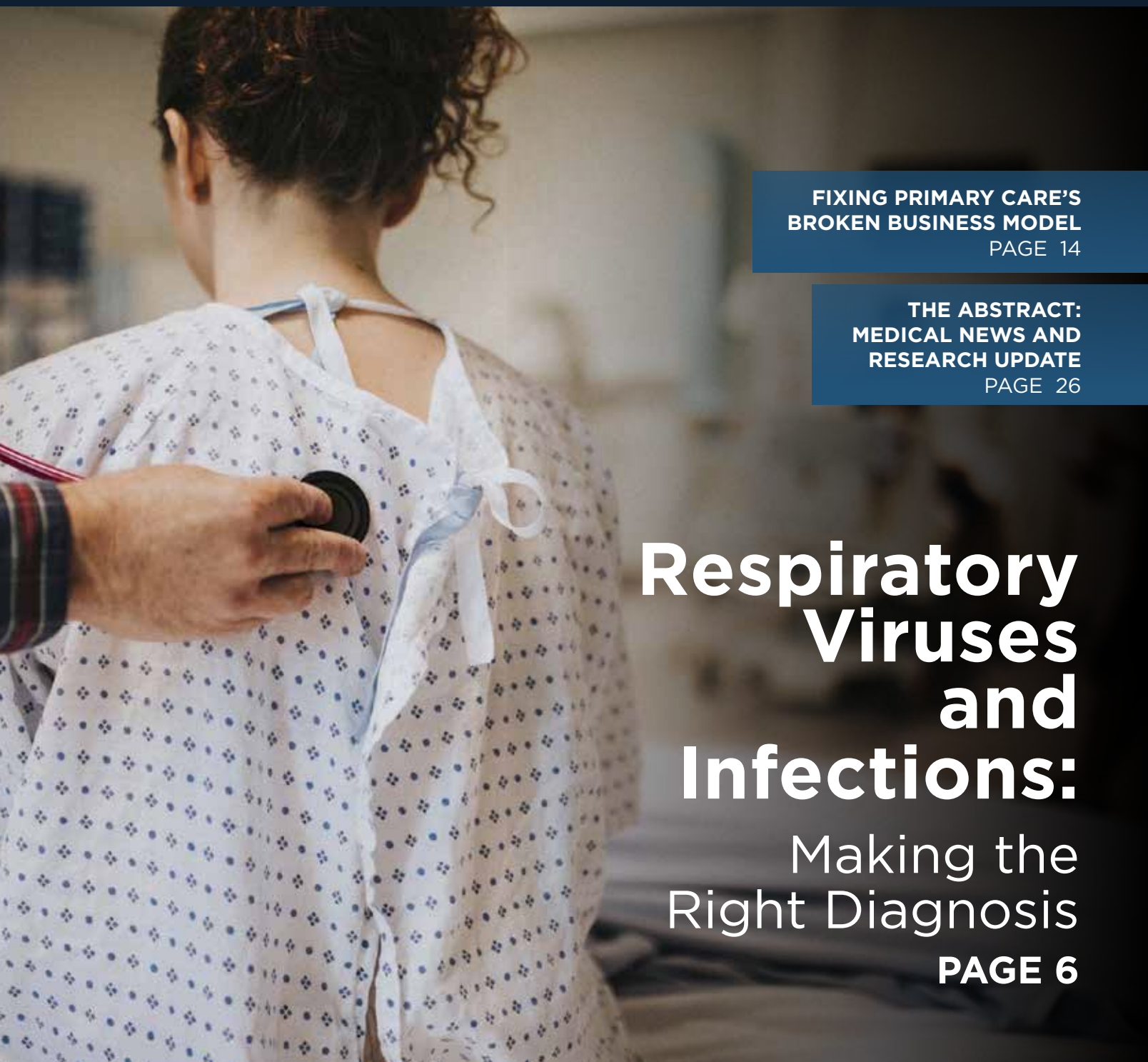
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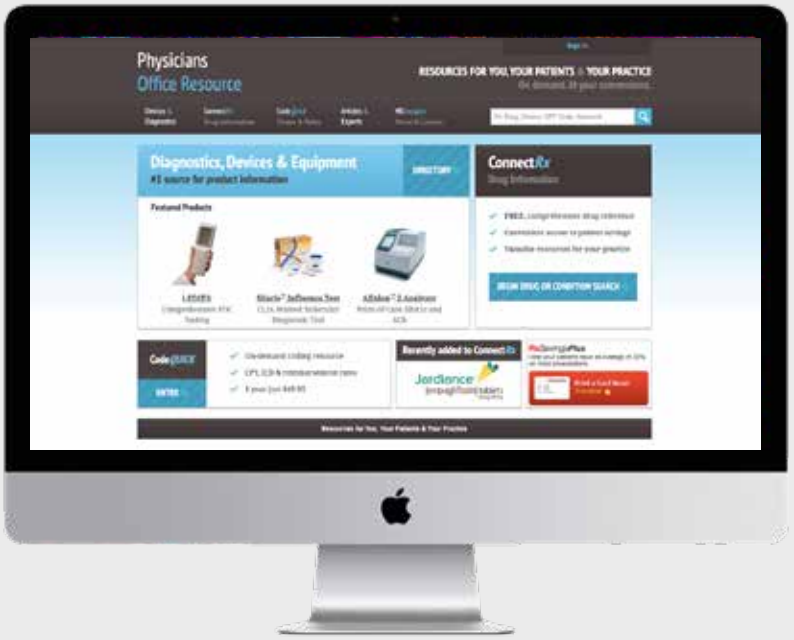
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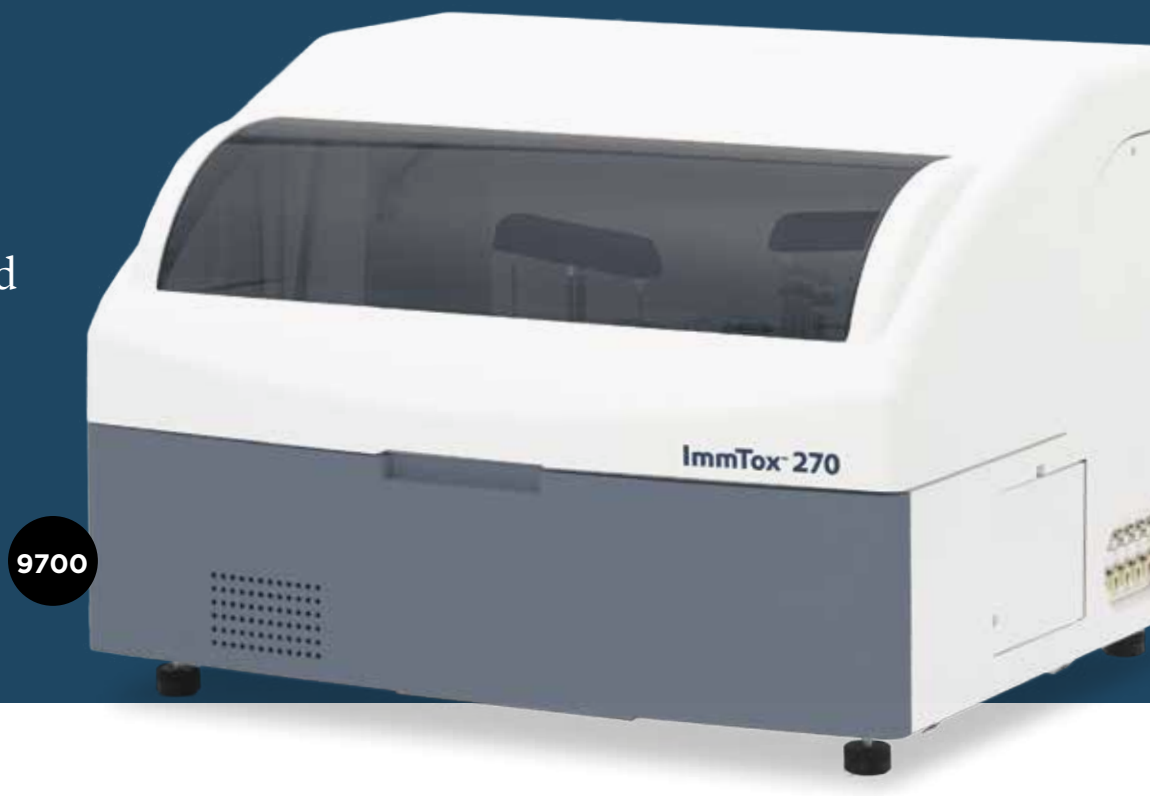
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Testing For Respiratory Viruses and Infections

When it comes to testing for flu, COVID, RSV, rhinovirus, and all the other respiratory viruses and infections out there, which test is best for you and your practice?

Learn About the Best Products for Your Practice on

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RESPIRATORY VIRUSES AND INFECTIONS

Last year as we hunkered down, to avoid the dreaded results of COVID-19, we also avoided the flu the and respiratory infections.

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FIXING PRIMARY CARE'S BROKEN BUSINESS MODEL

Primary care visits are never quick; we don't give advice over the phone; and we prioritize public agenda over patients' concerns.

26

THE ABSTRACT: MEDICAL NEWS AND RESEARCH

A new monthly column from Physicians Office Resource looking into current research and the future of medical science

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Influenza A - 96.0% (95% CI: 94.4% - 97.2%)
Influenza B - 98.1% (95% CI: 96.9% - 98.8%)

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Respiratory Viruses and Infections:

Making the Right Diagnosis

BY AARON MEDARIS, PUBLISHER PHYSICIANS OFFICE RESOURCE

Last year as we hunkered down, masked up, social distanced, and used gallons of hand sanitizer to avoid the dreaded results of COVID-19, we also avoided the flu the and a variety of other respiratory infections. Talk to any parent with young children and they'll most likely tell you that 2020 was the healthiest their kids had been in a long time. Now that we've emerged from our quarantines, shed the masks, and probably aren't as good as using the hand sanitizer as we were 12 months ago, respiratory infections are on the rise. Yes, it's true that most children who contract COVID-19 will be fine, but health officials are reporting an influx of patients, especially pediatric, with corona virus and other respiratory infections at the same time, presenting additional challenges in an already difficult situation. Are we entering in to the "perfect storm" of challenges for this cold and flu season? That is yet to be told, but rain is definitely in the forecast for the months ahead.

Assessing our current situation and looking at the forecast, what can you do to be better prepared for the increase of patients respiratory infections that will soon be entering your exam rooms? The first and one of the most important is to test for respiratory infections. That may seem simple, but this important step is often skipped because well, if it looks like a duck, and it talks like a duck, well then it's probably a duck…right? But what if there's more to it? A couple of years ago, I got really sick. Cough, fever, chills, body aches that came on hard and fast. I went to the doctor and after his examination, he told me he has seen this a lot lately and it was just a virus. I then asked if he thought it was the flu. He quickly replied, "I highly doubt it. I haven't seen any flu cases this year." This illness just felt different to me, and so I asked, "Is it ok if you test me for the flu?" He again stated he was quite certain it wasn't the flu, but that if I wanted the test he would have the nurse administer one. And wouldn't you know it, when I got the test results back, I had the flu. My good doctor prescribed an antiviral which helped immensely! A treatment I would have never received if I hadn't been tested. Could it be that all those that my physician had been seeing with similar symptoms as me had the flu as well, but were never tested for it?

Why Should You Test

Some physicians like in the example above choose not to test. Whether that's because doubts regarding the accuracy

of tests or feel that empirical treatment will be effective in most cases. Despite these concerns there are multiple reasons why you should test:

1. Empirical treatment can lead to more patients receiving antiviral treatment than actually need to receive it. This could possibly give rise to a antiviral shortage and delaying the correct care for another patient that actually needs it.

