



original contributions

# Novel Program Offering Remote, Asynchronous Subspecialist Input in Thoracic Oncology: Early Experience and Insights Gained During the COVID-19 Pandemic

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**QUESTION ASKED:** What are the leading lessons learned from a remote asynchronous consultation providing subspecialist input for cancer management function during its early development, coinciding with the COVID-19 pandemic?

**SUMMARY ANSWER:** AccessHope received and completed 110 thoracic oncology cases from April 2019 through November 2020, demonstrating increasing program volume over time despite the practical challenges of the pandemic, with a median report turnaround time of 5 days after requested records had been received. Expert recommendations disagreed with local management in 28% of cases and suggested refinements to improve clinical outcomes in 92% of cases, with recommendations to reduce low-value care associated with cost savings averaging \$19,062 in US dollars (USD) per patient.

**WHAT WE DID:** AccessHope, a remote consult and educational support service developed as a subsidiary of City of Hope Comprehensive Cancer Center working with client companies and selected medical insurers, retrospectively analyzed submissions over an interval of just over 1.5 years for the program. This effort focused on case volumes and key findings within thoracic oncology for potential candidates throughout the United States. Specifically, the focus of this review was on patient characteristics, the degree of concordance between subspecialist recommendations from the reviewer with management plans by the local oncology team, the anticipated clinical benefit and cost savings of new recommendations, and the patterns of molecular marker testing, routine positron emission tomography-computed tomography surveillance, and reported patient frailty or poor performance status limiting the ability of patients to pursue treatment approaches otherwise considered as standard of care.

**WHAT WE FOUND:** Cases represented a broad range of thoracic oncology, comprising the spectrum of clinical stages of small-cell lung cancer and non-small-cell lung cancer, including a range of histologic subtypes. Molecular marker testing was rare in small-cell lung cancer and far more common for nonsquamous than squamous non-small-cell

lung cancer, more commonly pursued with increasing stage; routine use of positron emission tomography-computed tomography surveillance was pursued in 11% of cases; 19% of the patient cohort was identified by their care team as having a performance status that precluded treatment that would have otherwise been standard of care.

**BIAS, CONFOUNDING FACTORS, DRAWBACKS:** These findings represented a limited cohort of patients who are both insured and provided supplemental case review services through their employer or medical insurer, limiting the generalizability of these findings to a patient population with less support and fewer resources. In addition, we do not have data to speak to the level of satisfaction with the program among patients or physicians who received the reviews featuring recommendations, nor do we know the extent to which suggested changes in management were implemented in practice; however, AccessHope is developing processes to assess satisfaction among other stakeholders and clarify the degree to which recommendations are adopted.

**REAL-LIFE IMPLICATIONS:** The AccessHope model of faculty from an National Cancer Institute-designated cancer center in a specific cancer type reviewing medical records to provide recommendations to local oncologists throughout the United States offers the opportunity to integrate subspecialist insight and support for remote cases without requiring patient travel and with a focus on having most patients receive their care through their local cancer care team, close to home. This service was compatible with the travel restrictions introduced by the COVID-19 pandemic and grew despite the limitations imposed over the time interval. AccessHope is now transitioning to a network of several geographically distributed foundational partner institutions equipped to scale the increased case volume conferred by new client partners and insurers. This novel platform offers a strategy for effective educational support for patients and physicians across the United States to avail themselves of the latest rapidly evolving changes in cancer subtype-specific care without requiring patients to travel or receive most care away from their local environment and support system.

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## ASSOCIATED CONTENT

### Appendix

Author affiliations and disclosures are available with the complete article at [ascopubs.org/journal/op](https://ascopubs.org/journal/op).

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# Novel Program Offering Remote, Asynchronous Subspecialist Input in Thoracic Oncology: Early Experience and Insights Gained During the COVID-19 Pandemic

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## abstract

**PURPOSE** AccessHope is a program developed initially by City of Hope to provide remote subspecialist input on cancer care for patients as a supplemental benefit for specific payers or employers. The leading platform for this work has been an asynchronous model of review of medical records followed by a detailed assessment of past and current management along with discussion of potential future options in a report sent to the local oncologist. This summary describes an early period of development and growth of this service, focusing on cases of lung cancer, particularly during the COVID-19 pandemic.

**METHODS** Cases were primarily identified by a trigger list of cancer diagnoses that included non–small-cell lung cancer and small-cell lung cancer. After medical records were obtained, a summary narrative was provided to a thoracic oncology specialist who wrote a case review sent to the local physician, followed by a direct discussion with the recipient. We focused on feasibility as measured by case volumes, the rates of concordance between the subspecialist reviewer with the local team, and cost savings from recommended changes, using descriptive statistics.

**RESULTS** From April 2019 to November 2020, 110 cases were reviewed: 55% male, median age 62.5 years (range, 33–92 years); 82% non–small-cell lung cancer (12% stage I or II, 16% stage III, and 57% stage IV), and 17% small-cell lung cancer (4% limited and 14% extensive). Median turnaround time for report send-out was 5.0 days. The review agreed with local management in 79 (72%) cases and disagreed in 31 (28%) cases; notably, specific additional recommendations were associated with evidence-based anticipated improvements in efficacy in 76 cases (69%) and improvement in potential for cure in 14 cases (13%). Recommendations leading to cost savings were identified in 14 cases (13%), translating to a projected cost savings of \$19,062 (USD) per patient for the entire cohort of patient cases reviewed.

**CONCLUSION** We demonstrate the feasibility of completing a rapid turnaround of cases of lung cancer either patient-initiated for review or prospectively triggered by diagnosis and stage. This program of asynchronous second opinions identified evidence-based management changes affecting current treatment in 28% and potential improvements to improve care in 92% of patients, along with cost savings realized by eliminating low-value interventions.

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## INTRODUCTION

With advances in cancer care arriving at an escalating pace, additional input from second opinions may provide invaluable insight, particularly if conferred by a subspecialist in a limited area of oncology. Reviews of second opinions in general,<sup>1,2</sup> as well as telemedicine-based second opinions in particular,<sup>3</sup> reveal that they are sought to provide additional certainty, supplemental communication, more personalized

attention, and potential identification of novel management options; diagnostic or therapeutic discrepancies are identified in a significant fraction (2%–69%) of cases.<sup>1–3</sup>

AccessHope is a subsidiary of City of Hope Comprehensive Cancer Center that provides remote subspecialist input on wide range of different cancer subtypes, most commonly offered as a supplemental employee benefit for specific companies or health care

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payers. Evaluations are commonly conducted as an asynchronous review of medical records, without patient travel required, followed by a detailed assessment of prior and current management along with recommendations for subsequent testing and treatment options. Importantly, patients may seek a remote opinion, but most cases are proactively identified on the basis of the anticipated impact of potential management changes on the basis of the diagnosis and stage of a cancer for which the prognosis is often unfavorable and practice patterns are dynamic. The reports are provided directly to the primary medical team, a strategy providing subspecialist guidance that typically incorporates treatment plans amenable to ongoing management close to their home and support system.

The feasibility of such an approach has yet to be clarified, but restrictions on mobility and direct access as a consequence of the COVID-19 pandemic only made it more challenging for people to seek additional opinions in person, raising the appeal of a remote alternative that offers an individualized assessment for patients.

