome; ECOG, Eastern Cooperative Oncology Group; HIV, human immunodeficiency virus; NOS, not otherwise specified; NSCLC, non-small cell lung cancer; Q, quartile; USA, United States of America.

- Real-World Disease-Free Survival (Figure 3)
- The median rwDFS was 42.4 months (95% CI: 36.3, 53.9) for patients with stage IB-IIIA disease (n=441). Median rwDFS was longest for patients diagnosed with stage IB disease (57.8 months, 95% CI: 41.3, 67.0). Median rwDFS was similar between patients diagnosed with stage II (36.6 months, 95% CI: 26.7, 46.2) and stage IIIA disease (34.4 months, 95% CI: 20.1, 58.6) in this patient sample.
 - The overall rwDFS probability for patients diagnosed with stage IB-IIIA disease (n=441) was 55.2% at 3 years (95% CI: 50.3%, 59.8%), and 42.1% at 5 years (95% CI: 37.2%, 46.9%).

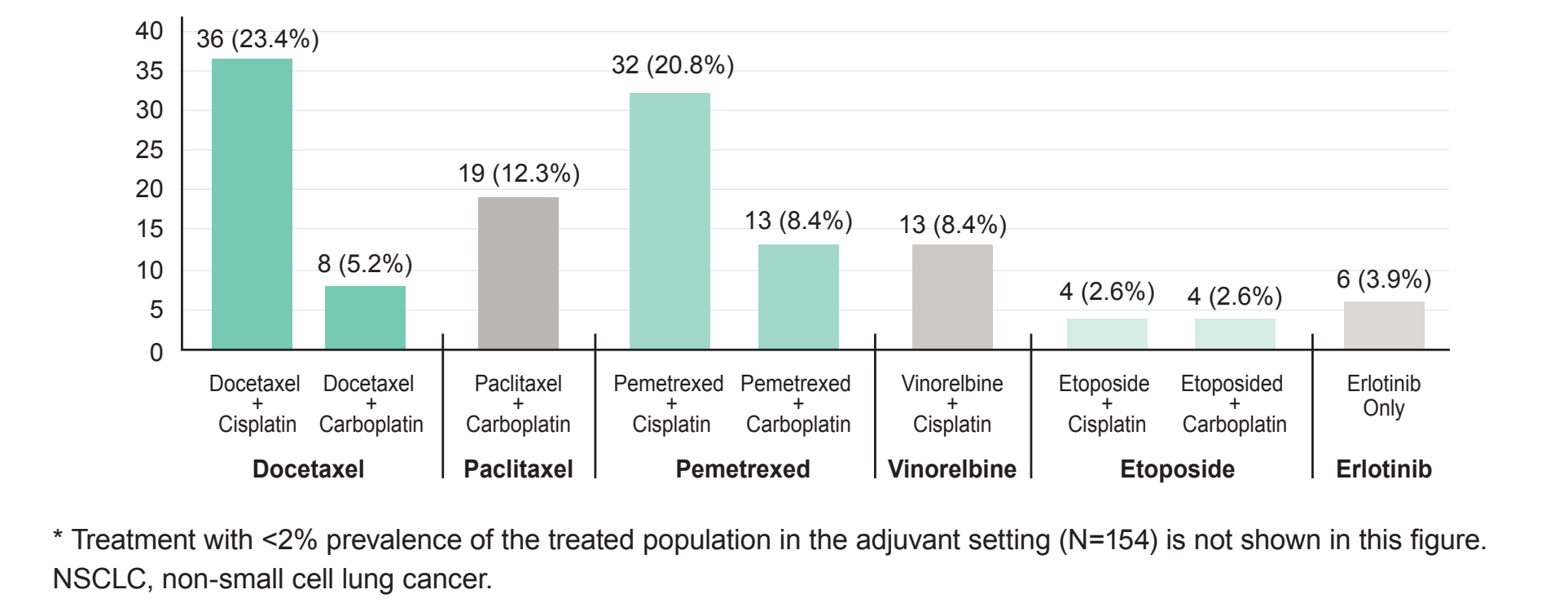
- Overall Survival (Figure 4)
- The median OS was 83.1 months (95% CI: 74.2, 90.6) for patients with stage IB-IIIA disease (n=441). Median OS was longest among those with stage IB disease (n=153), at 86.5 months (95% CI: 78.6, 101.5), followed by 79.4 months (95% CI: 68.7, 93.3) for those with stage II disease (n=183), and 71.7 months (95% CI: 59.1, 109.7) for those with stage IIIA disease (n=105).
 - The 5-year survival probability for patients with stage IB-IIIA disease was 65.7% (95% CI: 60.7%, 70.1%). The highest 5-year survival probability was observed for patients with stage IB disease, followed by patients with stage II disease and stage IIIA disease.

