New England Journal of Medicine publishes Phase III data showing Xolair® (omalizumab) significantly reduced allergic reactions across multiple foods in people with food allergies

Feb 25, 2024

- Detailed results from the NIH-sponsored Phase III OUtMATCH study showed treatment with Xolair increased the amount of peanuts, tree nuts, egg, milk and wheat that people as young as 1 year consumed without an allergic reaction
- The US FDA recently approved Xolair as the first and only medicine for children and adults with one or more food allergies
- Allergic reactions can be life-threatening and it is estimated that food-related anaphylaxis results in 30,000 medical events treated in emergency rooms in the US each year[1-3]

EAST HANOVER, N.J., Feb. 25, 2024 /PRNewswire/ -- Novartis announced today data from Stage 1 of the National Institutes of Health (NIH)-sponsored pivotal Phase III OUtMATCH study evaluating the efficacy and safety of Xolair® (omalizumab) in patients allergic to peanuts and at least two other common foods were published in the New England Journal of Medicine (NEJM) and featured in a late-breaking symposium at the 2024 American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting. The study showed treatment with Xolair increased the amount of peanuts, milk, egg, wheat and tree nuts (cashew, hazelnut and walnut) that it took to cause moderate to severe allergic reactions in multi-food allergic people as young as 1 year. Safety findings were consistent with the known safety profile of Xolair across its approved indications and in previous clinical trials[4]. The US Food and Drug Administration (FDA) recently approved the expanded use of Xolair in children and adults with IgE-mediated food allergies based on the OUtMATCH data.

"Over the past 35 years, I have seen how debilitating food allergies can be for patients and their loved ones, as they are consumed by the fear of accidental exposure," said Robert Wood, M.D., Director of the Eudowood Division of Allergy, Immunology and Rheumatology at Johns Hopkins Children's Center, and principal investigator of the OUtMATCH study. "While allergic reactions to exposures are common and often severe, there have been limited treatment advancements for food allergy. The results of the OUtMATCH study showed that anti-IgE therapy could significantly reduce the occurrence of allergic reactions across multiple foods in the event of an accidental exposure."

"Living with food allergies has a profound impact on patients and their families, causing significant stress and requiring constant vigilance," said R. Sharon Chinthrajah, M.D., Associate Professor of Medicine, Stanford School of Medicine, Sean N. Parker Center for Allergy and Asthma Research and OUtMATCH co-lead study investigator. "The OUtMATCH study demonstrated that anti-IgE therapy increased most patients' threshold for an allergic reaction. This presents an important new treatment option for patients and families in its potential to reduce the risk of allergic reactions from accidental exposures they may face in day-to-day life."

One hundred eighty patients ages 1 to 55 years old entered Stage 1 of the OUtMATCH study unable to tolerate up to 100 mg of peanut protein (equivalent to about one third of a peanut), and up to 300 mg of at least two other food

proteins among milk, egg, cashew, walnut, hazelnut and wheat. After 16 to 20 weeks of treatment with Xolair or placebo, each participant completed four separate blinded food challenges (including a placebo ingredient) to assess patients' ability to consume a single dose of at least 600 mg of peanut protein (primary endpoint), and a single dose of at least 1,000 mg of milk, egg, wheat, cashew, hazelnut or walnut protein (secondary endpoints) without experiencing moderate to severe allergic reactions.

Results showed that, compared to placebo, a statistically significant ($p<0.001$) higher proportion of patients receiving Xolair were able to consume at least 600 mg of peanut protein and at least 1,000 mg of milk, egg and cashew protein without experiencing moderate to severe allergic reactions. Additionally, compared to placebo, a higher proportion of patients receiving Xolair were also able to consume at least 1,000 mg of walnut, hazelnut and wheat protein without experiencing moderate to severe allergic reactions. Detailed results are included in the table below.