The purpose of this descriptive analysis is to retrospectively evaluate the cohort of patients with lung cancer whose cases were reviewed during the early period of this program, from April 2019 through November 2020. The focus of this work is on case volumes, rates of concordance versus alternative management recommendations compared with the plans from the local medical team, projected improvements in outcomes that may include cost savings, and observed clinical patterns that may be compared with published series from clinical trials. This work demonstrates the feasibility and growth of the program despite the practical challenges introduced by the COVID-19 pandemic and reveals opportunities for its ongoing evolution as AccessHope transitions into a network of geographically decentralized tertiary care institutions.

## METHODS

### Identification of Cases

Client companies or medical payers (see Appendix Fig A1, online only for distribution) retain AccessHope to offer expert reviews for their insured employees and dependents, in which AccessHope provides detailed reviews that may become eligible through either of two paths.

First, cases may be identified proactively through the *Accountfig Precision Oncology* (APO) program on the basis of prior authorizations and claims submissions identifying the top 20% of complex cancers, to address significant variability in treatment patterns and outcomes. This proactive process is designed to expedite identification of cases for which timely input is critical, including diagnosed lung cancer across many stages. Alternatively, a limited subset of client companies offers a program called *Expert Advisory Review*, a patient-initiated service in which

participants with any cancer diagnosis can request a review of their case materials and request answers to specific questions so that their reviewer can suggest management options to their treating physician.

This review includes cases of non-small-cell lung cancer (NSCLC), small-cell lung cancer (SCLC), or other chest malignancies that were conducted from April 2019 through November 2020.

### Case Review and Reporting Process

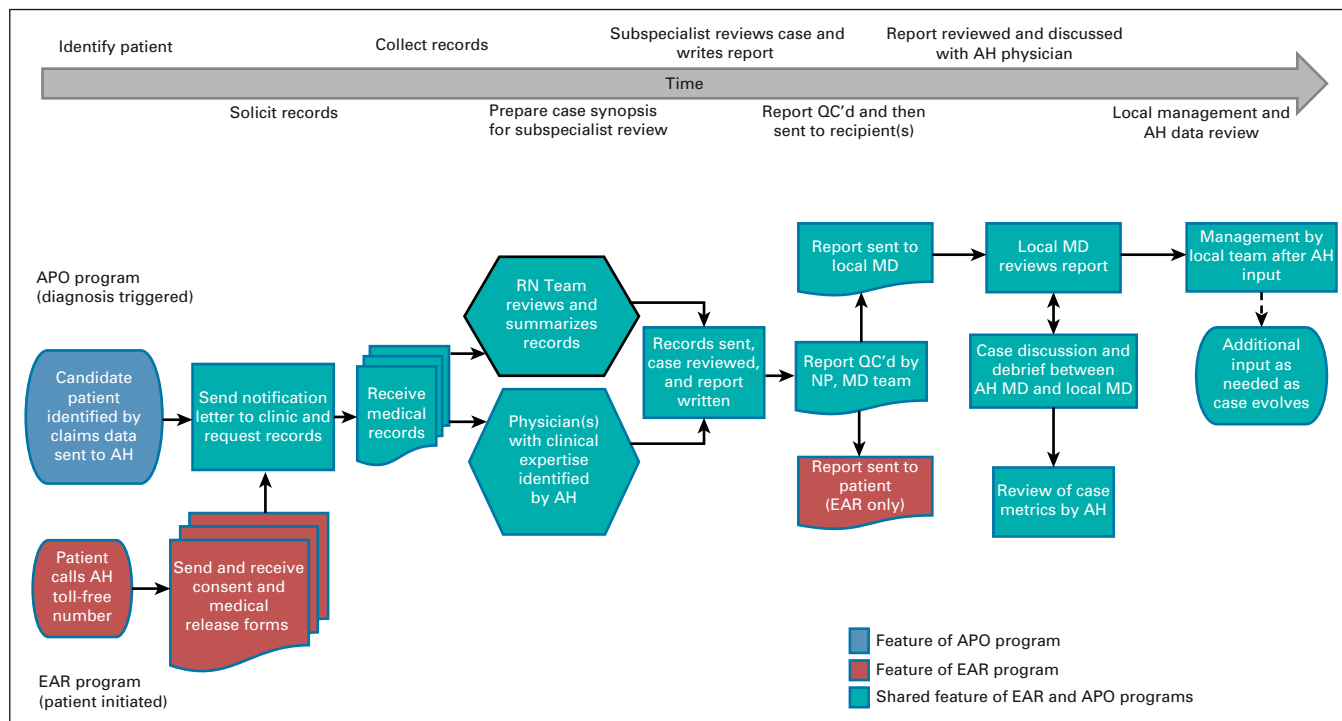
The process of collecting data, performing the case review, and sending completed reports is summarized in Figure 1. Once needed medical records were collected for each case, they were reviewed by an oncology specialist nurse who developed a synopsis of the chronology and key data; the Clinical Operations team then worked with an Access Hope oncologist as needed to identify the most relevant clinical expert(s) in hematology or oncology, radiation oncology, surgery, or potentially other experts who serve as active faculty at City of Hope to review the case. The narrative summary and original records are sent securely to the expert(s), who offer written commentary on the workup, prior therapy, current plans, and future management options for the patient.

Upon completion, reports undergo review and editing for quality control by a nurse practitioner followed by an additional hematology or oncology specialist on the AccessHope team before they are sent to the local physician in all cases, with a copy also sent to the requesting patient for Expert Advisory Review cases. The key components of a completed report are illustrated in Appendix Figure A2 (online only). For APO cases, the AccessHope team coordinates a call between an AccessHope physician and the oncologist or other leading member of the treatment team coordinating the patient's care. This is pursued to directly discuss the report and interval events in the patient's care, as well as to facilitate outreach back to AccessHope by the local physician in the future in the event that any further communication could be helpful.

### Assessing Metrics to Case Reviews

Metrics for each case were assessed in multiple dimensions, generally by a team of two or more physicians reviewing case reports and agreeing on an assignment of these metrics on the basis of defined criteria enumerated in the Appendix 1. The level of concordance of the expert reviewer with the planned management ranged from agreement (without additional recommendations) to disagreement, with significant recommendations. Notably, all categories other than agreement include additional recommendations anticipated to improve outcomes for the patient's care.

In addition, recommendations for a change in diagnosis or stage, treatment, additional testing or specifically precision medicine, a clinical trial, or other management recommendations such as bone-directed therapy were tabulated.



**FIG 1.** AccessHope work flow. Flowchart depicting the multistep process of case identification, intake of medical records, summary of a case narrative, distribution of the case to the subspecialist expert, editing of the report, delivery of the case to the recipient(s), subsequent case discussion with the local oncologist, and review of case metrics to assess the clinical and financial impact of each case. AH, AccessHope; APO, Accountig Precision Oncology; EAR, Expert Advisory Review; MD, physician; NP, AccessHope nurse; QC, quality control; RN, AccessHope registered nurse.