2. Testing frequently will provide the physician with valuable "market intelligence." It will help the physician understand what viruses are currently preading through the community and will allow them to provide a better treatment path.

3. Better patient experience. That might seem odd because what patient wants a stick shoved up their nose. The truth is, testing shows the patient that you want to provide the best possible care and it can bring peace of mind to the patient, even if they do test positive. They will know that they are being treated the correct way.

What to Know When Purchasing Tests

I'm sure that many of you are testing for respiratory infections. If you've talked to your distributor lately, you've probably noticed a lot of different respiratory tests out there. When it comes to testing for flu, COVID, RSV, rhinovirus, etc. which test is best for you and your practice? Here are some things to consider when evaluating which ones are best for you:

CLIA Complexity – A test is only good if you are able to administer it. Make sure that you are equipped with the correct CLIA certificate of perform the test. Check to see if the test is a Waived (most simple) or Moderately complex (requires additional certification). If you're a waived facility and are interested in purchasing a moderately complex test, that's fine, but make sure you take the steps before hand to become a certified compliance facility with CLIA.

Ease of Use – Is the test simple to perform? Difficult? Require additional equipment? Training? Will the additional equipment help me in the long run?

Performance – Sensitivity and specificity are essential. I would even be sensitive to the brand of test that I am purchasing. Especially when it comes to different COVID tests. Due to the EUA that the FDA has granted, there are many counterfeit and poor quality COVID tests that are being pushed on doctors.

Volume – How many tests are you planning on running? What's the average you use during a flu season? Will you need more this season?

Time to Results – How long does it take to run and receive test results? Is it important to get results back quickly to your patients?

Sample Type – is it a single sample type or does it allow for multiple sample types (nasal, nasopharyngeal, saliva, etc.)?

Connectivity – Is it important to have the results transmitted electronically?

Cost – Brand is important when it comes to getting accurate results. But brand can also be expensive. Be sure to check with different brand reps, distributors, websites, publications, and promo emails for discounts and specials. They're out there.

What Types of Tests are Available?

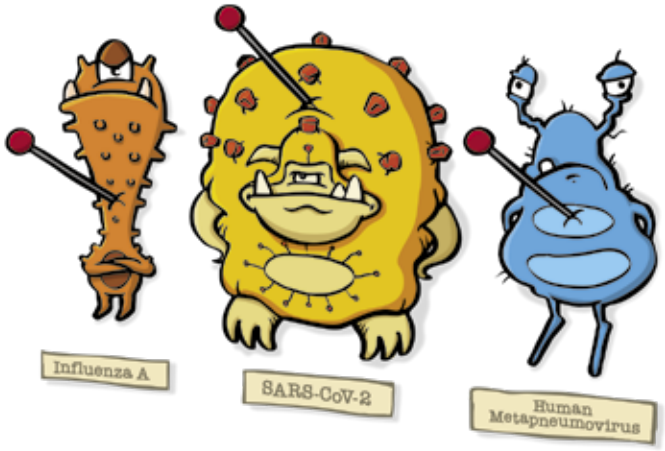
Rapid Lateral Flow Immunochemical Tests:
There are different varieties of these test which have been on the market for decades and are used to confirm the presence or absence of a specific antigen. Results of these types of tests can either be viewed visually or with the use of an instrument. May of these tests are CLIA Waived and can be completed in less than 15 minutes.

Molecular Tests:
Many flu and other respiratory infections can be run on molecular devices. These tests detect the presence of the genetic material of the virus and generally produce results in 30 minutes or less. Molecular results are the gold standard in testing. Be sure to verify the CLIA compliance that is needed for molecular tests, some are CLIA Waived and some require a moderate complexity license. CLIA Waived molecular test typically use rapid PCR detection and the device can be moved closer to the point of care. CLIA Waived molecular devices usually cost less than traditional molecular devices, but still offer the same reimbursement.

One important thing to note is that no respiratory test provides 100% accuracy. Results depend on a few different criteria: type of test used, virus strain, and integrity of the sample. For best results please review test instructions and be aware of any test limitations.

Be Prepared

I don't know if we are heading towards and "perfect storm" of challenges, but I do know that whatever the forecast is you can be prepared. Physicians Office Resource offers valuable insights on a variety of different respiratory infection tests and testing devices. Look for them in this issue or visit our website and learn more. Have questions feel free to reach out and we'll be sure to put you in contact with the right people.



Pinpoint SARS-CoV-2 and 18 other bugs.

The new BioFire® Respiratory 2.1-EZ (RP2.1-EZ) Panel[1] covers COVID-19 detection in your clinic.

SARS-CoV-2 is everyone's top suspect, but many other respiratory bugs can cause similar, overlapping symptoms. In your clinic, you can test for 19 common respiratory pathogens, including SARS-CoV-2, with the BioFire RP2.1-EZ Panel—now available under an FDA Emergency Use Authorization.[1,2]



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To learn more, visit **biofiredx.com**

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Syndromic Testing: The Right Test, The First Time.

1. This test has not been FDA cleared or approved. This test has been authorized by FDA under an EUA for use by authorized laboratories. This test has been authorized only for the detection and differentiation of nucleic acid of SARS-CoV-2 from multiple respiratory viral and bacterial organisms. This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.
2. For use with the CLIA-waived BioFire® FilmArray® 2.0 EZ configuration.

BFR0001-0515-01



CLIA-WAIVED BIOFIRE® FILMARRAY® RESPIRATORY PANEL (RP) EZ

From BioFire

The BioFire RP EZ accurately detects and identifies 14 viral and bacterial pathogens—not just Flu A and Flu B—so you can provide your patients with the right treatment, the first time. The test is easy and can be performed right in your office or clinic, with results in about an hour. The BioFire RP EZ is designed to run on a single computer/instrument configuration (EZ Configuration) of the BioFire® FilmArray® 2.0 System.

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BD VERITOR™ PLUS SYSTEM

From BD Veritor™

The BD Veritor™ Plus System is a portable, easy-to-use, testing solution for SARS-COV-2*, Flu A+ B and other respiratory tract infections that delivers results in 15 minutes or less. It features two analysis modes that adapt to your workflow, online education tools, and optional reporting capabilities including the BD Synapsys™ Informatics Solution—making it the point-of-care diagnostic tool you won't want to be without.

*EUA authorized by FDA

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FIRST EUA POINT-OF-CARE (POC/WAIVED/ FINGERSTICK) COVID-19 ANTIBODY TEST NOW AVAILABLE

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#1 MOST PRESCRIBED TREATMENT FOR TARDIVE DYSKINESIA[1]

THE SIMPLE CHOICE

FOR YOUR PATIENTS WITH TARDIVE DYSKINESIA (TD)



Not actual size.

ONLY INGREZZA OFFERS ALL THE EASE OF[2]:

- One capsule, once daily
- **3** Effective dosing options
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- Taken with or without food

Give your patients all the ease of INGREZZA. See more at **INGREZZAHCP.com/Dosing**

Important Information

INDICATION & USAGE

INGREZZA® (valbenazine) capsules is indicated for the treatment of adults with tardive dyskinesia.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

INGREZZA is contraindicated in patients with a history of hypersensitivity to valbenazine or any components of INGREZZA. Rash, urticaria, and reactions consistent with angioedema (e.g., swelling of the face, lips, and mouth) have been reported.

WARNINGS & PRECAUTIONS

Somnolence
INGREZZA can cause somnolence. Patients should not perform activities requiring mental alertness such as operating a motor vehicle or operating hazardous machinery until they know how they will be affected by INGREZZA.

QT Prolongation
INGREZZA may prolong the QT interval, although the degree of QT prolongation is not clinically significant at concentrations expected with recommended dosing. INGREZZA should be avoided in patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval. For patients at increased risk of a prolonged QT interval, assess the QT interval before increasing the dosage.

WARNINGS & PRECAUTIONS (continued)

Parkinsonism
INGREZZA may cause parkinsonism in patients with tardive dyskinesia. Parkinsonism has also been observed with other VMAT2 inhibitors. Reduce the dose or discontinue INGREZZA treatment in patients who develop clinically significant parkinson-like signs or symptoms.

ADVERSE REACTIONS

The most common adverse reaction (≥5% and twice the rate of placebo) is somnolence. Other adverse reactions (≥2% and >Placebo) include: anticholinergic effects, balance disorders/falls, headache, akathisia, vomiting, nausea, and arthralgia.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit MedWatch at **www.fda.gov/medwatch** or call 1-800-FDA-1088.

Please see the adjacent page for Brief Summary of Prescribing Information and visit Neurocrine.com/INGREZZAPI for full Prescribing Information.

REFERENCES: 1. Data on file. Neurocrine Biosciences, Inc. **2.** INGREZZA [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.

Neurocrine BIOSCIENCES

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INGREZZA® (valbenazine) capsules
for oral use

Brief Summary: for full Prescribing Information and Patient Information, refer to package insert.

INDICATION AND USAGE
INGREZZA® (valbenazine) capsules is indicated for the treatment of adults with tardive dyskinesia.

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WARNINGS AND PRECAUTIONS
Somnolence

INGREZZA can cause somnolence. Patients should not perform activities requiring mental alertness such as operating a motor vehicle or operating hazardous machinery until they know how they will be affected by INGREZZA.

QT Prolongation

INGREZZA may prolong the QT interval, although the degree of QT prolongation is not clinically significant at concentrations expected with recommended dosing. In patients taking a strong CYP2D6 or CYP3A4 inhibitor, or who are CYP2D6 poor metabolizers, INGREZZA concentrations may be higher and QT prolongation clinically significant. For patients who are CYP2D6 poor metabolizers or are taking a strong CYP2D6 inhibitor, dose reduction may be necessary. For patients taking a strong CYP3A4 inhibitor, reduce the dose of INGREZZA to 40 mg once daily. INGREZZA should be avoided in patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval. For patients at increased risk of a prolonged QT interval, assess the QT interval before increasing the dosage.

Parkinsonism

INGREZZA may cause parkinsonism in patients with tardive dyskinesia. Parkinsonism has also been observed with other VMAT2 inhibitors. In the 3 placebo-controlled clinical studies in patients with tardive dyskinesia, the incidence of parkinson-like adverse events was 3% of patients treated with INGREZZA and <1% of placebo-treated patients. Postmarketing safety reports have described parkinson-like symptoms, some of which were severe and required hospitalization. In most cases, severe parkinsonism occurred within the first 2 weeks after starting or increasing the dose of INGREZZA. Associated symptoms have included falls, gait disturbances, tremor, drooling, and hypokinesia. In cases in which follow-up clinical information was available, parkinson-like symptoms were reported to resolve following discontinuation of INGREZZA therapy. Reduce the dose or discontinue INGREZZA treatment in patients who develop clinically significant parkinson-like signs or symptoms.

ADVERSE REACTIONS
The following adverse reactions are discussed in more detail in other sections of the labeling:

- Hypersensitivity
- Somnolence
- QT Prolongation
- Parkinsonism

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Variable and Fixed Dose Placebo-Controlled Trial Experience

The safety of INGREZZA was evaluated in 3 placebo-controlled studies, each 6 weeks in duration (fixed dose, dose escalation, dose reduction), including 445 patients. Patients were 26 to 84 years of age with moderate to severe tardive dyskinesia and had concurrent diagnoses of mood disorder (27%) or schizophrenia/schizoaffective disorder (72%). The mean age was 56 years. Patients were 57% Caucasian, 39% African-American, and 4% other. With respect to ethnicity, 28% were Hispanic or Latino. All subjects continued previous stable regimens of antipsychotics; 85% and 27% of subjects, respectively, were taking atypical and typical antipsychotic medications at study entry.