Table 2. Rate of Adjuvant Therapy in Patients with Completely Resected Stage IB-IIIA NSCLC

Adjuvant Therapy, n (%)	Stage IB (N=153)	Stage II (N=183)	Stage IIIA (N=105)
Patients receiving adjuvant therapy	24 (15.7%)	77 (42.1%)	53 (50.5%)
Patients receiving a second adjuvant therapy	5 (3.3%)	11 (6.0%)	10 (9.5%)
Patients receiving a third adjuvant therapy	3 (2.0%)	3 (1.6%)	3 (2.9%)

NSCLC, non-small cell lung cancer.

Figure 2. Treatment Distribution for the First Adjuvant Therapy for Overall Completely Resected Stage IB-IIIA NSCLC Patients



* Treatment with <2% prevalence of the treated population in the adjuvant setting (N=154) is not shown in this figure. NSCLC, non-small cell lung cancer.

Figure 3. Kaplan-Meier Analysis of Real-World Disease-Free Survival from Complete Resection by Stage

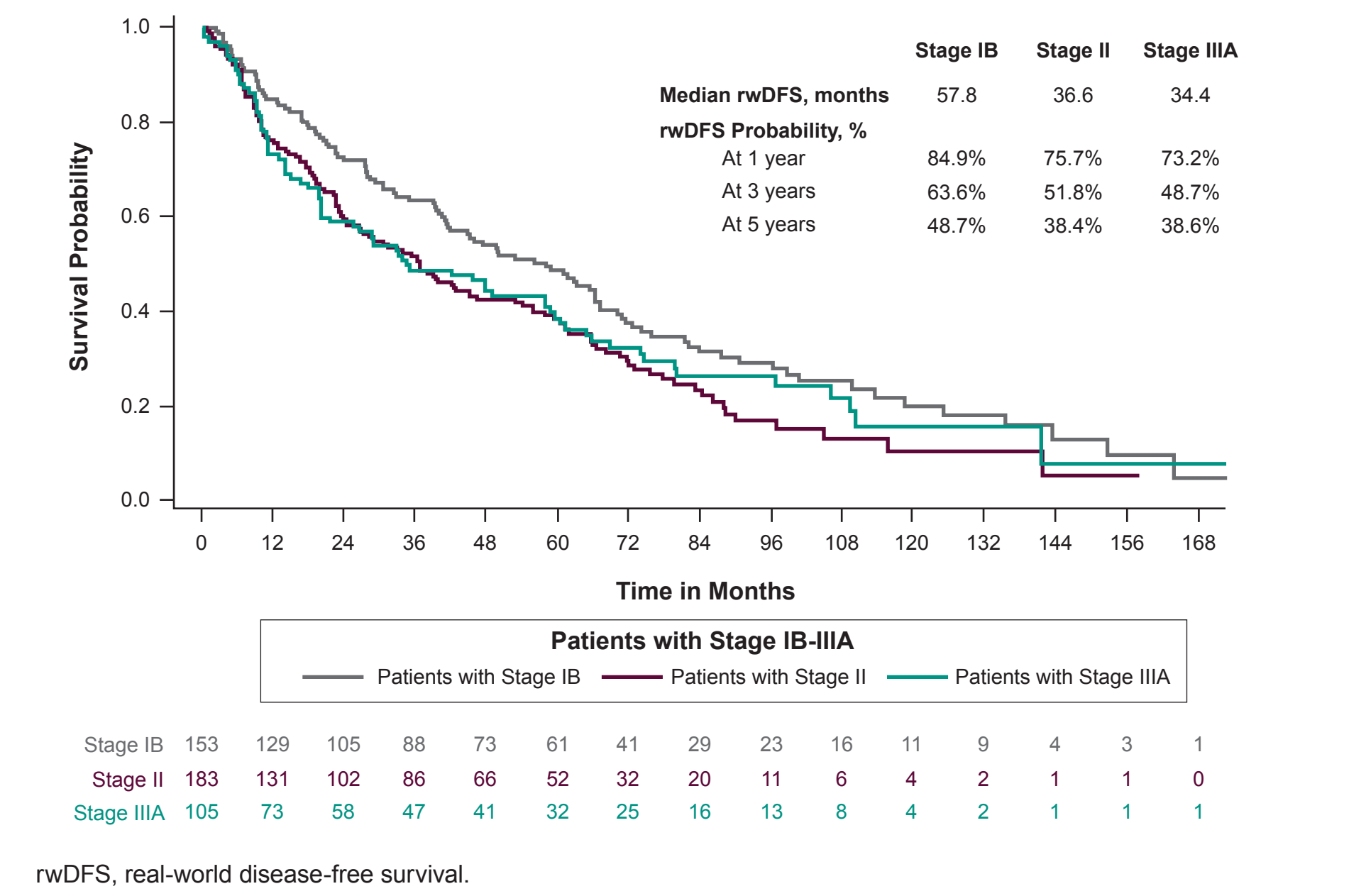
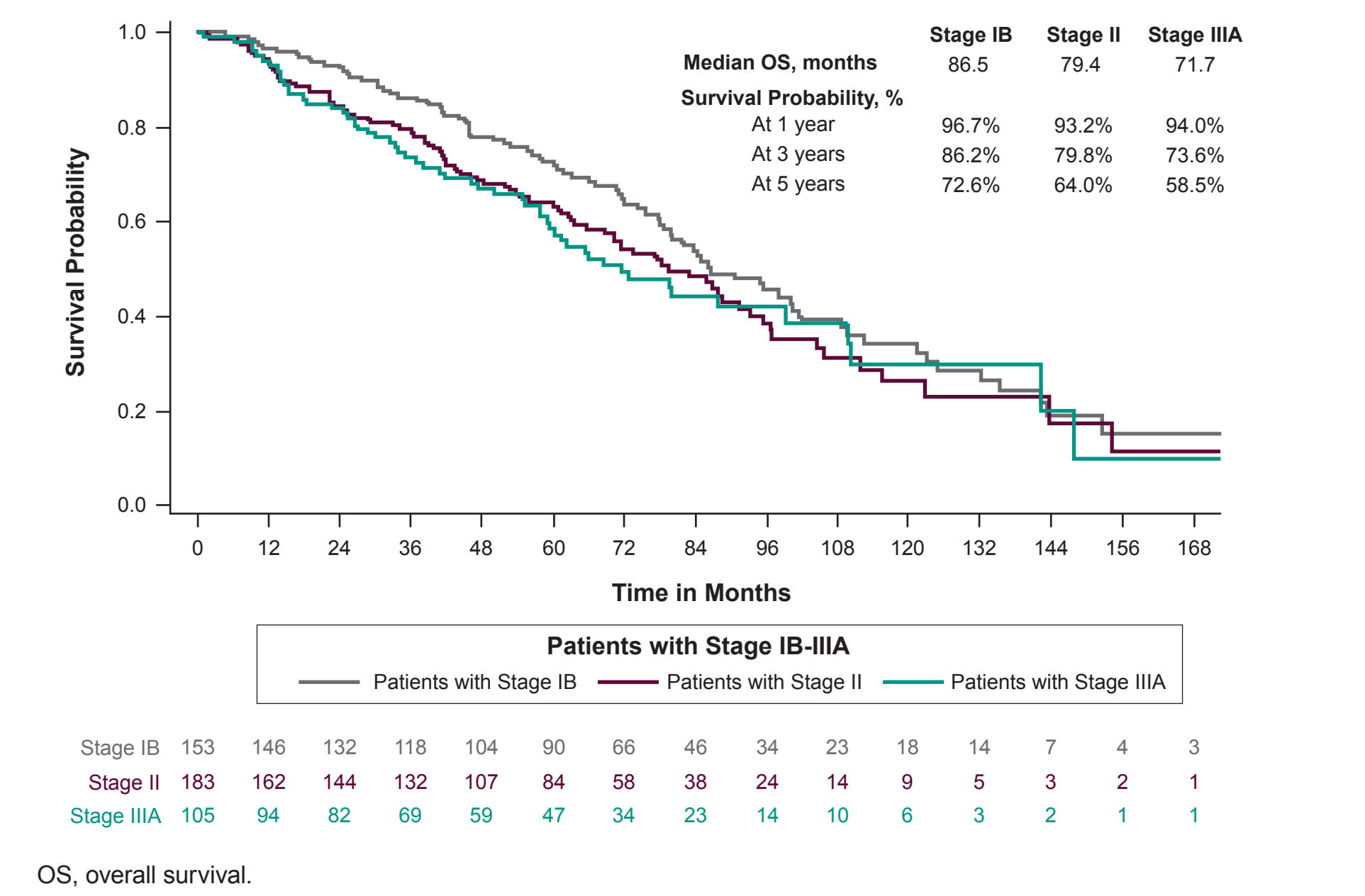


