Rubenstein, James 04-18 11am EDIT

Rubenstein, James 02-07-2019

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5:5 - 5:14	**Rubenstein, James 02-07-2019 (00:00:17)** 5:5 Q. Good afternoon, Doctor. 5:6 A. How are you? 5:7 Q. Great. 5:8 Please state your full name. 5:9 A. James Louis Rubenstein. 5:10 Q. Dr. Rubenstein, you are a medical doctor? 5:11 A. Correct. 5:12 Q. What kind of medical doctor are you? 5:13 A. I'm trained in internal medicine and in 5:14 medical oncology and hematology.	Rubenstein.1
5:15 - 5:18	**Rubenstein, James 02-07-2019 (00:00:06)** 5:15 Q. Okay. And hematology, the study of blood? 5:16 A. Right. 5:17 Q. Oncology, the study of cancer? 5:18 A. Correct.	Rubenstein.2
5:19 - 5:21	**Rubenstein, James 02-07-2019 (00:00:06)** 5:19 Q. You study blood cancers? 5:20 A. I study blood cancers and -- and treat 5:21 blood -- patients with blood cancers.	Rubenstein.3
6:1 - 6:15	**Rubenstein, James 02-07-2019 (00:00:50)** 6:1 Q. Okay. Please just give us a short summary 6:2 of your experience, how you got to be a specialist 6:3 in blood cancers here at the university. 6:4 A. Well, it goes back -- my interest in blood 6:5 cancers goes back through -- to medical school where 6:6 I trained at -- in Cornell where there was 6:7 impressive expertise in -- in blood cancers. 6:8 And beyond that, I did my residency at 6:9 Stanford where there was a lot of expertise in -- in 6:10 lymphomas. Remarkable expertise in lymphomas. 6:11 And -- and then coming here, UCSF, I 6:12 became more focused, and my fellowship training and 6:13 research training really became focused on 6:14 developing an expertise and research expertise in 6:15 lymphoma biology and treatment.	Rubenstein.4
6:22 - 7:2	**Rubenstein, James 02-07-2019 (00:00:17)** 6:22 Q. Would it be fair to say that you spend 6:23 your time either researching or treating patients in 6:24 non-Hodgkin's lymphoma as one of your specialties or	Rubenstein.5

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	6:25 perhaps your only one, I don't know?	
	7:1 A. Well, yeah, you have to -- it is really my	
	7:2 specialty.	
7:5 - 7:14	**Rubenstein, James 02-07-2019 (00:00:23)**	Rubenstein.6
	7:5 Q. Within the field of non-Hodgkin's lymphoma	
	7:6 research and treatment, do you particularly	
	7:7 emphasize any given subtype or kind of non-Hodgkin's	
	7:8 lymphoma?	
	7:9 A. Sure.	
	7:10 Well, I would regard -- I think people	
	7:11 would regard me as an expert in aggressive lymphoma	
	7:12 that involves the brain.	
	7:13 Q. And how long have you been an expert in	
	7:14 aggressive lymphomas that involve the brain?	
7:15 - 8:8	**Rubenstein, James 02-07-2019 (00:00:42)**	Rubenstein.67
	7:15 A. Well, I've been working in the area since	
	7:16 late 1990s.	
	7:17 Q. Okay.	
	7:18 A. You know, I would say my evolving	
	7:19 expertise first became manifested certainly by 2001.	
	7:20 Q. Okay.	
	7:21 A. With the, you know -- or 2000 when we put	
	7:22 together a protocol that we still use today.	
	7:23 Q. A protocol for what, sir?	
	7:24 A. Treatment.	
	7:25 Q. Oh, very good. For treatment of	
	8:1 aggressive --	
	8:2 A. Yeah.	
	8:3 Q. -- brain --	
	8:4 A. Lymphoma in the brain. Yeah.	
	8:5 Q. Okay. All right. And the jury's heard by	
	8:6 now, but have you published in the peer-reviewed	
	8:7 literature in this area?	
	8:8 A. Multiple papers on -- and -- yeah. Yes.	
8:8 - 8:8	**Rubenstein, James 02-07-2019 (00:00:00)**	Rubenstein.68
	8:8 A. Multiple papers on -- and -- yeah. Yes.	
8:9 - 9:5	**Rubenstein, James 02-07-2019 (00:00:55)**	Rubenstein.69
	8:9 Q. Okay. And did there come a time when	
	8:10 Alberta Pilliod was referred to you because of her	
	8:11 brain lymphoma?	