Adverse Reactions Leading to Discontinuation of Treatment

A total of 3% of INGREZZA treated patients and 2% of placebo-treated patients discontinued because of adverse reactions.

Common Adverse Reactions

Adverse reactions that occurred in the 3 placebo-controlled studies at an incidence of ≥2% and greater than placebo are presented in Table 1.

Table 1: Adverse Reactions in 3 Placebo-Controlled Studies of 6-week Treatment Duration Reported at ≥2% and >Placebo

Adverse Reaction[1]	INGREZZA (n=262) (%)	Placebo (n=183) (%)
General Disorders		
Somnolence (somnolence, fatigue, sedation)	10.9%	4.2%
Nervous System Disorders		
Anticholinergic effects (dry mouth, constipation, disturbance in attention, vision blurred, urinary retention)	5.4%	4.9%
Balance disorders/fall (fall, gait disturbance, dizziness, balance disorder)	4.1%	2.2%
Headache	3.4%	2.7%
Akathisia (akathisia, restlessness)	2.7%	0.5%
Gastrointestinal Disorders		
Vomiting	2.6%	0.6%
Nausea	2.3%	2.1%
Musculoskeletal Disorders		
Arthralgia	2.3%	0.5%

[1] Within each adverse reaction category, the observed adverse reactions are listed in order of decreasing frequency.

Other Adverse Reactions Observed During the Premarketing Evaluation of INGREZZA

Other adverse reactions of ≥1% incidence and greater than placebo are shown below. The following list does not include adverse reactions: 1) already listed in previous tables or elsewhere in the labeling, 2) for which a drug cause was remote, 3) which were so general as to be uninformative, 4) which were not considered to have clinically significant implications, or 5) which occurred at a rate equal to or less than placebo.

Endocrine Disorders: blood glucose increased

General Disorders: weight increased

Infectious Disorders: respiratory infections

Neurologic Disorders: drooling, dyskinesia, extrapyramidal symptoms (non-akathisia)

Psychiatric Disorders: anxiety, insomnia

During controlled trials, there was a dose-related increase in prolactin. Additionally, there was a dose-related increase in alkaline phosphatase and bilirubin, suggesting a potential risk for cholestasis.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of INGREZZA that are not included in other sections of labeling. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders: hypersensitivity reactions (including allergic dermatitis, angioedema, pruritis, and urticaria)

Skin and Subcutaneous Tissue Disorders: rash

DRUG INTERACTIONS
Drugs Having Clinically Important Interactions with INGREZZA

Table 2: Clinically Significant Drug Interactions with INGREZZA

Monoamine Oxidase Inhibitors (MAOIs)	
Clinical Implication:	Concomitant use of INGREZZA with MAOIs may increase the concentration of monoamine neurotransmitters in synapses, potentially leading to increased risk of adverse reactions such as serotonin syndrome, or attenuated treatment effect of INGREZZA.
Prevention or Management:	Avoid concomitant use of INGREZZA with MAOIs.
Examples:	isocarboxazid, phenelzine, selegiline
Strong CYP3A4 Inhibitors	
Clinical Implication:	Concomitant use of INGREZZA with strong CYP3A4 inhibitors increased the exposure (Cmax and AUC) to valbenazine and its active metabolite compared with the use of INGREZZA alone. Increased exposure of valbenazine and its active metabolite may increase the risk of exposure-related adverse reactions.
Prevention or Management:	Reduce INGREZZA dose when INGREZZA is coadministered with a strong CYP3A4 inhibitor.
Examples:	itraconazole, ketoconazole, clarithromycin
Strong CYP2D6 Inhibitors	
Clinical Implication:	Concomitant use of INGREZZA with strong CYP2D6 inhibitors increased the exposure (C_{max} and AUC) to valbenazine's active metabolite compared with the use of INGREZZA alone. Increased exposure of active metabolite may increase the risk of exposure-related adverse reactions.
Prevention or Management:	Reduce INGREZZA dose when INGREZZA is coadministered with a strong CYP2D6 inhibitor.
Examples:	paroxetine, fluoxetine, quinidine
Strong CYP3A4 Inducers	
Clinical Implication:	Concomitant use of INGREZZA with a strong CYP3A4 inducer decreased the exposure of valbenazine and its active metabolite compared to the use of INGREZZA alone. Reduced exposure of valbenazine and its active metabolite may reduce efficacy.
Prevention or Management:	Concomitant use of strong CYP3A4 inducers with INGREZZA is not recommended.
Examples:	rifampin, carbamazepine, phenytoin, St. John's wort[1]
Digoxin	
Clinical Implication:	Concomitant use of INGREZZA with digoxin increased digoxin levels because of inhibition of intestinal P-glycoprotein (P-gp).
Prevention or Management:	Digoxin concentrations should be monitored when coadministering INGREZZA with digoxin. Increased digoxin exposure may increase the risk of exposure-related adverse reactions. Dosage adjustment of digoxin may be necessary.

[1] The induction potency of St. John's wort may vary widely based on preparation.

Drugs Having No Clinically Important Interactions with INGREZZA

Dosage adjustment for INGREZZA is not necessary when used in combination with substrates of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2E1, or CYP3A4/5 based on *in vitro* study results.

OVERDOSAGE
Human Experience

The pre-marketing clinical trials involving INGREZZA in approximately 850 subjects do not provide information regarding symptoms with overdose.

Management of Overdosage

No specific antidotes for INGREZZA are known. In managing overdose, provide supportive care, including close medical supervision and monitoring, and consider the possibility of multiple drug involvement. If an overdose occurs, consult a Certified Poison Control Center (1-800-222-1222 or www.poison.org).

For further information on INGREZZA, call 84-INGREZZA (844-647-3992).

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CP-VBZ-US-0203v5 05/2020



Fixing primary care's broken business model

BY HANS DUVEFELT, MD

Primary care visits are never quick; we don't give much advice over the phone or online; and we prioritize the government's and insurance companies' public health agenda over our own patients' concerns.

Imagine health care as a retail customer experience for a few minutes:

Imagine you're going to Walmart to buy a bag of dog food, a new coffee maker or to equip a small kitchen in your newly built mother-in-law apartment.

1. You've bought dog food there before, so you know exactly where it is. You just want to quickly grab a bag and get out of there.

2. You have a rough idea of where the coffee makers are; you know some brands you trust, but you might have one or two questions before you select one, and if they don't have one you like, you might get it somewhere else. Or, you might even check their website to see which models they carry.

3. For the new kitchen, you have a list, but know you probably haven't thought of everything, so you plan to walk down the aisles in the kitchen and home departments. You plan to spend a fair amount of money, so you might be on the lookout for special sales or promotions. But, you definitely don't want someone else to choose all the items for you.

Can Walmart meet your needs in all these situations? Probably yes.

Now, think about how your doctor's office works

1. Can you quickly get in and out if you have a simple problem like conjunctivitis?

2. Are they able to give you information on what your options are for a recurring shoulder dislocation; could they refer you to a shoulder specialist without first waiting weeks to see your primary care doctor?

3. You have lots of issues and try to get an appointment to deal with them all at once; you think of it as a physical, but last time you had a physical, your doctor brought up all kinds of things you don't particularly see as priorities for yourself.

Here are the existing realities of primary care

We can't afford to just see you for something quick. Our quality indicators, which more and more will determine how we get paid, will go down if we don't screen you at every visit and offer interventions for depression, smoking, alcohol misuse, hypertension, weight management, immunization needs and much more.

We won't refer you without seeing you, and we often hesitate giving you medical advice over the phone. Our providers are not scheduled for anything else besides seeing patients, because the rules of how we are paid still emphasize face-to-face visits over "population management." So our providers are busy all day long seeing patients for visits that could have been simple but are loaded up with mandatory screenings and interventions and our medical assistants, besides being busy with all our screening questionnaires, are discouraged from giving medical advice they aren't formally trained to provide.

Is there a doctor shortage?

We are said to have a doctor shortage. We have an aging population with more and more chronic diseases, like diabetes and heart disease. The need for skilled and experienced medical providers is continually increasing.

We have no public health system to speak of in this country, so the government, through Medicare and Medicaid, has mandated that health care providers do the things the public health system does in other countries.

This is, plain and simple, what is clogging up the works in health care today: Too much non-doctor work is crammed into each patient visit, and we can't charge for giving advice or directing care except in a face-to-face visit.

You don't need to go to medical school to give immunizations, tell people smoking is bad for you, explain that "low fat" foods cause obesity, or promote regular exercise. You don't even need to be a doctor, PA or NP to screen for high blood pressure – only to treat it. (Some pundits, in utter desperation, have suggested we send pharmacists to school to learn how to treat hypertension, but there are of course plenty of licensed medical providers who are able and willing to do that if we get freed up from the less-skilled tasks I just listed above.)

Patients and doctors have no control

Now, why are we doing all those things we do if they are so inefficient? Quite simply, whoever pays us has the power to define our work. We call that "health insurance," but that is not exactly what we are dealing with. Insurance, for home, auto or employer liability, has nothing to do with predictable events or minor issues. Your car insurance doesn't pay for oil changes or tire wear, not even for a minor paint scratch. But somehow that is what we expect health insurance to cover for our bodies. In terms of auto insurance, most people probably figure an insurance job carries an inflated price tag and lots of paperwork. The same is true for health care, which should not be a surprise to anyone.

For example, years ago the overhead cost of insurance billing for each primary care doctor was reported to be $80,000. That, put very plainly, is money that patients and employers are ultimately paying through premiums and deductibles.

And all the mandated screenings are there because Medicare, in particular, has the right to micromanage doctors' work because they are paying for health care visits, which could be quicker and less costly if patients had control over their health care spending.

How could we do better?

We do three things in primary care, each with its own workflow and, really, each with its own economics.

1. We could do our part of public health more effectively. Allow us to promote immunizations and other primary preventions outside our already crammed fifteen-minute visits. Pay us a per patient per year stipend to reach out to target populations through mail, phone, web or, when appropriate, in person about general health issues. Stop imagining we can do all of it and still treat diseases, acute and chronic, in our measly fifteen minutes. Right now, that is just clicking boxes with little actual substance. Use some of the government money that should have been spent on a working public health system if you want us to step in and do the government's work.

2. Make it economically feasible for medical providers to oversee patient care by acknowledging that reading incoming reports, answering phone or web inquiries and coordinating care with specialists and hospitals are essential parts of being a medical home for patients. Such activities should not be unpaid services eked out at the expense of lunch, bathroom breaks or dinner with our families.

3. Allow us to define each office visit together with our patients. It is insulting to everyone involved to have to interrogate someone with a splitting headache, twisted ankle or bleeding laceration about their diet and alcohol habits. I could see many more patients if I could delegate those things to outreach staff or simply not do it every visit. Right now we are made to act as if we will never see that patient again. I was trained to provide care over time, in a relationship based practice. That is proven to be an effective and fiscally sound way to deliver health care.

The third task is the only one that makes sense to pay us for on a per-visit basis, whereas the first two deserve their own payment method. Personally, I wonder if the first few hundred dollars worth of primary care visits are worth churning through the expensive bureaucratic insurance machinery, or if it wouldn't make more sense to just allow each patient a set amount of spending at their discretion.

I am not writing about privately financed, direct primary care or concierge medicine. Those obviously exist, and may work well for many people, but the health care payment options for most Americans are what desperately need fixing.

Only if we acknowledge that public health, population health, and face-to-face visits are three separate aspects of health care can we move forward in reforming primary care. And only if we recognize and reimburse physicians' non-face-to-face work fairly will we see the improved customer service and doctor-patient communications we are now only paying lip service to.

