**ProjectXYZ - Clinical Trials Biomarker Testing - CompanyABC**

0:0:0.0 --> 0:0:12.960  
Angela Angle  
Great. So to start off this call would be helpful just if you could provide a brief description of your background and your experience that type of the size and type of companies that you've been at in any therapeutic areas of focus, that'd be great.

0:0:13.610 --> 0:0:33.850  
Edward Hewitt  
Yeah, sure. So I'm a trained physician. I've done a PhD in, in hematology and virology. So microbiology in a sense, I have the worked extensively in the clinic and the board certified clinician. I've been in the industry for.

0:0:34.360 --> 0:0:59.580  
Edward Hewitt  
Uh, a long time. I've worked with [Company], which is a key player in diabetes. I worked in the in the clinical development and primarily in phase one and phase two help have advanced an oral GLP 1 tablet and design the phase three program as well. I moved on to [Company].

0:1:0.780 --> 0:1:15.870  
Edward Hewitt  
Big Swiss player and that was mainly in the oncology space and primarily kind of more late stage. So medical affairs, certainly some level of clinical development but also commercialization.

0:1:16.790 --> 0:1:29.200  
Edward Hewitt  
I moved on to [Company] again in a in a medical affairs capacity and then focusing on oncology and and I'm currently with.

0:1:30.320 --> 0:1:32.200  
Edward Hewitt  
A smaller biotech.

0:1:33.500 --> 0:1:38.310  
Edward Hewitt  
There were about 60 to 70 people were working on.

0:1:38.390 --> 0:2:6.760  
Edward Hewitt  
And it tailored or customized personalized cancer vaccines as well as in the infectious disease space. And and here we are doing a lot of that, you know clinical development. And so I have 5 mark your experience stemming back from my time and diabetes, but most recently and perhaps more most in depth is or at least more crisp is on the oncology side of things.

0:2:8.670 --> 0:2:9.430  
Angela Angle  
OK, great.

0:2:8.320 --> 0:2:11.590  
Edward Hewitt  
Yeah, this afternoon provide the the insights that you need.

0:2:12.850 --> 0:2:30.310  
Angela Angle  
Yes, that's helpful. And we'll definitely ask about your experience in apology and with the the newer vaccine experience will be interesting to talk about cancer vaccines and any differences in testing needs between these therapeutic vaccines and prophylactic vaccines as well that be helpful.

0:2:30.60 --> 0:2:31.950  
Edward Hewitt  
Exactly. Exactly. Yeah.

0:2:33.240 --> 0:3:4.30  
Angela Angle  
Umm so I I guess maybe we helpful too since we haven't had as much feedback on that area yet. It might be helpful for us to start with the therapeutic vaccines and it'd be a guess at a high level what we're thinking about in terms of the different type of testing services for biomarkers is you have the radio mix types of tests and maybe this includes amino acids as well genomics histopathology and then immune monitoring. And this can include full cytometry.

0:3:4.250 --> 0:3:10.40  
Angela Angle  
Are there any other bigger biomarker classifications that you think about or are missing from this?

0:3:12.30 --> 0:3:12.620  
Edward Hewitt  
Umm.

0:3:13.700 --> 0:3:20.150  
Edward Hewitt  
So. So we typically we're looking at and maybe that's captured that the farmer could dynamics.

0:3:20.230 --> 0:3:22.890  
Edward Hewitt  
And for instance, if we were looking at.

0:3:24.390 --> 0:3:42.390  
Edward Hewitt  
And using a combination with checkpoint inhibitors such as temporalis IMAP, so kids through and and and similar drugs, we would be looking at some of the we call the PD1 occupancy. So you do that by flow so telemetry.

0:3:42.830 --> 0:3:54.950  
Edward Hewitt  
And and the sample that you use are PBMC is also essentially just take blood blood sample and so that would be an easy former pharma code dynamics space.

0:3:56.560 --> 0:3:59.150  
Edward Hewitt  
We would also be looking at.

0:3:59.880 --> 0:4:13.320  
Edward Hewitt  
Things like uh, she sell phenotyping again by flow cytometry, we would be looking at cytokines like TNF alpha interferon gamma.

0:4:14.90 --> 0:4:19.250  
Edward Hewitt  
And those would be at least look what springs to mind and and the.

0:4:19.860 --> 0:4:21.870  
Edward Hewitt  
When you come to dynamics space.

0:4:21.980 --> 0:4:22.690  
Edward Hewitt  
And.

0:4:24.500 --> 0:4:26.610  
Edward Hewitt  
And what we you talked about?

0:4:26.690 --> 0:4:34.160  
Edward Hewitt  
Yeah. Could you run that by me again? Some of the other examples that that you had mentioned?

0:4:35.230 --> 0:4:48.100  
Angela Angle  
Yeah. And I think some of the, the phenotyping and we might include that in in some of the telemetry, immune monitoring, type of tests, other categories where proteomics, genomics and histopathology.

0:4:48.840 --> 0:4:53.420  
Edward Hewitt  
Yeah, yeah. Hope so. We we've certainly looked into to some of these.

0:5:18.310 --> 0:5:18.620  
Angela Angle  
Mm-hmm.

0:4:54.600 --> 0:5:23.840  
Edward Hewitt  
Not sure it comes in the right category as a kind of a occurs to me, but and so for for some of the stuff that we're looking at, we're looking at specific T cells. So for typically we would in a personalized the vaccine setting we would be looking for the new antigens that we discovered and are then assigning the vaccines against. So you're looking for for these new antigen specific T cells. So those would be.

0:5:23.920 --> 0:5:42.410  
Edward Hewitt  
Sitting four positive cells as well as CD 8 positive T cells so so again it's the presence of these new antigen specific cells in the tumor. We believe to be associated with a better clinical outcomes. So I guess that is if you're looking into a group that would be a filmmaker dynamic.

0:5:44.210 --> 0:5:48.970  
Edward Hewitt  
Category as well and yeah, sure. So we do that by Ellie spot.

0:5:50.230 --> 0:5:50.490  
Angela Angle  
Umm.

0:5:50.730 --> 0:5:56.710  
Edward Hewitt  
Yeah, it's typically so if if that makes sense, we look at.

0:5:57.730 --> 0:6:23.400  
Edward Hewitt  
Tumor infiltrating lymphocytes and so the tilts so immune phenotyping account the composition spatial arrangement. So we look at the presence where the get the presence or whether they're abundant in the tumor. So that would be kind of a tumor microenvironment and way of looking at things again typically by flows atomic tree.

0:6:24.240 --> 0:6:33.230  
Edward Hewitt  
Maybe I HALS seeing. Yeah. So looking at different frequencies of these cell specific cell population relative to the total cell number.

0:6:34.410 --> 0:6:37.560  
Edward Hewitt  
Umm, we look at.

0:6:39.520 --> 0:6:43.170  
Edward Hewitt  
And certainly circulating tumor DNA.

0:6:46.90 --> 0:6:46.320  
Angela Angle  
Umm.

0:6:44.40 --> 0:6:51.90  
Edward Hewitt  
And it says CT DNA. Again, the presence of CT DNA in the blood is associated typically with the poor patient outcome.

0:6:51.640 --> 0:6:58.890  
Edward Hewitt  
And and and so. So there are different ways of doing that, but that's obviously by by by sequencing.

0:7:12.780 --> 0:7:13.100  
Angela Angle  
Mm-hmm.

0:6:59.140 --> 0:7:13.220  
Edward Hewitt  
And and you can do that either through a solid tumor solid scuse me a solid sample from from the tumor. But we're also looking into perhaps doing this as a liquid biopsy. So in the blood.

0:7:13.700 --> 0:7:28.830  
Edward Hewitt  
And so that kind of the wherever at this kind of debris tumor degree might be circulating. And so so so typically do digital PCR and forgotten just looking at the number of C DNA copies being found.

0:7:29.650 --> 0:7:38.670  
Edward Hewitt  
And we also look at circulating tumor cells. Again, the presence of these cells is associated with the poor patient outcome.

