AHRQ Healthcare Horizon Scanning System – Potential High Impact Interventions Report

Priority Area 13: Pulmonary Disease including Asthma

Potential High Impact Interventions Report

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Statement of Funding and Purpose

This report incorporates data collected during implementation of the Agency for Healthcare Research and Quality (AHRQ) Healthcare Horizon Scanning System by ECRI Institute under contract to AHRQ, Rockville, MD (Contract No. HHSA29020100006C). The findings and conclusions in this document are those of the authors, who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

This report's content should not be construed as either endorsements or rejections of specific interventions. As topics are entered into the System, individual Topic Profiles are developed for technologies and programs that appear to be closer to diffusion into practice in the United States. Drafts of those reports are sent to various experts with clinical, health systems, health administration, and/or research backgrounds for comment and opinions about potential for impact. The comments and opinions received are then considered and synthesized by ECRI Institute to identify those interventions that experts deem, through the comment process, to have potential for high impact. Please see the methods section for more details about this process. This report is produced twice annually, and topics included may change depending on expert comments received on interventions issued for comment during the preceding six months.

A representative from AHRQ served as a Contracting Officer's Technical Representative and provided input during the implementation of the horizon scanning system. AHRQ did not directly participate in the horizon scanning, assessing the leads for topics, or provide opinions regarding potential impact of interventions.

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Financial Disclosure Statement

None of the individuals compiling this information has any affiliations or financial involvement that conflicts with the material presented in this report.

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Preface

The purpose of the AHRQ Healthcare Horizon Scanning System is to conduct horizon scanning of emerging health care technologies and innovations to better inform patient-centered outcomes research investments at AHRQ through the Effective Health Care Program. The Healthcare Horizon Scanning System provides AHRQ a systematic process to identify and monitor target technologies and innovations in health care and to create an inventory of target technologies that have the highest potential for impact on clinical care, the health care system, patient outcomes, and costs. It will also be a tool for the public to identify and find information on new health care technologies and interventions. Any investigator or funder of research will be able to use the AHRQ Healthcare Horizon Scanning System to select potential topics for research.

The health care technologies and innovations of interest for horizon scanning are those that have yet to diffuse into or become part of established health care practice. These health care interventions are still in the early stages of development or adoption except in the case of new applications of already-diffused technologies. Consistent with the definitions of health care interventions provided by the Institute of Medicine and the Federal Coordinating Council for Comparative Effectiveness Research, AHRQ is interested in innovations in drugs and biologics, medical devices, screening and diagnostic tests, procedures, services and programs, and care delivery.

Horizon scanning involves two processes. The first is identifying and monitoring new and evolving health care interventions that are purported to or may hold potential to diagnose, treat, or otherwise manage a particular condition or to improve care delivery for a variety of conditions. The second is the analysis of the relevant health care context in which these new and evolving interventions exist to understand their potential impact on clinical care, the health care system, patient outcomes, and costs. It is NOT the goal of the AHRQ Healthcare Horizon Scanning System to make predictions on the future utilization and costs of any health care technology. Rather, the reports will help to inform and guide the planning and prioritization of research resources.

We welcome comments on this Potential High Impact report. Send comments by mail to the Task Order Officer named in this report to: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to effectivehealthcare@ahrq.hhs.gov.

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Background

Horizon scanning is an activity undertaken to identify technological and system innovations that could have important impacts or bring about paradigm shifts. In the health care sector, horizon scanning pertains to identification of new (and new uses of existing) pharmaceuticals, medical devices, diagnostic tests and procedures, therapeutic interventions, rehabilitative interventions, behavioral health interventions, and public health and health promotion activities. In early 2010, the Agency for Healthcare Research and Quality (AHRQ) identified the need to establish a national Healthcare Horizon Scanning System to generate information to inform comparative-effectiveness research investments by AHRQ and other interested entities. AHRQ makes those investments in 14 priority areas. For purposes of horizon scanning, AHRQ's interests are broad and encompass drugs, devices, procedures, treatments, screening and diagnostics, therapeutics, surgery, programs, and care delivery innovations that address unmet needs. Thus, we refer to topics identified and tracked in the AHRQ Healthcare Horizon Scanning System generically as "interventions." The AHRQ Healthcare Horizon Scanning System implementation of a systematic horizon scanning protocol (developed between September 1 and November 30, 2010) began on December 1, 2010. The system is intended to identify interventions that purport to address an unmet need and are up to 7 years out on the horizon and then to follow them for up to 2 years after initial entry into the health care system. Since that implementation, more than 7,000 leads about topics have resulted in identification and tracking of more than 900 topics across the 14 AHRQ priority areas.