Where would Google be if we had to make an appointment to sit down with a search consultant and pose our questions, fifteen minutes at a time? It may be an outlandish analogy, but health care needs some shaking up.

Hans Duvefelt, MD is a Family Physician, Writer, Teacher and Mentor. You can read more of his articles at acountrydoctorwrites.wordpress.com

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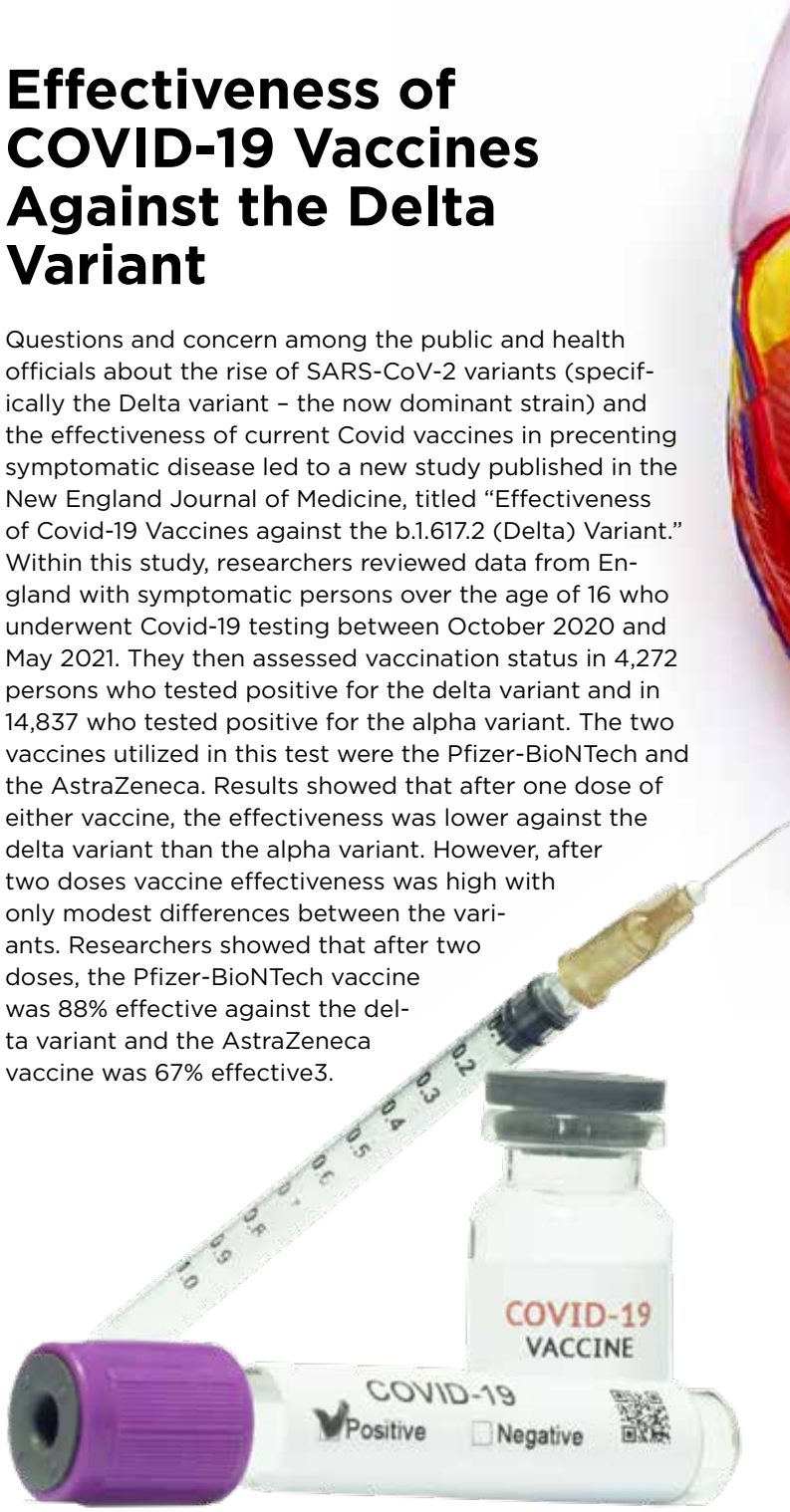
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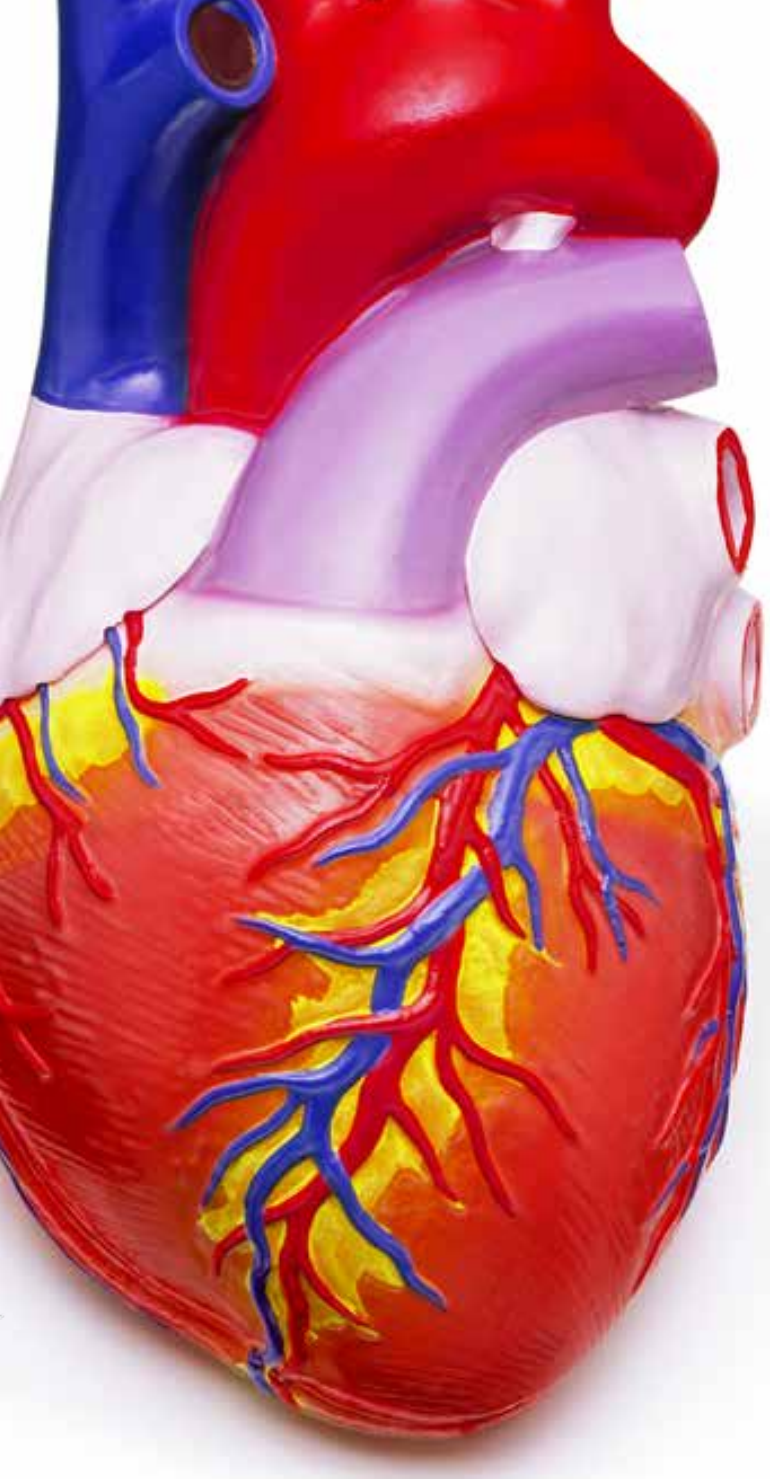
Artificial Intelligence Models Show 17 Potential FDA Approved Drugs to Help Treat COVID-19

While vaccines provide the best way to prevent COIVD-19, researchers have been working to find ways to treat COVID may have just found some hope in several drugs already FDA approved. In a recent study published in the Proceedings of the National Academy of Science of the United State of America5, researchers at the University of Michigan utilized artificial intelligence powered image analysis of human cell lines during infection with the coronavirus. In this computer model, cells were treated in over 1,400 individual FDA approved drugs either before or after viral infection. This resulted in 17 potential therapies, 10 of which were new to the science community. Dr. Johathan Sexton, Ph.D assistant professor of Internal medicine at the University of Michigan Medical School and one of the senior authors on the paper said, "Traditionally, the drug development process takes a decade—and we just don't have a decade. The therapies we discovered are well positioned for phase 2 clinical trials because their safety has already been established."6 One of the surprises of this study was the anti-viral activity of lactoferrin, a protein found naturally in human breast milk that can also be found over the counter in a dietary supplement derived from cow's milk. Dr. Sexton went on to say, "We found lactoferrin had remarkable efficacy for preventing infection, working better than anything else we observed."6 In their article published in PNAS, researchers mention that lactoferrin "inhibits SARS-CoV-2 infection in the nanomolar range in all cell models with multiple modes of action, including blockage of virus attachment to cellular heparan sulfate and enhancement of interferon responses."5

Effectiveness of COVID-19 Vaccines Against the Delta Variant

Questions and concern among the public and health officials about the rise of SARS-CoV-2 variants (specifically the Delta variant – the now dominant strain) and the effectiveness of current Covid vaccines in precenting symptomatic disease led to a new study published in the New England Journal of Medicine, titled "Effectiveness of Covid-19 Vaccines against the b.1.617.2 (Delta) Variant." Within this study, researchers reviewed data from England with symptomatic persons over the age of 16 who underwent Covid-19 testing between October 2020 and May 2021. They then assessed vaccination status in 4,272 persons who tested positive for the delta variant and in 14,837 who tested positive for the alpha variant. The two vaccines utilized in this test were the Pfizer-BioNTech and the AstraZeneca. Results showed that after one dose of either vaccine, the effectiveness was lower against the delta variant than the alpha variant. However, after two doses vaccine effectiveness was high with only modest differences between the variants. Researchers showed that after two doses, the Pfizer-BioNTech vaccine was 88% effective against the delta variant and the AstraZeneca vaccine was 67% effective3.