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	8:12 A. Sure.	
	8:13 Was there -- yeah, she was referred	
	8:14 because she had recurrent disease and there was --	
	8:15 well, fortunately, she's a local patient --	
	8:16 geographically, relatively local. So it was not	
	8:17 extraordinarily difficult for her to come up here.	
	8:18 Q. Sure.	
	8:19 Well, then, that's -- let me back up.	
	8:20 Patients are referred to you from other	
	8:21 areas besides the Bay Area. That's fair, isn't it?	
	8:22 A. Absolutely.	
	8:23 Q. All right. And -- and before we go too	
	8:24 much farther, within the field of non-Hodgkin's	
	8:25 lymphoma, there are -- are B-cell cancers and T-cell	
	9:1 cancers?	
	9:2 A. Uh-huh.	
	9:3 Q. And the kind of cancer that Alberta	
	9:4 Pilliod had in her brain was a form of B-cell	
	9:5 cancer?	
9:11 - 9:16	**Rubenstein, James 02-07-2019 (00:00:07)**	Rubenstein.7
	9:11 THE WITNESS: Well, I mean, it was -- I	
	9:12 can -- if you want me to check that out, because I	
	9:13 don't want to say anything wrong, but she was a --	
	9:14 it was an aggressive lymphoma that was -- might be a	
	9:15 B-cell-type, yes.	
	9:16 BY MR. MILLER:	
9:21 - 11:6	**Rubenstein, James 02-07-2019 (00:01:50)**	Rubenstein.8
	9:21 We're going to look at your medical	
	9:22 records in a minute. But the sub- -- was or was not	
	9:23 the subtype of B-cell lymphoma in her brain a PCN?	
	9:24 A. Yes, PCN. Primary central nervous system	
	9:25 lymphoma, which is the diagnosis that was worked up	
	10:1 when she presented to us.	
	10:2 Basically, that's a -- it's a form of	
	10:3 lymphoma, which the disease has a unique propensity	
	10:4 only to manifest itself in the brain.	
	10:5 So lymphoma is like a -- you can get	
	10:6 lymphomas in the skin. You can get lymphomas in the	
	10:7 bone. You can get lymphomas in virtually any organ	
	10:8 in the body.	

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10:9 But there is a distinct disease called
10:10 primary central nervous system lymphoma, which is a
10:11 unique set of molecular features that makes it grow
10:12 in the brain and -- and requires independent
10:13 treatment.
10:14 Q. Is PCN lymphoma such as the type Alberta
10:15 Pilliod had, is it an aggressive form of cancer?
10:16 A. It's a very aggressive -- it's a very
10:17 aggressive form, one of the most aggressive forms of
10:18 cancer. And it's -- there's only emerging evidence
10:19 that it can be cured.
10:20 Q. And we want to talk about the treatment
10:21 that you've -- well, let me back up.
10:22 Have you developed a chemical treatment
10:23 for this type of cancer?
10:24 A. Sure.
10:25 Well, we've -- we developed a regimen,
11:1 yeah. She -- we've developed -- she was influenced
11:2 by our regimen. Certainly at relapse we used our
11:3 regimen. And then because of her age, we used a
11:4 drug that we kind of pioneered in this disease.
11:5 Q. And what's the name of that drug?
11:6 A. Lenalidomide, or Revlimid.