0:7:39.430 --> 0:7:58.10  
Edward Hewitt  
And they are being isolated from, from blood, using different ways. Some use iron nanoparticles with the using antibodies to capture these. And then there are staying, typically with the nuclear stain and and and the fluorescent antibody.

0:7:59.210 --> 0:8:3.330  
Edward Hewitt  
So. So those would be some of the things that we'd be looking at and.

0:8:15.650 --> 0:8:15.960  
Angela Angle  
Umm.

0:8:4.660 --> 0:8:24.430  
Edward Hewitt  
Sometimes we've been looking at it. She cell receptor profiling is this becomes kind of maybe very specific for for what we did. I'm not sure how widely applicable this is, but again understanding the diversity of the the CR, the T cell receptor reference or and clonal Colonel appearance.

0:8:24.990 --> 0:8:25.800  
Angela Angle  
And that sequencing?

0:8:25.60 --> 0:8:32.840  
Edward Hewitt  
Uh, it's it, and that is done by deep sequencing, typically at the amplified M RNA and yeah.

0:8:33.630 --> 0:8:40.230  
Edward Hewitt  
And we use PMC for that, to the drugs and and we extract the flash frozen.

0:8:41.630 --> 0:8:46.320  
Edward Hewitt  
I'm so sorry and we typically use. Yeah, the RNA from PMC.

0:8:48.330 --> 0:8:48.700  
Angela Angle  
OK.

0:8:48.240 --> 0:8:54.640  
Edward Hewitt  
OK. And another, let me just stop you from this is not applicable to because again it's.

0:8:55.550 --> 0:9:4.560  
Edward Hewitt  
I I appreciate what we do is maybe not widely used, but but we are certainly interested in what we call the tumor mutational burden.

0:9:5.140 --> 0:9:24.870  
Edward Hewitt  
Uh, so looking at the the the number of mutations in a given tumor because that is associated again with with the outcome and the promise of the checkpoint inhibitor or the likelihood of success of using a checkpointing hitter.

0:9:25.340 --> 0:9:42.260  
Edward Hewitt  
And so so that is of interest. So that is more on the tumor genomic biomarkers and and within that sphere we also look for typically a DNA mismatch repair. So microsite satellite instability.

0:9:42.810 --> 0:9:56.640  
Edward Hewitt  
And again, the belief is if if there's a DNA repair deficiency that could suit lead to a generally a higher number of mutations and faster evolving tumors and seemingly microsite.

0:9:56.840 --> 0:10:10.50  
Edward Hewitt  
And Max microsatellite instability in our view and others refer to, you know, a higher degree of new mutations and.

0:10:11.50 --> 0:10:22.500  
Edward Hewitt  
Possibly because there is some kind of a impaired DNA mismatch and repair function. And again it's it's a poor prognostic marker.

0:10:23.620 --> 0:10:31.80  
Edward Hewitt  
Yeah. So, so, so this would be some, some of the issues or some of the areas that we look for in that too much anomic biomarker.

0:10:32.150 --> 0:10:40.560  
Edward Hewitt  
We look at any and HC 2 and 1 gene expressions, so again that would be M RNA.

0:10:41.490 --> 0:10:49.510  
Edward Hewitt  
And so sequencing we we use that for helping to design or vaccines.

0:10:50.30 --> 0:10:55.140  
Edward Hewitt  
And again, because it's a tailored approach, so that would be, yeah.

0:10:56.300 --> 0:10:58.530  
Edward Hewitt  
Some of the stuff that we're looking at and.

0:10:59.310 --> 0:10:59.580  
Edward Hewitt  
Yeah.

0:10:59.270 --> 0:11:0.660  
Angela Angle  
And and So what was that it was?

0:11:1.800 --> 0:11:2.870  
Angela Angle  
MHC 2.

0:11:6.10 --> 0:11:7.20  
Angela Angle  
And HC OK.

0:11:10.550 --> 0:11:11.0  
Angela Angle  
OK.

0:11:2.180 --> 0:11:15.50  
Edward Hewitt  
But so, so NHC and so the MHC is a major history. History compatibility. Yeah. Complex. So one and two. So so again for.

0:11:15.120 --> 0:11:24.700  
Edward Hewitt  
OK. One being tied, obviously two see AIDS and and and two for for the CD fours. So we should we look at that because it's it's part of the.

0:11:25.340 --> 0:11:30.90  
Edward Hewitt  
And algorithm that we use for designing these personalized vaccines.

0:11:30.770 --> 0:11:36.340  
Edward Hewitt  
I again, I appreciate what we do is maybe highly selective them not widely applicable.

0:11:37.0 --> 0:11:39.920  
Edward Hewitt  
And yeah, we also look at.

0:11:38.780 --> 0:11:40.190  
Angela Angle  
Yeah, like I said, be.

0:11:41.140 --> 0:11:41.760  
Edward Hewitt  
Go ahead.

0:11:41.50 --> 0:11:50.980  
Angela Angle  
So I just wanted to clarify with some of the technologies that you mentioned so far. So it sounds like so then the new antigen specific T cells, that's of course gonna be for the therapeutic vaccines.

0:11:58.990 --> 0:12:0.540  
Edward Hewitt  
Yes, yes.

0:12:3.310 --> 0:12:3.730  
Edward Hewitt  
Yes.

0:11:52.370 --> 0:12:15.620  
Angela Angle  
And then MHC one and two testing, is that also specific for just the therapeutic vaccine? So I'm just trying to understand which technologies compared to a traditional oncology drug, which ones are specific to the vaccine space and are there on the flip side, are there any commonly run biomarker tests in the broader oncology space that are not as relevant to vaccines?

0:12:16.170 --> 0:12:21.900  
Edward Hewitt  
Yeah. So I would say that the MHC is probably more specific for.

0:12:22.290 --> 0:12:37.970  
Edward Hewitt  
And for helping us to to design the vaccine so so it's a it's more probably not something you would encounter is frequently in kind of a small molecule kind of off the shelf.

0:12:39.140 --> 0:12:50.0  
Edward Hewitt  
And some would say it's the beta in terms of the prognostic value. Looking at the image MC generally speaking, but we certainly use it, it's it's a it's a.

0:12:50.80 --> 0:12:54.270  
Edward Hewitt  
And it's a must, a component it's it's a.

0:12:55.40 --> 0:13:19.250  
Edward Hewitt  
And it's it's a key component in how we decide the vaccines. Again, the vaccine is decide based on the absurd mutations. So the new antigens being presented, but it's also coupled or associated with the host, the host in this case being represented by the NHC.

0:13:19.530 --> 0:13:40.890  
Edward Hewitt  
And obviously you and I probably don't share the same tissue type heads, our MC ways of presenting or being presented with antigens or are different. So, so you and I would require different designs. So so that is taken into account when we design the vaccine. So that is a very I think.

0:13:42.70 --> 0:13:48.130  
Edward Hewitt  
Specific piece to to how we design the vaccine. So it's yeah, yeah.

0:13:49.160 --> 0:13:59.280  
Angela Angle  
And for the MC testing what sort of assets is that? Are you sequencing the genes or doing some sort of immunoassay for their reactivity or or what's involved there?

0:14:10.530 --> 0:14:10.850  
Angela Angle  
OK.

0:14:0.280 --> 0:14:15.950  
Edward Hewitt  
You can certainly do the sequencing and typically RNA sequencing. So we're really looking at expression levels. So Mr. so we're looking at expression values essentially.

0:14:16.650 --> 0:14:19.680  
Edward Hewitt  
Based on tumor biopsies, so these would be the.

0:14:20.490 --> 0:14:31.50  
Edward Hewitt  
And yeah, typically you'd put this in into either a fresh frozen or an RNA RNA. Later you. We could also use.

0:14:32.550 --> 0:14:34.240  
Edward Hewitt  
It blocks FP.

0:14:34.350 --> 0:14:35.60  
Edward Hewitt  
And.

0:14:36.460 --> 0:14:40.290  
Edward Hewitt  
To the tissue being being in paraffin and embedded.