New Heart Disease Drug Approved in the UK Hailed as "Life Changing"

It's long been known that too much LDL cholesterol can lead to a buildup of plaques in the blood vessels. Plaque build-ups deprive the flow of oxygen rich blood to the heart which can lead to heart attacks and strokes. A new drug developed by Novaris called Inclisiran is the first drug to utilize RNA interference to help remove LDL from the bloodstream. Inclisiran silences a gene called PCSK9, by doing so Inclisiran helps the liver absorb more LDL cholesterol from the blood and break it down. The therapy is delivered via injection and could cut LDL cholesterol levels by 50%. Studies also noted that Inclisiran when combined with a statin could reduce cholesterol levels by 75-80%. The National Health Service of England and Wales estimate that if "300,000 people receive the drug as planned, a projected 30,000 people could avoid premature death due to heart attacks and stroke."8

Maternal Speech Increases Oxytocin Levels and Decreases Pain Scores in Preterm infants During Painful Procedures

15 MILLION premature infants are born worldwide every year and are often faced with early maternal separation and painful procedures which can have short and long term effects on their neurodevelopment. In an article in Nature published on August 27, 2021, researchers wanted to see "whether the mother's voice could provide an effective and safe analgesia for preterm infants and whether endogenous oxytocin (OXT) could be linked to pain modulation."4 In this study, 20 preterm infants when undergoing painful procedures had their OXT levels in saliva and plasma cortisol levels measured, and the Premature Infant Pain Profile was blindly coded by trained psychologist. When the mother was speaking to the child during the procedure, Premature Infant Pain Profile scores significantly decreased, along with an increase of OXT levels over the baseline. No effects on cortisol levels were found.4

Ultrasound Activates Genetically Engineered Immune Cells to Safely Attack Tumors in Mice

CAR T Cell (chimeric antigen receptor) therapy is a type of treatment in which a patient's T cells are changed in the laboratory so they will attack cancer cells. Large numbers of these CAR T cells are grown in a laboratory and given to the patient by infusion. This type of treatment has been used to treat certain blood caners, but not solid tumors. The reason being is the CAR T cells are always turned on and are very potent – destroying not only cancer cells, but normal healthy cells. In a recent article published in Nature Biomedical Engineering titled, "Control of the activity of CAR-T cells within tumours via focused ultrasound,"7 researchers at UC San Diego took CAR T cells and re-engineered them so that they only express the CAR protein when ultrasound energy is applied. Thus, allowing the researchers to turn on the CAR T proteins and focus them on a specific spot in the body. The scientist tested their hypothesis on mice with solid tumors. Taking the mice and injecting them with the re-engineered CAR T cells, they then used an ultrasound transducer on the area of the skin on top of the tumor. The heat from the ultrasound activated the CAR T cells over the tumor, attacking the tumor but keeping surrounding tissue and cells safe. Though still early in its research, the work looks promising for new therapies to treat solid tumors.

Pulmonary Fibrosis Reversed in Mice Utilizing Existing FDA-approved Drug

Pulmonary fibrosis occurs when lung tissue becomes damaged and scarred, leading to thick and stiff tissue making it more difficult for lungs to function properly. Scarring is caused by a multitude of factors and in most cases doctors are not able to pinpoint the exact cause. Currently there is no cure, and mortality often happens within a few years; though there are certain therapies can sometimes ease symptoms1. Promising results were published recent article in the journal Nature, researchers at the University of Alabama are starting to make headway on a possible reversal of this disease. Utilizing mice models and an already approved FDA drug called ABT-199 (currently approved for treating types of leukemia), scientists treated the mice with lung fibrosis with the drug and after 21 days the mice's lung architecture had returned to normal. This specific test was initiated when researchers discovered that human patients with pulmonary fibrosis exhibited higher amounts of Bcl-2, a regulator of apoptosis, in their lung immune cells. With higher levels of Bcl-2, macrophages refused to die off after completing their work, which lead to lung damage caused by pulmonary fibrosis. Research is still in the early stages but scientists are hopeful this will lead to new therapies for treating pulmonary fibrosis in humans.2

Sources

1. Mayo Clinic
Pulmonary Fibrosis
https://www.mayoclinic.org/diseases-conditions/pulmonary-fibrosis/symptoms-causes/syc-20353690

2. Nature
Targeting Cpt1a-Bcl-2 interaction modulates apoptosis resistance and fibrotic remodeling
https://www.nature.com/articles/s41418-021-00840-w

3. New England Journal of Medicine
Effectiveness of Covid-19 Vaccines against the b.1.617.2 (Delta) Variant
https://www.nejm.org/doi/full/10.1056/NEJMoa2108891?query=featured_coronavirus

4. Nature
Maternal speech decreases pain scores and increases oxytocin levels in preterm infants during painful procedures
https://www.nature.com/articles/s41598-021-96840-4

5. Proceedings of the National Academy of Science of the United State of America
Morphological cell profiling of SARS-CoV-2 infection identifies drug repurposing candidates for COVID-19
https://www.pnas.org/content/118/36/e2105815118

6. Existing drugs kill SARS-CoV-2 in cells
https://labblog.uofmhealth.org/lab-report/existing-drugs-kill-sars-cov-2-cells

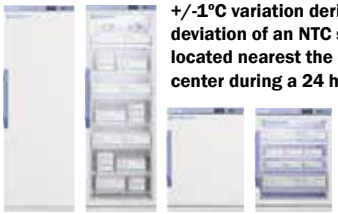
7. Nature Biomedical Engineering
Control of the activity of CAR-T cells within tumours via focused ultrasound
https://www.nature.com/articles/s41551-021-00779-w

8. Cholesterol-lowering jab could save over 30,000 lives
https://www.medicalnewstoday.com/articles/cholesterol-lowering-jab-could-save-over-30000-lives#Why-inclisiran-is-deemed-life-changing

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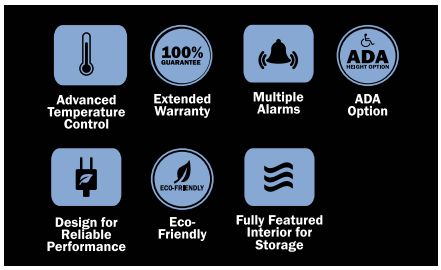


Refrigeration designed and purpose-built for pharmacy, medication, and vaccination applications to support meeting CDC/VFC vaccine storage guidelines

9741

Advanced Temperature Control & Durable Performance

- Intelligent microprocessor digital temperature controller
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Pharma-Vac Refrigerators

Accucold	Capacity	Height	Width	Depth	Door	PRICE
ARS1PV	1 cu.ft.	21.5"	17.5"	19.5"	White	**865.00**
ARG1PV	1 cu.ft.	21.5"	17.5"	20"	Glass	**878.00**
ARS3PV	3 cu.ft.	33.75"	18.5"	19"	White	**965.00**
ARG3PV	3 cu.ft.	33.75"	18.5"	19.5"	Glass	**969.00**
ARS6PV	6 cu.ft.	32.5"	23.5"	24.5"	White	**1,060.00**
ARG6PV	6 cu.ft.	32.5"	23.5"	25"	Glass	**1,072.00**
ARS8PV	8 cu.ft.	50"	23.38"	24.5"	White	**1,284.00**
ARG8PV	8 cu.ft.	50"	23.38"	25"	Glass	**1,349.00**
ARS12PV	12 cu.ft.	61.75"	23.38"	24.5"	White	**1,788.00**
ARG12PV	12 cu.ft.	61.75"	23.38"	25"	Glass	**1,801.00**
ARS15PV	15 cu.ft.	72"	23.5"	24.5"	White	**1,970.00**
ARG15PV	15 cu.ft.	72"	23.5"	25"	Glass	**1,983.00**

models with data loggers are available

Pharma-Lab Refrigerators

Accucold	Capacity	Height	Width	Depth	Door	PRICE
ARS23ML	23 cu.ft.	83.75	27.5	31	(1) Stainless	**2,466.00**
ARG23ML	23 cu.ft.	83.75	27.5	31	(1) Glass	**2,811.00**
ARS49ML	49 cu.ft.	83.75	55.25	31	(2) Stainless	**3,634.00**
ARG49ML	49 cu.ft.	83.75	55.25	31	(2) Glass	**4,186.00**

Pharma-Lab Freezers

Accucold	Capacity	Height	Width	Depth	Door	PRICE
AFS23ML	23 cu.ft.	83.75	27.5	31	(1) Stainless	**2,804.00**
AFS49ML	49 cu.ft.	83.75	55.25	31	(2) Stainless	**4,299.00**

visit www.medicaldevicedepot.com for all product information and options

Choosing the Right Sized Unit

Below are a few handy steps for determining the ideal Accucold refrigerator size for your clinic:

1 Estimate the maximum number of doses of publicly-provided vaccine and privately purchased vaccine that will be in your refrigerator.

Refrigerator: Add the number of doses on hand (current inventory) from your last order form.

Public Vaccine _____

Private Vaccine + _____

Total doses = _____

Multiply (max inventory) **x 1.25**

Maximum doses = _____

2 Match your maximum doses with the minimum cubic feet needed to safely store your vaccine

Max. Doses	Minimum Cubic Ft.
2,000+ doses	may need more than one refrigerator
1000-2000	40 cu.ft
900-1000	36 cu.ft
801-900	21-23 cu.ft
701-800	17-19.5 cu.ft
400-700	11-16.7 cu.ft
100-399	4.9-6.1 cu.ft

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PORTABLE, SINGLE CLICK OPERATION SPIROMETER

From MicroDirect

The MicroDirect SpiroUSB many features include single click operation of all main functions, full ATS/ERS test quality checks, real time Flow/Volume and Volume/ Time traces, a choice of child incentive displays, choice of predicted values, estimated lung age, pre/post bronchodilator comparisons and can be used on multiple PC's with dongle software protection key. The child incentive display and ATS quality checks ensure maximal results every time. Use with a laptop for true portability.

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Unless the equipment is easy to use, it will not be fully utilized by your staff. The MicroLab and MicroLoop are menu driven via a large graphic display and the test takes less than five minutes to perform. The easy-to-read reports, quality checks and built-in interpretation assist with your diagnosis. Your office sees patients with indications for spirometry on a daily basis. Accurately and quickly diagnosis them so you can properly treat them.

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LIBTAYO®
(cemiplimab-rwlc)
Injection 350 mg

LIBTAYO is indicated for the first-line treatment of patients with non–small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [tumor proportion score (TPS) ≥50%] as determined by an FDA-approved test, with no EGFR, ALK, or ROS1 aberrations, and is[1]:

- **Locally advanced where patients are not candidates for surgical resection or definitive chemoradiation or[1]**
- **Metastatic[1]**



NOW APPROVED

As a first-line treatment option in **advanced NSCLC**

Overall survival with LIBTAYO vs platinum-based chemotherapy in EMPOWER-Lung 1[1-3]*

ITT patient population (N=710)[1]

32% reduction in risk of death HR=0.68, *P*=0.0022[1]
Median OS: 22.1 months (95% CI, 17.7-NE) vs 14.3 months (95% CI, 11.7-19.2) (chemotherapy†), HR=0.68, *P*=0.0022[1]
Number of deaths: 30% of patients (108 out of 356 patients) with LIBTAYO and 40% of patients (141 out of 354 patients) with chemotherapy[1]

The EMPOWER-Lung 1 study was designed to enroll patients with PD-L1 ≥50%.[2]

- A total of 710 patients were enrolled and randomized. For some patients, it was later determined that PD-L1 biomarker testing was not conducted according to the instructions for use, and required retesting[2]
- An analysis was conducted in a subset of patients with known PD-L1 ≥50% (n=563). The analysis excluded 91 patients from the overall population whose PD-L1 status was unknown because their tumors could not be retested, and 56 patients from the overall population who had <50% PD-L1 expression[2] (LIBTAYO is not indicated in patients with <50% PD-L1 expression)

Known PD-L1 ≥50% patient population (n=563)[2,3]

43% reduction in risk of death HR=0.57, *P*=0.0002[2,3]
Median OS: NR (95% CI, 17.9-NE) vs 14.2 months (95% CI, 11.2-17.5) (chemotherapy†), HR=0.57, *P*=0.0002[2,3]
Number of deaths: 25% of patients (70 out of 283 patients) with LIBTAYO and 38% of patients (105 out of 280 patients) with chemotherapy[2,3]

PD-L1 expression was determined using the PD-L1 IHC 22C3 pharmDx assay.[1-3]

***Investigator's choice: Paclitaxel + cisplatin or carboplatin; gemcitabine + cisplatin or carboplatin; or pemetrexed + cisplatin or carboplatin followed by optional pemetrexed maintenance in patients with nonsquamous histology.[1-3]**

† Platinum-based.[1-3]

ALK=anaplastic lymphoma kinase; EGFR=epidermal growth factor receptor; HR=hazard ratio; IHC=immunohistochemistry; ITT=intention-to-treat; NE=not evaluable; NR=not reached; NSCLC=non–small cell lung cancer; OS=overall survival; PD-L1=programmed death ligand 1; ROS1=ROS proto-oncogene 1, receptor tyrosine kinase.