11:13 - 12:5 **Rubenstein, James 02-07-2019 (00:00:44)** Rubenstein.9

11:13 Q. And -- and we're going to get to the --
11:14 the course of her treatment for Alberta.
11:15 But first let me ask you, something called
11:16 a Ki-67, are you familiar with that?
11:17 A. Sure.
11:18 Q. What is that?
11:19 A. That's a proliferative index. It's a
11:20 marker. It's an -- well, what it is, is a marker of
11:21 how many cells within the tumor are actually
11:22 dividing or mitosing. So it's a particular antigen
11:23 that is recognized by an antibody tool that can tell
11:24 you whether the cells are in mitosis or not. And
11:25 generally, you know, that's a -- it's -- it's a
12:1 marker of aggressiveness of the tumor.
12:2 Q. And as we look through her records, I see
12:3 a Ki-67 of 80 percent.

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	12:4 What does that tell us?	
	12:5 A. Well, it's consistent with being an	
12:6 - 12:25	**Rubenstein, James 02-07-2019 (00:00:53)**	Rubenstein.70
	12:6 aggressive lymphoma. It doesn't -- it doesn't --	
	12:7 it -- that's rapidly dividing. It's -- and	
	12:8 mitotically active. This is an -- this is a	
	12:9 lymphoma that, if you didn't treat it, she would	
	12:10 likely be dead within three months and -- at the	
	12:11 time of presentation, because 80 percent of the	
	12:12 cells are dividing at any given time.	
	12:13 Q. Wow.	
	12:14 A. And so you -- you can imagine, when you	
	12:15 present, you need a billion cells just to have a	
	12:16 mass that you can see on an MRI. So if you have --	
	12:17 that's 80 percent of the cells are dividing. That	
	12:18 you can imagine how that could wreak havoc -- havoc	
	12:19 in the brain.	
	12:20 Q. Is PCN lymphoma in the brain such as	
	12:21 Alberta Pilliod had, is it susceptible to	
	12:22 reoccurrence after its initial --	
	12:23 A. Yes.	
	12:24 Q. -- presentation?	
	12:25 A. Yes, definitely. Definitely.	
13:1 - 13:4	**Rubenstein, James 02-07-2019 (00:00:12)**	Rubenstein.10
	13:1 Q. And let's look first at your record when	
	13:2 you first saw Alberta Pilliod.	
	13:3 MR. MILLER: And I will mark that document	
	13:4 as Exhibit 1.	RJ1.1
13:20 - 13:25	**Rubenstein, James 02-07-2019 (00:00:09)**	Rubenstein.11
	13:20 BY MR. MILLER:	
	13:21 Q. Okay. So Alberta Pilliod first came to	
	13:22 you for treatment in September of 2016?	RJ1.1.1
	13:23 A. Correct.	
	13:24 Q. And how was she referred to you,	
	13:25 Dr. Rubenstein?	
14:3 - 14:15	**Rubenstein, James 02-07-2019 (00:00:25)**	Rubenstein.71
	14:3 because of, I think, insurance reasons, she was	
	14:4 initially going to see people at Stanford, and they	
	14:5 referred her to me because of my local reputation.	
	14:6 Q. I see.	