OUtMATCH Primary and Secondary Endpoints Results in Pediatric Population (n=177)
Percentage of Patients Successfully Consuming Predefined Threshold Dose of Seven Foods

	Approximate Equivalents[5]	Xolair Treated Patients	Placebo Treated Patients	Number of Patients
Primary Endpoint				
Peanut (≥600 mg) 95% CI for difference: 47 to 70; p<0.001	2.5 peanuts or 1/2 teaspoon of regular peanut butter	67 %	7 %	177
Key Secondary Endpoints				
Cashew (≥1,000 mg) 95% CI for difference: 19 to 52; p<0.001	3.5 cashews	41 %	3 %	99
Egg (≥1,000 mg) 95% CI for difference: 46 to 79; p<0.001	1/4 of an egg	67 %	0 %	71
Milk (≥1,000 mg) 95% CI for difference: 30 to 74; p<0.001	2 tablespoons of 1% milk	66 %	10 %	62
Additional Secondary Endpoints				
Walnut (≥1,000 mg) 95% CI for difference: 27 to 68	3 walnut halves	64 %	13 %	78

Hazelnut (≥1,000 mg)	4.5 hazelnuts	65 %	14 %	24
95% CI for difference: -2 to 78				
Wheat (≥1,000 mg)	3.5 saltine crackers	75 %	13 %	20
95% CI for difference: 13 to 88				

Additionally, out of three adult OUtMATCH participants, two completed Stage 1 of the study; the adult who received Xolair met the primary endpoint compared to the placebo-enrolled adult patient.

Adverse event rates in the study were similar between Xolair and placebo. The most common adverse event in Xolair-treated children and adolescents was injection site reaction (9%).

"These pivotal results show promise for children, families and adults living with the constant risk of potentially life-threatening allergic reactions to common food allergens following an accidental exposure," said Angelika Jahreis, M.D., Ph.D., Development Unit Head, Immunology, Novartis. "We are proud to partner with the National Institutes of Health and leading research institutions on this study and are thrilled that Xolair is an important new treatment option for people with food allergies."

While efficacy cannot be established from uncontrolled, open-label studies, for 38 children who continued Xolair for 24-28 weeks in an open-label extension, the percentage of patients who were able to consume 600 mg or more of peanut protein and 1,000 mg or more of egg, milk and/or cashew protein without moderate to severe dose-limiting symptoms was maintained.

About 3.4 million children and 13.6 million adults in the US will have been diagnosed with IgE-mediated food allergies, based on estimates for 2024[1,2]. Food allergy prevalence has been on the rise for the past 20 years[6]. There are 160 different foods that cause IgE-mediated food allergy[7]. Allergic reactions can range from mild to moderate, including hives and swelling, to severe and life-threatening, such as anaphylaxis[3]. More than 40% of children and more than half of adults with food allergies have experienced a severe reaction at least once, and it is estimated that food-related anaphylaxis results in 30,000 medical events treated in emergency rooms in the US each year[1,2,3].

On February 16, 2024, the FDA approved Xolair for the reduction of allergic reactions, including anaphylaxis, that may occur with accidental exposure to one or more foods in adult and pediatric patients aged 1 year and older with IgE-mediated food allergy. People taking Xolair for food allergies should continue to avoid all foods they are allergic to (commonly referred to as "food allergen avoidance"). Xolair should not be used for the emergency treatment of any allergic reactions, including anaphylaxis. Xolair is the first and only FDA-approved medicine to reduce allergic reactions in people with one or more food allergies.

In the US, Novartis Pharmaceuticals Corporation and Genentech, a member of the Roche Group, work together to develop and co-promote Xolair.

About the OUtMATCH Study

The Omalizumab as Monotherapy and as Adjunct Therapy to Multi-Allergen Oral Immunotherapy in Food Allergic Children and Adults (OUtMATCH; NCT03881696) study is an NIH-sponsored, three-stage, multicenter, randomized, double-blind, placebo-controlled study evaluating Xolair safety and efficacy in patients aged 1 to 55 years who are allergic to peanuts and at least two other common foods.

Stage 1 included 180 patients (177 children and adolescents; 3 adults) who were randomly assigned to receive

placebo or Xolair injections either every two weeks or every four weeks for 16 to 20 weeks. The Xolair dose and dosing interval were determined by total serum IgE level and body weight at baseline.

