

Notes from Dr. Mark Moyad

“My last drug, which really, all of these could be supplements. This came from the French Lilac, a natural source, it’s been generic for well over a decade. 21 studies right now suggesting that **metformin** use, the number one drug used in the world for Type 2 diabetics, the number one drug used in the world for pre-diabetes, suggests that **metformin** might reduce the risk of biochemical recurrence, but maybe not all-cause mortality. We do have an LHRH study published in The British Journal of Urology many years ago where they put patients on 850 mg BID and gave them their LHRH or not, and then follow them over six months. Tell me where in the LHRH world, or the ADT world, you see numbers like this. You actually lose weight, your BMI comes down, your body fat comes down, your blood pressure gets better, and there’s no change in lipids. That’s what **metformin** did in this trial, and that’s what we see it do in the breast cancer trials. So, it’s not just potentially going after the progression of the disease, in the worst-case scenario it reduces some of the side effects of hormone therapy, which I think makes it incredibly exciting at about a quarter of it a week. Remember, it’s about a quarter a week; it’s generic. Now, the Swiss just did a new small trial on CRPC patients on **metformin** suggesting that newly diagnosed CRPC patients put on **metformin**, it actually might slow the progression of the disease. They saw other benefits with markers. Again, does the benefit outweigh the risk for these patients? Absolutely. My final thoughts; a lot of patients will start **metformin** on ADT or another situation, they’ll immediately jump to 1,000 or 1,500 with their primary care. We like to recommend 500, the lowest possible dose. Then you take that for two or three weeks, always with a meal, regardless of what it says on the label. You want to take it with a meal, and then that keeps the GI side effects down to that of a placebo, and then you titrate up to the dose you want to get every two to three weeks, and that’s what they’re doing in all the major cancer trials. Keep in mind that this drug is in over 100 clinical trials right now on clinicaltrials.gov with a variety of cancers. It can cause soft stool, you can’t use it with contrast, so basically if you’re going to get contrast, you want to stop it for 48 hours, and the two biggest concerns I actually have on **metformin** is that we do recognize B12 and magnesium deficiencies, so those two levels have to be monitored with their primary care doctor. The primary cares know this; they know it well. My last point on **metformin** on this slide is quite remarkable. I wonder how many people in this audience know that in the United States right now there’s a Phase III trial, and adjuvant trial of **metformin** for breast cancer patients. They just reported on the mid-term analysis of that trial, and the average patient in that trial getting **metformin**, the average woman in that trial who has a BMI about 28, 29, has already lost about 6 or 7 lbs., blood sugar is down about 1 or 2 points, their numbers are all better across the board, cardiovascular-wise, versus the placebo group. So, we’re at least seeing them benefit in terms of the potential for side effect reduction. Whether or not it’s going to reduce the risk of breast cancer recurrence, we’ll know in the next few years. But either way, it goes after

side effects. My final point about lifestyle, because I don't want you to leave here thinking that I'm pushing these pills over lifestyle. This is a slide that no one ever gets to see in the primary care world. The trial that made metformin a billion-dollar drug was called the Diabetes Prevention Trial. It showed that within three years patients in one arm on metformin who weren't even diabetics, they were prediabetics, reduce their risk of getting diabetes by 31% and it made every newspaper. There was a third arm in that trial; it was a lifestyle group that exercised 150 minutes per week. They cut back on about 450 calories a day. They lost about 7% of their body weight, and in that group there was a 58% reduction. It significantly beat metformin in the head-to-head trial, and both beat placebo, and people still walk out of that trial thinking metformin, when they should be thinking intensive lifestyle changes beat the drug."

If you are interested in getting Mark's thoughts on this based on the particulars of your clinical status (especially if you're willing to make a donation to his research foundation), feel free to email him with the details of your laboratory results and clinical status. I've copied him on this treatise in case that's of interest.