Review Article

Changes in store for early-stage non-small cell lung cancer

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Contributions: (I) Conception and design: All authors; (II) Administrative support: All authors; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Abstract: The management of advanced non-small cell lung cancer (NSCLC) has been revolutionized in recent years with the introduction of biomarker-targeted molecular therapies and immune checkpoint inhibitors. In contrast, since adjuvant chemotherapy was first established twenty years ago as the standard of care, little has changed for resected early-stage (IB-IIIA) patients for whom the potential for cure is greatest. In this manuscript we will review recently presented data as well as ongoing/planned studies in this arena. So far, investigative efforts have yielded mixed results regarding the use of tyrosine kinase inhibitors (TKIs) in early-stage NSCLC, though a series of now better planned, biomarker-driven ongoing phase III trials may be more informative. Several innovative immunotherapy studies have already shown promising results principally in the neoadjuvant setting with a large number of pivotal neo-adjuvant and adjuvant trials now in progress. Given the more robust design and biomarker-focused approach of the new generation of studies, significant advances in the optimal curative treatment of early stage NSCLC are anticipated.

Keywords: Lung cancer; neoadjuvant therapy; adjuvant therapy; immunotherapy

Submitted Feb 26, 2019. Accepted for publication May 07, 2019.
doi: 10.21037/jtd.2019.05.34
View this article at: http://dx.doi.org/10.21037/jtd.2019.05.34

Introduction

There has been dramatic progress with the introduction of targeted therapies and immune checkpoint inhibitors in the management of advanced non-small cell lung cancer (NSCLC). Biomarker-driven targeted therapy has revolutionized the management of oncogene-driven lung adenocarcinomas. Multiple generations of agents are now available for the treatment of epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), and ROS-aberrant lung adenocarcinomas. Furthermore, effective agents are either available or rapidly-emerging for BRAF/RET/MET/NTRK/ErbB2-positive subsets. In addition, immune biomarkers such as programmed death-ligand 1 (PD-L1) inform clinicians as to proper choices of immunotherapies, alone or in combination with chemotherapy, as treatment for the large majority of patients without actionable alterations. In fact, by now there is very little justification for the use of conventional chemotherapy alone as first-line therapy. We have similarly witnessed a major sea-change in the management of locally-advanced disease. The PACIFIC study has established a new standard with adjuvant durvalumab (Imfinzi) following concurrent chemoradiation leading to major survival benefits (1).

In this context, it is extremely disappointing that for the early-stage patients for whom cure is the most reachable, and for whom the impact of new systemic therapies could be the most substantial, little—if anything—has changed since the acceptance of adjuvant chemotherapy for resected NSCLC about two decades ago. While there have been advances in the treatment of early stage lung cancer through the use of stereotactic radiotherapy (2), robotic surgical techniques (3), and other interventions to avoid post-resection pulmonary complications (4), there have been few novel systemic therapies to offer. Instead, we have

witnessed failed attempts at improving on the status quo, with negative results as to postoperative radiation (PORT meta-analysis) (5), anti-angiogenic (ECOG 1505) (6), and vaccine therapies (MAGRIT) (7). Furthermore, outside of nodal involvement and tumor size, no validated biomarkers exist in this setting to guide patient management. Adjuvant chemotherapy remains the standard of care for patients with resected NSCLC. The landmark International Adjuvant Lung Cancer Trial (IALT) showed that cisplatin-based postoperative chemotherapy improved survival, marking a new era in NSCLC management (8). The Lung Adjuvant Cisplatin Evaluation (LACE) meta-analysis of the key five trials of this era echoed these results, showing an overall survival benefit of 5.4% at five years (though adjuvant chemotherapy was found to be harmful in stage IA NSCLC) (9). Nonetheless, outcomes remain poor; the modest benefit offered by adjuvant chemotherapy indeed seems to lessen over time due to significant toxicities and other long-term complications of treatment. These complications are of particular concern in the elderly population of NSCLC patients, for whom the limited data suggest a survival benefit with chemotherapy, but at the expense of greater toxicity relative to their younger counterparts (10). The time is thus ripe to re-energize research with a focus on improving our curative strategies in this setting.