After 16 to 20 weeks of treatment with Xolair or placebo, each participant completed four separate blinded food challenges where they were given gradually increasing amounts of peanut protein, two other food proteins they were allergic to, and a placebo ingredient. The food challenges were conducted in a carefully controlled setting with investigators looking for signs and symptoms of allergic reaction to assess patients' ability to consume a single dose of at least 600 mg of peanut protein (primary endpoint), and a single dose of at least 1,000 mg of milk, egg, wheat, cashew, hazelnut or walnut protein (secondary endpoints) without experiencing dose-limiting symptoms, which were defined as moderate to severe allergic reactions, including skin, respiratory or gastrointestinal symptoms.

The OUtMATCH study is being sponsored and funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH, and conducted by the NIAID-funded Consortium for Food Allergy Research (CoFAR) at 10 clinical sites across the US led by Johns Hopkins Children's Center and co-led by Stanford School of Medicine. The study is also supported by Genentech and Novartis Pharmaceuticals Corporation.

About Xolair
In the US, Xolair is the only approved antibody designed to target and block immunoglobulin E (IgE). By reducing free IgE, down-regulating high-affinity IgE receptors and limiting mast cell degranulation, Xolair minimizes the release of mediators throughout the allergic inflammatory cascade.

Indications and Important Safety Information
What is XOLAIR?

XOLAIR® (omalizumab) for subcutaneous use is an injectable prescription medicine used to treat:

- moderate to severe persistent asthma in people 6 years of age and older whose asthma symptoms are not well controlled with asthma medicines called inhaled corticosteroids. A skin or blood test is performed to see if you have allergies to year-round allergens. It is not known if XOLAIR is safe and effective in people with asthma under 6 years of age.

- chronic rhinosinusitis with nasal polyps (CRSwNP) in people 18 years of age and older when medicines to treat CRSwNP called nasal corticosteroids have not worked well enough. It is not known if XOLAIR is safe and effective in people with CRSwNP under 18 years of age.

- food allergy in people 1 year of age and older to reduce allergic reactions that may occur after accidentally eating one or more foods to which you are allergic. While taking XOLAIR you should continue to avoid all foods to which you are allergic. It is not known if XOLAIR is safe and effective in people with food allergy under 1 year of age.

- chronic spontaneous urticaria (CSU, previously referred to as chronic idiopathic urticaria (CIU), chronic hives without a known cause) in people 12 years of age and older who continue to have hives that are not controlled with H1 antihistamine treatment. It is not known if XOLAIR is safe and effective in people with CSU under 12 years of age.

XOLAIR should not be used for the emergency treatment of any allergic reactions, including anaphylaxis. XOLAIR should also not be used to treat other forms of hives, or sudden breathing problems.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about XOLAIR?
Severe allergic reaction. A severe allergic reaction called anaphylaxis can happen when you receive XOLAIR. The

reaction can occur after the first dose, or after many doses. It may also occur right after a XOLAIR injection or days later. Anaphylaxis is a life-threatening condition and can lead to death. Go to the nearest emergency room right away if you have any of these symptoms of an allergic reaction:

- wheezing, shortness of breath, cough, chest tightness, or trouble breathing
- low blood pressure, dizziness, fainting, rapid or weak heartbeat, anxiety, or feeling of "impending doom"
- flushing, itching, hives, or feeling warm
- swelling of the throat or tongue, throat tightness, hoarse voice, or trouble swallowing

Your healthcare provider will monitor you closely for symptoms of an allergic reaction while you are receiving XOLAIR and for a period of time after treatment is initiated. Your healthcare provider should talk to you about getting medical treatment if you have symptoms of an allergic reaction.

Do not receive and use XOLAIR if you are allergic to omalizumab or any of the ingredients in XOLAIR.