Methods

As part of the Healthcare Horizon Scanning System activity, a report on interventions deemed as having potential for high impact on some aspect of health care or the health care system (e.g., patient outcomes, utilization, infrastructure, costs) is aggregated twice annually. Topics eligible for inclusion are those interventions expected to be within 0 to 4 years of potential diffusion (e.g., in phase III trials for pharmaceuticals or biotechnologies or in phase II or a trial with some preliminary efficacy data on the target population for devices and programs) in the United States or that have just begun diffusing and that have completed an expert feedback loop.

The determination of impact is made using a systematic process that involves compiling a profile on topics and issuing topic profile drafts to a small group of various experts (selected topic by topic) to gather their opinions and impressions about potential impact. Those impressions are used to determine potential impact. Information is compiled for expert comment on topics at a granular level (i.e., similar drugs in the same class are read separately), and then topics in the same class of a device, drug, or biologic are aggregated for discussion and impact assessment at a class level for this report. The process uses a topic-specific structured form with text boxes for comments and a scoring system (1 minimal to 4 high) for potential impact in seven parameters. Participants are required to respond to all parameters.

The scores and opinions are then synthesized to discern those topics deemed by experts to have potential for high impact in one or more of the parameters. Experts are drawn from an expanding database ECRI Institute maintains of approximately 350 experts nationwide who were invited and agreed to participate. The experts comprise a range of generalists and specialists in the health care sector whose experience reflects clinical practice, clinical research, health care delivery, health business, health technology assessment, or health facility administration perspectives. Each expert uses the structured form to also disclose any potential intellectual or financial conflicts of interest (COI).

Perspectives of an expert with a COI are balanced by perspectives of experts without COIs. No more than two experts with a possible COI are considered out of a total of the seven or eight experts who are sought to provide comment for each topic. Experts are identified in the system by the perspective they bring (e.g., clinical, research, health systems, health business, health administration, health policy).

The topics included in this report had scores *and/or* supporting rationales at or above the overall average for all topics in this priority area that received comments by experts. Of key importance is that topic scores alone are not the sole criterion for inclusion—experts' rationales are the main drivers for the high impact potential designation. We then associated topics that emerged as having potentially high impact with a further subcategorization of "lower," "moderate," or "higher" within the potential high impact range. As the Healthcare Horizon Scanning System grows in number of topics on which expert opinions are received, and as the development status of the interventions changes, the list of topics designated as potential high impact is expected to change over time. This report is being generated twice a year.

For additional details on methods, please refer to the full AHRQ Healthcare Horizon Scanning System Protocol and Operations Manual published on AHRQ's Effective Health Care Web site.

Results

The material on interventions in this Executive Summary and report is organized alphabetically by disease state. Readers are encouraged to read the detailed information on each intervention that follows the Executive Summary. The table below lists the three topics for which (1) preliminary phase III were available for drugs, or phase II, III or later data were available for devices; (2) information was compiled by November 2011 in this priority area; *and* (3) we received six to eight sets of comments from experts between February and November 1, 2011. (A total of 30 topics in this priority area were being tracked in the system as of November 2011.) For purposes of the Potential High Impact Interventions Report, we aggregated related topics for summary and discussion (e.g., individual drugs into a class). We present two summaries on two topics (indicated below by an asterisk) that emerged as potential high impact on the basis of experts' comments and their assessment of potential impact.

Priority Area 13: Pulmonary Disease (including Asthma)
1. *Bronchial thermoplasty (Alair System) for treatment-resistant asthma
2. *Ivacaftor (Kalydeco, VX-770) for treatment of cystic fibrosis in patients with G551D-*CFTR* mutation
3. Roflumilast (Daliresp) for treatment of chronic obstructive pulmonary disease

Discussion

Pulmonary disease is another priority area in which relatively few topics have been identified as meeting criteria for the AHRQ Healthcare Horizon Scanning System and high potential impact report. The two topics that experts deemed as having potential high impact were a technology for treatment-resistant asthma and a new disease-modifying drug targeted at one of the genetic mutations seen in patients with cystic fibrosis (CF).