0:14:41.880 --> 0:14:46.910  
Edward Hewitt  
That the RNA leader of fresh frozen. This is the preferred sample requirement.

0:14:47.780 --> 0:14:48.30  
Angela Angle  
Umm.

0:14:48.490 --> 0:14:52.480  
Edward Hewitt  
OK, it gets the best quality eventually that that expression values yes.

0:14:53.140 --> 0:15:13.720  
Angela Angle  
Umm so for the MHCC sequencing as well as the new antigen specific T cell flow cytometry experiments. Is this, are these something that you're doing just in the design, maybe manufacturing stages of the vaccine or are you performing any of these tests during preclinical or clinical trials?

0:15:14.600 --> 0:15:18.230  
Edward Hewitt  
We we certainly used them in the preclinical setting as well.

0:15:18.410 --> 0:15:19.30  
Edward Hewitt  
Uh.

0:15:21.420 --> 0:15:26.830  
Edward Hewitt  
Yes, yes, the the the that, that, that that would be pretty much the same I'd say.

0:15:29.170 --> 0:15:29.380  
Edward Hewitt  
Yeah.

0:15:30.950 --> 0:15:31.390  
Angela Angle  
And then.

0:15:30.470 --> 0:15:33.460  
Edward Hewitt  
Same same type of thing. Yeah, testing.

0:15:33.270 --> 0:15:47.650  
Angela Angle  
And when you get to clinical testing or the clinical stage trials, are there any biomarker testing that you would need to perform because you're working with a therapeutic vaccine compared to some other more typical oncology drug?

0:15:49.910 --> 0:15:51.130  
Edward Hewitt  
Umm.

0:15:52.460 --> 0:15:54.860  
Edward Hewitt  
Yeah. Well, I, I mean we are looking at.

0:15:54.960 --> 0:16:2.610  
Edward Hewitt  
I didn't mention that we're also looking at the the PD, L1 and PD that you one level. So so the ligands.

0:16:2.710 --> 0:16:15.420  
Edward Hewitt  
Uh, uh and and again be the both the occupancy and and the expression levels, you know some have higher and lower levels and just just to kind of wrap that up and and again that's.

0:16:15.540 --> 0:16:19.600  
Edward Hewitt  
And related to the fact that we use checkpoint inhibitors.

0:16:19.890 --> 0:16:29.600  
Edward Hewitt  
Yeah. Yeah. So, so, so again, depends on on the type of trial that that you're looking for and that that at least that's that's.

0:16:30.370 --> 0:16:43.400  
Edward Hewitt  
Part of what we do and and I know it was part of what Merck and others did that as part of the culture, the trials and and the BMS trials and the Divo, etcetera, that they they also looked at the P1 levels PS1.

0:16:43.360 --> 0:16:43.650  
Angela Angle  
Umm.

0:16:44.130 --> 0:16:47.460  
Edward Hewitt  
And but specific for.

0:16:48.210 --> 0:16:48.780  
Edward Hewitt  
Umm.

0:16:50.290 --> 0:17:1.360  
Edward Hewitt  
Yeah. So I, I mean, because we're talking, you know, this is in therapy, right and the the tumor mutational burden is something which is.

0:17:1.830 --> 0:17:2.710  
Edward Hewitt  
And.

0:17:19.660 --> 0:17:19.930  
Angela Angle  
Umm.

0:17:3.410 --> 0:17:28.660  
Edward Hewitt  
Key to to what we about, man, it's it's how we help select the indication in the 1st place. So the indication like skin cancer and Melanoma, you have typically higher mutation to a mutational burden. So that's that's also kind of a key to what we look for versus pancreatic cancer just to mention one example which is very low. So that's kind of being ruled out.

0:17:29.390 --> 0:17:30.100  
Edward Hewitt  
And.

0:17:52.60 --> 0:17:52.370  
Angela Angle  
Umm.

0:17:31.550 --> 0:18:0.400  
Edward Hewitt  
Yeah. I mean, we basically we we sequence the tumor and we compare against normal tissue and we need to find a number of I wanna say promising new antigens that is core. If we can't find any meaningful differences to then decide and training in system it makes no sense. So it is yeah so so that's kind of the gatekeeper you need to absolutely need to find relevant.

0:18:1.640 --> 0:18:2.800  
Edward Hewitt  
Even the genic.

0:18:5.340 --> 0:18:7.210  
Edward Hewitt  
Mutations, yeah.

0:18:18.320 --> 0:18:18.670  
Edward Hewitt  
That's.

0:18:8.890 --> 0:18:19.880  
Angela Angle  
Are you to to find these new antigens? Are you doing some sort of spatial sequencing or a more traditional NGS on like a resuspended? Make sure of tumor sample.

0:18:20.510 --> 0:18:26.40  
Edward Hewitt  
And I mean this just hold, hold or excellent sequencing I should say, yeah.

0:18:26.760 --> 0:18:28.610  
Edward Hewitt  
So I said we we do the entire Excel.

0:18:31.520 --> 0:18:37.600  
Angela Angle  
OK. So it's not like a sequencing within the the spatial context of a tissue slice, it's more of a.

0:18:38.690 --> 0:18:39.40  
Edward Hewitt  
No.

0:18:40.640 --> 0:18:40.890  
Edward Hewitt  
Yes.

0:18:38.530 --> 0:18:42.160  
Angela Angle  
A holistic scan of what's in that sample.

0:18:42.790 --> 0:19:13.160  
Edward Hewitt  
Exactly what we've been looking into doing, you know single cell but but the and and we're touring around with this, but we're not based the vaccines on this so far and and you touch upon a kind of a sensitive issue because what we're you know given the nature of this being cancer, we also looking at clonality as this really a true representation of kind of the the tumor and you know universally or looking at this from from.

0:19:13.250 --> 0:19:19.330  
Edward Hewitt  
Kind of a higher up perspective is, is this a good representation of what is, you know, across?

0:19:20.220 --> 0:19:31.440  
Edward Hewitt  
And the tumor. But we have not done a spatial like either one anatomical location versus another, like different sites of the body or within the tumor.

0:19:31.720 --> 0:19:34.620  
Edward Hewitt  
And no door or the particular.

0:19:36.80 --> 0:19:36.800  
Edward Hewitt  
Yeah.

0:19:38.680 --> 0:19:48.530  
Edward Hewitt  
Yeah, piece of the tumor. We would not gone in and and and done one side versus another within one specific location.

0:19:50.710 --> 0:20:10.700  
Angela Angle  
OK. And for the the new antigens, are you performing any sort of amino assays for the levels of that antigen that's present in different tumors may be before and after treatment or is it primarily monitoring the new antigen specific T cells by flow cytometry throughout the clinical trials?

0:20:11.800 --> 0:20:33.550  
Edward Hewitt  
So so typically we were able to. So we have a payload of 10 to 15 new antigens that we put into the vaccine and we're able to then you know the you. You can then look at, do you get a generally speaking a spike or an increase in the CD agency for levels. So so you know.

0:20:33.860 --> 0:20:34.510  
Edward Hewitt  
Uh.

0:20:37.70 --> 0:20:40.600  
Edward Hewitt  
And a new spike with these specific.

0:20:40.740 --> 0:20:57.160  
Edward Hewitt  
And she sells, but we can also go in, you know, the level of granularity. So say you have a payload of 10 different new antigens where you can actually go in and and look at each of these 10 and maybe that you know based on our.

0:21:9.740 --> 0:21:9.990  
Angela Angle  
Umm.

0:20:57.480 --> 0:21:27.870  
Edward Hewitt  
And this is an AI to write platform that's so it's kind of that prediction on what is, you know, supposedly the most immunogenic, again based on on the on the host and then what we find in the tumor and and we would ran those and just very quickly. So in in a in a Melanoma setting you'd oftentimes you'd find at least maybe 300 mutations sometimes more than 1000, but let's yeah 300 and we picked the top.

0:21:27.960 --> 0:21:28.870  
Edward Hewitt  
1015.