Humanistic outcomes such as an anticipated reduction in side effects or long-term complications, improvement in patient support or distress, and potential improvement in anticipated survival or cure rate on the basis of evidence-based recommendations were recorded. Finally, anticipated cost savings from overutilization or inappropriate utilization of services (such as imaging or treatment interventions) not supported as an appropriate standard of care was identified. Cost savings were valued (in US dollars) on the basis of differences in the cost of the plan by the treatment team compared with that proposed by Access Hope. In keeping with established practices,<sup>4</sup> we relied on the methodology for measuring return on investment for oncology pathways. Specifically, savings are based on a payer perspective and account for direct costs associated with treatments and procedures, whereas for chemotherapy or supportive care agents, savings are associated with the drug reimbursement. Costs are based on Medicare reimbursement fees and adjusted with a conversion factor for private carriers. Cost savings are only captured for future activities; assessments or treatments that were delivered and completed were not subject to savings.

### Project Scope and Statistics

This project was submitted to the institutional review board and determined to be exempt.

The aims of this analysis are as follows:

1. To assess the changes in case volumes and characterize the stage and histologic distribution of remote consultations for lung cancer over time during the interval noted above.
2. To evaluate the level of concordance of subspecialist expert recommendations in remote consults on cases compared with management pursued or proposed by the local medical team for the case.
3. To identify the proportion of patients with anticipated improvements in clinical outcomes.
4. To identify trends in patterns on the basis of aggregate review of cases, including molecular marker testing, surveillance with positron emission tomography-computed tomography (PET-CT), and marginal performance status limiting treatment options.

These variables were characterized using descriptive statistics.

## RESULTS

### Feasibility of Reviews and Case Volumes

A total of 110 cases with a diagnosis of NSCLC or SCLC were reviewed during the interval being evaluated, the majority (107 [97%]) coming through the APO program. As shown in Figure 2, case volume increased over time, despite the disruption of workflows and many health care processes and workups in the spring of 2020, albeit with marked

variation month to month because of variance in client company case input. The characteristics of patients for whom reviews were conducted are shown in [Table 1](#).

The median turnaround time from receipt of the case materials by the expert to the report being sent to the local oncologist or other intended recipient was 5.0 days. Multidisciplinary reviews were conducted for 3 of 110 cases (3%).

At the time of the case review, 14 (13%) patients had not initiated treatment for their current treatment stage and setting, 68 (62%) were receiving or had received their primary treatment without progression, and 28 (25%) had disease progression and were receiving or planned to receive second line or later treatment.

### Review Outcomes and Case Metrics

The distribution of concordance by the AccessHope expert with the recommendations from the local oncology team for the cohort of cases is illustrated in [Appendix Figure A3](#). The most common level of concordance was agreement, with minor recommendations in 71 cases (65%); followed by disagreement, with moderate recommendations in 25 cases (23%); agreement, with no recommendations in eight cases (7%); and disagreement, with significant recommendations in six cases (5%). The recommendations were associated with evidence-based anticipated improvements in efficacy in 76 cases (69%) and improvement in potential for cure in 14 cases (13%, only feasible in patients with curable disease). Examples of suggested changes for the 31 cases (28%) with disagreement are briefly summarized in [Appendix Table A1](#) (online only).

Recommendations accompanied by cost savings were identified in 14 cases (13%), with a total cost savings of

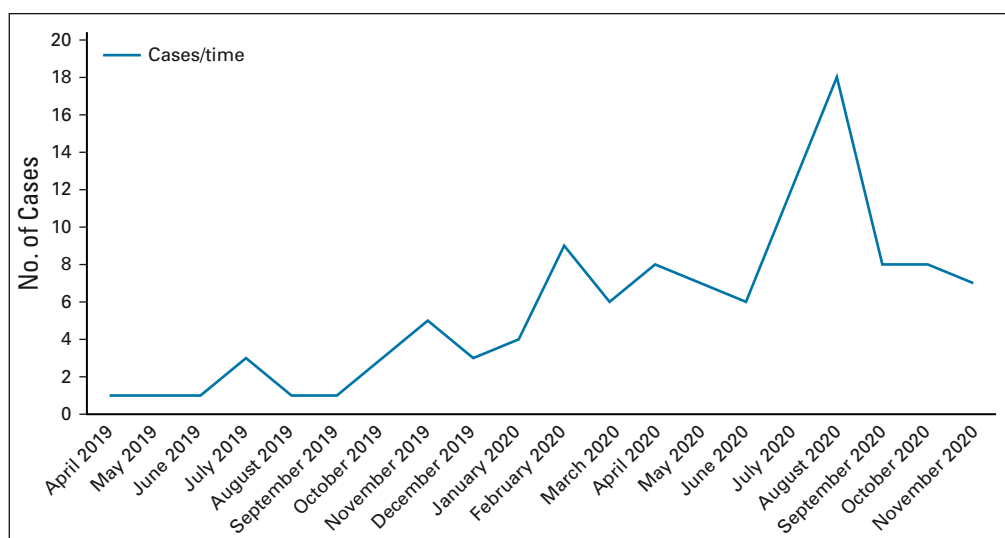
\$149,776 (USD) per patient within this subset, or \$19,062 (USD) per patient for the full cohort of cases reviewed.

### Specific Features of Reviews

**Molecular testing patterns.** As shown in [Figure 3](#), molecular marker testing was rare in SCLC, ordered for only one of 19 (5%) cases of SCLC, consistent with the lack of any clear role for it in this setting.<sup>5</sup> For patients with NSCLC, molecular marker testing was more commonly ordered for patients with nonsquamous compared with squamous NSCLC at all stages (66% and 0% for early-stage nonsquamous and squamous NSCLC, respectively; 57% v 25% for stage III nonsquamous and squamous NSCLC, respectively; 94% v 75% for stage IV nonsquamous NSCLC, respectively) and most commonly ordered for stage IV NSCLC, all consistent with clinical guidelines.<sup>5</sup>

**Routine surveillance with PET-CT.** Among the cohort of 110 cases, surveillance PET-CT scans were identified as the prevailing imaging studies to assess ongoing treatment response in 12 cases (11%). In these cases, the reviews noted that there is no evidence demonstrating that PET-CT offers a significant incremental benefit in terms of clinical outcomes and that routine monitoring of response by CT may be an appropriate alternative.

**Frail or marginal performance status.** A total of 21 patients (19%) were identified by their local cancer care team as having a poor performance status, as reflected in clinic notes, limiting treatment considerations relative to standard of care for more fit patients. Although this cohort included nine patients (8%) age 80 years or older, only three (33%) of this subset were noted to be frail enough on the basis of clinic notes to limit the treatment recommendations.



**FIG 2.** Case volume over time: there was a clear increase over time, despite the COVID-19 pandemic, although marked variability from month to month was a product of changes in some client company priorities.