Mixed results from tyrosine kinase inhibitors (TKIs)

The introduction of targeted therapies in the adjuvant setting highlights this general disappointment. Over the past 15 years, EGFR TKI therapies have been tested in several adjuvant studies, yielding mixed results—partly due to misguided patient selection and partly due to poor trial design (*Table 1*). The non-molecularly selected NCIC CTG BR19 trial found no improvement in survival for patients receiving gefitinib compared to placebo in stage IB-IIIA surgically-resected patients, even in a subset analysis based on EGFR mutation status—although this subset was very small, leading to underpowered analyses (11). The RADIANT study randomized resected stage IB-IIIA IHC/FISH EGFR-positive patients to receive erlotinib or placebo following receipt of optional adjuvant chemotherapy, and similarly did not find any difference in disease-free or overall survival—not surprisingly, in retrospect, given incorrect biomarker choice (12). While a subset of patients with deletion 19 or L858R EGFR mutations in fact showed a disease-free survival advantage, the results were not significant owing to the hierarchical study design, and overall survival appeared identical. The subsequent multicenter phase II SELECT study of erlotinib for two years following resection of stage IB-IIIA EGFR-mutated NSCLC used more scientifically-valid biomarker selection and included only patients with EGFR mutations (13). The study certainly demonstrated excellent overall results and reached its endpoint of improved disease-free survival (DFS) as compared to historical controls, but the results are difficult to interpret in the absence of a true control group. Furthermore, a significant relapse rate soon after stopping adjuvant therapy is worrisome. This highlights the specific concern that adjuvant targeted therapy might lack actual curative effect, possibly leading only to delays in recurrence. The results, therefore, are not viewed as practice-changing. Yet another recent study, the phase II EVAN trial, showed improved disease-free survival (2 years) in stage IIIA patients receiving adjuvant erlotinib alone versus chemotherapy (14). The latest major trial to conclude, ADJUVANT, a randomized phase 3 Chinese study comparing adjuvant chemotherapy with gefitinib, did reach its primary endpoint of significant DFS improvement (median DFS of 28.7 *vs.* 18 months) (15). However, available overall survival (OS) data argue against a substantial true benefit, and the study is criticized for not offering standard of care chemotherapy in the gefitinib arm. Based on these studies, adjuvant EGFR TKIs may be beneficial to delaying recurrence, but clear benefits as to overall survival—the key endpoint in such studies—remain elusive.

Erlotinib has also been studied in the neoadjuvant setting. The phase II study (CSLC 0702) by Zhong *et al.* demonstrated the feasibility of administering neoadjuvant erlotinib, stratified by EGFR mutation status, and showed a higher response rate in the EGFR+ erlotinib arm (16). Xiong *et al.* (ML25444) examined erlotinib's role in achieving operability and demonstrated a radical resection rate of 68.4% in their sample (17). Most importantly, the multicenter phase II EMERGING study demonstrated a significant increase in progression-free survival (PFS) in the erlotinib arm (median PFS 21.5 *vs.* 11.9 months), although it did not reach statistical significance in its primary endpoint of objective response rate (18) Although OS data are immature and will warrant review to ascertain whether the survival benefit is durable, this study supports continued investigation of erlotinib and other TKIs in the neoadjuvant setting for early-stage EGFR+ NSCLC.