Bronchial Thermoplasty for Treatment-resistant Asthma in Adults

- **Key Facts**: An estimated 7% of the U.S. population has asthma and about 5% to15% of these patients have severe, persistent asthma that does not respond sufficiently to high doses of asthma medications. Bronchial thermoplasty (Alair® Bronchial Thermoplasty System,

Asthmatx, Inc., acquired by Boston Scientific Corp., Natick, MA) is a minimally invasive outpatient procedure that uses a system approved by the U.S. Food and Drug Administration (FDA) in April 2010 to treat adults (aged 18 years and older) with severe asthma that has not responded adequately to standard medical therapy. The FDA approval included conditions requiring conduct of two 5-year postapproval studies. A pulmonologist delivers thermal energy using the Alair system to accessible airway walls during a series of three bronchoscopy procedures. The procedure is intended to reduce the thickness of smooth muscle mass without causing charring or scarring. By reducing, debulking, or partially eliminating excess smooth muscle tissue in the patient's distal airways, the hope is that the number of severe asthma attacks will decrease on a long-term basis.

Uptake of the use of BT was slow during the first year after its approval; however, the rate of BT's availability more than doubled from January 2011, with 22 clinical sites in 15 states to 51 clinical sites in 24 states by November 2011. The increase may be due to the acquisition of Asthmatx by Boston Scientific and increased marketing efforts. Additionally, data reported after the expert comments were collected for this report indicated that patients with severe persistent asthma treated with BT maintained reductions in severe exacerbations for at least 2 years and maintained stable lung function in the absence of clinical complications over a 5-year period. These longer-term results may increase acceptance of the treatment.

The list price of the Alair ATS 200 Controller System, which includes a radiofrequency controller and a footswitch, is $49,000. The patient return electrode is not included in the system and must be supplied by the provider. The list price of a disposable, single-use Alair Catheter Model ATS 2-5 is $2,500. Searches of 11 representative, large U.S. private third-party payers that provide online medical coverage policies found that 10 payers that have specific policies that deny coverage and one payer that has no policy (i.e., CIGNA). Effective January 1, 2012, the Alair catheter is eligible for Medicare reimbursement through a separate "pass-through" payment when the procedure is performed in an outpatient hospital setting. The 2012 national unadjusted Hospital Prospective Payment System payment is $2,023.82.

- **Key Expert Comments**: Overall, experts commenting on this topic were cautiously optimistic about its potential to offer an option for some patients with severe asthma that does not respond to medical therapies. However, experts also cited the small evidence base, lack of long-term data, serious risks associated with BT, required investment in equipment and training, and relatively small number of qualified bronchoscopists as barriers to widespread diffusion.
- **Potential for High Impact**: Lower range of high impact

Ivacaftor (Kalydeco, VX-770) for Treatment of Cystic Fibrosis in Patients with G551D-CFTR Mutation

- **Key Facts**: Current therapies for cystic fibrosis (CF) have improved median survival times, but patients with CF still have a shorter-than-normal life expectancy and require extensive treatment over a lifetime to maintain as good health as possible. Thus, an unmet need exists need for novel, effective therapy to improve outcomes in this patient population. Ivacaftor (Kalydeco™, VX-770, Vertex Pharmaceuticals, Inc., Cambridge, MA) is an oral tablet that targets the defective CF transmembrane conductance regulator (CFTR) protein that causes

CF. The drug is intended as first-line treatment for patients with the G551D-*CFTR* mutation—about 10% of patients with CF. In clinical trials, ivacaftor is administered in doses of 150 mg every 12 hours. The drug is in several phase III clinical trials cosponsored by the Cystic Fibrosis Foundation. In trials, effects on pulmonary function were reported as early as 2 weeks, and a statistically significant treatment effect was reported to be maintained through week 48. Also through week 48, investigators reported that patients given ivacaftor were 55% less likely to have a pulmonary exacerbation than patients given placebo. In October 2011, the company submitted a new drug application to FDA with a request for priority review, which FDA granted and set a decision date for April 2012.

Some financial analysts expect this drug to be priced as high as $300,000 per year, and expect that third-party payers would cover it because other effective therapies for CF are lacking. For patients without insurance or with lifetime insurance limits, the high cost could make the therapy out of reach.