**TABLE 1.** Patient Characteristics

Characteristic	N = 110
Sex, No. (%)	
Male	61 (55)
Female	49 (45)
Age, years, median (range)	62.5 (33-92)
Smoking status, No. (%)	
Never	20 (18)
Prior	63 (57)
Current	26 (24)
Unknown	1 (1)
Diagnosis and stage at the time of review, No. (%)	
NSCLC	90 (82)
Stage I-II	13 (14 of NSCLC)
Stage III	18 (20 of NSCLC)
Stage IV	59 (66)
SCLC	19 (17)
Limited	4 (21 of SCLC)
Extensive	15 (79)
Other	1 (1)
NSCLC histology, No. (%)	
Squamous	19 (21 of NSCLC)
Adenocarcinoma	63 (70)
Neuroendocrine	3 (3)
Not otherwise specified	5 (6)
Local treatment setting, No. (%)	
Community	94 (85)
Academic	16 (15)

Abbreviations: NSCLC, non-small-cell lung cancer; SCLC, small-cell lung cancer.

## DISCUSSION

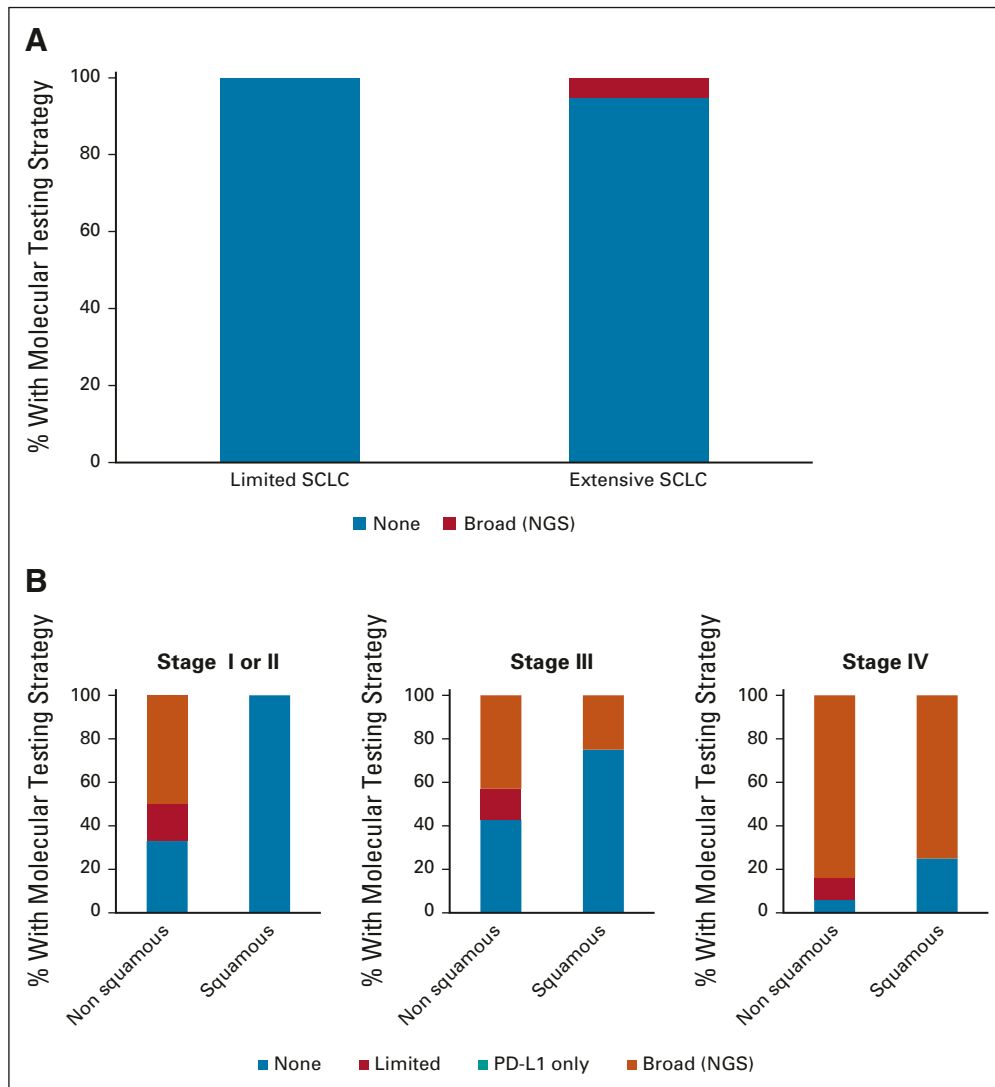
The program developed by AccessHope represents a new model for cancer care that remotely incorporates input from a subspecialist oncologist into a report to a patient's local medical team, thereby enabling delivery of optimal care without an expectation that a patient present to a tertiary care center. Our experience over slightly more than 1.5 years demonstrates that this model is not only feasible to implement but revealed increasing uptake over that time, despite disruption of workflows and many health care processes throughout much of 2020.<sup>6</sup>

Reviewing the results of these reports in aggregate demonstrated that although our expert agreed with the general management approach in the majority (72%) of cases, 92% of cases included recommendations to refine management, largely on the basis of strategies for surveillance, subsequent treatment options, surveillance, and/or supplemental evidence-based recommendations such as

bone-directed therapy for patients with bone metastases. Two-thirds of cases included recommendations for current or future care associated with an anticipated improvement in efficacy, and 13% included a proposed plan associated with improved chance of cure. Moreover, even when commenting on past management, identifying teaching points for completed therapies is prone to improve outcomes for other patients treated by the same physician; similarly, outlining and suggesting optimal subsequent therapy options for a patient is not recorded as discordant with current therapy but stands to improve that patient's outcome later, while also providing guidance that can also be translated to many other patients. Overall, for more than one of every four cases, expert recommendations proposed an alternative management approach for current treatment associated with a significantly superior survival on the basis of available data. Moreover, by recommending against low-value imaging or treatments that are not concordant with clinical guidelines for that setting, marked cost savings could be identified that averaged more than \$19,000 (USD) per patient.

Surveying the broad range of case materials submitted also affords an opportunity to understand the features of the patient population and clinical decision making of a diverse array of oncology practice across the United States. Through this lens, we observed that PET scan-based imaging was pursued or planned to assess for response or progression in 11% of cases despite it having no demonstrated incremental benefit over CT scan surveillance. We noted that 19% of patients were limited by marginal or poor performance status for which individualized judgment is left to fill the void of scant clinical evidence; importantly, this proportion is based on local assessment and includes only the subset of patients for whom their functional status was specifically documented within clinic notes as poor candidates for standard therapies favored for more fit patients. Assessment of molecular testing patterns revealed that testing in this broad sample far exceeded that reported in some prior reports<sup>7-9</sup>; overall, even very recent broad data sets have shown that community-based molecular marker testing follows clinical guidelines in < 50% of cases.<sup>9</sup> Consistent with clinical guidelines, molecular testing was far more likely to be ordered for patients with NSCLC than SCLC, more commonly ordered for advanced- compared with early-stage disease, and more likely to be ordered in patients with nonsquamous versus squamous NSCLC histology.