Table 1 Key completed studies of TKIs in early stage NSCLC

Reference (trial)	Phase	Stage	A/NA	Other key selection criteria*	Agent	No. of participants	Primary endpoint	Key results
Goss 2013 (NCIC CTG BR19)	III	IB–IIIA	A		Gefitinib *vs.* placebo	503	OS; DFS	Median DFS 4.2 years (*vs.* not reached with placebo, P=0.15); OS 5.1 years, versus not reached, HR, 1.22, P=0.14)
Kelly 2015 (RADIANT)	III	IB–IIIA	A	IHC/FISH EGFR +	Erlotinib *vs.* placebo	973	DFS	Median, 50.5 months (*vs.* placebo 48.2 months, HR, 0.9, P=0.324)
Zhong 2018 (ADJUVANT)	III	II–IIIA	A	No prior chemotherapy, EGFR mutation +	Gefitinib *vs.* VC	222	DFS	Median, 28.7 months (*vs.* chemo 18.0 months, HR, 0.6, P=0.0054)
Yue 2018 (EVAN)	II	IIIA	A	No prior chemotherapy, EGFR mutation +	Erlotinib *vs.* VC	102	2-year DFS	81.4% (*vs.* 44.6% with chemo, RR, 1.823, P=0.0054)
Pennell 2019 (SELECT)**	II	IA–IIIA	A	EGFR mutation +	Erlotinib	100	2-year DFS	90% (compared to historical control of 76%)
Zhong 2015 (CSLC 0702)	II	IIIA (N2)	NA	EGFR mutation + assigned to erlotinib (*vs.* GC for wild-type)	Erlotinib *vs.* GC	24	Response rate	58.3% (*vs.* 25% for wild-type GC arm, P=0.18)
Xiong 2018 (ML25444)**	II	IIIA (N2)	NA	EGFR mutation +	Erlotinib	19	Radical resection rate	68.40%
Zhong 2018 (CTONG 1103/EMERGING)	II	IIIA (N2)	NA	EGFR mutation +	Erlotinib *vs.* GC	72	Objective response rate	54.1% (*vs.* GC 34.3%, OR 2.26, P=0.092)

*, for the adjuvant studies when not specifically indicated, routine adjuvant chemotherapy permitted prior to study entry; **, indicates single-arm study. TKI, tyrosine kinase inhibitor; NSCLC, non-small cell lung cancer; A, adjuvant; NA, neoadjuvant; EGFR, epidermal growth factor receptor; VC, vinorelbine/cisplatin; GC, gemcitabine/cisplatin; SOC, standard of care; OS, overall survival; DFS, disease-free survival; PFS, progression-free survival; HR, hazard ratio; RR, relative risk; OR, odds ratio; ALK, anaplastic lymphoma kinase.

There is a continued effort to demonstrate the value of TKIs for early-stage NSCLC (*Table 2*), in the United States principally through the ALCHEMIST randomized controlled trials originally designed to test adjuvant targeted therapies (erlotinib for EGFR mutation, crizotinib for ALK rearrangement) versus placebo in resected stage IB-IIIA patients following receipt of adjuvant chemotherapy (19). Despite high hopes for ALCHEMIST, accrual has been slow, leading to concerns as to whether it can be successfully completed and—of more concern—whether it is becoming obsolete as more effective EGFR- and ALK-targeted agents have by now shown great success in the advanced setting. The potential of another first-generation TKI, icotinib, as adjuvant therapy for stage II-IIIA NSCLC is currently being investigated in a number of phase III studies in China, including ICWIP (NCT02125240), EVIDENCE (NCT02448797), and ICTAN (NCT01996098).

The important ADAURA study (NCT02511106) being conducted in a similar setting utilizes adjuvant osimertinib, a third-generation EGFR TKI with greater CNS penetrance that targets the T790M resistance mutation. Osimertinib has become the standard of care frontline option in advanced disease, thereby making ADAURA the most relevant of ongoing targeted adjuvant trials. In general, the lack of investment in adjuvant studies clearly has led to a series of missed opportunities over the last