- **Key Expert Comments**: Overall, experts commenting on this topic were moderately confident that this drug could meet the need for a novel effective oral treatment for CF, though this view was tempered by the fact that the drug is intended for only the 10% or so CF patients with the mutation. Because the drug would be the first genetically targeted CF therapy, and because it might have the potential to slow CF progression, the drug's greatest impact would be in shifting care models and patient management for this subgroup of CF patients, the experts thought. In addition, some experts noted that ivacaftor may have activity in patients with the F508del mutation (present in approximately 90% of all patients with CF) alone or in combination with another Vertex drug, VX-809, which is currently in phase II development. They thought that off-label use in patients with F508del and future pursuit of an indication in this population might further increase the impact of ivacaftor.
- **Potential for High Impact**: Moderately high

Pulmonary Disease, Including Asthma, Interventions

Intervention

Bronchial thermoplasty (Alair System) for treatment-resistant asthma

Asthma, a chronic inflammatory disorder of the respiratory system, is characterized by airway inflammation, airway narrowing, and bronchial hyperresponsiveness. The U.S. Centers for Disease Control and Prevention reports that about 7.3% of the adult population in the U.S. has asthma, and 5% to 15% of patients with asthma have severe, persistent asthma that does not respond sufficiently to high doses of asthma medications.[1,2]

Bronchial thermoplasty (BT) is a minimally invasive outpatient procedure used to treat adults with severe asthma that has not responded adequately to standard medical therapy. To perform the procedure, a pulmonologist delivers thermal energy using the Alair® Bronchial Thermoplasty System (Asthmatx, Inc., acquired by Boston Scientific Corp., Natick, MA). The energy is delivered to accessible airway walls (i.e., from 3 to 10 mm in diameter and distal to main stem bronchi) to a sedated patient during a series of three bronchoscopy procedures. Using a radiofrequency controller, the physician delivers energy to heat smooth muscle in the airway wall to approximately 150º F (66º C) for a period of 10 seconds. This reduces the thickness of smooth-muscle tissue mass and is intended to do so without causing charring or scarring.[3] The physician withdraws the catheter within the specific bronchial area from that site and moves to the next ablation site.[4]

BT is intended to decrease the number of severe asthma attacks on a long-term basis by reducing, debulking, or partially eliminating excess smooth muscle tissue in the patient's distal airways.[5] Each session takes less than an hour, and three sessions are needed to treat the entire lung.[5] BT is intended to treat patients with no other treatment options and might reduce, but will not eliminate, the need for asthma medication. Thus, BT is used as an adjunct to the continued use of rescue and controller medications.

In a clinical trial, the effectiveness and safety of BT versus a sham procedure in patients (n = 288) with severe asthma who remain symptomatic despite treatment with high-dose inhaled corticosteroids and long-acting beta$_2$-agonists (LABA) were evaluated.[6] Investigators reported that patients treated with BT showed superior improvement from baseline in the integrated Asthma Quality of Life Questionnaire (AQLQ) score compared with sham (BT: 1.35 ± 1.10; sham: 1.16 ± 1.23). They also reported that 79% of patients treated with BT and 64% of patients treated with sham achieved changes in AQLQ of 0.5 or greater. Six percent more BT-treated patients were hospitalized during the treatment period (up to 6 weeks after BT). In the posttreatment period (6 to 52 weeks after BT), the BT group experienced fewer severe exacerbations, emergency department (ED) visits, and days missed from work/school than the sham group.[6] In a recent followup, BT was shown to maintain reductions in severe exacerbations experienced by patients with severe persistent asthma for at least 2 years.[7]

The pulmonologist must exercise care when selecting patients suitable for BT because several other respiratory complications are associated with an increased risk of adverse events.[5,8] Although BT is intended to decrease the number of severe asthma attacks on a long-term basis, the procedure may cause a transient worsening of respiratory symptoms that generally resolves within 7 days, using standard care.[9] Consequently, physicians treat patients undergoing BT prophylactically with a systemic corticosteroid (i.e., prednisone).[10] Other potential adverse events include atelectasis, hemoptysis, anxiety, headaches, and nausea.[11]

In April 2010, the U.S. Food and Drug Administration (FDA) granted marketing approval through the premarket approval process for the Alair System "for the treatment of severe persistent asthma in patients 18 years and older whose asthma is not well controlled with inhaled corticosteroids and long acting beta agonists."[11] As a condition of approval, Asthmatx must conduct two 5-year postapproval

studies to investigate the system's long-term safety and effectiveness.[12] The diffusion of the system more than doubled from January 2011 to November 2011, perhaps as a result of acquisition of Asthmatx by Boston Scientific. In July 2010, Health Canada licensed the Alair Bronchial Thermoplasty System. Asthmatx has received Conformité Européene (CE) mark approval for the system permitting distribution in the European Union.