Clinical safety data[1]

- LIBTAYO was permanently discontinued due to adverse reactions in 6% of patients;
- Adverse reactions resulting in permanent discontinuation in at least 2 patients were pneumonitis, pneumonia, ischemic stroke, and increased aspartate aminotransferase
- Serious adverse reactions occurred in 28% of patients receiving LIBTAYO;
- The most frequent serious adverse reactions in at least 2% of patients were pneumonia and pneumonitis

Important Safety Information

Warnings and Precautions

Severe and Fatal Immune-Mediated Adverse Reactions

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue at any time after starting treatment. While immune-mediated adverse reactions usually occur during treatment, they can also occur after discontinuation. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously. Early identification and management are essential to ensuring safe use of PD-1/PD-L1–blocking antibodies. The definition of immune-mediated adverse reactions included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. Monitor closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

No dose reduction for LIBTAYO is recommended. In general, withhold LIBTAYO for severe (Grade 3) immune-mediated adverse reactions.

Please see additional Important Safety Information and Brief Summary of full Prescribing Information on the following pages.

LIBTAYO safety profile in EMPOWER-Lung 1[1]

Adverse reactions in ≥10% of patients[1]

Adverse reactions	LIBTAYO (n=355)		Chemotherapy (n=342)	
	All Grades, %	Grade 3-4, %	All Grades, %	Grade 3-4, %
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain*	26	0.6	27	1.5
Skin and subcutaneous tissue disorders				
Rash†	15	1.4	6	0
Blood and lymphatic system disorders				
Anemia	15	3.4	50	16
General disorders and administration site conditions				
Fatigue‡	14	1.1	26	2
Metabolism and nutrition disorders				
Decreased appetite	12	0.6	18	0.3
Infections and infestations				
Pneumonia§	11	5	12	5
Respiratory, thoracic, and mediastinal disorders				
Cough‖	11	0	8	0.3

*Musculoskeletal pain is a composite term that includes back pain, arthralgia, pain in extremity, musculoskeletal pain, musculoskeletal chest pain, bone pain, myalgia, neck pain, spinal pain, and musculoskeletal stiffness.

†Rash is a composite term that includes rash, dermatitis, urticaria, rash maculopapular, erythema, rash erythematous, rash pruritic, psoriasis, autoimmune dermatitis, dermatitis acneiform, dermatitis allergic, dermatitis atopic, dermatitis bullous, drug eruption, dyshidrotic eczema, lichen planus, and skin reaction.

‡Fatigue is a composite term that includes fatigue, asthenia, and malaise.

§Pneumonia is a composite term that includes atypical pneumonia, embolic pneumonia, lower respiratory tract infection, lung abscess, paracancerous pneumonia, pneumonia, pneumonia bacterial, and pneumonia klebsiella.

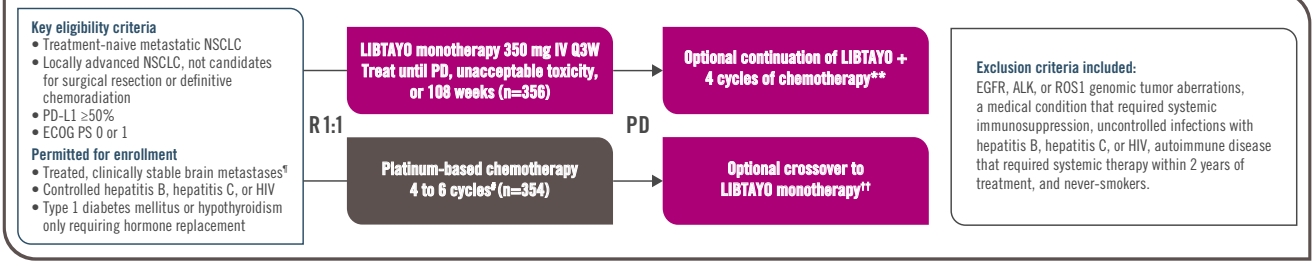
‖Cough is a composite term that includes cough and productive cough.

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v4.03.

In patients who had no EGFR, ALK, or ROS1 aberrations:

EMPOWER-Lung 1 was designed to enroll advanced NSCLC patients with PD-L1 ≥50%[1]

Phase 3, large, randomized, multicenter, open-label, active-controlled trial (ITT population, N=710)[1,2]



Primary endpoints[1]:
- OS and PFS

Secondary endpoints included[1,2]:
- ORR (key), DOR, and safety and tolerability

LIBTAYO was examined in a clinical study that included historically underrepresented patients with advanced NSCLC[1,2]:

In the LIBTAYO arm (ITT patient population) at baseline, 12% of patients had pretreated and stable brain metastases,¶ 18% had locally advanced disease, and 2% had controlled hepatitis B or hepatitis C. Patients with HIV were permitted to enroll, but none were recruited.[1,2,4]

¶Patients were eligible if they had been adequately treated and had neurologically returned to baseline for at least 2 weeks prior to randomization.[1]

#Investigator's choice: Paclitaxel + cisplatin or carboplatin; gemcitabine + cisplatin or carboplatin; or pemetrexed + cisplatin or carboplatin followed by optional pemetrexed maintenance in patients with nonsquamous histology.[1]

**Patients who experienced IRC-assessed RECIST 1.1-defined progressive disease on therapy with LIBTAYO were permitted to continue treatment with LIBTAYO 350 mg Q3W for up to 108 additional weeks, along with the addition of histology-specific chemotherapy for 4 cycles until further disease progression was observed.[1]

††Patients who experienced IRC-assessed RECIST 1.1-defined progressive disease on chemotherapy were permitted to receive treatment with LIBTAYO for up to 108 weeks.[1,2]

Randomization was stratified by histology (nonsquamous vs squamous) and geographic region (Europe vs Asia vs rest of world).[1]

Median duration of exposure was 27.3 weeks (range, 9 days-115 weeks) for LIBTAYO vs 17.7 weeks (range, 18 days-86.7 weeks) for chemotherapy.[1]

DOR=duration of response; ECOG=Eastern Cooperative Oncology Group; IRC=independent review committee; IV=intravenous; ORR=objective response rate; PD=progressive disease; PFS=progression-free survival; PS=performance status; Q3W=every 3 weeks; R=randomization; RECIST=Response Evaluation Criteria in Solid Tumors.

For more information, visit LIBTAYOhcp.com

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Permanently discontinue LIBTAYO for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated adverse reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids.

Withhold or permanently discontinue LIBTAYO depending on severity. In general, if LIBTAYO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids.

Please see additional Important Safety Information and Brief Summary of full Prescribing Information on the following pages.

LIBTAYO®
(cemiplimab-rwlc)
Injection 350 mg

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated pneumonitis: LIBTAYO can cause immune-mediated pneumonitis. In patients treated with other PD-1/PD-L1–blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 4 (0.5%), Grade 3 (0.5%), and Grade 2 (2.1%). Pneumonitis led to permanent discontinuation in 1.4% of patients and withholding of LIBTAYO in 2.1% of patients. Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis resolved in 58% of the 26 patients. Of the 17 patients in whom LIBTAYO was withheld, 9 reinitiated after symptom improvement; of these, 3/9 (33%) had recurrence of pneumonitis. Withhold LIBTAYO for Grade 2, and permanently discontinue for Grade 3 or 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated colitis: LIBTAYO can cause immune-mediated colitis. The primary component of immune-mediated colitis was diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1–blocking antibodies. In cases of corticosteroid-refractory immune-mediated colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 2.2% (18/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (1.1%). Colitis led to permanent discontinuation in 0.4% of patients and withholding of LIBTAYO in 1.5% of patients. Systemic corticosteroids were required in all patients with colitis. Colitis resolved in 39% of the 18 patients. Of the 12 patients in whom LIBTAYO was withheld, 4 reinitiated LIBTAYO after symptom improvement; of these, 3/4 (75%) had recurrence. Withhold LIBTAYO for Grade 2 or 3, and permanently discontinue for Grade 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated hepatitis: LIBTAYO can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 2% (16/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (1.4%), and Grade 2 (0.2%). Hepatitis led to permanent discontinuation of LIBTAYO in 1.2% of patients and withholding of LIBTAYO in 0.5% of patients. Systemic corticosteroids were required in all patients with hepatitis. Additional immunosuppression with mycophenolate was required in 19% (3/16) of these patients. Hepatitis resolved in 50% of the 16 patients. Of the 5 patients in whom LIBTAYO was withheld, 3 reinitiated LIBTAYO after symptom improvement; of these, none had recurrence.

For hepatitis with no tumor involvement of the liver: Withhold LIBTAYO if AST or ALT increases to more than 3 and up to 8 times the upper limit of normal (ULN) or if total bilirubin increases to more than 1.5 and up to 3 times the ULN. Permanently discontinue LIBTAYO if AST or ALT increases to more than 8 times the ULN or total bilirubin increases to more than 3 times the ULN.

For hepatitis with tumor involvement of the liver: Withhold LIBTAYO if baseline AST or ALT is more than 1 and up to 3 times ULN and increases to more than 5 and up to 10 times ULN. Also, withhold LIBTAYO if baseline AST or ALT is more than 3 and up to 5 times ULN and increases to more than 8 and up to 10 times ULN. Permanently discontinue LIBTAYO if AST or ALT increases to more than 10 times ULN or if total bilirubin increases to more than 3 times ULN. If AST and ALT are less than or equal to ULN at baseline, withhold or permanently discontinue LIBTAYO based on recommendations for hepatitis with no liver involvement.

Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated endocrinopathies: For Grade 3 or 4 endocrinopathies, withhold until clinically stable or permanently discontinue depending on severity.

- **Adrenal insufficiency:** LIBTAYO can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold LIBTAYO depending on severity. Adrenal insufficiency occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.4%). Adrenal insufficiency led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. LIBTAYO was not withheld in any patient due to adrenal insufficiency. Systemic corticosteroids were required in all patients with adrenal insufficiency; of these, 67% (2/3) remained on systemic corticosteroids. Adrenal insufficiency had not resolved in any patient at the time of data cutoff
- **Hypophysitis:** LIBTAYO can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue depending on severity. Hypophysitis occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.1%) adverse reactions. Hypophysitis led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient and withholding of LIBTAYO in 1 (0.1%) patient. Systemic corticosteroids were required in 67% (2/3) of patients with hypophysitis. Hypophysitis had not resolved in any patient at the time of data cutoff
- **Thyroid disorders:** LIBTAYO can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity
- **Thyroiditis:** Thyroiditis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including Grade 2 (0.2%) adverse reactions. No patient discontinued LIBTAYO due to thyroiditis. Thyroiditis led to withholding of LIBTAYO in 1 patient. Systemic corticosteroids were not required in any patient with thyroiditis. Thyroiditis had not resolved in any patient at the time of data cutoff. Blood thyroid stimulating hormone increased and blood thyroid stimulating hormone decreased have also been reported
- **Hyperthyroidism:** Hyperthyroidism occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 2 (0.9%). No patient discontinued treatment and LIBTAYO was withheld in 0.5% of patients due to hyperthyroidism. Systemic corticosteroids were required in 3.8% (1/26) of patients. Hyperthyroidism resolved in 50% of 26 patients. Of the 4 patients in whom LIBTAYO was withheld for hyperthyroidism, 2 patients reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of hyperthyroidism
- **Hypothyroidism:** Hypothyroidism occurred in 7% (60/810) of patients receiving LIBTAYO, including Grade 2 (6%). Hypothyroidism led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. Hypothyroidism led to withholding of LIBTAYO in 1.1% of patients. Systemic corticosteroids were not required in any patient with hypothyroidism. Hypothyroidism resolved in 8.3% of the 60 patients. Majority of the patients with hypothyroidism required long-term thyroid hormone replacement. Of the 9 patients in whom LIBTAYO was withheld for hypothyroidism, 1 reinitiated LIBTAYO after symptom improvement; 1 required ongoing hormone replacement therapy
- **Type 1 diabetes mellitus, which can present with diabetic ketoacidosis:** Monitor for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold LIBTAYO depending on severity. Type 1 diabetes mellitus occurred in 0.1% (1/810) of patients, including Grade 4 (0.1%). No patient discontinued treatment due to type 1 diabetes mellitus. Type 1 diabetes mellitus led to withholding of LIBTAYO in 0.1% of patients