Table 2 Key ongoing studies of TKIs in early stage NSCLC

Trial (NCT identifier)	Phase	Stage	A/NA	Other key selection criteria	Agent	Estimated enrollment	Primary endpoint
ALCHEMIST (NCT02201992; NCT02193282)	III	IB–IIIA	A	EGFR-mutation + or ALK-translocation +	EGFR+: Erlotinib *vs.* observation; ALK+: crizotinib *vs.* observation	828	OS
ICWIP (NCT02125240)	III	II–IIIA	A	EGFR mutation +	Icotinib *vs.* placebo	124	DFS
EVIDENCE (NCT02448797)	III	II–IIIA	A	EGFR mutation +	Icotinib *vs.* placebo	320	DFS
ICTAN (NCT01996098)	III	IIA–IIIA	A	EGFR mutation +	Icotinib *vs.* placebo	318	DFS
ADAURA (NCT02511106)	III	IB–IIIA	A	EGFR mutation +	Osimertinib *vs.* placebo	700	DFS

TKI, tyrosine kinase inhibitor; NSCLC, non-small cell lung cancer; A, adjuvant; NA, neoadjuvant; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase; OS, overall survival; DFS, disease-free survival.

Table 3 Key completed studies of immunotherapy in early stage NSCLC

Reference (trial)	Phase	Stage	A/NA	Other key selection criteria	Agent	No. of participants	Primary endpoint	Key results
Yi 2017 (TOP1201)**	II	IB–IIIA	NA	–	Ipilimumab ×2 cycles, with platinum doublet chemotherapy ×3 cycles	24	% of subjects with detectable circulating T cells after treatment	Increased activation of CD4/CD8 T cells with ipilimumab, though primary endpoint not met
Yang 2018 (TOP1201)**	II	II–IIA	NA	–	Ipilimumab ×2 cycles, with platinum doublet chemotherapy ×3 cycles	13	Surgical outcomes	90-day mortality (1% and 0%) in preoperative chemotherapy alone versus ipilimumab groups, respectively. No increase in adverse surgical outcomes (P values not reported)
Forde 2018 (NA_00092076)**	II	I–IIA	NA	–	Nivolumab ×2 cycles	21	Safety	Few side effects, no treatment-related delays in surgery, and major pathological response in 45% of resected tumors

**, indicates single-arm study. NSCLC, non-small cell lung cancer.

decade and a half, hopefully informing us now with regard to the next wave of studies ahead.

Immunotherapy in early stage NSCLC

Immunotherapy represents the next frontier of oncology, with checkpoint inhibitors already approved for a growing variety of cancer types by the United States Food and Drug Administration, including two anti-PD-1 and two anti-PD-L1 agents for the management of advanced and locally-advanced NSCLC (20). While checkpoint inhibitors are currently in widespread use for stage III/IV NSCLC, they remain investigational for early stages when their efficacy would likely be the most robust, and when their impact could be the most significant. Clearly, great efforts urgently need to be expanded to assess these agents. To this end, a variety of studies are ongoing in both the adjuvant and neoadjuvant settings (*Tables 3*,*4*).