Results reported at the 2011 annual meeting of the American Thoracic Society stated that patients with severe refractory asthma treated with BT maintained stable lung function in the absence of clinical complications over a 5-year period.[13]

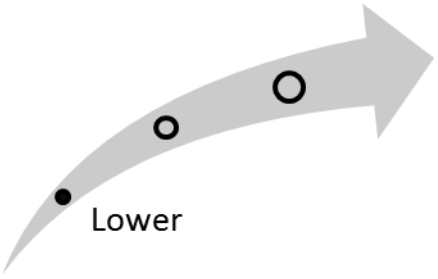
The list price of the Alair ATS 200 Controller System, which includes a radiofrequency controller and a footswitch, is $49,000. The patient return electrode is not included in the system and must be supplied by the provider. The list price of a disposable, single-use Alair Catheter Model ATS 2-5 is $2,500.

Searches of 11 representative U.S. private third-party payers that provide online medical coverage policies (i.e., Aetna, Anthem, Blue Cross/Blue Shield Alabama, Blue Cross/Blue Shield Massachusetts, CIGNA, HealthPartners, Humana, Medica, Regence, United Healthcare, Wellmark) found 10 payers that have specific policies that deny coverage and one payer that has no policy (i.e., CIGNA). On January 1, 2012, the Alair catheter becomes eligible for Medicare reimbursement through a separate "pass-through" payment when the procedure is performed in an outpatient hospital setting. The 2012 national unadjusted Hospital Prospective Payment System payment is $2,023.82.

Clinical Pathway at Point of This Intervention

Standard treatments for asthma involve establishing environmental controls of allergens and irritants, avoiding risk factors that trigger symptoms, and maintaining comprehensive pharmacologic therapy.[14] Quick-relief medications for acute asthma exacerbations and prevention of exercise-induced asthma symptoms include short-acting beta-agonists, anticholinergics, and systemic corticosteroids. Long-term control medications include inhaled corticosteroids, cromolyn sodium, nedocromil, LABAs, combination inhaled corticosteroids and LABAs, methylxanthines, and leukotriene antagonists.[14] The monoclonal antibody omalizumab selectively binds to human immunoglobulin E on the surface of mast cells and basophils, which precipitates asthmatic symptoms and can be used for patients with moderate to severe or severe allergic asthma.[14] Some patients have severe asthma that responds poorly to all forms of medical therapy.[3] At least half of these patients may be candidates for bronchial thermoplasty.[10]

Figure 1. Overall High Impact Potential: Bronchial thermoplasty (Alair System) for treatment-resistant asthma



Overall, the experts commenting on this intervention were cautiously optimistic about the potential of BT for adults with severe treatment-resistant asthma. However, the experts cited the small evidence base, lack of long-term data, serious adverse events reported, required investment in equipment and training, and lack of qualified bronchoscopists as barriers to widespread diffusion. That said, diffusion increased significantly after Boston Scientific acquired Asthmatx in fall 2010, and the number of centers and clinicians trained in the procedure more than doubled between January 2011 and November 2011. Based on this input, our overall assessment is that this intervention is in the lower end of the high potential impact range.

Results and Discussion of Comments

Seven experts with clinical, health systems, and/or research backgrounds offered their perspectives on this procedure.[15-21] The experts agreed that patients with persistent severe asthma that is unresponsive to therapy present a significant unmet medical need. The experts were split regarding their certainty of the underlying concept of BT to effectively treat severe asthma; some experts still thought the mechanism of BT action was poorly understood and had limited data to support the technology. Although some of the experts were optimistic about the early efficacy results, experts were concerned about the initial worsening of symptoms after BT and the lack of long-term efficacy/safety data. In addition, one expert with a health systems perspective pointed out that the need to still use inhalers demonstrates that this is an adjunctive therapy and may moderately improve health outcomes.