Figure 4. Kaplan-Meier Analysis of Overall Survival from Complete Resection by Stage



OS, overall survival.

Limitations

- Findings from this study should be generalized only to the underlying population who satisfy the study eligibility criteria. Patients selected from the ConcertAI Patient360™ database may differ from the underlying NSCLC population.
- Patients in this study were mainly treated within community oncology practices in the USA. Treatment patterns in the adjuvant setting may vary in academic centers or in practices outside of the USA.
- With the advance of therapies in early-stage NSCLC, this study may not be reflective of future NSCLC treatment patterns in the adjuvant setting.
- The results of the study should be interpreted in consideration of its retrospective design and the known limitations of chart review. The analyses were limited to the extent of data availability as recorded in the database.

Conclusions

- Although adjuvant chemotherapy is recommended by clinical guidelines, the rate of adjuvant chemotherapy delivery was low in this patient sample with early-stage NSCLC following complete resection in USA oncology practices.
- Worse outcomes were observed in patients with higher disease stage at diagnosis, including both rwDFS and OS.
- Overall survival rates at 5 years were higher for completely resected patients with stage II (64%) and IIIA (58.5%) NSCLC than historical benchmarks (45% for stage II and 30% for stage III among completely resected NSCLC patients²; 49%-57% for stage II and 36% for stage IIIA among overall NSCLC patients⁶).

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Disclosures

H West reports financial relationships with Amgen, AstraZeneca, Eli Lilly, Genentech/Roche, Merck, Mirati, Pfizer, and Regeneron.

X Hu, T Burke, and A Samkari are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA and own stocks of Merck & Co., Inc., Kenilworth, NJ, USA.

M Walker and Y Wang are employees of ConcertAI, Memphis, TN, USA.

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Contact Information

Contact Dr. Hu at xiaohan.hu@merck.com for questions or comments.

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