We must also acknowledge the limitations of this work. First, this analysis represents a growing but still relatively small cohort that limits our ability to draw strong conclusions about patient features or practice patterns; our ability to see these with greater resolution will undoubtedly improve as the size of this cohort grows with the trajectory of this program. Findings are also gleaned from a population of patients who are not only insured but have an employer



**FIG 3.** Molecular marker testing patterns by local oncologists by lung cancer histology and clinical setting for SCLC and NSCLC. Cases are categorized as SCLC (limited [n = 4]; extensive [n = 14]) and NSCLC (early stage, squamous [n = 7]; nonsquamous [n = 6]; stage III, squamous [n = 4]; stage III, nonsquamous [n = 14]; stage IV, squamous [n = 8]; stage IV, nonsquamous [n = 53]). Testing is categorized as none, limited mutation panel, PD-L1 expression only, or broad testing, eg, NGS. NGS, next generation sequencing; NSCLC, non-small-cell lung cancer; SCLC, small-cell lung cancer; PD-L1, programmed death-ligand 1.

or insurance payer providing a high level of support; the observations cannot be extrapolated to a broader population of uninsured or underinsured patients in the United States. In addition, the expert input has been provided by only a limited group of experts in this early interval of the program. Given the value in obtaining input from a plurality of experts as well as the steadily growing case volume, the AccessHope program is now increasingly distributing cases not only among City of Hope faculty but also to faculty that include two additional National Cancer Institute–designated cancer centers (Northwestern Medicine and Dana-Farber Cancer Institute) as foundational partners, with others planned, to create a geographically diverse network of experts reviewing an escalating number of candidate cases.

Importantly, we do not directly assess patient or local physician satisfaction, nor the rates at which articulated recommendations have been followed or clinical outcomes associated with them. AccessHope is striving to pursue follow-up at one or more defined time points, which should enable us to assess which recommendations have been pursued in the interval since the initial review was submitted.

Those interested in these services may question whether this work constitutes telemedicine that would require physicians to be licensed by the state in which the patient is located. AccessHope provides educational and support services to the local treating physicians who are licensed in the state where the patient resides and who provide direct

care for the patient. AccessHope does not establish a doctor-patient relationship, provide care, or practice telemedicine. Therefore, although patients may be located throughout the United States, there is no requirement for AccessHope physicians to be licensed in the state in which a specific patient resides.

Multiple mechanisms for second opinions exist to provide reassurance to patients and potentially their care team, although the experience of many of these programs has not been summarized and published. As one option with some similarities to AccessHope, Meyer et al<sup>10</sup> describe their experience with an asynchronous patient-initiated second opinion service (Best Doctors) covering all aspects of medicine that included 588 patients with hematology or oncology diagnoses, with opinions in this subset estimated to have moderate or major clinical impact in 38% of cases. Another option that provides a multidisciplinary approach is virtual tumor boards or case conferences, which have been pursued for testicular cancer,<sup>11</sup> sarcoma,<sup>12</sup> and lung cancer,<sup>13</sup> with success in improving care while overcoming geographic barriers.

AccessHope has prioritized proactive identification of cases with high potential for impact by triggering cases on the

basis of diagnosis and stage, with a rationale that many patients and oncologists may be unaware of when supplemental subspecialist input could improve outcomes. Only 3% of our reviewed cases with lung cancer were patient-initiated, likely reflecting the disinclination of so many patients with cancer, often particularly patients with lung cancer, to seek a second opinion.<sup>14</sup>

The AccessHope program is also designed to minimize turnaround time and maximize flexibility to accommodate a variable volume of patients with a potentially wide array of cancer diagnoses. Although a regular cadence of multidisciplinary tumor boards or case conferences could potentially provide support for patients with specific tumor types, this incurs a delay before feedback is available, cannot be readily offered across a wide range of tumor types simultaneously, and is challenging to modulate in response to variable patient volumes over time.

As new employers contract with this AccessHope network, this program can offer oncologists in practice the input and support of a subspecialist while preserving the autonomy of the local medical team, without requiring patient travel, and keeping the patient's care close to home.

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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## DATA SHARING STATEMENT

Because of legal restrictions and the proprietary nature of several of the processes included, data represented in this work cannot be shared

beyond that which is included here or published elsewhere by representatives of AccessHope.

## AUTHOR CONTRIBUTIONS

**Conception and design:** Howard (Jack) West, Yuan Angela Tan

**Administrative support:** Howard (Jack) West, Todd Sachs

**Provision of study materials or patients:** Howard (Jack) West

**Collection and assembly of data:** Howard (Jack) West, Yuan Angela Tan, Afsaneh Barzi, Robert Parsley

**Data analysis and interpretation:** Yuan Angela Tan, Afsaneh Barzi, Debra Wong, Todd Sachs

**Manuscript writing:** All authors

**Final approval of manuscript:** All authors

**Accountable for all aspects of the work:** All authors

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**AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**

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**Consulting or Advisory Role:** Merck, Genentech/Roche, AstraZeneca, Takeda, Mirati Therapeutics, Regeneron

**Speakers' Bureau:** Takeda, Merck, AstraZeneca

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**Honoraria:** AstraZeneca, Genentech/Roche, Merck, Takeda, Mirati Therapeutics, Regeneron, Merck, Genentech/Roche, AstraZeneca, Takeda, Mirati Therapeutics, Regeneron

**Speakers' Bureau:** Takeda, Merck, AstraZeneca

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**Leadership:** Cardiff Oncology

**Consulting or Advisory Role:** Merrion, bioTheranostics, Bayer Technology System, Daiichi Sankyo/Astra Zeneca

**Research Funding:** Bayer (Inst), Merck (Inst)

**Debra Wong**

**Consulting or Advisory Role:** Bristol Myers Squibb, Genentech/Roche, Sanofi/Aventis, Blueprint Medicines, Regeneron, Pfizer

**Speakers' Bureau:** Pfizer

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**Robert Parsley**

**Employment:** AccessHope, Optum

No other potential conflicts of interest were reported.

## APPENDIX 1. SUPPLEMENTAL MATERIALS

### Definitions of Case Metrics

**Agree.** The clinical expert agrees with current management and has no suggestions for clinically significant changes in management. This category should only be selected when outcome of review is validation of current care.

**Agree, with minor recommendations.** The clinical expert has recommendations for additional tests, interventions, or changes in management that are not associated with significant evidence-based improvements in cancer outcome and may be secondary to anticancer treatment and/or on the basis of preference.

**Disagree, with moderate recommendations.** The clinical expert recommends a change in anticancer therapy that is anticipated to be associated with an evidence-based, clinically significant improvement in cancer outcome, whether greater efficacy or reduced toxicity or both; OR the clinical expert recommends a management plan in the

absence of any default treatment recommendations by the local medical team.

**Disagree, with significant recommendations.** The clinical expert recommends a change in anticancer therapy that is anticipated to be associated with an evidence-based, clinically significant improvement in cancer outcome that is provided as an alternative to a treatment plan by the local medical team that is associated with greater anticipated harm than benefit or represents a treatment plan clearly below the standard of care for that clinical setting.

### Records Requested

Medical records including most recent three clinic notes from relevant specialists (as applicable), pathology reports including all molecular marker testing, and initial and most recent imaging reports for each case were requested as pdf files, although an original history and physical examination and any additional relevant records were also welcomed. Imaging and pathology were reviewed on the basis of reports and not direct review of source materials.