The experts stated that if BT is shown to be successful, it has the potential to change treatment and management paradigms for severe asthma because it promotes the use of a surgical/bronchoscopic option instead of some of the pharmacologic options. The experts generally agreed that the use of BT would require the purchase of equipment, put additional demand on endoscopic facilities, and necessitate the training of interventional pulmonologists. Two clinical experts disagreed about the amount of training required to implement this procedure. One expert with a health systems perspective stated that since BT will be used to treat only a subset of asthma patients, it would likely be performed in large tertiary facilities that already perform complicated procedures and this should limit time to implementation.

The experts expect the implementation of BT to increase the cost of care by requiring additional facilities, capital and disposable equipment expenditures, training, and skilled personnel; however some of these costs to the health care system may be offset by reducing the frequency of ED visits due to acute asthma attacks. Equipment and training costs are expected by some of the experts to provide a barrier to clinical acceptance. Also cited by a clinical expert as a source of controversy is a potential divide between pulmonologists and allergists regarding the procedure. One expert with a health systems perspective also cited the altered risk-benefit ratio of BT compared with pharmaceutical interventions as a potential source of controversy. Although the experts expected many patients with severe asthma to request the surgery, serious risks are also associated with the procedure, thus providing a potential barrier to acceptance.

Overall, the experts were cautiously optimistic about the potential of BT. As a new treatment modality BT may provide effective treatment for some patients with severe asthma that does not respond to current therapies. However, the experts cited the small evidence base, lack of long-term data, serious risks associated with BT, required investment in equipment and training, and lack qualified bronchoscopists as barriers to widespread diffusion.

Intervention

Ivacaftor (Kalydeco, VX-770) for treatment of cystic fibrosis in patients with G551D-CFTR mutation

Current therapies for cystic fibrosis (CF) have improved median predicted survival, but patients with CF still have a shorter-than-normal life expectancy and require extensive treatment over a lifetime to maintain good health as much as possible. Thus, an unmet need exists for novel, effective medications to improve outcomes in this patient population. Ivacaftor (Kalydeco™, VX-770, Vertex Pharmaceuticals, Inc., Cambridge, MA) is a small-molecule, cystic fibrosis transmembrane conductance regulator (*CFTR*) modulator that improves the function of the *CFTR* gene by increasing CFTR activity in transporting ions across the cell membrane to the cell surface.[22] Ivacaftor also promotes activity for two other mutations of *CFTR* (F508del and R117H) and has some effect on the wild-type *CFTR* gene. Ivacaftor targets the defective protein that causes CF and is intended as first-line treatment for the 10% of CF patients with the G551D mutation.[23] In clinical trials, ivacaftor is administered as an oral tablet in doses of 150 mg every 12 hours.[24]

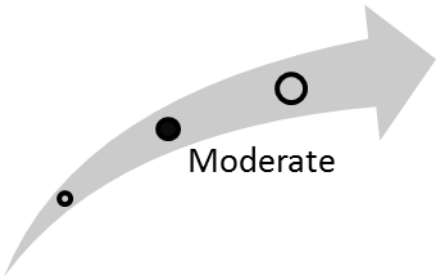
Ivacaftor is being investigated in several phase III clinical trials. In a randomized, double-blind, placebo-controlled, phase III, clinical trial, cosponsored by the Cystic Fibrosis Foundation and manufacturer, patients (n = 161) with at least one copy of CF mutation G551D given ivacaftor had a predicted forced expiratory volume in 1 second measurement that was 10.6 percentage points higher than patients treated with placebo through week 24 ($p < 0.001$).[25] Effects on pulmonary function were observed as early as 2 weeks, and a significant treatment effect was maintained through week 48. Also through week 48, patients given ivacaftor were 55% less likely to have a pulmonary exacerbation than patients given placebo ($p < 0.001$). Patients treated with ivacaftor also demonstrated a significant improvement in quality of life ($p < 0.001$). By 48 weeks, patients treated with ivacaftor had gained significantly more weight and secreted significantly less chloride in sweat samples (a key indicator for *CFTR* activity; $p < 0.001$ for both measures). The incidence of adverse events was similar with ivacaftor and placebo, with a lower proportion of serious adverse events with ivacaftor than with placebo (24% vs. 42%).[25]

In October 2011, the company submitted a new drug application to FDA for ivacaftor for treatment of CF in patients with at least one copy of the G551D-*CFTR* mutation.[26] The regulatory submission included a request for priority review, which would shorten the anticipated review time by 4 months.[26] The company was also expected to file for marketing approval in the E.U. in October 2011.[26] Some financial analysts expect this drug to be priced as high as $300,000 per year and expect third-party payers to cover it because other effective therapies for CF are lacking.