Before receiving XOLAIR, tell your healthcare provider about all of your medical conditions, including if you:

- have a latex allergy or any other allergies (such as seasonal allergies). The needle cap on the XOLAIR prefilled syringe contains a type of natural rubber latex.
- have sudden breathing problems (bronchospasm)
- have ever had a severe allergic reaction called anaphylaxis
- have or have had a parasitic infection
- have or have had cancer
- are pregnant or plan to become pregnant. It is not known if XOLAIR may harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if XOLAIR passes into your breast milk. Talk with your healthcare provider about the best way to feed your baby while you receive and use XOLAIR.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I receive and use XOLAIR?

- When starting treatment XOLAIR should be given by your healthcare provider in a healthcare setting.
- If your healthcare provider decides that you or a caregiver may be able to give your own XOLAIR prefilled syringe or autoinjector injections, you should receive training on the right way to prepare and inject XOLAIR.
- Do not try to inject XOLAIR until you have been shown the right way to give XOLAIR prefilled syringe or autoinjector injections by a healthcare provider. Use XOLAIR exactly as prescribed by your healthcare provider.
- The XOLAIR autoinjector (all doses) is intended for use only in adults and adolescents aged 12 years and older. For children 12 years of age and older, XOLAIR prefilled syringe or autoinjector may be self-injected under adult supervision. For children 1 to 11 years of age, XOLAIR prefilled syringe should be injected by a caregiver.
- See the detailed Instructions for Use that comes with XOLAIR for information on the right way to prepare and inject XOLAIR.
- XOLAIR is given in 1 or more injections under the skin (subcutaneous), 1 time every 2 or 4 weeks.
- In people with asthma, CRSwNP and food allergy, a blood test for a substance called IgE must be performed before starting XOLAIR to determine the appropriate dose and dosing frequency.
- In people with chronic hives, a blood test is not necessary to determine the dose or dosing frequency.
- Do not decrease or stop taking any of your other asthma, CRSwNP, hive medicine, food allergy medicine or allergen immunotherapy, unless your healthcare providers tell you to.
- You may not see improvement in your symptoms right away after XOLAIR treatment. If your symptoms do not improve or get worse, call your healthcare provider.

- If you inject more XOLAIR than prescribed, call your healthcare provider right away.

What are the possible side effects of XOLAIR?

XOLAIR may cause serious side effects, including:

- Cancer. Cases of cancer were observed in some people who received XOLAIR.
- Inflammation of your blood vessels. Rarely, this can happen in people with asthma who receive XOLAIR. This usually, but not always, happens in people who also take a steroid medicine by mouth that is being stopped or the dose is being lowered. It is not known whether this is caused by XOLAIR. Tell your healthcare provider right away if you have rash; chest pain; shortness of breath; or a feeling of pins and needles or numbness of your arms or legs.
- Fever, muscle aches, and rash. Some people get these symptoms 1 to 5 days after receiving a XOLAIR injection. If you have any of these symptoms, tell your healthcare provider.
- Parasitic infection. Some people who are at a high risk for parasite (worm) infections, get a parasite infection after receiving XOLAIR. Your healthcare provider can test your stool to check if you have a parasite infection.
- Heart and circulation problems. Some people who receive XOLAIR have had chest pain, heart attack, blood clots in the lungs or legs, or temporary symptoms of weakness on one side of the body, slurred speech, or altered vision. It is not known whether these are caused by XOLAIR.

The most common side effects of XOLAIR:

- In adults and children 12 years of age and older with asthma: joint pain especially in your arms and legs, dizziness, feeling tired, itching, skin rash, bone fractures, and pain or discomfort of your ears.
- In children 6 to less than 12 years of age with asthma: swelling of the inside of your nose, throat, or sinuses, headache, fever, throat infection, ear infection, abdominal pain, stomach infection, and nose bleeds.
- In adults with chronic rhinosinusitis with nasal polyps: headache, injection site reactions, joint pain, upper abdominal pain, and dizziness.
- In people with chronic spontaneous urticaria: nausea, headaches, swelling of the inside of your nose, throat or sinuses, cough, joint pain, and upper respiratory tract infection.
- In people with food allergy: injection site reactions and fever.

These are not all the possible side effects of XOLAIR. Call your doctor for medical advice about side effects.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555 or Novartis Pharmaceuticals Corporation at (888) 669-6682.