Please see additional Important Safety Information and Brief Summary of full Prescribing Information on the following pages.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated nephritis with renal dysfunction: LIBTAYO can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 3 (0.1%), and Grade 2 (0.4%). Nephritis led to permanent discontinuation in 0.1% of patients and withholding of LIBTAYO in 0.4% of patients. Systemic corticosteroids were required in all patients with nephritis. Nephritis resolved in 80% of the 5 patients. Of the 3 patients in whom LIBTAYO was withheld, 2 reinitiated LIBTAYO after symptom improvement; of these, none had recurrence. Withhold LIBTAYO for Grade 2 or 3 increased blood creatinine, and permanently discontinue for Grade 4 increased blood creatinine. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated dermatologic adverse reactions: LIBTAYO can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS) has occurred with PD-1/PD-L1–blocking antibodies. Immune-mediated dermatologic adverse reactions occurred in 1.6% (13/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (0.6%). Immune-mediated dermatologic adverse reactions led to permanent discontinuation in 0.1% of patients and withholding of LIBTAYO in 1.4% of patients. Systemic corticosteroids were required in all patients with immune-mediated dermatologic adverse reactions. Immune-mediated dermatologic adverse reactions resolved in 69% of the 13 patients. Of the 11 patients in whom LIBTAYO was withheld for dermatologic adverse reactions, 7 reinitiated LIBTAYO after symptom improvement; of these, 43% (3/7) had recurrence of the dermatologic adverse reaction. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold LIBTAYO for suspected SJS, TEN, or DRESS. Permanently discontinue LIBTAYO for confirmed SJS, TEN, or DRESS. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Other immune-mediated adverse reactions: The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% in 810 patients who received LIBTAYO or were reported with the use of other PD-1/PD-L1–blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.

- **Cardiac/vascular:** Myocarditis, pericarditis, and vasculitis. Permanently discontinue for Grades 2, 3, or 4 myocarditis
- **Nervous system:** Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, and autoimmune neuropathy. Withhold for Grade 2 neurological toxicities and permanently discontinue for Grades 3 or 4 neurological toxicities. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids
- **Ocular:** Uveitis, iritis, and other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada–like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss
- **Gastrointestinal:** Pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis, stomatitis
- **Musculoskeletal and connective tissue:** Myositis/polymyositis, rhabdomyolysis, and associated sequelae including renal failure, arthritis, polymyalgia rheumatica
- **Endocrine:** Hypoparathyroidism
- **Other (hematologic/immune):** Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection

Infusion-related reactions

Severe infusion-related reactions (Grade 3) occurred in 0.1% of patients receiving LIBTAYO as a single agent. Monitor patients for signs and symptoms of infusion-related reactions. The most common symptoms of infusion-related reaction were nausea, pyrexia, rash, and dyspnea. Interrupt or slow the rate of infusion for Grade 1 or 2, and permanently discontinue for Grade 3 or 4.

Complications of allogeneic HSCT

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1–blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1–blocking antibody prior to or after an allogeneic HSCT.

Embryo-fetal toxicity

LIBTAYO can cause fetal harm when administered to a pregnant woman due to an increased risk of immune-mediated rejection of the developing fetus resulting in fetal death. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose.

Adverse Reactions

- In the pooled safety analysis of 810 patients, the most common adverse reactions (≥15%) with LIBTAYO were musculoskeletal pain, fatigue, rash, and diarrhea
- In the pooled safety analysis of 810 patients, the most common Grade 3-4 laboratory abnormalities (≥2%) with LIBTAYO were lymphopenia, hyponatremia, hypophosphatemia, increased aspartate aminotransferase, anemia, and hyperkalemia

Use in Specific Populations

- **Lactation:** Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO
- **Females and males of reproductive potential:** Verify pregnancy status in females of reproductive potential prior to initiating LIBTAYO

Please see Brief Summary of full Prescribing Information on the following pages.

References: 1. LIBTAYO (cemiplimab-rwlc) injection full U.S. prescribing information. Regeneron Pharmaceuticals, Inc., and sanofi-aventis U.S. LLC. **2.** Sezer A, Kilickap S, Gümüş M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. *Lancet.* 2021;397(10274):592-604. Supplementary material available at: https://www.sciencedirect.com/science/article/abs/pii/S0140673621002282. Accessed February 13, 2021. **3.** PD-L1 IHC 22C3 pharmDx [instructions for use]. Carpinteria, CA: Dako, Agilent Pathology Solutions; 2021. **4.** Data on file. Regeneron Pharmaceuticals, Inc.

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LIBTAYO®
(cemiplimab-rwlc)
Injection 350 mg

LIBTAYO® (cemiplimab-rwlc) injection, for intravenous use

Brief Summary of Prescribing Information

1 INDICATIONS AND USAGE

1.3 Non-Small Cell Lung Cancer

LIBTAYO is indicated for the first-line treatment of patients with non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [Tumor Proportion Score (TPS) ≥ 50%] as determined by an FDA-approved test *[see Dosage and Administration (2.1) in the full prescribing information]*), with no EGFR, ALK or ROS1 aberrations, and is:

- locally advanced where patients are not candidates for surgical resection or definitive chemoradiation or
- metastatic.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Severe and Fatal Immune-Mediated Adverse Reactions

LIBTAYO is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting PD-1/PD-L1 blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1 blocking antibodies, immune-mediated adverse reactions can also manifest after discontinuation of PD-1/PD-L1 blocking antibodies. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue LIBTAYO depending on severity *[see Dosage and Administration (2.3) in the full prescribing information]*. In general, if LIBTAYO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids.

Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below.

Immune-Mediated Pneumonitis

LIBTAYO can cause immune-mediated pneumonitis. The definition of immune-mediated pneumonitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. In patients treated with other PD-1/PD-L1 blocking antibodies the incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

Immune-mediated pneumonitis occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 4 (0.5%), Grade 3 (0.5%), and Grade 2 (2.1%) adverse reactions. Pneumonitis led to permanent discontinuation of LIBTAYO in 1.4% of patients and withholding of LIBTAYO in 2.1% of the patients.

Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis resolved in 58% of the 26 patients. Of the 17 patients in whom LIBTAYO was withheld for pneumonitis, 9 reinitiated LIBTAYO after symptom improvement; of these, 3/9 (33%) had recurrence of pneumonitis.

Immune-Mediated Colitis

LIBTAYO can cause immune-mediated colitis. The definition of immune-mediated colitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. The primary component of the immune-mediated colitis was diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1 blocking antibodies. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated colitis occurred in 2.2% (18/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (1.1%) adverse reactions. Colitis led to permanent discontinuation of LIBTAYO in 0.4% of patients and withholding of LIBTAYO in 1.5% of patients.

Systemic corticosteroids were required in all patients with colitis. Colitis resolved in 39% of the 18 patients. Of the 12 patients in whom LIBTAYO was withheld for colitis, 4 reinitiated LIBTAYO after symptom improvement; of these, 3/4 (75%) had recurrence of colitis.

Immune-Mediated Hepatitis

LIBTAYO can cause immune-mediated hepatitis. The definition of immune-mediated hepatitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology.

Immune-mediated hepatitis occurred in 2% (16/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (1.4%), and Grade 2 (0.2%) adverse reactions. Hepatitis led to permanent discontinuation of LIBTAYO in 1.2% of patients and withholding of LIBTAYO in 0.5% of patients.

Systemic corticosteroids were required in all patients with hepatitis. Nineteen percent (19%) of these patients (3/16) required additional immunosuppression with mycophenolate. Hepatitis resolved in 50% of the 16 patients. Of the 5 patients in whom LIBTAYO was withheld for hepatitis, 3 patients reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of hepatitis.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

LIBTAYO can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold LIBTAYO depending on severity *[see Dosage and Administration (2.3) in the full prescribing information]*.

Adrenal insufficiency occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.4%) adverse reactions. Adrenal insufficiency led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. LIBTAYO was not withheld in any patient due to adrenal insufficiency. Systemic corticosteroids were required in all patients with adrenal insufficiency; of these 67% (2/3) remained on systemic corticosteroids. Adrenal insufficiency had not resolved in any patient at the time of data cutoff.

Hypophysitis

LIBTAYO can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity *[see Dosage and Administration (2.3) in the full prescribing information]*.

Hypophysitis occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.1%) adverse reactions. Hypophysitis led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient and withholding of LIBTAYO in 1 (0.1%) patient. Systemic corticosteroids were required in 67% (2/3) patients with hypophysitis. Hypophysitis had not resolved in any patient at the time of data cutoff.

Thyroid Disorders

LIBTAYO can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity *[see Dosage and Administration (2.3) in the full prescribing information]*.

Thyroiditis: Thyroiditis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including Grade 2 (0.2%) adverse reactions. No patient discontinued LIBTAYO due to thyroiditis. Thyroiditis led to withholding of LIBTAYO in 1 patient. Systemic corticosteroids were not required in any patient with thyroiditis. Thyroiditis had not resolved in any patient at the time of data cutoff.

Blood thyroid stimulating hormone increased and blood thyroid stimulating hormone decreased have also been reported.

Hyperthyroidism: Hyperthyroidism occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 2 (0.9%) adverse reactions. No patient discontinued treatment due to hyperthyroidism. Hyperthyroidism led to withholding of LIBTAYO in 0.5% of patients.

Systemic corticosteroids were required in 3.8% (1/26) of patients with hyperthyroidism. Hyperthyroidism resolved in 50% of the 26 patients. Of the 4 patients in whom LIBTAYO was withheld for hyperthyroidism, 2 patients reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of hyperthyroidism.

Hypothyroidism: Hypothyroidism occurred in 7% (60/810) of patients receiving LIBTAYO, including Grade 2 (6%) adverse reactions. Hypothyroidism led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. Hypothyroidism led to withholding of LIBTAYO in 1.1% of patients.

Systemic corticosteroids were not required in any patient with hypothyroidism. Hypothyroidism resolved in 8.3% of the 60 patients. The majority of patients with hypothyroidism required long-term thyroid hormone replacement.

Of the 9 patients in whom LIBTAYO was withheld for hypothyroidism, 1 reinitiated LIBTAYO after symptom improvement; 1 required ongoing hormone replacement therapy.

Type 1 Diabetes Mellitus, which can present with diabetic ketoacidosis.

Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold LIBTAYO depending on severity *[see Dosage and Administration (2.3) in the full prescribing information]*.

Type 1 diabetes mellitus occurred in 0.1% (1/810) of patients, including Grade 4 (0.1%) adverse reactions. No patient discontinued treatment due to Type 1 diabetes mellitus. Type 1 diabetes mellitus led to withholding of LIBTAYO in 0.1% of patients.