Table 4 Key ongoing studies of immunotherapy in early stage NSCLC

Trial (NCT identifier)	Phase	Stage	A/NA	Other key selection criteria*	Agent	Estimated enrollment	Primary endpoint
ANVIL (ALCHEMIST trial) (NCT02595944)	III	IB–IIIA	A	EGFR-, ALK-; PD-L1 tested	Nivolumab *vs.* observation	714	OS, DFS
PEARLS/ KEYNOTE-091 (NCT02504372)	III	IB–IIIA	A	PD-L1 tested	Pembrolizumab *vs.* placebo	1,080	DFS
NCT02273375	III	IB–IIIA	A	–	Durvalumab *vs.* placebo	1,360	DFS
IMpower010 (NCT02486718)	III	IB–IIIA	A	–	Atezolizumab *vs.* best supportive care	1,127	DFS
NCT03447769	III	II–IIIA, resected IIIB	A	–	Canakinumab *vs.* placebo	1,500	DFS
NCT03148327	I	I	A	Medically-inoperable (or surgery refused)	Phase 1: Durvalumab + SBRT; Phase 2: SBRT alone *vs.* durvalumab + SBRT	105	PFS
CheckMate 816 (NCT02998528)	III	IB–IIIA	NA	–	3 arms: (I) Nivolumab + ipilimumab; (II) Nivolumab + platinum doublet chemotherapy; (III) Platinum doublet chemotherapy alone	642	Event-free survival; pathological complete response
IMpower030 (NCT03456063)	III	II–IIIA, select IIIB	NA	–	Neoadjuvant atezolizumab (or placebo) + platinum-based chemotherapy ×4 cycles, then adjuvant atezolizumab (or placebo) ×16 cycles	302	Major pathologic response (% with ≤10% residual viable tumor at time of resection)
KEYNOTE-671 (NCT03425643)	III	IIB–IIIA	NA	–	Platinum doublet chemotherapy + pembrolizumab/placebo (×4 cycles neoadjuvant + 13 cycles adjuvant)	786	Event-free survival
TOP1501** (NCT02259621)	II	IB–IIA	NA	–	Pembrolizumab then surgery followed by adjuvant chemotherapy + pembrolizumab	32	Surgical feasibility rate
NEOSTAR (NCT03158129)	II	I–IIIA	NA	–	3 arms: (I) nivolumab; (II) nivolumab + ipilimumab; (III) nivolumab + platinum doublet chemotherapy	66	Major pathologic response (% w ≤10% residual viable tumor at time of resection)
NCT03081689**	II	IIIA	NA	–	Nivolumab + platinum doublet chemotherapy	46	Progression free survival
IONESCO** (NCT03030131)	II	IB–II	NA	No prior neoadjuvant chemotherapy or radiotherapy	Durvalumab ×3 cycles	81	Percentage of surgical resection R0
LCMC3** (NCT02927301)	II	IB–IIA, selected IIB resectable	NA	–	Atezolizumab ×2 cycles then adjuvant atezolizumab for 12 months	180	Major pathologic response

Table 4 *(continued)*

Table 4 *(continued)*

Trial (NCT identifier)	Phase	Stage	A/NA	Other key selection criteria	Agent	Estimated enrollment	Primary endpoint
PRINCEPS (NCT02994576)	II	IB–IIIA	NA	–	Atezolizumab ×1	60	Rate of patients without major toxicities or morbidities from treatment to 1 month after surgery
NCT02716038**	II	IB–IIIA	NA	–	Atezolizumab + platinum doublet chemotherapy	60	DFS
NCT02904954	II	I–IIIA	NA	–	Arm 1: Durvalumab ×2 cycles; Arm 2: Durvalumab ×2 cycles + SBRT	–	–
NCT02572843**	II	IIIA	NA	–	Durvalumab ×3 cycles following cisplatin/docetaxel ×2 cycles, then adjuvant durvalumab ×1 yr (following radiotherapy in subset with incomplete resection)		Event-free survival at 12 months

*, for the adjuvant studies when not specifically indicated, routine adjuvant chemotherapy permitted prior to study entry; **, indicates single-arm study. NSCLC, non-small cell lung cancer; DFS, disease-free survival; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase; PD-L1, programmed death-ligand 1; OS, overall survival; PFS, progression-free survival; SBRT, stereotactic body radiation therapy.