Clinical Pathway at Point of This Intervention

Routine use of inhaled medications and ventilators and/or chest physiotherapy helps to release the thick mucus associated with CF, which damages lung tissue over time. Patients with CF often require chronic use of inhaled, intravenous, or oral antibiotics to prevent or treat acute infections in lungs already weakened by disease. Lung transplantation can reduce the effects of CF for some individuals.[27] As disease progresses, some patients require mechanical breathing support, especially while asleep. Ivacaftor is intended as first-line treatment for CF patients with the G551D-*CFTR* mutation, and it can be used in conjunction with physiotherapy, mechanical devices, and antibiotics as needed.

Figure 2. Overall High Impact Potential: Ivacaftor (Kalydeco, VX-770) for treatment of cystic fibrosis in patients with G551D-CFTR mutation



Overall, experts commenting on this topic expressed some confidence that this drug had potential to meet the need for a novel treatment for CF, though this view was tempered by the facts that CF is relatively rare and this drug is intended for only the approximately 10% of CF patients with this specific mutation. Because the drug would be the first genetically targeted therapy for this disease, and because it might have potential to slow CF progression, experts thought the greatest impact would be that it would offer the first disease-modifying treatment and require genetic testing to determine which CF patients have the mutation. Because the drug is intended to be delivered orally, it is not expected to have a major impact on health care processes, such as staffing or infrastructure requirements, and thus, the experts expected it could be easily adopted. Based on this input, our overall assessment is that this intervention is in the moderate high potential impact range.

Results and Discussion of Comments

Six experts with backgrounds in clinical practice, health systems, or research offered their perspectives on this intervention.[28-33] Experts generally agreed that the unmet need for novel treatments for CF is important, particularly if those treatments are disease-modifying instead of merely palliative. However, two research-oriented experts opined that the importance of this unmet need is tempered by the fact that CF is a rare condition and that within the small population affected by CF, 90% of patients would not be eligible for this treatment.

Based on positive clinical trial results, ivacaftor appears to have a sound theory underlying its mechanism of action and potential to improve patient outcomes, the experts said. However, one health systems expert noted that clinical trials should evaluate reductions in mucus buildup in the lung and that trial results would be more meaningful if there were some improvement reported in reducing mucus production. Additionally, a clinical expert stated that it is difficult to assess how improvements in lung function correlate with quality of life. Additionally longer-term studies in younger patients are needed.

Experts were most optimistic about this drug's potential to shift the current understanding of CF by elucidating the disease state and progression. A health-systems-based expert noted, "The more we find successful gene therapies, the more we continue to search for them and the [greater the] likelihood that we will be able to find additional targeted approaches to specific illnesses."

Experts anticipated that this drug would affect current care processes and patient management by offering patients the first gene-based treatment approach for CF and shifting the focus from symptom management to treating the underlying problem. It might also obviate the need for ventilation equipment or transplantation, if the drug halts disease progression. The availability of the drug would also mean that CF patients would need to be screened for G551D-*CFTR* to determine whether they are potential candidates for the drug.

Because the drug is intended to be administered as an oral, twice-daily treatment and because of the rarity of CF, it was not anticipated to have a major impact on health care operations such as staffing and infrastructure needs by experts providing comments. However, some experts suggested that if this drug is proven to be effective, it might reduce frequency of outpatient visits and inpatient care for flares and complications for patients with the affected mutation, requiring significantly less treatment resources.

The price of the drug is currently unknown, and most experts were reluctant to predict its effect on current per-patient costs, but a couple suggested that the drug would likely be expensive. However, ivacaftor could also reduce overall care costs, if proven effective. Experts commenting on this topic thought it likely that if ivacaftor is approved, it would likely be adopted into third-party payers' formularies. Experts predicted wide and rapid patient and clinical acceptance of this drug because, aside from screening for G551D-*CFTR*, prescribing the drug does not appear to be substantially different from prescribing any other drug.

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