**TABLE A1.** Illustration of Recommendations for Cases of Disagreement

Case	Proposed or Initiated Management	Recommended Change(s)
A	Stage IIIA N2 NSCLC with major pathologic response, resected after concurrent cCRT followed by consolidation durvalumab for up to 1 year	Cited there is no evidence to support consolidation durvalumab; additional two cycles of platinum-based chemotherapy in the postoperative setting is supported by limited evidence
B	Stage IV squamous NSCLC s/p palliative radiation to painful bone metastases, proposed to start carboplatin/paclitaxel/bevacizumab/atezolizumab	Strongly advised against bevacizumab-containing regimen for squamous NSCLC, especially after recent radiation that included midchest; recommended alternative combinations for squamous NSCLC
C	At least stage IIIA NSCLC per outside workup, with PET-avid pleural nodules, planned to receive concurrent cCRT followed by consolidation durvalumab	Favored chemoimmunotherapy combination as optimal first-line standard of care for stage IV NSCLC without a driver mutation, potentially followed by consolidation local therapy if limited residual disease
D	Received pembrolizumab and radiation for T3N0M0 NSCLC invading chest wall, followed by chest wall resection with path CR, followed by ongoing pembrolizumab for more than two years despite pneumonitis and postoperative persistent air leaks requiring repeat surgery	Advised of the lack of evidence to support ongoing adjuvant pembrolizumab, particularly in the absence of residual viable cancer and with significant treatment-related complications
E	Unresectable stage IIIB NSCLC with plan for total of four cycles of chemotherapy and concurrent chest radiation to 76 Gy; no mention of consolidation durvalumab	Recommended against consolidation chemotherapy for which there is no evidence; also, advised radiation dose exceeds evidence-based guidelines; favored consideration of consolidation durvalumab
F	Multifocal lung nodules being treated as stage IIIA NSCLC on right, proposed to receive cCRT followed by surgery ± postoperative durvalumab, along with SBRT to left-sided lesion	Favored biopsy of left-sided disease to compare pathologic findings, brain MRI to complete staging, benefit of doubt to patient for staging, but favor durvalumab, not surgery after cCRT
G	SCLC with T9 lesion proposed to receive cCRT with atezolizumab, followed by maintenance atezolizumab, as well as denosumab for prophylaxis against skeletal-related events	Strongly favored brain MRI to complete staging, then reasonable if negative to treat as LS-SCLC, as radiation can be all within one port, with cCRT, while omitting immunotherapy if treating as LS-SCLC
H	Relapsed squamous NSCLC, heavily pretreated (including nivolumab), declining PS after docetaxel/ramucirumab × one cycle, considering gemcitabine or vinorelbine or another immunotherapy	Advised significant clinical benefit from gemcitabine or vinorelbine is quite unlikely after many lines and inability to tolerate prior chemotherapy; no data for repeat immunotherapy after PD, favor afatinib or BSC
I	Advanced nonsquamous NSCLC with progression on CT scan done 2 weeks after initiation of chemotherapy doublet, no immunotherapy, without clear plan for how to proceed	Noted that scan done within first few weeks after initiation of systemic therapy may not reflect cancer being refractory; favor adding pembrolizumab to carboplatin/pemetrexed in the absence of contraindication
J	Advanced nonsquamous NSCLC with low PD-L1 expression receiving pembrolizumab monotherapy, no chemotherapy because of concern about COVID-19, now with CT showing PD	Reviewed evidence supporting potential benefit of chemotherapy, concluding anticipated benefit of platinum doublet or docetaxel-based chemotherapy exceeds risk, no alternative with known benefit

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**TABLE A1.** Illustration of Recommendations for Cases of Disagreement (continued)