0:21:29.950 --> 0:21:40.660  
Edward Hewitt  
That we can then see afterwards that maybe yes, one and two and #7 turned out to be the most immunogenic so we can go back and and and do that kind of.

0:21:41.100 --> 0:21:46.300  
Edward Hewitt  
And assessment or measurement afterwards.

0:21:47.20 --> 0:21:57.40  
Edward Hewitt  
And yeah, and and and yeah. And then there's the learning in that as well and obviously and and it was the prediction, did it hold true or not?

0:22:0.790 --> 0:22:1.10  
Edward Hewitt  
Yeah.

0:22:5.630 --> 0:22:5.900  
Edward Hewitt  
Yes.

0:21:59.180 --> 0:22:17.570  
Angela Angle  
Yeah, that makes sense. I guess for use in the clinic and I guess you're probably test some preclinic too, but are there certain safety types of assessments that you're using biomarkers for to ensure that the immune response isn't is appropriate for lack of a better word?

0:22:18.460 --> 0:22:19.370  
Edward Hewitt  
Umm.

0:22:24.580 --> 0:22:25.710  
Edward Hewitt  
Yeah, yeah.

0:22:20.600 --> 0:22:26.630  
Angela Angle  
Like not a causing cytokine storms or auto reactivity if yeah.

0:22:27.540 --> 0:22:33.350  
Edward Hewitt  
Yeah. So I previously with Novartis, I worked in the Carthy space and there are certainly the cytokines where.

0:22:33.550 --> 0:22:39.390  
Edward Hewitt  
Umm with with concern and we we don't really see so.

0:22:40.610 --> 0:22:46.480  
Edward Hewitt  
Knock on wood, but you know. But for now, what we've seen in terms of the adverse events.

0:22:46.560 --> 0:22:47.130  
Edward Hewitt  
Yeah, right.

0:22:47.210 --> 0:23:17.0  
Edward Hewitt  
And I'm, you know, very mild, there were transient self limiting. It is what you'd expect from any ordinary vaccine injection site as one is a little bit swelling, maybe a slight brief fever. That's about it. So. So there are no real concerns safety wise and so we're not monitoring anything in particular, no kind of spikes in liver enzymes or like.

0:23:17.210 --> 0:23:19.900  
Edward Hewitt  
OK. Yeah, we, we haven't come across that.

0:23:20.800 --> 0:23:27.870  
Angela Angle  
Umm are you performing any larger scale proteomics experiments or are you primarily working at the M RNA level?

0:23:29.300 --> 0:23:33.590  
Edward Hewitt  
So we we've looked into that, but but we're not, it's not.

0:23:35.200 --> 0:23:43.550  
Edward Hewitt  
Yeah, core to what we do in a clinical setting. So it's more on a testing space. So I I I wouldn't claim that that we were at this stage.

0:23:43.630 --> 0:23:47.880  
Edward Hewitt  
And and to to do the whole lot in that in that space.

0:23:49.940 --> 0:23:52.910  
Angela Angle  
OK, I want to ask a little bit about.

0:23:54.130 --> 0:24:22.780  
Angela Angle  
The outsourcing considerations for some of these tests and then I just wanted to after that touch a little bit on the infectious disease vaccine work. But for the therapeutic vaccines, are there certain types of tests that you are there may be more challenging to perform in house that they require a lot of asset development that you may outsource this type of testing or what are kind of the main drivers that would lead you to look for a partner to help develop and perform testing?

0:24:23.630 --> 0:24:35.590  
Edward Hewitt  
Yeah. So I I think what one of our main challenges operationally has been, this may sound silly, but it's simply the handling of the PMC's.

0:24:36.190 --> 0:24:38.30  
Edward Hewitt  
And and and.

0:24:39.770 --> 0:25:4.190  
Edward Hewitt  
Sometimes it just works. Change we had as trial running in Perth, Australia, WA. I don't know what they did. They maybe they had extended coffee breaks but things didn't work. And then we shipped the lab. It worked from day one and it's not a difficult protocol. So. So it's not. It's not always a technical challenge, but that was simply the handling of the PBMC's.

0:25:4.900 --> 0:25:9.290  
Edward Hewitt  
For shipment, we would then be on the receiving end that we would do all of its testing.

0:25:9.980 --> 0:25:18.410  
Edward Hewitt  
Uh. Another kind of more of a English to logistic or operational issue have been has been on the.

0:25:19.640 --> 0:25:36.720  
Edward Hewitt  
And preserving the sample. So again for take Melanoma, you take a sample of the search and needs to be instructed. You cannot leave it on the table for half an hour because again, it's M RNA. It's it's it's frail, it's you know, so you need to to observe.

0:25:37.460 --> 0:26:0.470  
Edward Hewitt  
Uh, some specific procedures. It's not difficult. It's more kind of a top of mind issue. Again, more of an operational thing. So those those have been our main challenges. Other than that, I think so taking the the trial in Australia as an example, you know opposite ends of the globe, obviously this you know.

0:26:0.780 --> 0:26:9.720  
Edward Hewitt  
And these samples are then sent the ship to Denmark, but the tumor samples are actually set for a California.

0:26:11.30 --> 0:26:11.320  
Angela Angle  
Umm.

0:26:10.420 --> 0:26:35.870  
Edward Hewitt  
And being sequenced there and we get the results and and it's it's it's it's been a non issue and these are highly professional, well trained and logistics work in that setting. Once it's been in the initial whatever shipment conditions and container at the you know I I'm actually quite impressed by by the speed it's like it's easy and and the.

0:26:36.620 --> 0:26:44.850  
Edward Hewitt  
Yeah, and quality and and like. Yeah. And I think it's, it's actually been it's.

0:26:45.790 --> 0:27:3.70  
Edward Hewitt  
It's progressed and improved quite a bit since we started 567 years ago. And so yeah, it it actually works. So so for the sequencing we have we get that done and personnel as we've done have others.

0:27:3.180 --> 0:27:5.180  
Edward Hewitt  
And and.

0:27:6.0 --> 0:27:14.980  
Edward Hewitt  
Everything else we pretty much do in house because it's it's again we we have a big lab, we have a.

0:27:16.110 --> 0:27:27.840  
Edward Hewitt  
We grew from being an AI company into doing preclinical lots of scientists in, in the company and only recently moved into the clinic. So it kind of.

0:27:28.590 --> 0:27:34.860  
Edward Hewitt  
It's it's been built on on a, on a pretty solid base technical base, if that makes sense.

0:27:36.280 --> 0:27:42.700  
Angela Angle  
Do you have a GMP lab in house to perform some of the clinical tests? Or do does that stage get outsourced to different company?

0:27:43.510 --> 0:27:45.100  
Edward Hewitt  
No, no, we we did that in House.

0:27:45.730 --> 0:27:46.50  
Angela Angle  
OK.

0:27:47.360 --> 0:27:56.740  
Angela Angle  
And for the the company in California that you said is doing the sequencing, are they just doing the sequencing or are they involved in any of the analysis of the sequencing results?

0:27:57.540 --> 0:28:22.630  
Edward Hewitt  
No. So so they just sent us, you know, a huge file and and there are multiple I I forget how many times each sequence is sequenced or each area of the genome, because sometimes not there errors in sequencing or you know and again coming back to the clonality it's so it's it's it's it's a pretty deep sequencing and so we just get the sent to we received the files.

0:28:23.70 --> 0:28:53.400  
Edward Hewitt  
Yeah, and and then it's our by informaticians that that handle the the whole procedure. And I'm not well versed in that. I I stand on the side and awe and that's and they I know they put this into a high end computer and a digestives and spends I don't know 1215 hours and spits out there suggested ranking of the identified mutations yeah so that is done by us and it's actually.

0:28:54.100 --> 0:29:13.610  
Edward Hewitt  
Alright, claim to fame is actually this, this prediction tool or or the tool for identified the meaningful or the most immunogenic, new antigens that and everything else is built on top of that. But that's kind of the Forte of the company is, is to do just that.