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	14:7 It says here, "History of Present	RJ1.1.2
	14:8 Illness." Can you read that for us, please.	
	14:9 A. Sure.	
	14:10 You want me to read it or you want me to	
	14:11 explain -- expound on it by explaining what this	
	14:12 means?	
	14:13 Q. I think it makes more sense to expound on	
	14:14 it and tell us what it means.	
	14:15 A. Sure.	
14:18 - 17:2	**Rubenstein, James 02-07-2019 (00:02:55)**	Rubenstein.76
	14:18 She has -- she has presented with new	
	14:19 onset double vision, loss of balance, and -- and --	
	14:20 and vertigo, dizziness, instability in terms of	
	14:21 where she is in the world. These are signs of	
	14:22 cerebellar dysfunction.	
	14:23 As well as problems with hearing in her	
	14:24 right ear. Also could be related to cerebellar or	
	14:25 brain stem or cranial nerve dysfunction.	
	15:1 And vision -- dysfunction of vision in the	
	15:2 left eye. So that's also consistent with a lymphoma	
	15:3 that could involve the optic nerve, the retina, or	
	15:4 the occipital cortex or any of the pathway between	
	15:5 the -- pathway and processing of vision.	
	15:6 She also had problems with handwriting and	
	15:7 with speech. So that suggests multiple areas in the	
	15:8 brain that are involved because you have multiple	
	15:9 foci -- multiple functions of the brain that are	
	15:10 disrupted.	
	15:11 So she had a brain biopsy at Stanford, and	
	15:12 that diagnosed the most common histologic type of	
	15:13 this disease, which is large B-cell lymphoma. All	
	15:14 that means is this is a -- a garden-variety,	
	15:15 aggressive lymphoma, B-cell type. 98 percent of	
	15:16 these are B-cells.	
	15:17 The cells are large cells. They're not	
	15:18 small cells. That just means that under the	
	15:19 microscope these cells are bigger than other cells	
	15:20 in the field that the pathologist was looking at.	
	15:21 The other cells being macrophages or endothelial	
	15:22 cells. That's how we determine whether it's a large	

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15:23 cell or not, okay.
15:24 And those are the cells that -- when they
15:25 look at a Ki-67 index, those are the cells that
16:1 they're looking at. The large cells that are Ki-67.
16:2 Because the other cells are generally not
16:3 mitotically active. They're not -- they don't take
16:4 up Ki-67.
16:5 So they do a brain biopsy and that showed
16:6 large B-cell lymphoma. That's kind of the classic
16:7 course.
16:8 And then she had systemic staging that was
16:9 negative. That means they did a CAT scan of the
16:10 body, and that showed no evidence of lymphoma in the
16:11 body, okay. So that means, by exclusion, that this
16:12 is not stage IV lymphoma with body and brain
16:13 involvement, which we sometimes see, but this is
16:14 exclusive -- exclusively primary central nervous
16:15 system lymphoma, PCNSL.
16:16 And -- and at Stanford she was treated
16:17 with the regimen we actually -- we -- we pioneered,
16:18 but she didn't get a consolidation -- some of it was
16:19 at Stanford and some of it was at Eden Medical
16:20 Center. So she got half of it at Stanford, half of
16:21 it at Eden. And many of her symptoms went away.
16:22 But for whatever reason, she -- they -- they stopped
16:23 after the MTR, okay.
16:24 Q. What is MTR?
16:25 A. MTR is a methotrexate, temozolomide,
17:1 rituximab, okay.
17:2 So sometimes we recommend -- it's not

17:3 - 17:21 **Rubenstein, James 02-07-2019 (00:00:51)** Rubenstein.77

17:3 proven, and -- and it's -- sometimes we recommend
17:4 doing consolidation chemotherapy after the MTR, but
17:5 there's no randomized data showing that what's --
17:6 what happened to her was necessarily wrong in terms
17:7 of the chemotherapy.
17:8 Q. Sure.
17:9 A. Okay. But I will say that we -- now -- or
17:10 for these patients, we -- we definitely do something
17:11 different at UCSF.