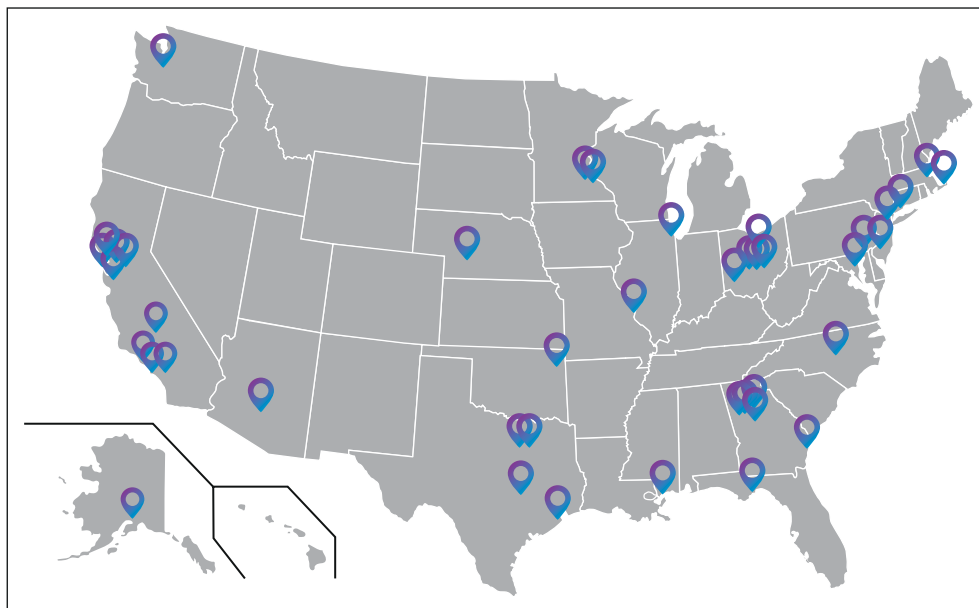
Case	Proposed or Initiated Management	Recommended Change(s)
K	Clinical stage II NSCLC in 92-year-old frail man felt not candidate for surgery or cCRT; received definitive RT, with plan to pursue immunotherapy in event of relapse; PD-L1 not assessed	Presented data supporting immunotherapy or possibly chemoimmunotherapy depending on his tumor's PD-L1 status and assessment of his PS and goals of care, with caveats about lack of data in his age range
L	Newly diagnosed patient with advanced nonsquamous NSCLC with recurrent symptomatic pleural effusions, mild renal insufficiency, and no articulated systemic therapy plan yet	Discussed range of chemoimmunotherapy options supported by evidence, favoring carboplatin/pemetrexed/pembrolizumab as a leading option, also highlighting the utility of indwelling pleural catheter
M	Progressing nonsquamous NSCLC with PD-L1 0%, started on cisplatin/pemetrexed, extensive new bone and brain metastases noted before pembrolizumab added in cycle 2; declining PS despite addition of pembrolizumab and radiation to brain metastases	Noted need for repeat imaging to clarify whether progression is occurring despite current interventions, possible docetaxel-based treatment but leading option likely initiation of palliative care in face of clinical decline in the setting of likely further disease progression
N	Newly diagnosed metastatic squamous NSCLC diagnosed in a fit 90-year-old man, no PD-L1 or molecular testing, started on nivolumab monotherapy, tolerating well thus far	Outlined value of testing for tumor PD-L1 expression to help guide optimal systemic therapy; favor chemoimmunotherapy as per KEYNOTE-407 trial or potentially pembrolizumab if PD-L1–positive
O	Stage IV lung adenocarcinoma with PD-L1 0%, dose-attenuated chemotherapy/immunotherapy as per KEYNOTE-189, progression on PET-CT but continued pemetrexed/pembrolizumab because of interpretation that progression may have preceded start of treatment	Recommended pursuing CT imaging to reassess for progression v stability or shrinkage, continue maintenance therapy if no progression, v docetaxel-based treatment or supportive care if PD; also emphasized lack of established role for PET-CT over CT scan for routine assessment of response
P	Indolent, multifocal lepidic adenocarcinoma, PD-L1 20%, single lesion progressing, most recent PET-CT > 3 months old. Considering SBRT, then pembrolizumab as consolidation	Advised repeat CT, not repeat PET-CT, indicated to assess for interval change, supportive of SBRT if solitary or limited progression if no change in background lesions, no role for post-SBRT immunotherapy
Q	Nonsquamous NSCLC with high tumor PD-L1 with progression months after initial pembrolizumab, now on chemotherapy, being recommended for alternate immunotherapy	Noted lack of evidence to support pursuing similar immunotherapy after clear progression after pembrolizumab, favoring docetaxel ± ramucirumab as a stronger evidence-based option
R	Patient with ambiguous staging of NSCLC, most recent imaging a PET-CT showing suspicious PET-avid nodules along chest wall months to evaluation; felt to be a candidate for surgery	Highlighted imaging that was so suspicious should be repeated to look for interval change, ideally with VATS or transthoracic biopsy of persistent or worse findings; outlined leading options stage by stage
S	Multifocal moderately differentiated lung adenocarcinomas in a single lobe are now confluent and associated with new PET-avid mediastinal nodes; surgery is planned	Conveyed concern that patient is at risk for N2 (or greater) nodal involvement, therefore favor preoperative mediastinal staging; discussed neoadjuvant standard of care for N2+ NSCLC, also adjuvant therapy data
T	Progressing advanced squamous NSCLC after KEYNOTE-407 regimen, proposed to start gemcitabine/ramucirumab as next treatment approach	Agreed with prior therapy decisions but noted that regimen of gemcitabine/ramucirumab is not well studied as second-line treatment option, enumerating data supporting docetaxel/ramucirumab instead
U	Patient with mixed response on pemetrexed/pembrolizumab maintenance therapy, although more progression than response, with worse pain from observed left acetabular metastasis	Favor transition to docetaxel ± ramucirumab rather than continued pemetrexed/pembrolizumab, given predominant pattern of progression, no role for switch to another immunotherapy, favor radiation to hip
V	Staging of squamous NSCLC that is most consistent with oligometastatic stage IV disease, planned to receive cCRT followed by consolidation durvalumab	Noting risk of pneumonitis from large radiation field required to treat all identified disease with initial cCRT, proposed initial chemoimmunotherapy followed by consolidation local therapy if good response
W	Advanced nonsquamous NSCLC with multiple brain metastases, now on ongoing steroids, proposed to receive chemoimmunotherapy with KEYNOTE-189 regimen	Recommended complete molecular marker testing, and agree with KEYNOTE-189 regimen if testing negative, but advocate tapering steroids expeditiously, given potential for worse outcomes with immunotherapy
X	Extensive-stage SCLC treated with chemotherapy and concurrent chest RT, developed relapse, treated with pembrolizumab, complicated by severe ocular toxicity, responded to steroids or discontinuation of therapy, now with response, proposed to start nivolumab	Recommended against initiating nivolumab, given lack of progression, severity of adverse event potential for sustained response to immunotherapy after discontinuation for toxicity, and in light of same mechanism of action of these agents; outlined several alternative options for treatment upon progression
Y	Single focus of slowly progressing, biopsy-confirmed lung adenocarcinoma years after surgery for stage IIIA N2 NSCLC, then chemotherapy and radiation, no treatment plan yet	Favor molecular marker testing of progressing lesion, consideration of local therapy most likely amenable to SBRT, potential for serial local therapy as needed over time, no anticipated need for systemic therapy

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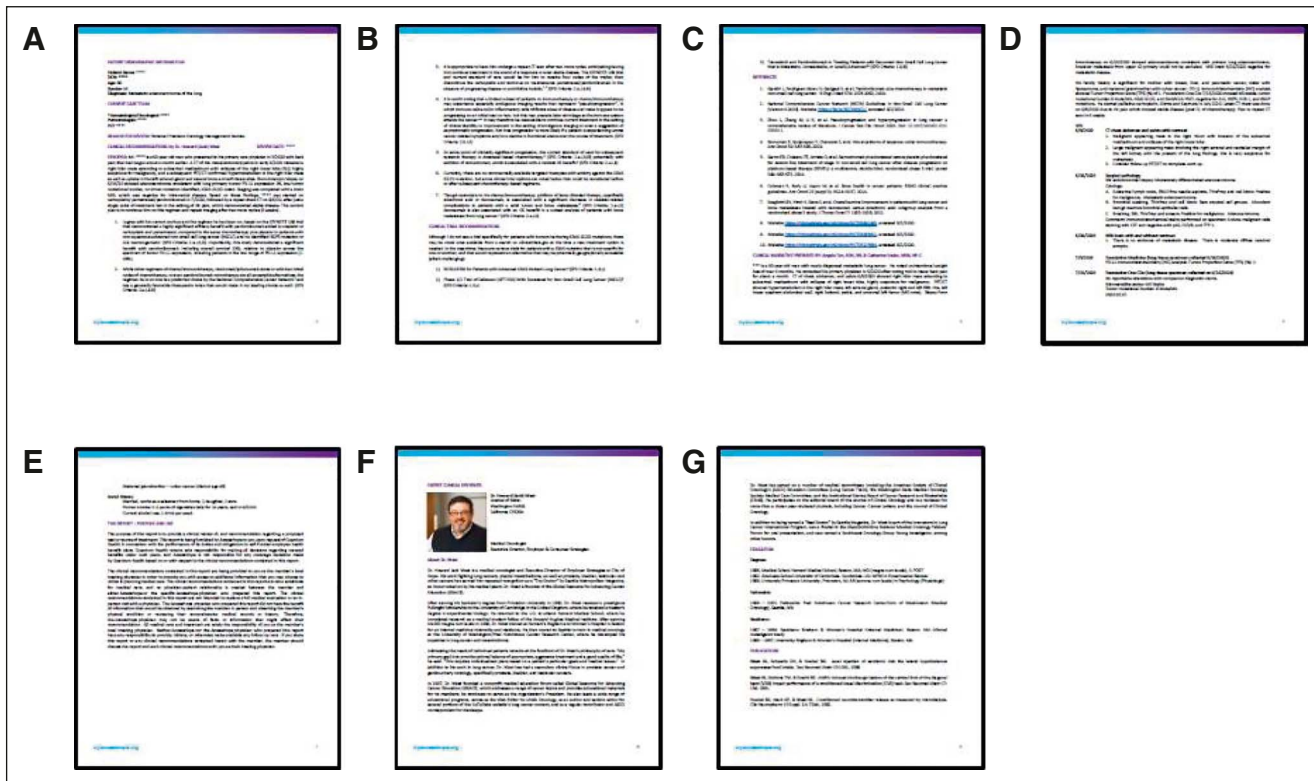
**TABLE A1.** Illustration of Recommendations for Cases of Disagreement (continued)