0:29:16.0 --> 0:29:19.870  
Angela Angle  
OK, uh, going back to some of the other types of tests that you mentioned.

0:29:20.990 --> 0:29:36.560  
Angela Angle  
Ellie spots tumor infiltrating lymphocyte testing. Circulating tumor DNA. Are these things that you're that are also being performed in traditional oncology programs or or any of these specific at all to the cancer vaccines that you've been working on?

0:29:37.650 --> 0:29:39.580  
Edward Hewitt  
I I would say that so for.

0:29:41.910 --> 0:29:42.550  
Edward Hewitt  
Uh.

0:29:44.730 --> 0:29:45.520  
Edward Hewitt  
Let me see.

0:29:46.690 --> 0:29:47.390  
Edward Hewitt  
Umm.

0:29:50.150 --> 0:30:1.790  
Edward Hewitt  
Some have probably in the summer micro environment like this cytokine status I and and the tills that tumor infiltrating looks like I would assume that is.

0:30:3.320 --> 0:30:6.270  
Edward Hewitt  
Common outside of of the space that we're operating in.

0:30:8.190 --> 0:30:19.620  
Edward Hewitt  
There are different tumor microenvironment markers that are kind of coming onto the scene and there's one called I delete S 100 if I recall correctly.

0:30:20.130 --> 0:30:36.370  
Edward Hewitt  
And certainly the PD1 and PDL one expression levels I I would assume that this is quite common. Again it's it's it's it talks about you know the profile of the tumor, how amenable or?

0:30:38.10 --> 0:30:39.450  
Edward Hewitt  
Receptive this this.

0:30:39.550 --> 0:30:45.160  
Edward Hewitt  
Alright, and tumor against for instance checkpoint inhibitor treatment and?

0:30:47.300 --> 0:30:57.960  
Edward Hewitt  
Yeah. So some look at in against staying with the tumor microline somewhere, talking about or looking into potential activation of NK cells from anti PD one.

0:30:59.440 --> 0:31:9.340  
Edward Hewitt  
Something to talk about cancer stem cells. I'm not too well versed in that, but those would be areas that I I assume could hold an interest outside of what we do.

0:31:11.320 --> 0:31:14.980  
Edward Hewitt  
I'm pretty sure like moving into the till so.

0:31:15.60 --> 0:31:31.390  
Edward Hewitt  
And trying to training on the sides. Yeah, I'm pretty sure others would be looking at people. One expression in in that regard. I mean, we look at new entity and reactivity, but that's specific to us, but.

0:31:32.540 --> 0:31:36.530  
Edward Hewitt  
Yeah. So and PD one expression and CD 8 positive T cells.

0:31:37.700 --> 0:31:51.440  
Edward Hewitt  
And PD one expression in T red. So so regulatory itself, uh, maybe looking at the ratio against CD8 positive T cells and those could be areas that might hold an interest.

0:31:53.800 --> 0:31:56.150  
Edward Hewitt  
I think moving into the PBMC.

0:32:5.150 --> 0:32:5.410  
Angela Angle  
Mm-hmm.

0:31:59.370 --> 0:32:11.310  
Edward Hewitt  
We look at what we call cytotoxic T cell assay, so it's kind of a T cell killing. And I think that that could be relevant for others as well. And that's not, you know unique to what we do.

0:32:13.150 --> 0:32:15.460  
Edward Hewitt  
Some look at 2 so phenotyping.

0:32:17.90 --> 0:32:23.890  
Edward Hewitt  
Yeah. And that, that, that, that would be some of the things and moving into.

0:32:24.430 --> 0:32:28.410  
Edward Hewitt  
I the Sarah, you know Sally, Sally table, saleable.

0:32:28.720 --> 0:32:38.610  
Edward Hewitt  
And P1PPL1 sidelines, you know, we talked about those TNF alpha and network gamma.

0:32:39.190 --> 0:32:58.780  
Edward Hewitt  
Uh grandson B or some of this stuff that people are looking at their, they're looking at literate sounds like LBH and so on that that is definitely not specific for what we do that that's more of a kind of a general biomarker talks about the it's it's associated with the stage of the Seas.

0:32:59.880 --> 0:33:1.40  
Edward Hewitt  
So yeah.

0:33:2.200 --> 0:33:2.710  
Edward Hewitt  
And.

0:33:19.760 --> 0:33:20.220  
Edward Hewitt  
Yes.

0:33:2.220 --> 0:33:24.830  
Angela Angle  
And for some of these, biomarkers just went to to clarify, are these well established biomarkers that people have been testing for for years or are these like relatively new biomarkers that people are using to understand to microenvironment immune response? Just trying to understand how much innovation there is in the biomarker space and how many new biomarkers are being developed?

0:33:25.300 --> 0:33:27.80  
Edward Hewitt  
Yeah, that's that's a good point.

0:33:35.300 --> 0:33:35.530  
Angela Angle  
Yep.

0:33:27.160 --> 0:33:42.130  
Edward Hewitt  
Umm, I would so 68 and C4A. Certainly a, you know, run-of-the-mill, I say looking at three, one and PDL 1 levels and it's certainly common as well, cytokines for sure.

0:33:44.420 --> 0:33:52.170  
Edward Hewitt  
We talked about LPH absolutely it's it's probably one of the oldest ways of measuring on monitoring.

0:33:53.810 --> 0:33:59.460  
Edward Hewitt  
Just to make, just to mention one of these kind of more common.

0:34:1.510 --> 0:34:5.70  
Edward Hewitt  
Once you start talking about till phenotyping.

0:34:9.30 --> 0:34:10.10  
Edward Hewitt  
We talked about.

0:34:10.90 --> 0:34:10.660  
Edward Hewitt  
Yeah.

0:34:12.110 --> 0:34:12.970  
Edward Hewitt  
And.

0:34:25.900 --> 0:34:26.160  
Angela Angle  
No.

0:34:14.570 --> 0:34:44.820  
Edward Hewitt  
Yeah, she's selling. Filtration was perhaps coming more, you know, online and, but both those I I would assume are kind of more new to the game and the T cell receptor sequencing is is I think new as well as as well as C receptor reference wire again using both PMCS and tumors those would be new the we talked about the expression level so anything.

0:34:44.960 --> 0:34:52.130  
Edward Hewitt  
To do related to M RNA and you know the expression levels of of these expressed.

0:34:52.210 --> 0:34:56.30  
Edward Hewitt  
Yeah, and and product such as the?

0:34:56.180 --> 0:34:59.630  
Edward Hewitt  
Would you like HLE expression? I I think it's.

0:35:0.790 --> 0:35:11.720  
Edward Hewitt  
It's more of a novelty and in the middle of this I would put the tumor mutational burden. It's it's growing in recognition.

0:35:12.650 --> 0:35:21.730  
Edward Hewitt  
As as a way of of looking at the you know how likely is the patient in in terms of responding another.

0:35:22.400 --> 0:35:36.200  
Edward Hewitt  
Peace, and this is perhaps quite important, is the CTL DNA, the circulating tumor DNA. There is more and more evidence that kind of underpins or or or emphasizes.

0:35:36.860 --> 0:36:3.410  
Edward Hewitt  
And points to the fact that this can be used as as a monitoring. You know what stage are we in? Is that therapy working? And but it also talks about it's a prognostic factor as well. And there you were probably I think the last time I read on this on this was so for lung cancer it is more acknowledged the more recognized bigger.

0:36:30.140 --> 0:36:30.420  
Angela Angle  
Umm.

0:36:4.120 --> 0:36:32.410  
Edward Hewitt  
And evidence pool, I said suggest, I suppose other indications less so, but so. So it's CT DNA is coming on to the scene and for reasons that I cannot speak to this, I simply don't know. But the, the the level of evidence and and and the confidence is this and this is slightly depending on the on the indication but that is you know some of the stuff that is coming on to the scene that makes the does that make sense.

0:36:33.850 --> 0:36:34.140  
Edward Hewitt  
It.