The administration of immunotherapy prior to surgical resection might be particularly advantageous, as larger tumors are thought to generate greater immune activity than micro-metastatic disease. Furthermore, the pathologic specimen allows for an early and robust readout of therapeutic activity, which might be particularly helpful in the selection of combination regimens for further studies. Completed efforts investigating this theory include TOP1201 and the pilot study by Forde and colleagues. The phase II TOP1201 study by Yi *et al.* [2017] demonstrated significant activation of CD4/CD8 lymphocytes after chemotherapy and ipilimumab in stage II-IIIA NSCLC, though it did not meet the primary endpoint of detecting a significant increase in circulating T cells with specificities against tumor-associated antigens (21). Yang *et al.* [2018] subsequently demonstrated the safety and feasibility of surgical resection in this study population (22). Forde and colleagues treated a cohort of 22 patients with resectable stage I-IIA NSCLC with 2 cycles of nivolumab prior to surgical resection (23). Neoadjuvant nivolumab was not only safe and feasible but was also associated with a 45% pathologic response rate in 9 of 20 patients who underwent resection, and a complete response in 3 patients. In addition, biomarker analysis of this cohort yielded remarkable data as to neoantigen discovery and identification of activated T cell clones, providing an excellent platform for future studies.

Trials in the neoadjuvant setting

The single arm nature of the above pilot studies nonetheless limits further interpretation of the data. While there are many phase II studies actively investigating neoadjuvant immunotherapy, the most notable include a series of now pivotal and potentially practice-changing phase III trials. IMpower030 (NCT03456063) is studying the role of neoadjuvant atezolizumab in resectable II, IIIA, or select IIIB NSCLC. KEYNOTE-671 (PEARLS, NCT03425643) is investigating the combination of neoadjuvant doublet chemotherapy with neoadjuvant/adjuvant administration of pembrolizumab versus placebo in patients with resectable stage IIB or IIIA NSCLC. Finally, CheckMate 816 (NCT02998528) is studying whether either combined nivolumab and ipilimumab, or nivolumab plus platinum doublet chemotherapy, is superior to doublet chemotherapy alone in the neoadjuvant treatment of stage IB–IIIA NSCLC.

Another immune checkpoint inhibitor, durvalumab, was recently approved for treatment of unresectable

stage III NSCLC following the findings of the PACIFIC trial. This agent is now being investigated in a number of phase II neoadjuvant studies, including IONESCO (NCT03030131), NCT02572843, and NCT02904954. In addition to studying durvalumab therapy, NCT02904954 also examines whether there is an added benefit from the administration of stereotactic body radiation therapy (SBRT) prior to, or concurrently with, durvalumab therapy. Another ongoing trial, NCT03148327, examines this combination as adjuvant therapy in patients who are medically inoperable or who decline surgery. The investigation of SBRT in conjunction with durvalumab could further expand treatment options for early-stage patients who are undergoing immunotherapy thanks to the phenomenon known as the abscopal effect, through which local irradiation of the primary tumor is followed by regression of disease at non-irradiated metastatic sites—a phenomenon hypothesized to occur due to generation of a systemic immune response following the release of neoantigens from the irradiated tumor (24). Within the past decade, as the use of immunotherapy has been on the rise, there has been a growing consensus that a combination of radiotherapy and immunotherapy is superior to either modality alone, which certainly warrants further investigation in earlier-stage NSCLC. With the expanding use of curative radiation-based strategies in lung cancer management, these studies will provide key data for large groups of patients.

Trials in the Adjuvant Setting Studies are also ongoing into the use of immunotherapy in the adjuvant setting. The pivotal ANVIL trial (NCT02595944) is a component of the phase III ALCHEMIST trial studying the effects of adjuvant nivolumab versus observation for EGFR/ALK-negative patients, while the KEYNOTE-091 trial (NCT02504372) is investigating the adjuvant use of pembrolizumab versus placebo, with or without standard adjuvant chemotherapy, in resected NSCLC. Additional key adjuvant studies currently recruiting participants with stage IB-IIIA NSCLC are NCT02273375, investigating durvalumab versus placebo, and IMpower010 (NCT02486718), comparing adjuvant atezolizumab to best supportive care following 4 cycles of doublet chemotherapy. Another study currently in the recruitment phase, NCT03447769, aims to study the role of canakinumab as adjuvant therapy in patients with stage II-IIIA and completely-resected stage IIIB NSCLC. Canakinumab, a monoclonal antibody against the pro-inflammatory cytokine IL-1β, was originally approved for treatment of a spectrum of autoinflammatory conditions. Analysis of the results of the 2017 CANTOS cardiovascular study incidentally revealed a highly-significant reduction in lung cancer incidence and mortality in the canakinumab group relative to placebo, prompting further interest in its potential as a lung cancer therapy and opening novel avenues into the exploration of the role of the myeloid cell compartment in the tumor microenvironment (25).