Immune-Mediated Nephritis with Renal Dysfunction

LIBTAYO can cause immune-mediated nephritis. The definition of immune-mediated nephritis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology.

Immune-mediated nephritis occurred in 0.6% (5/810) patients receiving LIBTAYO, including fatal (0.1%), Grade 3 (0.1%) and Grade 2 (0.4%) adverse reactions. Nephritis led to permanent discontinuation of LIBTAYO in 0.1% of patients and withholding of LIBTAYO in 0.4% of patients.

Systemic corticosteroids were required in all patients with nephritis. Nephritis resolved in 80% of the 5 patients. Of the 3 patients in whom LIBTAYO was withheld for nephritis, 2 reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of nephritis.

Immune-Mediated Dermatologic Adverse Reactions

LIBTAYO can cause immune-mediated rash or dermatitis. The definition of immune-mediated dermatologic adverse reaction included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. Exfoliative dermatitis, including Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and DRESS (Drug Rash with Eosinophilia and Systemic Symptoms), has occurred with PD-1/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold or permanently discontinue LIBTAYO depending on severity *[see Dosage and Administration (2.3) in the full prescribing information]*.

Immune-mediated dermatologic adverse reactions occurred in 1.6% (13/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (0.6%) adverse reactions. Dermatologic adverse reactions led to permanent discontinuation of LIBTAYO in 0.1% of patients and withholding of LIBTAYO in 1.4% of patients.

Systemic corticosteroids were required in all patients with immune-mediated dermatologic adverse reactions. Immune-mediated dermatologic adverse reactions resolved in 69% of the 13 patients. Of the 11 patients in whom LIBTAYO was withheld for dermatologic adverse reaction, 7 reinitiated LIBTAYO after symptom improvement; of these 43% (3/7) had recurrence of the dermatologic adverse reaction.

Other Immune-Mediated Adverse Reactions

The following clinically significant immune-mediated adverse reactions occurred at an incidence of < 1% in 810 patients who received LIBTAYO or were reported with the use of other PD-1/PD-L1 blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.

Cardiac/Vascular: Myocarditis, pericarditis, vasculitis

Nervous System: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome / myasthenia gravis (including exacerbation), Guillain-Barre syndrome, nerve paresis, autoimmune neuropathy

Ocular: Uveitis, iritis, and other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

Gastrointestinal: Pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis, stomatitis

Musculoskeletal and Connective Tissue: Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatica

Endocrine: Hypoparathyroidism

Other (Hematologic/Immune): Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection

5.2 Infusion-Related Reactions

Severe infusion-related reactions (Grade 3) occurred in 0.1% of patients receiving LIBTAYO as a single agent. Monitor patients for signs and symptoms of infusion-related reactions. The most common symptoms of infusion-related reaction were nausea, pyrexia, rash and dyspnea.

Interrupt or slow the rate of infusion or permanently discontinue LIBTAYO based on severity of reaction *[see Dosage and Administration (2.3) in the full prescribing information]*.

5.3 Complications of Allogeneic HSCT

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1 blocking antibody. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1 blocking antibody prior to or after an allogeneic HSCT.

5.4 Embryo-Fetal Toxicity

Based on its mechanism of action, LIBTAYO can cause fetal harm when administered to a pregnant woman. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus resulting in fetal death. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose *[see Use in Specific Populations (8.1, 8.3)]*.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling.

- Severe and Fatal Immune-Mediated Adverse Reactions *[see Warnings and Precautions (5.1)]*
- Infusion-Related Reactions *[see Warnings and Precautions (5.2)]*
- Complications of Allogeneic HSCT *[see Warnings and Precautions (5.3)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described in Warnings and Precautions reflect exposure to LIBTAYO as a single agent in 810 patients in three open-label, single-arm, multicohort studies (Study 1423, Study 1540 and Study 1620), and one open-label randomized multi-center study (Study 1624). These studies included 219 patients with advanced CSCC (Studies 1540 and 1423), 132 patients with advanced BCC (Study 1620), 355 patients with NSCLC (Study 1624), and 104 patients with other advanced solid tumors (Study 1423). LIBTAYO was administered intravenously at doses of 3 mg/kg every 2 weeks (n=235), 350 mg every 3 weeks (n=543), or other doses (n=32; 1 mg/kg every 2 weeks, 10 mg/kg every 2 weeks, 200 mg every 2 weeks). Among the 810 patients, 57% were exposed for ≥ 6 months and 25% were exposed for ≥ 12 months. In this pooled safety population, the most common adverse reactions (≥15%) were musculoskeletal pain, fatigue, rash, and diarrhea. The most common Grade 3-4 laboratory abnormalities (≥2%) were lymphopenia, hyponatremia, hypophosphatemia, increased aspartate aminotransferase, anemia, and hyperkalemia.

Non-Small Cell Lung Cancer (NSCLC)

The safety of LIBTAYO was evaluated in 355 patients with locally advanced or metastatic NSCLC in Study 1624 *[see Clinical Studies (14.3) in the full prescribing information]*. Patients received LIBTAYO 350 mg every 3 weeks (n=355) or investigator's choice of chemotherapy (n=342), consisting of paclitaxel plus cisplatin or carboplatin; gemcitabine plus cisplatin or carboplatin; or pemetrexed plus cisplatin or carboplatin followed by optional pemetrexed maintenance. The median duration of exposure was 27.3 weeks (9 days to 115 weeks) in the LIBTAYO group and 17.7 weeks (18 days to 86.7 weeks) in the chemotherapy group. In the LIBTAYO group, 54% of patients were exposed to LIBTAYO for ≥ 6 months and 22 % were exposed for ≥ 12 months.

The safety population characteristics were: median age of 63 years (31 to 79 years), 44% of patients 65 or older, 88% male, 86% White, 82% had metastatic disease and 18% had locally advanced disease and ECOG performance score (PS) of 0 (27%) and 1 (73%).

LIBTAYO was permanently discontinued due to adverse reactions in 6% of patients; adverse reactions resulting in permanent discontinuation in at least 2 patients were pneumonitis, pneumonia, ischemic stroke and increased aspartate aminotransferase. Serious adverse reactions occurred in 28% of patients. The most frequent serious adverse reactions in at least 2% of patients were pneumonia and pneumonitis.

Table 6 summarizes the adverse reactions that occurred in ≥ 10% of patients and Table 7 summarizes Grade 3 or 4 laboratory abnormalities in patients receiving LIBTAYO.

Table 6: Adverse Reactions in ≥ 10% of Patients with Locally Advanced or Metastatic NSCLC Receiving LIBTAYO in Study 1624

Adverse Reactions	LIBTAYO N=355		Chemotherapy N=342	
	All Grades %	Grades 3-4 %	All Grades %	Grades 3-4 %
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain[a]	26	0.6	27	1.5
Skin and subcutaneous tissue disorders				
Rash[b]	15	1.4	6	0
Blood and lymphatic system disorders				
Anemia	15	3.4	50	16
General disorders and administration site conditions				
Fatigue[c]	14	1.1	26	2
Metabolism and nutrition disorders				
Decreased appetite	12	0.6	18	0.3
Infections and infestations				
Pneumonia[d]	11	5	12	5
Respiratory, thoracic and mediastinal disorders				
Cough[e]	11	0	8	0.3

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v.4.03

a. Musculoskeletal pain is a composite term that includes back pain, arthralgia, pain in extremity, musculoskeletal pain, musculoskeletal chest pain, bone pain, myalgia, neck pain, spinal pain, and musculoskeletal stiffness
b. Rash is a composite term that includes rash, dermatitis, urticaria, rash maculo-papular, erythema, rash erythematous, rash pruritic, psoriasis, autoimmune dermatitis, dermatitis acneiform, dermatitis allergic, dermatitis atopic, dermatitis bullous, drug eruption, dyshidrotic eczema, lichen planus, and skin reaction
c. Fatigue is a composite term that includes fatigue, asthenia, and malaise
d. Pneumonia is a composite term that includes atypical pneumonia, embolic pneumonia, lower respiratory tract infection, lung abscess, paracancerous pneumonia, pneumonia, pneumonia bacterial, and pneumonia klebsiella
e. Cough is a composite term that includes cough and productive cough

Table 7: Grade 3 or 4 Laboratory Abnormalities Worsening from Baseline in ≥1% of Patients with Locally Advanced or Metastatic NSCLC Receiving LIBTAYO in Study 1624

Laboratory Abnormality	LIBTAYO N=355	Chemotherapy N=342
	Grades 3-4[a] %	
Chemistry		
Increased aspartate aminotransferase	3.9	1.2
Increased alanine aminotransferase	2.7	0.3
Increased alkaline phosphatase	2.4	0.3
Increased blood bilirubin	2.1	0.3
Hypoalbuminemia	1.8	1.3
Increased creatinine	1.2	1.6
Hematology		
Lymphopenia	7	9
Anemia	2.7	16
Electrolytes		
Hyponatremia	6	7
Hyperkalemia	4.2	1.9
Hypocalcemia	3.9	3.4
Hypophosphatemia	2.4	4.1
Hypermagnesemia	2.1	1.6
Hypokalemia	1.5	2.2
Hypercalcemia	1.2	2.2

Toxicity graded per NCI CTCAE v. 4.03

a. Percentages are based on the number of patients with at least 1 post-baseline value available for that parameter.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to cemiplimab-rwlc in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

Anti-drug antibodies (ADA) were tested in 823 patients who received LIBTAYO. The incidence of cemiplimab-rwlc treatment-emergent ADAs was 2.2% using an electrochemiluminescent (ECL) bridging immunoassay; 0.4% were persistent ADA responses. In the patients who developed anti-cemiplimab-rwlc antibodies, there was no evidence of an altered pharmacokinetic profile of cemiplimab-rwlc.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on its mechanism of action, LIBTAYO can cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1) in the full prescribing information]*. There are no available data on the use of LIBTAYO in pregnant women. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus resulting in fetal death *(see Data)*. Human IgG4 immunoglobulins (IgG4) are known to cross the placenta; therefore, LIBTAYO has the potential to be transmitted from the mother to the developing fetus. Advise women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

Animal reproduction studies have not been conducted with LIBTAYO to evaluate its effect on reproduction and fetal development. A central function of the PD-1/PD-L1 pathway is to preserve pregnancy by maintaining maternal immune tolerance to the fetus. In murine models of pregnancy, blockade of PD-L1 signaling has been shown to disrupt tolerance to the fetus and to result in an increase in fetal loss; therefore, potential risks of administering LIBTAYO during pregnancy include increased rates of abortion or stillbirth. As reported in the literature, there were no malformations related to the

blockade of PD-1/PD-L1 signaling in the offspring of these animals; however, immune-mediated disorders occurred in PD-1 and PD-L1 knockout mice. Based on its mechanism of action, fetal exposure to cemiplimab-rwlc may increase the risk of developing immune-mediated disorders or altering the normal immune response.

8.2 Lactation

Risk Summary

There is no information regarding the presence of cemiplimab-rwlc in human milk, or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating LIBTAYO *[see Use in Specific Populations (8.1)]*.

Contraception

LIBTAYO can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*.

Females

Advise females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose.

8.4 Pediatric Use

The safety and effectiveness of LIBTAYO have not been established in pediatric patients.

8.5 Geriatric Use

Of the 810 patients who received LIBTAYO in clinical studies, 32% were 65 years up to 75 years and 22% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

Of the 219 patients with mCSCC or laCSCC who received LIBTAYO in clinical studies, 34% were 65 years up to 75 years and 41% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

Of the 132 patients with BCC who received LIBTAYO in Study 1620, 27% were 65 years up to 75 years, and 32% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

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