0:36:33.390 --> 0:36:47.580  
Angela Angle  
Yeah, like a couple of follow up questions for TCR sequencing. Are there specific areas and oncology where this more important like liquid versus solid tumors, very specific indications that this is important for our modalities that this is important for?

0:36:52.470 --> 0:36:52.870  
Edward Hewitt  
Yeah.

0:36:54.580 --> 0:36:58.470  
Edward Hewitt  
I I think it's important for what we do in the personalized setting.

0:36:59.100 --> 0:36:59.800  
Edward Hewitt  
And.

0:37:1.950 --> 0:37:12.750  
Edward Hewitt  
I'm not sure that it is equally important. I I I don't think so in in more kind of an off the shelf at a type of drug.

0:37:14.610 --> 0:37:14.850  
Angela Angle  
Umm.

0:37:13.500 --> 0:37:18.190  
Edward Hewitt  
Umm, I may be overseeing something or or you know or overlooking.

0:37:19.120 --> 0:37:22.260  
Edward Hewitt  
And missing something that it's probably.

0:37:24.250 --> 0:37:25.40  
Edward Hewitt  
That's important.

0:37:26.150 --> 0:37:26.540  
Edward Hewitt  
Yeah.

0:37:26.430 --> 0:37:39.400  
Angela Angle  
And what about uh, circulating tumor DNA? I guess I'm trying to find areas and to types of tests or areas. I'm oncology, where there's gonna be a new types of testing or more frequent types of testing in the future.

0:37:40.100 --> 0:37:40.740  
Edward Hewitt  
Yeah.

0:37:52.260 --> 0:37:52.550  
Angela Angle  
Umm.

0:37:55.200 --> 0:37:55.500  
Angela Angle  
OK.

0:37:44.40 --> 0:37:58.60  
Edward Hewitt  
For it is CT DNA I my assumption so I'm I'm more familiar with the solid tumors in this setting. I I really can't speak to hematology, so leukemia and other, I I simply don't know.

0:37:58.390 --> 0:38:2.710  
Edward Hewitt  
And I I haven't come across that that is not to say it can't be important.

0:38:13.100 --> 0:38:13.390  
Angela Angle  
Mm-hmm.

0:38:3.310 --> 0:38:14.430  
Edward Hewitt  
And what I would advise you to do if if you're not familiar, you're a U.S. company called grail, like in the Holy Grail, but this is just a grail.

0:38:14.990 --> 0:38:25.340  
Edward Hewitt  
And they are looking at essentially they're looking at at circulating tumor DNA, but they're doing this as a kind of a as a first.

0:38:25.800 --> 0:38:56.50  
Edward Hewitt  
And I said diagnostic tool as if you could, you know, ultimately I I think there are vision is that that you and I and everyone else as part of our, I don't know annual checkup we would have a blood sample and they would do the sequencing and they would be able to pinpoint. Yes you have you know the very very very early in the minute you know early stages of say bladder cancer or whatever that they might find way before imaging and kind of symptoms.

0:38:56.130 --> 0:39:26.80  
Edward Hewitt  
Any kind of you know, whatever. So so, so picking up these pieces way before anything else. And that is again based on essentially looking for these tumor specific DNA pieces floating around. So so you you might find it interesting and they just had they they were bought by the personalities and then I believe the a year ago and then the deal fell through just.

0:39:26.810 --> 0:39:27.240  
Angela Angle  
Mm-hmm.

0:39:30.720 --> 0:39:30.920  
Angela Angle  
Yeah.

0:39:26.420 --> 0:39:35.430  
Edward Hewitt  
A week or so ago, because, for reasons I don't know anyway. So so it's it's sequencing, it's early diagnostics it it's it's.

0:39:36.330 --> 0:39:41.210  
Edward Hewitt  
I'm quite sure that you will see this having more and more.

0:39:41.290 --> 0:39:50.90  
Edward Hewitt  
Yeah, and and recognition and being used more, more, more and more frequently, perhaps more broadly. Again, I can't speak to him at topology. I I simply don't know.

0:40:13.320 --> 0:40:13.900  
Edward Hewitt  
Yeah.

0:39:51.0 --> 0:40:14.870  
Angela Angle  
Yeah, that makes sense. You mentioned you have a lot of the capabilities and how to do a lot of the tests that you mentioned so far. And I'm curious how common that is amongst other mid size or smaller companies in the space or if there's a lot more reliance on CRO's to do acid development or just to perform testing if they're the capacity is not available internally.

0:40:15.980 --> 0:40:25.610  
Edward Hewitt  
I I think we're an outlier in that respect and we some extent prior to ourselves with this, but but these are also super specific.

0:40:25.770 --> 0:40:44.170  
Edward Hewitt  
And and test that we have developed ourselves and because they they are directly linked to the design of our vaccine. Again, being able to to to identify which of the new antigens were actually triggering it and relevant and meaningful.

0:40:44.720 --> 0:40:54.980  
Edward Hewitt  
No, I mean logical response is so, so we we're we come from a different vantage point. I think this is not common and.

0:40:55.50 --> 0:40:55.350  
Angela Angle  
But.

0:40:56.780 --> 0:41:10.500  
Edward Hewitt  
A lot of this you would probably just die. You would buy this from various C zeros or you know whatever and companies that are out there specializing this and you'd be, you know, perfectly fine doing that.

0:41:11.740 --> 0:41:12.690  
Edward Hewitt  
Yeah, yeah.

0:41:14.650 --> 0:41:15.160  
Edward Hewitt  
Yeah.

0:41:13.790 --> 0:41:18.460  
Angela Angle  
OK, I did wanna touch upon a. Sorry. Did do you have another?

0:41:17.990 --> 0:41:36.910  
Edward Hewitt  
No. Yeah, no, I I just wanted to just just to give you one example. So just circulating tumor cells, we talked about the those just briefly and the plasma maybe associated with poor poor patient outcome. I know that there's a an assay which is commercially available.

0:41:37.470 --> 0:41:45.830  
Edward Hewitt  
And it's been FDA approved and it costs six 700US per per so. So you you can you can do that.

0:41:45.910 --> 0:41:46.360  
Edward Hewitt  
Yeah.

0:41:46.900 --> 0:42:8.530  
Edward Hewitt  
And yeah, so so so there are definitely \*\*\*\*\* out there that so you don't need to invent everything yourself. And you can either buy some of the activities or you can ask someone to to to to to to carry out the ideas, the different tests. So I again, I think we're we're not the your regular case in that respect.

0:42:10.210 --> 0:42:34.510  
Angela Angle  
OK. Yeah, that's helpful. I I did want to touch a little bit upon the infectious disease vaccines that you're also working on and just wanted to understand, I mean oncologists and area that we're hearing really significant use of biomarkers being a genetic disease and there's a lot of very targeted therapies. Just curious how you would compare the importance and the level of?

0:42:35.320 --> 0:42:46.620  
Angela Angle  
I don't know, like involvement of biomarker testing in infectious disease vaccines and if there is a reasonable amount of biomarker testing, what are the the main approaches used there?

0:42:47.290 --> 0:42:48.980  
Edward Hewitt  
Yeah, so so.

0:42:49.220 --> 0:42:49.800  
Edward Hewitt  
And M.

0:42:50.900 --> 0:43:20.150  
Edward Hewitt  
Cancer, obviously is is a lot different from, you know, an infectious disease. What what we've been looking at. And so for cancer, you know, it's not like flipping a switch and you know, by a day or two whether the therapy works or not. So you have these kind of surrogate markers, biomarkers whatever we are in the cancer space, we're looking to see we able to activate the most powerful tool that we have namely your immune system.

0:43:20.900 --> 0:43:32.580  
Edward Hewitt  
And all of this stuff that we've been talking about, Fast forward or moving, jumping into the infectious disease space. We're we're developing a staff Oreos vaccine.

0:43:33.460 --> 0:43:47.650  
Edward Hewitt  
Yes, it is. Has two components. One is on the toxin and one related to you know, directed against the toxin and the other is related to another piece of the.

