

that maternal COVID-19 vaccination protects against severe illness both among pregnant women and their infants up to 6 months of age who are too young to be vaccinated.^{2,3,7,9} During the omicron period, it remains crucial to convey that COVID-19 vaccination primarily prevents severe illness, including hospitalisation and death, in the general population; Villar and colleagues show this is also true for pregnant women.⁷ COVID-19 vaccination among pregnant women is effective against severe illness and complications during the omicron period, but immunity wanes over time.² Receipt of a booster regardless of the type of primary series received was highly effective.⁷ Additionally, a recent 2022 study among the general US population showed that bivalent mRNA boosters (containing components both from the ancestral SARS-CoV-2 strain and omicron sublineages) provide significant additional protection against symptomatic SARS-CoV-2 infection compared with receipt of monovalent mRNA boosters.¹⁰ To prevent adverse outcomes associated with SARS-CoV-2 infection during pregnancy, pregnant women should stay up to date with recommended COVID-19 vaccines, including, if available, a bivalent mRNA booster when they are eligible.^{10,11}

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New medications to mitigate attacks of hereditary angioedema: does one size fit all?



Hereditary angioedema has received renewed attention in the past two decades, with the elucidation of the biochemical pathways resulting in bradykinin overproduction in patients with congenital C1esterase inhibitor (C1INH) deficiency, leading to recurrent attacks of tissue swelling due to uncontrolled vascular permeability.¹ Oedema attacks affecting the lingual or laryngeal area can become lethal as a result of asphyxiation.² Several new treatments have emerged, 143 years after Quincke's first description of hereditary angioedema and 15 years after the introduction of the first specific bradykinin B2 receptor inhibitor

(icatibant). These drugs specifically target crucial steps in the kallikrein-kinin (contact) cascade downstream of bradykinin production.³ Many of these agents have shown their efficacy and safety in acute (on-demand) treatment and prophylaxis of hereditary angioedema attacks, saving lives and revolutionising patients' quality of life.⁴ These modalities fit well into the modern paradigm in hereditary angioedema treatment, supporting patients' autonomy, recommending self-administration, and reducing reliance on hospital emergency rooms, health-care providers, and medical points of care.⁵



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Some traditional on-demand treatments for hereditary angioedema, given parenterally or subcutaneously, are often challenging to self-administer since they require training and preparation, require venous access, and can cause pain and discomfort. Despite being cheaper, other previously offered acute treatments were proven ineffectual (ie, fresh-frozen plasma, danazol).

The study by Emel Aygören-Pürsün and colleagues⁶ published in *The Lancet* aimed to identify an effective medication to treat hereditary angioedema attacks in the acute, on-demand setting. This outpatient, randomised, double-blind, placebo-controlled, crossover phase 2 trial investigated the efficacy and safety of a new oral plasma kallikrein (PKa) inhibitor, sebetralstat. Eligible attacks (abdominal, arms and legs, genital, or others, but not laryngeal) had to be treated within the first hour of onset before developing into a more severe level. Patients evaluated their attack severity on a Global Impression of Severity scale and self-administered the experimental drug or placebo at home.⁶ Of the 84 patients with physician-diagnosed hereditary angioedema screened, 68 (mean age 38.3 years [SD 13.2], 37 [54%] female, 31 [46%] male, 68 [100%] White) received an oral dose of 600 mg sebetralstat or placebo, 42 (62%) completed pharmacokinetic measurements, and 113 attacks were treated per protocol. The trial achieved its primary goals by showing a reduction in time to symptom relief and increased time to conventional attack treatment (ie, the use of rescue medications such as intravenous C1INH or icatibant), and no serious safety signals were detected. Sebetralstat was rapidly absorbed, reaching high plasma concentration within 15 min, complementing phase 1 data showing nearly complete PKa inhibition within 20–30 min of administration, and ex-vivo suppression of high-molecular-weight kininogen cleavage (a surrogate for bradykinin generation).⁶