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	17:12 In any case -- so she was doing pretty	
	17:13 well. She had a resolution of a lot of her	
	17:14 symptoms. But by July of 2016, she had a new	
	17:15 right-sided occipital lobe lesion and her balance	
	17:16 was getting worse, okay.	
	17:17 So that means that was consistent with	
	17:18 recurrent disease, okay. That's -- the time course	
	17:19 is very consistent with the natural history of this	
	17:20 disease, which is to respond to chemotherapy, then	
	17:21 they come back, okay.	
18:2 - 19:25	**Rubenstein, James 02-07-2019 (00:02:32)**	Rubenstein.12
	18:2 Q. This is your new patient. You've	
	18:3 explained to us what happened at Stanford.	
	18:4 What did you decide to do once you began	
	18:5 treating her in September of 2016?	
	18:6 A. Yes.	
	18:7 So generally what we do is assess whether	
	18:8 this patient is, you know, a good candidate for more	
	18:9 therapy or not. And generally, we think this is a	
	18:10 disease that we can prolong survival and	
	18:11 progressively -- survival pretty well. And we try	
	18:12 to get people out -- out of a tough -- a tough	
	18:13 situation with more therapy and to do something	
	18:14 different at the end. So keep them out of trouble.	
	18:15 So, you know, she presented with a lot of	
	18:16 neurologic symptoms, mainly problems with gait and	RJ1.2.1
	18:17 vision. Cerebellar dysfunction which -- and -- but	
	18:18 we felt that she was strong enough to tolerate more	
	18:19 chemotherapy, okay.	
	18:20 Q. Yes, sir.	
	18:21 A. So that was in September of 2016.	
	18:22 So generally, what we do is then I	
	18:23 assessed her. I gave her an ECOG factor of 2, which	RJ1.4.1
	18:24 is a pretty -- pretty -- you know, pretty	
	18:25 impaired --	
	19:1 Q. Explain to us --	
	19:2 A. -- performance status.	
	19:3 Q. -- what ECOG is.	
	19:4 A. It's a -- it's a manifestation of her	
	19:5 performance status. Basically, it's a scale that	

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	19:6 oncologists use that determines their overall 19:7 functional capacity and as -- to be -- in terms of 19:8 activities of daily living. Can they dress 19:9 themselves? Can they feed themselves? Can they 19:10 organize themselves? Can they do work? Do they 19:11 need help with walking? Are they completely 19:12 unambulatory? 19:13 She needed help with walking. She had 19:14 problems with balance, but she -- okay. 19:15 Q. Uh-huh. 19:16 A. But she could walk. And so that's why we 19:17 gave her an ECOG of 2. And we put her in the 19:18 hospital as soon as possible. 19:19 And the plan was to restage her, get a 19:20 repeat eye examination, and then -- and then give 19:21 her high-dose methotrexate-based salvage. And then 19:22 initially the plan was either give her high-dose 19:23 dose-intensive consolidation chemotherapy or the 19:24 regimen that we're studying, which is lenalidomide 19:25 maintenance.	
20:24 - 21:12	**Rubenstein, James 02-07-2019 (00:00:42)** 20:24 BY MR. MILLER: 20:25 Q. Okay. And MTR, that's... 21:1 A. Methotrexate, temozolomide, which is a 21:2 drug that is a alkylating agent, chemotherapy drug 21:3 that gets in the brain, and it's minimally toxic. 21:4 Q. And so you would have anticipated that she 21:5 would undergo how many cycles of methotrexate? 21:6 A. Generally, the plan course is eight. And 21:7 that's like -- that's a convention that is -- that 21:8 we use here and use at other sites -- centers. 21:9 Q. Was Alberta Pilliod able to tolerate eight 21:10 cycles of methotrexate? 21:11 A. She was, yeah. We're very skilled at 21:12 giving it, I guess.	Rubenstein.13
21:16 - 21:17	**Rubenstein, James 02-07-2019 (00:00:02)** 21:16 A. It's not just me. We have a great team, 21:17 so...	Rubenstein.14
21:18 - 24:9	**Rubenstein, James 02-07-2019 (00:03:09)** 21:18 Q. And, you know, for those of us who don't	Rubenstein.72 clear