0:43:52.870 --> 0:43:53.280  
Angela Angle  
Mm-hmm.

0:43:48.320 --> 0:43:53.770  
Edward Hewitt  
I said let's see end bacterium it itself. So. So the cell itself.

0:43:54.670 --> 0:44:13.80  
Edward Hewitt  
And you can monitor those and and redo that, but that's that's it. You know, it's it's you. You can monitor, you know? Do you get an appropriate immunological response to what's that? But really, what we're looking for is colonization. You know, you either you have various.

0:44:13.580 --> 0:44:31.720  
Edward Hewitt  
Yeah, you have the tissue, you have different models in which you do superficial skin infection. You can do deep tissue models, you know, different animals, Guinea pigs, et cetera, and moving into the clinical testing. Of course, you don't do.

0:44:31.800 --> 0:44:41.170  
Edward Hewitt  
Yeah. The challenge to the trials and such there, there you look at the at the colonization.

0:44:42.460 --> 0:44:56.260  
Edward Hewitt  
So so this this is a whole different ball game in terms of looking at this, this work or not and and the time perspective is much more appealing because you will know pretty fast whether it's so looking at mice.

0:45:13.420 --> 0:45:13.710  
Angela Angle  
Mm-hmm.

0:44:56.340 --> 0:45:19.360  
Edward Hewitt  
In my, in my or in, we recently had a Guinea pig model coming through and and you're looking at a couple of months for the readout and and and you're looking at the size of an absence, for instance, you're looking at just the general infectious disease components.

0:45:27.830 --> 0:45:28.120  
Angela Angle  
OK.

0:45:19.440 --> 0:45:49.770  
Edward Hewitt  
Yeah, you know, look, sites, you know just the, the, the, the, the usual suspects, it's nothing out of the ordinary and so so it's it's I I think it's a lot more simple. At least we've approached it and we may be wrong, but it's to us it's it's more simple in terms of even the clinical readout for now we are using healthy volunteers and we're just looking at you know if you go out in the street and you do a swab in the nose.

0:45:49.850 --> 0:45:57.890  
Edward Hewitt  
You know, 100 people, I don't know, five, 1015% will will harbor whatever bacteria in the knows and we're just looking at you know.

0:46:7.580 --> 0:46:7.930  
Angela Angle  
Mm-hmm.

0:46:22.370 --> 0:46:22.800  
Angela Angle  
OK.

0:46:25.200 --> 0:46:25.640  
Angela Angle  
Yeah.

0:45:58.620 --> 0:46:27.250  
Edward Hewitt  
From from the baseline due to the end of the immunization, how does it? How does the colonization levels compare? We're hoping to see them drop. It's a crude measure, but really that's all you want. You just want to see that you're helping the immune system or the body to eradicate the in this case staff areas so that it's a lot more simple than that. Does that make sense or?

0:46:30.200 --> 0:46:30.490  
Edward Hewitt  
Yeah.

0:46:31.540 --> 0:46:31.820  
Edward Hewitt  
Yeah.

0:46:33.160 --> 0:46:33.790  
Edward Hewitt  
And.

0:46:27.790 --> 0:46:44.120  
Angela Angle  
Yeah, that makes sense. And that's helpful. Just to understand the overall kind of need there, I did wanna go back a little bit to the some of the geographic trends. I mean, you mentioned earlier that you were conducting a study in Australia and had to deal with the logistics of having the samples shipped in the.

0:46:50.540 --> 0:46:51.60  
Edward Hewitt  
Yeah.

0:46:46.210 --> 0:47:5.160  
Angela Angle  
And in a way that made the PBMC stable enough to get back to your lab. Curious kind of. Just in the APEC region in general, where you're seeing a lot of oncology trials as Australia like a hotspot for that kind of study or there are other countries or regions that are also important.

0:47:6.200 --> 0:47:9.900  
Edward Hewitt  
So which shows Australia? Because these are.

0:47:10.420 --> 0:47:28.60  
Edward Hewitt  
Uh white people living in a spot in which of the globe, where there they, you know, don't belong ritually. So the incidence of Melanoma is very high. There is a high degree of awareness.

0:47:28.220 --> 0:47:32.150  
Edward Hewitt  
And highly professionalized uh setting.

0:47:32.790 --> 0:47:43.520  
Edward Hewitt  
And there is a tax incentive in in running clinical trials. It's well organized and and it's too us, it's been really easy. We set up the trial starting in.

0:47:44.330 --> 0:48:15.100  
Edward Hewitt  
Exactly three years ago, just as COVID hit us and and we were able to conclude the trial without even being able to visit the sites after the initial visit, we're because we couldn't get entry. And so, so so that, so we have not moved outside of Australia, but I do know because we're been involved in talks with the various agencies in Singapore and they have it. There's something called a star, but that would probably transgressing a little bit.

0:48:15.210 --> 0:48:17.500  
Edward Hewitt  
And that that they they have a strong.

0:48:18.760 --> 0:48:32.90  
Edward Hewitt  
And let's set up and and well organized as well within oncology as well. We just at this stage have not entered into any clinical testing within this. Yeah, there were some strong.

0:48:32.290 --> 0:48:35.710  
Edward Hewitt  
Yeah, she owes out there. There's one called novotech.

0:48:36.430 --> 0:48:53.740  
Edward Hewitt  
And they offer a number of different uh services. We have mainly been involved in the, you know, trial management side of things, but I'm quite sure that they they manage a lot of other stuff as well. And there are strong in the Asia Pacific region.

0:48:55.910 --> 0:49:28.90  
Angela Angle  
And from my understanding for from the background you mentioned earlier that it's been a few years since you relied on zeros to perform the assay. Since you have a lot of the capabilities internally now. But I guess thinking back to some of the work at the larger companies you were previously at, were there the zeros that you were working with there, who performed biomarker testing? Were they providing any other services besides biomarker testing? And here I'm thinking, I mean it could be in terms of trial management recruiting but other things could be.

0:49:29.190 --> 0:49:33.180  
Angela Angle  
Logistics services, maybe other testing types like PK.

0:49:33.820 --> 0:49:34.170  
Edward Hewitt  
Mm-hmm.

0:49:34.420 --> 0:49:35.680  
Angela Angle  
Anything else that comes to mind?

0:49:36.870 --> 0:50:2.960  
Edward Hewitt  
But I mean, some of the bigger players that I currently we're working with in a LabCorp and and you know it's the menu goes on and on. It's just you know when do you get tired of ticking the boxes, I mean it's they they they have lots of offerings and I think you know looking at for instance diabetes and they're the biomarkers are quite simple no oftentimes done at the local lab.

0:50:4.320 --> 0:50:4.700  
Angela Angle  
Mm-hmm.

0:50:3.740 --> 0:50:13.980  
Edward Hewitt  
You know the the the the markers of efficacy quite simple and could be handled by a I wanna say any any regional lab for sure.

0:50:14.250 --> 0:50:16.760  
Edward Hewitt  
And and so oftentimes.

0:50:17.760 --> 0:50:37.630  
Edward Hewitt  
They were not. We we did not use zeros for that and but you. Yeah. I mean, most of these certainly have it as part of their offering and at least some of the more simple ones, some of the stuff that we've been talking about today, I think there are not that many players.

0:50:38.850 --> 0:50:41.790  
Edward Hewitt  
That were able to do that then, yeah.

0:50:44.690 --> 0:50:45.60  
Angela Angle  
OK.

0:50:46.770 --> 0:50:50.90  
Angela Angle  
And I guess for some of the more specialized biomarker testing like.

0:50:50.860 --> 0:50:52.420  
Angela Angle  
Cardiome mixed genomics where?

0:50:53.740 --> 0:51:10.30  
Angela Angle  
You you might need to go to more specialized location to do this testing. Do those testing service providers often offer other types of services, or if they did offer those, or what services could those more specialized zeros offer? That would be interesting to you.

0:51:11.520 --> 0:51:11.710  
Edward Hewitt  
I.

0:51:11.850 --> 0:51:14.80  
Edward Hewitt  
And from my understanding.