However, one of the study's major limitations was the absence of data on the efficacy and safety of sebetralstat in patients with abdominal or oropharyngeal attacks, or both. Abdominal attacks are highly frequent in hereditary angioedema, most notorious for being difficult to detect, prone to misdiagnosis and unnecessary surgeries, and frequently imitating other gastrointestinal conditions. Indeed, abdominal attacks pose a major clinical dilemma, affecting more than

70% to 90% of patients, sometimes with high frequency. In many cases involving the gastrointestinal tract, a high prevalence of nausea and vomiting accompanies the initial symptoms of hereditary angioedema attacks.^{7–10}

Evidently, certain locations of hereditary angioedema attacks (ie, oropharyngeal, laryngeal, and gastrointestinal) could become a potential impediment to administering acute or on-demand treatment, which might pertain to sebetralstat, as well as other oral agents already in development and clinical trials.

In the study by Aygören-Pürsün and colleagues,⁶ patients were requested to treat their attacks within the first hour of onset and before reaching mild to moderate severity, assuming that quick absorption would mitigate the attack before nausea and vomiting ensue. As such, the study design approach aligns with widely accepted international guidelines; on-demand treatment should be administered at the early onset of the attack to modify and shorten the time to resolution.⁵

In the era of delegated patient autonomy, and given the high price of some of the new treatments, physician–patient dialogue is a highly desired goal.^{11,12} Personal treatment plans should reflect the patient's experience, ability to recognise early signs and symptoms of an oncoming attack (prodromes), reasonable assessment of the severity of attacks, and training to increase the proficiency of self-administration techniques.

Despite its limitations, the study's encouraging results support the addition of sebetralstat to the armamentarium of pharmaceutical agents already used for the on-demand treatment of hereditary angioedema. Further trials are needed to fully address the place of oral medications in on-demand treatment strategies.

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Stemming commercial milk formula marketing: now is the time for radical transformation to build resilience for breastfeeding



One of the striking messages of the *Lancet* Breastfeeding Series^{1–3} is that the consumption of commercial milk formula (CMF) by infants and young children has been normalised. More children are consuming CMF than ever before.² Only 48% of the world's infants and young children are breastfed as recommended,⁴ despite the huge body of evidence on the lifelong benefits of breastfeeding. This situation reflects the stranglehold the CMF industry has on governments, health professionals, academic institutions, and increasingly on caregivers and families through pervasive social media. CMF companies exert undue control on the infant and young child feeding discourse, and the value of CMF sales have increased year on year.² This dire situation, interventions to address it, and the economic, health, and survival benefits to society of optimal breastfeeding practices have been outlined in three previous *Lancet* Series^{5–7} since 2003. The 2023 *Lancet* breastfeeding Series underlines, yet again, inadequate progress in improving breastfeeding practices globally, with the powerful addition of quantifying the association between sales of CMF and national breastfeeding rates.² The Series provides evidence of the overwhelming influence of CMF marketing in the promotion of CMF as a positive choice and the solution to every feeding challenge, thereby eroding breastfeeding practices.^{1–3}

This *Lancet* Series recommends programmatic and policy actions to support women who want to breastfeed, including the adoption of a framework convention on the commercial marketing of foods for infants and young children.³ Although a framework convention to restrict CMF marketing could be a potentially impactful high-level action, the International Code of Marketing of Breast-milk Substitutes (hereafter referred to as the Code) that regulates the marketing of CMF has been in existence for 40 years.⁸ The Code and subsequent resolutions explicitly state that “there should be no advertising or other form of promotion to the general public” and that “manufacturers and distributors should not provide...to pregnant women, mothers or members of their families, samples of products”.⁸ Promotion through any type of sales device, including special displays, discount coupons, and special sales, is prohibited.⁸ In terms of health-care settings, the Code and subsequent resolutions call for a total prohibition of any type of promotion of products that fall within their scope in the health services. The evidence analysis in the *Lancet* Series shows clearly how marketing has continued, irrespective of the Code. Notably, advertising expenditure by CMF manufacturers has grown by 164% during the past decade,² despite 144 (74%)

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