Liberty Nasal Polyp Study Newsletter

Enrollment update

448 Randomized patients

Early Discontinuation of Treatment

Ongoing Treatment

Completed Treatment

Warm wishes for the new year from the study team

Dear all,

First, let us wish you and your loved ones a very happy new year!

This past year was a great year full of major milestones for dupilumab, patients, and health providers. Dupilumab, sold under the brand name Dupixent, was approved by the FDA in March as a breakthrough therapy for the treatment of adult patients with moderate to severe atopic dermatitis (AD) whose disease is not adequately controlled with topical prescription therapies. The European Commission also granted marketing authorization for Dupixent for AD in September 2017. Dupixent is now approved in many other regions and countries worldwide.

Later in the year, results of the pivotal phase 3 studies demonstrated the efficacy of dupilumab in a broad population of patients with uncontrolled, persistent asthma. Dupilumab, when added to standard therapies, reduced severe asthma attacks (exacerbations) and improved lung function. Dupilumab is also the first biologic to show improvement in a severe, steroid-dependent asthma population that enrolled patients regardless of blood eosinophil levels or any other type 2 biomarkers at baseline.

To start off this new year, we'd like to take the opportunity to thank all the investigators and site staff participating in the Liberty Nasal Polyps program. Thanks to your dedication and excellent work, in less than one year, we could potentially enroll about 800 patients with moderate to severe nasal polyposis uncontrolled by the current standard of care. This is the first and largest-ever phase 3 program with a biologic in nasal polyps. With phase 3 results expected before the end of the year, 2018 is a critical year for the program. We look forward to it with hope and excitement.

Warmest regards,

Gianluca Pirozzi,
Dupixent Global Project Head

Leda Mannent,
Senior Clinical Research Director and Clinical Leader for Nasal Polyps – Dupilumab

News concerning last database extraction

Thank you for your dedication to eCRF data collection and cleaning over the last year! Database extraction was successfully performed on schedule by the December 22 deadline. Database collection was very well done, and we are still investigating data quality.

We are working toward many milestones and the database lock planned for this year. We will keep you informed of updates as they come.

Study reminders

Pregnancy tests

Please remember to conduct pregnancy tests at visits per the protocol schedule. Additionally, the pregnancy test results entered by the patient in the LogPad beginning at Week 12 should be monitored via StudyWorks. In the case of a positive or an inconclusive result, please contact the patient for follow-up.

PPD reminders

Collection condition

According to the latest PPD reports, some samples have been collected with the wrong condition of collection.

In order to avoid any collection issues and re-testing, please always refer to the collection flowchart (v3.0) and strictly follow the instructions for the collection and shipment process.

Frozen versus ambient

On a similar note, several samples have been stored and shipped in the wrong condition. Please be aware that samples wrongly frozen or not frozen, even for storage or shipment, cannot be processed and analyzed. This may lead to losing study data and wasting patient samples.

Please always refer to the collection flowchart (v3.0) for the ambient/frozen collection instructions and be sure to follow them.

Expired kits

Please always check the expiration date of a kit before using it, as some samples have been received with an exceeded expiration date. Be aware that any samples received with an expired date cannot be analyzed and will be disposed of.

Sample labeling

After analysis, it seems that most queries are related to labeling and date of collection. Before shipment, please check that all tubes and requisition have been completed with the visit label and date of the visit. This is extremely important in order to avoid additional work for all the contributors.

ERT acquires Biomedical Systems

ERT has acquired Biomedical Systems, a well-recognized provider of reliable imaging, cardiac safety, and respiratory data collection solutions. ERT completed this acquisition in early September 2017 and shared the news via press release, social media, and email.

We wanted you to be aware of this news, as you might see both a logo and a name change in correspondence you receive from BMS, but this should not impact you in any other way.

Error on page three of the November newsletter

Non-readable Nasal Endoscopy Video Procedures

If one of the readers or adjudicators marks a Visit 8 video as non-readable, the site will be asked to repeat the examination for that patient. If a video of the new exam is **available**, the site can use the same patient number, upload the exam, and submit it in the same manner as used previously at Visit 1. If possible, please perform the new video within four weeks of the first non-readable video. Please refer to Section 3.5 of the Site Procedure Manual v3.0 for more information.

Clinician's corner: Management of rescue treatment

Patients may experience worsening of nasal polyp symptoms over the course of the study, necessitating treatment intensification. According to the protocol, in these conditions, rescue treatment can be provided (see the "Rescue Treatment" section of the protocol). This can be nasal lavage and/or systemic antibiotics, short course oral corticosteroids, or sino-nasal surgery for nasal polyps.

The number of patients requiring rescue treatment is one of the secondary endpoints for this study. Therefore, correct reporting of rescue treatment is key. The question "Did the patient receive any rescue treatment?" is asked at every visit (see the chapter titled, "Rescue Treatment" in CRF Completion Instructions). If the answer is yes, additional questions will appear that are related to the type of rescue treatment and to address if clinical and/or endoscopic worsening of symptoms was observed. We ask that you fill in this information about rescue treatment so the patient can be labeled and identified by the study team as "rescued."