Looking for better biomarkers

As the role of targeted therapies and immunotherapy in early-stage lung cancer continues to be explored, it is crucial that further investments be made in the development of better biomarkers to facilitate patient selection and risk stratification. Research continues into additional biomarkers beyond EGFR and ALK that either represent actionable therapeutic targets, or that are associated with risk of progression of early-stage NSCLC. For instance, the myPlan Lung Cancer proprietary prognostic test developed by Myriad Genetics, Inc. measures cell cycle progression genes; it has been validated in a cohort of 650 stage I-II NSCLC patients and found to be a more significant indicator of mortality than pathologic cancer stage (26). Another important biomarker being explored is tumor mutational burden (TMB), a measure of the number of mutations in a given tumor, and a surrogate marker for a tumor's potential to generate an immune response to specific neoantigens. Initial studies in NSCLC have demonstrated an association between higher TMB and better response to immunotherapy; it appears that TMB might serve as a complimentary biomarker to PD-L1 IHC in patient selection (27). Further studies will be necessary in the setting of early-stage NSCLC as this biomarker is further elucidated and refined. Finally, plasma-derived circulating tumor DNA (ctDNA) holds the potential to further expand the role of personalized therapy—making it available to those patients not amenable to tissue biopsy and enabling non-invasive repeat sampling so that therapy can be modified as needed over the course of treatment, as the molecular profile of an individual's cancer changes (28). Its most promising role in the definitive setting might be as a biomarker of residual microscopic disease, allowing patient enrichment in adjuvant studies following delivery of definitive surgery or radiation-based therapy. Indeed, the recently published study by Chaudhuri *et al.* highlights the potential tremendous utility of ctDNA testing for risk stratification in this context (29). Among the outcome measures of the ALCHEMIST Screening Trial

(NCT02194738) are the identification of new mutations at time of cancer recurrence, and the correlation of ctDNA level with survival measures in these patients. Another study that has recently started recruitment (NCT03465241) is investigating the role of ctDNA dynamic monitoring of stage II-IIIA NSCLC to verify its prognostic/predictive effect.

Better data are emerging

In summary, following two decades of significant lull in this critical area of research, we are now seeing much better-designed neoadjuvant and adjuvant studies based on proper biomarker selection, and optimized treatment choices founded upon recent advances in the metastatic setting. As a result, there is real hope that in the coming years we will indeed see tremendous changes in the management of early-stage lung cancer. The only way this can be achieved is through support by all relevant thoracic disciplines to allow timely completion of important studies whose results could hold the key to improving cure rates for the large number of patients diagnosed with early-stage lung cancer worldwide.

Acknowledgments

None.

Footnote

Conflicts of Interest: Dr. B Halmos is receiving clinical research support from Merck, BMS, AbbVie, Novartis, GSK, Mirati, Boehringer-Ingelheim, Pfizer, Astra-Zeneca, Takeda and Guardant Health and has received consulting fees from Astra-Zeneca, Pfizer, Novartis, Guardant Health, Foundation Medicine, Merck, BMS, Genentech, Spectrum, Ignyta, Takeda and Boehringer-Ingelheim. The other authors have no conflicts of interest to declare.

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Cite this article as: Sandler JE, D'Aiello A, Halmos B. Changes in store for early-stage non-small cell lung cancer. J Thorac Dis 2019;11(5):2117-2125. doi: 10.21037/jtd.2019.05.34