21:19 know a lot of about this, I mean, did she lose her
21:20 hair?
21:21 A. No.
21:22 Q. Okay. Did -- you talked about in your
21:23 records EA treatment or --
21:24 A. Right.
21:25 Q. -- EA therapy after the methotrexate.
22:1 What is that in lay terms? What are we
22:2 doing?
22:3 A. Sure.
22:4 Etop- -- it's an acronym for a drug
22:5 combination that we often use in -- in this disease.
22:6 It consists of two chemotherapy drugs. One's called
22:7 ara-C, also known as cytarabine. And the other drug
22:8 is called etoposide, also known as VP-16. And the
22:9 two-drug combination is really a dose-intensive,
22:10 very intensive chemotherapy.
22:11 The idea is these are drugs that get in
22:12 the brain, cross the blood brain barrier, and are
22:13 able to kill lymphoma cells. And they work
22:14 differently from the previous drugs she's received.
22:15 Do you follow me?
22:16 Q. Yes.
22:17 A. So it's analogous to if you have a
22:18 bacterial infection and you treat it, you know, a
22:19 very bad bacterial infection, you -- that comes back
22:20 and you keep treating with penicillin, what do you
22:21 get? You get a penicillin-resistant form of it.
22:22 So cancer is the same way. We -- you
22:23 know, we -- here we gave her eight cycles of
22:24 methotrexate. Whatever is left is undoubtedly going
22:25 to be somewhat or outright resistant to
23:1 methotrexate. So we give her some really strong
23:2 drugs that work through different mechanisms of
23:3 action.
23:4 The idea is that we hope that those -- we
23:5 believe that those are going to eradicate the
23:6 remaining cells and that we have evidence that that
23:7 can work. That does work. And that's a practice
23:8 that people -- it's actually a standard practice now

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	23:9 in the country to use EA consolidation, etoposide	
	23:10 and ara-C.	
	23:11 It's a very -- a very tough chemotherapy	
	23:12 combination, however, and given some of her cerebral	
	23:13 signs, her problems with gait and dysfunction, I	
	23:14 felt that maybe she wasn't such a great candidate	
	23:15 for that combination because of the -- one of the	
	23:16 side -- many side effects of the EA regimen is that	
	23:17 those drugs can injure the brain, particularly the	
	23:18 cerebellum, in older people.	
	23:19 Q. And is that called encephalopathy?	
	23:20 A. Well, encephalopathy is -- can be caused	
	23:21 by multiple things. Chemotherapy can cause	
	23:22 encephalopathy. The -- the tumor can cause	
	23:23 encephalopathy.	
	23:24 Q. Sure. I understand.	
	23:25 A. Metabolic changes.	
	24:1 But certainly, ara-C is a very toxic drug	
	24:2 that you have to be very careful with giving in	
	24:3 people over 60, or in anybody, but somebody with --	
	24:4 who has cerebellar dysfunction you -- you really	
	24:5 need to be wary of giving more ara-C to somebody.	
	24:6 Q. It's a tough disease and you have to	
	24:7 figure out what you can -- where you can navigate to	
	24:8 treat this patient.	
	24:9 A. Correct.	
25:9 - 25:10	**Rubenstein, James 02-07-2019 (00:00:07)**	Rubenstein.15
	25:9 Q. Was she hospitalized on February 4th,	
	25:10 2017, through March 1st, 2017?	
25:13 - 25:13	**Rubenstein, James 02-07-2019 (00:00:03)**	Rubenstein.16
	25:13 A. Yeah. If I didn't do my -- help, if I	
25:24 - 25:25	**Rubenstein, James 02-07-2019 (00:00:04)**	Rubenstein.17
	25:24 So what happened was, so she ended up	
	25:25 getting -- we decided to give her the -- the EA.	
26:3 - 26:3	**Rubenstein, James 02-07-2019 (00:00:01)**	Rubenstein.18
	26:3 A. And that was on March -- that was in --	
26:4 - 26:4	**Rubenstein, James 02-07-2019 (00:00:05)**	Rubenstein.73
	26:4 she got those drugs back in -- so we were -- we were	RJ2.1.1
26:5 - 26:5	**Rubenstein, James 02-07-2019 (00:00:04)**	Rubenstein.74
	26:5 assessing her in -- in February of 2017. And she	