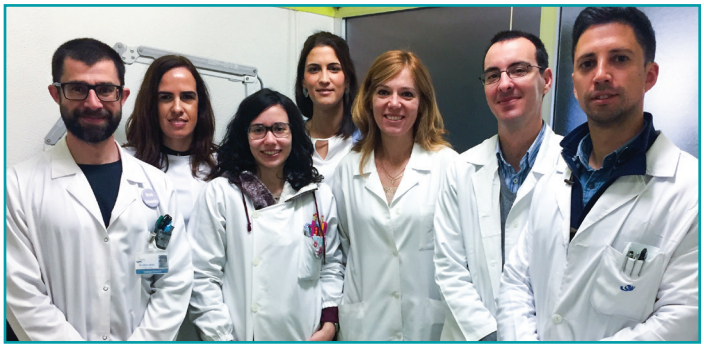
When reporting newly initiated treatment, you will be asked for the reason why this treatment was provided. If, for instance, systemic corticosteroids for nasal polyposis are being prescribed and this is reported in the Medication – Systemic Corticosteroid Form, please select "Reason = Nasal Polyposis" (see the chapter titled, "Medication – Systemic Corticosteroid" in CRF Completion Instructions). This will enable us to correlate the appropriate medication to the rescue treatment. The same applies for other medications (see the chapter titled, "Other Medications" in CRF Completion Instructions). In case systemic antibiotics are prescribed as rescue treatment for nasal polyposis, please select "Reason for Treatment = Rescue Therapy."

Thank you for your efforts and cooperation.

Sincerely,

Maarten Boomsma and
Steven Draikiwicz

Interview with Portugal's top recruiter



From left to right: Dr. Ricardo Leitão – Pharmacist, Dr. Patricia Barbosa (back) – Pharmacist, Bárbara Maia – Study Coordinator, Diana Soares (back) – Study Coordinator, Dr. Luísa Azevedo – Principal Investigator, Dr. Joaquim Vieira – Sub-investigator and Dr. Mario Nuno Branco – Sub-investigator

Dr. Luísa Azevedo | Aveiro, Portugal | Site 6200004

Q. What most interested and motivated you to take part in this study?

A. Nasal polyposis is a complex disease with a large number of failed treatments and repeated surgeries. After reading about the study, I believe dupilumab could be an alternative treatment for patients with moderate to severe signs and symptoms of nasal polyps not controlled by standard-of-care treatment. Participating in this study gives our patients the opportunity to test a new drug with special focus on safety and efficacy, possibly enhancing their quality of life. The three main reasons why I decided to participate in this clinical trial are:

1. The fact that the drug has been developed by a global healthcare leader like Sanofi.
2. Because dupilumab was in the approval stage for the treatment of moderate to severe atopic dermatitis at the time. It has since been approved in March 2017, supporting its safety.
3. Because of the preliminary clinical evidence from phase 2 of this study.

Q. To what do you attribute your success?

A. A doctor does not work by him- or herself, so a good relationship with the patients is essential for successful prevention and treatment of diseases. And this is no different for clinical trials. Without the patients' cooperation and understanding of the potential benefits of participating, these studies simply wouldn't be possible.

So the key to a large recruitment is a good relationship between patient and doctor that's based on trust. Having a very dynamic team is important too. My team is comprised of six ENTs, two nurses, two study coordinators, and two pharmacists.

I also attribute the success of our center to our hard work, the strong relationship between the study team members, and the excellent and effective collaboration of each member in every activity/function that they're delegated to perform.

The months of pre-planning before our first screening and the early selection of patients who could be eligible have also optimized our recruitment.

A well-selected group of patients is key to avoiding screening failures and making well-structured source documents. This makes it easier to conduct visits and take our time.

And finally, we immediately correct any mistakes at our center that are identified by the monitoring team to optimize our performance.

Q. What have been your patients' reactions/ receptivity toward the clinical trial? What do you think could be done to raise awareness and trust in clinical trials or, in particular, this study?

A. As a doctor, my main concern and commitment is to my patient. And I believe that with dupilumab, we have an alternative treatment for patients with moderate to severe signs and symptoms of nasal polyps not controlled by standard-of-care treatment.

A good relationship between doctor and patient is essential to offering the best treatment to our patients. So we need to believe in the clinical trial we're working on to transmit that confidence to them. In conclusion, a well-informed patient with a good relationship with his or her doctor results in good receptivity to the new treatment.

Another important factor is having the knowledge of the patient's profile to know if he or she is able to go further in the study. I am pleased to say that all the patients we proposed to include in the study have accepted it.

Q. Do you anticipate patient retention issues? How are you acting to prevent eventual patient demotivation?

A. Our team doesn't anticipate any retention issues. Our study patients are all motivated by the study treatment, clinical monitoring, and all study-specific procedures. Patient feedback is very positive during scheduled clinical consultations. We think the key to success in patient retention is the total commitment to patients that our whole research team shows in every patient contact.

Q. Finally, your site was recently audited in September 2017 with excellent results (no major or critical findings). How was this experience and what were the main lessons learned?

A. The main and most important lesson learned is that we must document all contacts and events that take place during the course of the study – and we understand the importance of the physical proof of everything (all documents) that is relative to the medical history of each patient.

Watch for the next issue of this newsletter with additional and updated information. And thank you for your continued dedication and support! If you have any questions, please contact your monitoring team.