0:51:17.0 --> 0:51:25.790  
Edward Hewitt  
This is kind of the the pinnacle if if if you're able to do these kind of the, the, the stuff that you mentioned, you can also do some of the more.

0:51:26.650 --> 0:51:38.780  
Edward Hewitt  
Common stuff. So. So the does that make sense? So it's kind of the you you're building on, you know this this is that at the top range of of what they offer and and they would oftentimes also offer.

0:51:39.540 --> 0:51:46.420  
Edward Hewitt  
Just a general. Yeah. Yeah, more more common. And biomarker testing for, you know, general lab testing.

0:51:48.30 --> 0:51:52.250  
Edward Hewitt  
But again, we we haven't engaged that deeply with them.

0:51:53.950 --> 0:51:59.180  
Edward Hewitt  
Because, yeah, for the reasons that we talked about that that we kept most most in the House.

0:52:1.790 --> 0:52:3.270  
Angela Angle  
OK. That makes sense.

0:52:6.50 --> 0:52:22.800  
Angela Angle  
Umm, I guess looking more broadly and oncology are there certain biomarker testing areas that you see as real growth opportunities and and maybe this is something like Janelle mix or spatial omics or or other specific technologies or any?

0:52:23.440 --> 0:52:28.770  
Angela Angle  
Kind of up and coming biomarkers or sets of biomarkers that you're seeing a lot more interested in today?

0:52:30.40 --> 0:52:30.900  
Edward Hewitt  
And.

0:52:31.860 --> 0:52:36.430  
Edward Hewitt  
Well, certainly the you know this this spatial piece, the single cell.

0:52:36.530 --> 0:53:1.900  
Edward Hewitt  
Uh sequencing? I I'm I. I'm intrigued. You know, years ago in my PhD, I I spent. I don't how many hours doing stuff that today you would do in a split second. You know things have really moved on. I said I'm just I'm I just stand on the sidelines and that you know my head is but so those would be some of this stuff I know.

0:53:4.340 --> 0:53:6.400  
Edward Hewitt  
Uh, some of our.

0:53:6.480 --> 0:53:16.810  
Edward Hewitt  
Uh scientists and talked about immunoperoxidase, amics and and and I'm not well versed in this and I think that is.

0:53:18.190 --> 0:53:20.140  
Edward Hewitt  
Gaining some traction.

0:53:20.920 --> 0:53:23.610  
Edward Hewitt  
And there is a.

0:53:24.540 --> 0:53:46.380  
Edward Hewitt  
An academic institution in Speaking of Australia in Monash University, in in, in Australia, they are really strong and you have oftentimes it comes from whatever research done at and it demic institution, whatever and it's being recognized and ultimately commercialized. So I think you will see some growth in that area as well.

0:53:46.540 --> 0:53:51.410  
Edward Hewitt  
Yeah, it's expensive and it's it's you need, you know, you need to have.

0:53:52.100 --> 0:53:57.220  
Edward Hewitt  
Yeah, and there needs to be a purpose obviously for this. Again, those could be some of the.

0:53:57.900 --> 0:54:6.400  
Edward Hewitt  
And I think something like the the the deep immune phenotyping and could be, you know something.

0:54:7.270 --> 0:54:9.960  
Edward Hewitt  
That that you see and yeah.

0:54:10.610 --> 0:54:11.470  
Edward Hewitt  
And.

0:54:13.440 --> 0:54:14.180  
Edward Hewitt  
What's it called the?

0:54:13.50 --> 0:54:15.800  
Angela Angle  
And so could you clarify the deep immunophenotyping?

0:54:16.620 --> 0:54:17.530  
Angela Angle  
Like what that involves?

0:54:16.530 --> 0:54:17.620  
Edward Hewitt  
It's so good.

0:54:18.350 --> 0:54:23.820  
Edward Hewitt  
And so there's something called the MDSC myeloid derived suppressor selves.

0:54:24.580 --> 0:54:29.830  
Edward Hewitt  
That's kind of a heterogeneous population among myeloid cells.

0:54:31.220 --> 0:54:38.370  
Edward Hewitt  
And apparently they have the, you know, potent mechanism to inhibit both T cell and NK NK cell activity.

0:54:38.970 --> 0:54:49.120  
Edward Hewitt  
And and which that promotes tumor growth and and and that and and simply contributes to the resistance of the against the and that therapy.

0:54:49.600 --> 0:55:3.460  
Edward Hewitt  
And I I I just listen in recently and and and that is an area that's at least our scientists or are looking into it's not established but it's something and you know they they would.

0:55:4.530 --> 0:55:11.130  
Edward Hewitt  
The the way it was presented to me was this is that they don't have like this. That's a deep immune phenotyping.

0:55:12.160 --> 0:55:12.430  
Angela Angle  
Umm.

0:55:12.890 --> 0:55:22.150  
Edward Hewitt  
Yeah, and and and that that's at least one area that that springs to mind that that could be, you know seeing some growth could be seeing some growth.

0:55:23.690 --> 0:55:28.490  
Angela Angle  
OK. And then I guess just there's a couple minutes. I've just one last question.

0:55:29.830 --> 0:55:37.980  
Angela Angle  
Around some of the more going back to some of the therapeutic vaccine testing that you're doing, how?

0:55:38.880 --> 0:56:1.390  
Angela Angle  
I guess what you get to late stage clinical trials, are you still performing circulating tumor DNA testing? Are you still analyzing the new antigen specific T cells and some of those other more detailed tests or does it become more general testing at that point for I don't know like efficacy endpoints rather than looking at the the mechanism of the therapeutic?

0:56:2.10 --> 0:56:25.800  
Edward Hewitt  
Yeah, I I I I think you're and and you're right in in the assumption that as you mature you're clinical pipeline and move further towards commercialization and you have a better understanding of the mechanism of action etcetera, you don't need to go further proof you you move away from understanding the signs to then proving the.

0:56:25.880 --> 0:56:30.740  
Edward Hewitt  
This one and so I I think you're absolutely right in the sense that you're looking at.

0:56:40.450 --> 0:56:40.900  
Angela Angle  
Yeah.

0:56:32.20 --> 0:56:43.10  
Edward Hewitt  
Something you know to go outcome measures, which would be, you know, overall survival which is not a test that's you know you know relapse free survival.

0:56:43.90 --> 0:56:49.50  
Edward Hewitt  
Uh progression free survival, though those kind of things you would still be looking at.

0:56:50.350 --> 0:57:20.680  
Edward Hewitt  
So there was something called the resist criteria, so that talks about the the size of the lesions and there are different ways of calculating that recessed. Our EC IST and and and and there you need imaging and and I don't think that will go away I think that would be part of a phase three you know a registrational trial that will certainly be there also looking at it late stage trial my expectation is that you would still be looking at.

0:57:21.410 --> 0:57:41.910  
Edward Hewitt  
Uh, she forward CD 8 positive T cells that that, the novel responds. Maybe not, you know, fully granular level into each of the antigens that you, you know, put into your vaccine. But just looking more kind of as a lump of the seeing seeing these spiking?

0:57:42.600 --> 0:58:0.330  
Edward Hewitt  
I think also for the city DNA, simply because it's gaining more traction, I think it's it's it makes sense from a biological perspective to be monitoring this. So. So I think those you know the imaging CD4 CD 8, the CTD DNA on top of the regular stuff again.

0:58:0.850 --> 0:58:2.0  
Edward Hewitt  
Uh, it's from.

0:58:3.390 --> 0:58:4.680  
Edward Hewitt  
The gamma.

0:58:10.500 --> 0:58:12.100  
Angela Angle  
OK. Yeah.

0:58:4.950 --> 0:58:12.210  
Edward Hewitt  
And LTH that, that's not going anywhere. That that's still gonna be there, but that's that would be my.

0:58:13.610 --> 0:58:24.380  
Angela Angle  
OK, let's say we're up on a time like to thank you for taking the time to speak this way. There's been really helpful and appreciate your feedback and looking forward to potentially speaking with you on a future project.