

Dear friend,

This is Jane Gutkovich, a Vice-president of The EHE Foundation and a Director of Research. I would like to share with you the outcome of a very important milestone EHE meeting that took place on May 29 in Chicago during the ASCO Annual Meeting.

We had 13 leading sarcoma specialists, EHE experts from around the world talking about what should be done to bring EHE cure closer. I started the meeting with a 15 minutes presentation about certain aspects of EHE biology that might give us a good low toxic preventive maintenance regiment to prevent EHE from becoming more aggressive.

Doctors response was " it's all good and definitely makes sense .But we learned that in cancer many things make sense but don't necessarily work. So yes, it would be great to come up with some prophylactic measures but we need assurance that it works and don't do harm " . The conversation then started on what kind of biomarkers it is possible to use in order to determine the slight changes in EHE progression or response to treatment that can't be seeing on the scans yet. Dr Rubin came up with several ideas of what can be such a biomarker , something that can be easily detected in blood work ,

The most promising hypothesis Dr Rubin is planning to work on is the protein CTGF that EHE cells probably excrete and which is responsible for all that fibrotic tissue always associated with EHE . This protein is quite easy to catch in a blood. The idea is, if this protein numbers are growing, EHE is progressing ,if the numbers are going down during the treatment, the treatment is actually working.

Doctors all agreed that it would be a great tool,

Dr Seth Pollack from Seattle came up with a few ideas how we can measure immune response to the progressing EHE . Dr Pollack is a sarcoma specialist working in immunology..He and Dr Rubin agreed to collaborate. Next day after the meeting I took dr Rubin and Dr Pollack out for a lunch and they were discussing the details. The problem, as always is money. Dr Pollack has a clear idea of how to approach EHE from immunological angle. He is currently working on the vaccine for another sarcoma and is willing to do it for EHE .At this point Dr Rubin can't really financially cover a full immunotherapy project. But dr Pollack agreed to make some basic tests. Hopefully, our fundraising efforts will enable him for a real immunotherapy project for EHE . For now, he will run some tests and hopefully will identify some markers of immunoresponse of the body to EHE which can be used to monitor EHE progression.

The topic of best treatment for advance progressing EHE was of course in a center of the meeting. Dr Rubin and Dr Schutze from Michigan University are working on a design of the Mekinist clinical trial. Dr Rubin identified Mekinist as a targeted therapy for EHE in his lab. Now we have to see if it works in patients. The trial has been dragging for several years already. The bitter reality of a rare cancer, the pharmaceutical company is not really rushing to help us. But Dr. Schultze and his fellow, who also attended the meeting seems to be very involved now and working out the details with Dr Rubin.

Doctors asked Dr Rubin about EHE patients that have been already treated with Mekinist . We had so far 4 patients put on this drug. Two of them were too sick to

tolerate it and could not stay on it long enough to see if it is working. The other two, actually had a good initial response, but one patient developed resistance and started progressing. So of course, it doesn't seem to be a magic bullet that will keep EHE at bay forever, but it will help some patient to stay stable for a long time. Dr Rubin actually hopes that Mekinist can be used in lower doses for EHE than for other more aggressive cancers with lower side effects. I will definitely keep you informed about the progress of this trial.

There was a discussion about EHE response to mTor inhibitor Sirolimus. There is definitely a good response seeing in a certain subgroup of EHE patients. Dr Stacchiotti from Milan gave a short summary of her experience which is very encouraging. Out of 15 patients she has had on Sirolimus 11 showed good response. It is very very encouraging!

I helped Dr Adams from Cincinnati Children hospital to get in touch with a few oncologists who have been putting their patients on sirolimus . She is in a process of publishing a retrospective study . I would like to take an opportunity and ask you to let me know if your doctor is considering a treatment for you now. I will send you my file on Sirolimus which includes a few publications and the data from our group. Maybe your doctor will be willing to try it. It's not a very toxic drug and usually well tolerated. Most of post transplant patients are put on this drug for the rest of their life.

Then discussion turned to the lack of clear guidelines for EHE treatment. Different doctors and different institutions have their preferences. The lack of solid information on what works better on what type of EHE is definitely a huge problem. All doctors agreed that the establishment of a solid patient registry that can be used for collecting , combining and analyzing data is THE ONLY way doctors can learn real statistics. You all know very well that not much is published about EHE

Dr Rubin will take a lead in creating such registry. We might use the one that many of you already entered **Patientcrossroads** , (that what we are hoping for). Unfortunately, rules and regulations are so strict that if we want published guidelines that would come from our registry we have to comply with those rules . I had a separate meeting with Dr. Rubin just discussing the EHE registry. Dr Rubin wants to have a professional involved and he does have a person .at Cleveland Clinic who Dr Rubin will ask to work with us. I will keep you informed on the decision. Another big issue that doctors brought up is a correct EHE diagnosis. It's hard to believe but even today many patients are still misdiagnosed. We agreed to come up with the list of reputable institutions. You will receive the list once it becomes available. We also agreed to come up with the list of "EHE specialists", doctors who not only have experience with EHE but really invested in **understanding it** and interested in collaboration with others. It will take some time for us to create such a list. We have to review carefully many sarcoma specialists. I would like to ask your input I it. If you are very happy (or had a bad experience) with a sarcoma specialist, please get back to me and share your thought. It will be extremely helpful to identify right doctors..once the list is complete we will post it on a facebook, on our website and will send it to you.

I am happy to tell you that the fundraising efforts of our group evoked a lot of interest at the meeting. It is a sad reality, but it is... When doctors see there **is** money out there

for this particular cancer, they take it seriously. Because they know that no matter what discussions they have it will all come down to the **funding to support the ideas**.

The meeting that we had was just an hour and a half lunch during a big ontological conference. Dr Rubin suggested having **a full day EHE conference** within a year so doctors will have time to get down to details without time pressure. Most of the doctors expressed their willingness to fly for it. I got very nervous about the cost but Dr. Rubin promised to get funds for the conference from pharmaceutical company.

Dear friend; I would like to remind you again how incredibly lucky we are to have Dr Rubin on our site. Not only he is a great researcher, a true workaholic who deprives his family of his presence to work on EHE, but he assumed a role of a clinical coordinator of **all EHE related efforts** which is completely NOT HIS JOB !!! The time he spends on it could be spent on more publications, more lectures, more of the things that would benefit his resume. But he chose to manage all EHE efforts with no what so ever benefits to his career. Just because **your life is more important to him than his career** .! I usually receive emails from Dr Rubin way past midnight. If he works 18 hours a day to find cure for EHE , what excuse do we have not to help him? Again, I am asking you to think what you can do to support his research.. I visited many presentations during this conference and I could clearly see that the tools to study cancers are already here, they are just not free. And no matter how much bitterness we might feel and how unfair it is that we don't have an access to them, this is a reality and the sooner we realize that it's up to us to put that tools to work on EHE the sooner we will beat this monster.

Please feel free to write to me with any questions. Whether it's the meeting or Dr Rubin's work or work of our (your!!!) foundation, I will be happy to answer them.

Best of luck to you!

Jane

About ASCO

Founded in 1964, the American Society of Clinical Oncology (ASCO) is the world's leading professional organization representing physicians who care for people with cancer. With more than 35,000 members, ASCO is committed to improving cancer care through scientific meetings, educational programs and peer-reviewed journals. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation, which funds ground-breaking research and programs that make a tangible difference in the lives of people with cancer. For ASCO information and resources, visit www.asco.org.