Please see full Prescribing Information, including Medication Guide for additional Important Safety Information and Instructions for Use.

Disclaimer
This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as "potential," "can," "will," "plan," "may," "could," "would," "expect," "anticipate," "look forward," "believe," "committed," "investigational," "pipeline," "launch," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that

such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis
Novartis is a focused innovative medicines company. Every day, we work to reimagine medicine to improve and extend people's lives so that patients, healthcare professionals and societies are empowered in the face of serious disease. Our medicines reach more than 250 million people worldwide.

Reimagine medicine with us: Visit us at https://www.novartis.com and https://www.novartis.us and connect with us on LinkedIn, LinkedIn US, Facebook, X/Twitter, X/Twitter US and Instagram.

References

1. Gupta RS, Warren CM, Smith BM, et al. Prevalence and Severity of Food Allergies Among US Adults. JAMA Netw Open. 2019;2(1):e185630. doi:10.1001/jamanetworkopen.2018.5630.
2. Gupta RS, Warren CM, Smith BM, et al. The Public Health Impact of Parent-Reported Childhood Food Allergies in the United States. Pediatrics. 2018;142(6):e20181235. doi:10.1542/peds.2018-1235.
3. USDA Food Safety and Inspection Service. Food Allergies. https://www.fsis.usda.gov/food-safety/safe-food-handling-and-preparation/food-safety-basics/food-allergies. Accessed November 2023.
4. Xolair (omalizumab) Prescribing Information. Genentech, Inc. and Novartis Pharmaceuticals Corporation 2024.
5. Groetch M, Mudd K, Woch M, et al. Retail Food Equivalents for Post-Oral Immunotherapy Dosing in the Omalizumab as Monotherapy and as Adjunct Therapy to Multi-Allergen Oral Immunotherapy in Food-Allergic Children and Adults (OUtMATCH) Clinical Trial. J Allergy Clin Immunol Pract. 2023;11(2):572-580.e2. doi:10.1016/j.jaip.2022.10.022.
6. Benedé S, Blázquez AB, Chiang D, Tordesillas L, Berin MC. The Rise of Food Allergy: Environmental Factors and Emerging Treatments. EBioMedicine. 2016;7:27-34.
7. US FDA. Food Allergies. https://www.fda.gov/food/food-labeling-nutrition/food-allergies. Accessed February 2024.

# # #

Novartis Media Relations

E-mail: media.relations@novartis.com

North America Julie Masow +1 862 579 8456

Michael Meo +1 862 274 5414

Marlena Abdinoor +1 617 335 9525

Novartis Investor Relations

E-mail: investor.relations@novartis.com

North America

Sloan Simpson +1 862 345 4440

Jonathan Graham +1 201 602 9921

Parag Mahanti +1 973 876 4912

SOURCE DNA/Novartis Pharmaceuticals Corporation

---

w0m4ezZxEQEl0ptafXN2M99VRIk39pf49PAc8NbK93Pxp3uaSBQkAf8oEnzWXG8Sk%24
24. https://instagram.com/novartis?igshid=MzRlODBiNWFlZA%3D%3D__%3B%21%21N3hqHg43uw%21pjp8z253J5NjaOYrW65UbAAlHeHRdQ-w0m4ezZxEQEl0ptafXN2M99VRIk39pf49PAc8NbK93Pxp3uaSBQkAf8oEnzWXG8Sk%24
25. https://instagram.com/novartis?igshid=MzRlODBiNWFlZA%3D%3D__%3B%21%21N3hqHg43uw%21pjp8z253J5NjaOYrW65UbAAlHeHRdQ-w0m4ezZxEQEl0ptafXN2M99VRIk39pf49PAc8NbK93Pxp3uaSBQkAf8oEnzWXG8Sk%24
26. https://www.fsis.usda.gov/food-safety/safe-food-handling-and-preparation/food-safety-basics/food-allergies
27. https://www.fda.gov/food/food-labeling-nutrition/food-allergies
28. mailto:media.relations@novartis.com
29. mailto:investor.relations@novartis.com