



Message to FOP community,

On behalf of the Clinical Trials Committee of the International Clinical Council on FOP (The ICC): The ICC is aware of the recent publication by the Palhares group regarding FOPCon and a new YouTube video (available in some countries, but appears to be not available in the USA or Europe) supporting FOPCon. FOPCon is a proposed therapy composed of ascorbic acid (vitamin C) and propranolol.

At this time and with the currently published evidence, the ICC feels **that the evidence presented for public review does not support the use of FOPCon as a therapy for FOP.**

Specifically, the ICC has requested the following:

- **FOPCon should not be advertised as a definitive therapy for FOP.** The FOPCon paper and video do not provide proof of efficacy or safety because the evidence presented and available for review is insufficient to make this judgement. Although FOPCon may eventually provide insights into therapeutic options, we strongly recommend caution for patients with FOP and physicians who treat FOP against drawing therapeutic conclusions.
- **FOPCon should be described as an investigative therapy,** until its efficacy and safety have been reviewed by a national regulatory agency, and accepted by the international community.
- **The risks of FOPCon need to be fully presented.** These include, but are not limited to, concerns about increased risks of cardiac arrhythmias, slow heart beat, low blood pressure, dizziness, passing out (syncope), increased risks of kidney stones, and death.
- **Subjects receiving FOPCon are portrayed to be in a clinical trial; thus, all subjects should be treated according to internationally-recognized standards.** This includes formal written and voluntary consents, a full discussion of potential risks and benefits, standardized clinical and safety monitoring, and standardized endpoints to understand the potential efficacy of an investigational therapeutic intervention. The ICC also confirms that all investigation studies should follow key clinical trial recommendations previously agreed on by FOP clinicians worldwide (<https://bpspubs.onlinelibrary.wiley.com/doi/pdf/10.1111/bcp.13777>). This will help ensure the safety and ethical treatment of subjects with FOP and scientific validity of the results. This is important so that the community can understand how well FOPCon works compared to other potential therapies.

The ICC confirms that the treatment recommendations recently reviewed in detail and published in the 2019 FOP treatment guidelines ([https://www.ifopa.org/updated\\_fop\\_treatment\\_guidelines\\_released](https://www.ifopa.org/updated_fop_treatment_guidelines_released)) are unchanged at this point. We and others await the review of additional published data about how the proposed therapy FOPCon may benefit the FOP community. We also encourage the FOP community to critically assess the risks, benefits, and strength of the supporting data for any other proposed therapy for FOP. **Patients with FOP who are considering any medication changes should discuss their options, and potential risks and benefits, with their doctors and medical team before starting any potential treatment.**

The International Clinical Council on FOP (The ICC) is an autonomous and independent group of 21 internationally-recognized physicians who are clinical experts in FOP from 13 nations (Argentina, Australia, Brazil, China, France, Germany, Italy, Japan, Netherlands, South Africa, South Korea, United Kingdom, and United States) and six continents (Africa, Asia, Australia, Europe, North America and South America). The ICC was established to coordinate and consolidate a global voice for the best practices for clinical care and clinical research for people who suffer from FOP. The ICC publishes the FOP Clinical Treatment Guidelines, which is used internationally to guide the management of patients with FOP. The ICC also has published key recommendations for clinical trials testing potential therapies for FOP.

Follow up response May , 2019

The ICC strives to provide the best possible advice from an international consortium of physicians familiar with FOP. The goal is to encourage safe, accurate, and scientific research into effective treatments and care for FOP patients. There have been many proposed therapies for FOP, some which have not proven to be effective and some which have hurt patients with FOP.

As detailed in the ICC's open letter, the ICC currently does not have an opinion on the efficacy of FOPCon at this time. The fact is that many of the claims of efficacy have been through social media or TV publicity and not through the internationally accepted scientific review process. We, as a community, do not have enough data to say it works or it doesn't work.

The ICC encourages the Palhares team to publically share their data in a peer-reviewed, open manner before they publically claim that they have a treatment. This is critical so that others can help understand, replicate, and determine how well FOPCon works. To date, all public claims of safety and efficacy in the 40 patients they say have been treated with FOPCon have been limited to a case report of 3 subjects and scattered individual case reports in the literature. Understanding how the other 37 subjects fared, with objective data, is critical before anyone jumps to a conclusion about FOPCon.

The ICC simply requests that FOPCon be described as a potential therapy, not an actual therapy, as it is currently portrayed in social media.

The ICC also advises that there be a discussion with a patients' medical team before taking FOPCon or any other potential therapy. Medication interactions and individual risks vary, and so this must be discussed at the individual level. Social media claims of safety are not the same as an open discussion of potential risks. The ICC believes in individual choice. Whether someone takes a potential therapy, or

feels that a therapy works, is an individual judgment that must be made with all available risks and benefits clearly presented.

The ICC agrees that future research should be supported and encourages the IFOPA and funding agencies to support efforts based on the potential merit of a drug. In the case of FOPCon, we agree that the individual reports suggest that more detailed investigation needs to be done. However, since existing data has been collected, the full data set should be shared via publications so that everyone can assess if this is the right therapy for them and the appropriate research studies can be done. This is the same standard that is applied universally before anyone can claim that a potential therapy is a therapy.

The ICC respects the Palhares group and the many other international teams that are seeking treatments for FOP. The ICC simply feels that the public claims for efficacy and safety are premature without the systematic data to back it up. The ICC believes that the FOP community deserves to have an open, objective discussion about FOPCon or any other potential therapy, where the data can be openly reviewed and the potential as a treatment can be objectively assessed.