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26:6 - 26:13	**Rubenstein, James 02-07-2019 (00:00:20)**	Rubenstein.78
	26:6 got the drugs in February.	
	26:7 Q. The EA drugs?	
	26:8 A. Yeah. Yes. And -- and she had -- those	
	26:9 drugs in everybody will cause immunosuppression,	
	26:10 neutropenia, low blood count. So she had some	
	26:11 infections from that. Infection with a bacteria in	
	26:12 the blood, okay.	
	26:13 Q. Right.	
26:14 - 26:14	**Rubenstein, James 02-07-2019 (00:00:02)**	Rubenstein.84
	26:14 A. And she was treated with antibiotics for	clear
26:15 - 26:15	**Rubenstein, James 02-07-2019 (00:00:03)**	Rubenstein.83
	26:15 that. And she -- sometimes when you have an	
26:16 - 26:16	**Rubenstein, James 02-07-2019 (00:00:08)**	Rubenstein.82
	26:16 infection, you can have some neurocognitive changes	
26:17 - 26:20	**Rubenstein, James 02-07-2019 (00:00:26)**	Rubenstein.85
	26:17 as well. And she did have some increased cerebellar	
	26:18 signs and problems with speech. But then those --	
	26:19 and she was evaluated by -- evaluated by neurology.	
	26:20 And the assessment was that her MRI was --	
26:21 - 26:21	**Rubenstein, James 02-07-2019 (00:00:00)**	Rubenstein.79
	26:21 was stable. No evidence of lymphoma. And -- I'm	
26:21 - 26:21	**Rubenstein, James 02-07-2019 (00:00:02)**	Rubenstein.81
	26:21 was stable. No evidence of lymphoma. And -- I'm	
26:22 - 27:9	**Rubenstein, James 02-07-2019 (00:00:32)**	Rubenstein.80
	26:22 sorry.	
	26:23 She was -- and -- and there's no evidence	
	26:24 of lymphoma in the eyes. And she was doing pretty	
	26:25 well when I saw her in -- in mid March, 2017.	
	27:1 Q. She was discharged on March 1st?	
	27:2 A. Yeah. I saw her two weeks later and she	
	27:3 was pretty -- doing quite -- doing quite well.	
	27:4 Q. Excellent. Excellent.	
	27:5 And after the eight rounds of methotrexate	
	27:6 and then after the EA therapy, you -- you felt --	
	27:7 and again, we're certainly yielding to your	
	27:8 expertise.	
	27:9 A. Yeah.	
27:10 - 28:17	**Rubenstein, James 02-07-2019 (00:01:20)**	Rubenstein.19
	27:10 Q. You felt that she needed to go on this new	

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27:11 drug that you had such hope and promise for,
27:12 Revlimid?
27:13 A. Well, it doesn't seem that -- somebody who
27:14 is in this situation, has relapsed disease, this age
27:15 group, you don't want to be going through this
27:16 having another relapse too often, right?
27:17 Q. Sure.
27:18 A. Because every time this thing comes back
27:19 you're going to be causing more brain injury. And
27:20 so -- hope and promise, well, we -- I felt like the
27:21 risk benefit of her being on another drug certainly
27:22 favored a maintenance approach at this point.
27:23 Q. Would it be fair to call it maintenance
27:24 chemotherapies?
27:25 A. I would call it more of a maintenance
28:1 immunotherapy.
28:2 Q. Okay.
28:3 A. At the -- at the drug -- at the doses
28:4 she's getting, I would call it more of an
28:5 immunotherapy.
28:6 Q. And what would be --
28:7 A. Why?
28:8 Q. Yeah, I don't know the difference.
28:9 A. Sure.
28:10 Q. I'm asking.
28:11 A. Yeah.
28:12 So chemotherapy is basically cytotoxic to
28:13 cancer cells and kills cancer cells by inhibiting
28:14 cell division. This drug, lenalidomide, at low
28:15 doses can promote the immune system to attack the --
28:16 the lymphoma, okay, and so -- and restore the immune
28:17 function, okay.