Case	Proposed or Initiated Management	Recommended Change(s)
Z	T4 adenocarcinoma with ambiguous nodal imaging, no mediastinal staging, possible small brain lesion, EGFR mutation noted, chemotherapy/radiation followed by planned surgery	Recommended cCRT followed by surgery only if repeat imaging, including repeat brain imaging of suspicious lesion, shows no PD or evidence of metastatic disease; osimertinib favored if advanced disease identified
AA	Clinical and pathologic findings ambiguous for lung v GI cancer, treated with carboplatin/nab-paclitaxel/pembrolizumab, now progressing, considering FOLFIRINOX as next treatment	Joint opinion between thoracic and GI oncologist favoring test for albumin RNA-ish, biopsy a lesion in tail of pancreas, recommend docetaxel ± ramucirumab if findings not consistent with GI origin
BB	Extensive-stage SCLC treated with chemotherapy/durvalumab, then maintenance chemotherapy, with PD seen quickly after transition to maintenance durvalumab, return to same chemotherapy planned	Favor lurbinectedin as next treatment option on the basis of short CFI, rather than return to same chemotherapy, which is more favored after longer CFI; consider denosumab for bone metastases
CC	Extensive-stage SCLC with symptomatic brain metastases and bone metastases, started on chemotherapy/durvalumab, not yet treated with local therapy for brain metastases	Recommend close surveillance of intracranial disease and likely need for local therapy of whole-brain radiation therapy or possibly stereotactic radiosurgery; consider denosumab for bone metastases
DD	Stage IV disease with oligometastatic focus of likely pericardial nodule, PET-avid, receiving cCRT to total radiation dose 50.4 Gy, then potential right pneumonectomy	Highlighted risk of right pneumonectomy, particularly for what appears to be stage IV disease, favoring cCRT to higher dose of radiation followed by durvalumab, or chemotherapy/immunotherapy for stage IV
EE	Stage III NSCLC, completed two cycles of cisplatin/pemetrexed followed by same with chest radiation, undefined plans for subsequent management after cCRT	Agreed that induction chemotherapy followed by cCRT is an appropriate strategy for some patients with stage III NSCLC, advised against consolidation chemotherapy and favored consolidation durvalumab
FF	Stage III NSCLC, recently started weekly carboplatin/paclitaxel with chest radiation, plan is articulated to give two additional cycles of chemotherapy, then durvalumab consolidation	Noted that there is no evidence to support consolidation chemotherapy after cCRT, evidence only shows increased toxicity with no clinical benefit, favor transition to subsequent consolidation durvalumab next
GG	Stage IIIA N2 NSCLC, underwent neoadjuvant chemotherapy × four cycles, minor response on CT, surgery revealing 95% residual viable tumor and multiple positive N1 and N2 nodes	Discussed lack of evidence of survival benefit but improvement in disease-free survival and local control with radiation; recommended testing for possible EGFR mutation and adjuvant osimertinib if detected

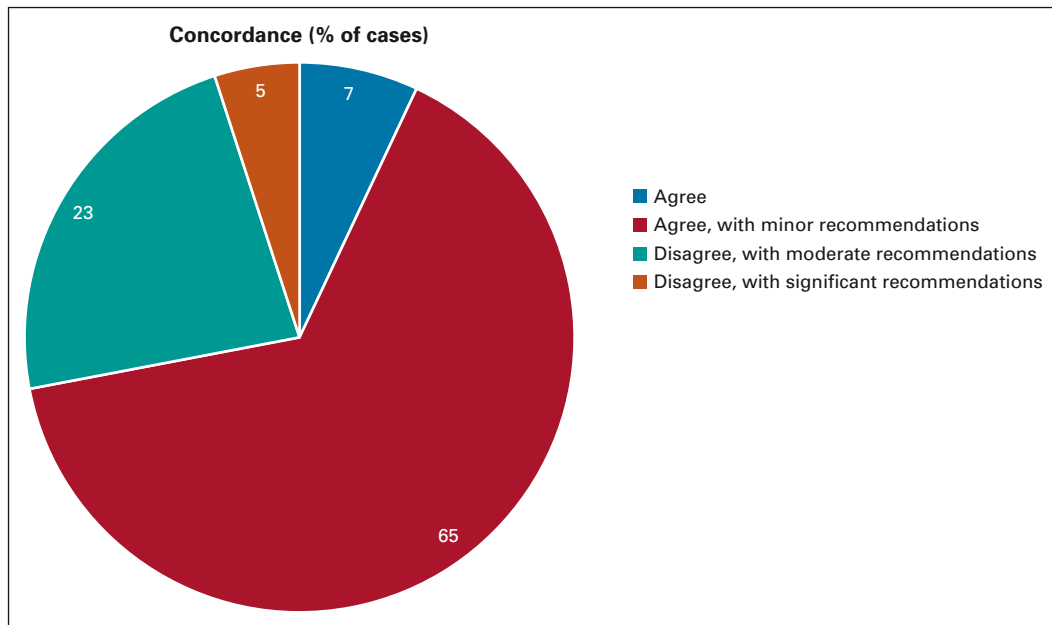
Abbreviations: BSC, best supportive care; cCRT, chemoradiation; CFI, chemotherapy-free interval; CR, complete response; CT, computed tomography; EGFR, epidermal growth factor receptor; FOLFIRINOX, fluorouracil, leucovorin, irinotecan, oxaliplatin; LS-SCLC, limited stage small cell lung cancer; MRI, magnetic resonance imaging; NSCLC, non-small-cell lung cancer; PD, progression of disease; PD-L1, programmed death-ligand 1; PET, positron emission tomography; PS, performance status; RT, radiotherapy; SBRT, stereotactic body radiotherapy; s/p: status-post; VATS, video-assisted thoracoscopic surgery.



**FIG A1.** Geographic distribution of client companies working with AccessHope. At the present time, AccessHope works with 43 companies in 21 states to cover approximately 2.3 million lives.



**FIG A2.** Content of Sample Report from AccessHope. (A) Summary data on patient, then local clinical team, name of expert reviewer, date of review, followed by brief synopsis of case by expert physician, and numbered points of commentary on workup and treatment thus far. (B) Continued numbered points of commentary on treatment and potential alternatives, surveillance and subsequent management options, as well as supportive care, followed by suggested clinical trial options, as applicable. (C) Numbered references cited in review commentary, followed by narrative summary of case as prepared by nurse. (D) Additional narrative summary by nurse, followed by chronologic summary of case data and medical history (continues for additional pages). (E) Program disclaimers. (F) Introduction to expert reviewer, with biography. (G) The summary of education, training, and papers authored by the expert reviewer (continues for additional pages).



**FIG A3.** Concordance with local oncologist or medical team. The breakdown of measures of concordance or disagreement with diagnosis and current or proposed management as defined by AccessHope. Note that agree, with minor recommendations includes recommendations for changes in management applied to past or future care. Dr Howard West's image is visible and recognizable within Appendix [Figure A3](#) (online only), which illustrates the faculty biography portion of the provided case report. Dr West has provided his explicit consent for his likeness to be included in the context of this publication.