28:18 - 29:13 **Rubenstein, James 02-07-2019 (00:00:56)** Rubenstein.75

28:18 Q. During the time you were -- you're still
28:19 treating Alberta Pilliod?
28:20 A. Yep.
28:21 Q. I think you saw her -- when was the last
28:22 time you saw her?
28:23 A. Last week.
28:24 Q. Okay. And is she still on Revlimid?

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	28:25 A. Yeah. Yeah. 29:1 Q. And how much does that cost per month? 29:2 A. Well, it varies. I mean, some people 29:3 pay -- pay thousands of dollars a month. You know, 29:4 $3,000 a month or more. It depends on their -- on 29:5 their insurance. It depends on the program you're 29:6 on. 29:7 Q. Are you recommending that she stay on 29:8 Revlimid for the rest of her life? 29:9 A. Our experience suggests that there isn't a 29:10 downside. Somebody who has relapsed disease could 29:11 be on Revlimid the rest of their life because -- 29:12 why? Because she's already proven that lymphoma 29:13 will come back.	
30:8 - 31:7	**Rubenstein, James 02-07-2019 (00:01:02)** 30:8 Q. Right now, you have Ms. Pilliod on 21 days 30:9 on, seven off? 30:10 A. Yeah. Yeah. 30:11 Q. Okay. And that's something that right now 30:12 you're recommending she continue through her life? 30:13 A. I do, yeah, until we have evidence that 30:14 it's going to be causing bad things to patients. 30:15 But I think, you know, you only live once, so we 30:16 want to make sure that people -- we don't want to -- 30:17 you know, I think of her in this study -- this in a 30:18 bigger study would recommend probably stopping after 30:19 two years. But in relapsed disease, I think you got 30:20 to just keep -- keep it on. 30:21 Q. Sure. 30:22 A. Yes. 30:23 Q. And what -- what was the course of -- of a 30:24 relapse patient like Alberta Pilliod before you were 30:25 able to offer them Revlimid? 31:1 A. Well, somebody in her -- in her age 31:2 group -- it's very interesting. Somebody in her age 31:3 group, the median survival would be less than a 31:4 year. Certainly all -- everybody would be dead in 31:5 two years. And so -- 31:6 Q. With the benefit of Revlimid, do you think 31:7 she can live a normal life expectancy?	Rubenstein.20

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31:9 - 31:15	**Rubenstein, James 02-07-2019 (00:00:25)** 31:9 THE WITNESS: She's already -- yeah, I 31:10 think -- I think -- well, I -- I -- my gut is, yeah, 31:11 we have evidence that in a small -- in a small 31:12 set -- set of patients, that -- that -- who respond, 31:13 that their remission's gone on a long time and some 31:14 of them are dying of other causes unrelated to 31:15 cancer, lymphoma.	Rubenstein.21
32:2 - 32:7	**Rubenstein, James 02-07-2019 (00:00:10)** 32:2 BY MR. MILLER: 32:3 Q. And this is a blood cancer that we have in 32:4 Alberta Pilliod? 32:5 A. She has a cancer of -- of malignant 32:6 transformation of lymphocytes, which are blood 32:7 cancer, yes.	Rubenstein.22
38:7 - 38:20	**Rubenstein, James 02-07-2019 (00:00:25)** 38:7 Have you talked with Dr. Nabhan? 38:8 A. No. 38:9 Q. Have you talked with any of the 38:10 plaintiffs' experts in this case? 38:11 A. No. 38:12 Q. Do you know who they are? 38:13 A. I assume that you're referring to somebody 38:14 like Dr. Weisenburger? 38:15 Q. Dr. Weisenburger, yes. 38:16 A. Weisenburger, yes, of course. 38:17 Q. You've spoken to him? 38:18 A. No. 38:19 Q. Okay. You've spoken to Dr. Portier? 38:20 A. No.	Rubenstein.87
44:7 - 44:14	**Rubenstein, James 02-07-2019 (00:00:17)** 44:7 So let me ask you personally, when did 44:8 this interest in the association or potential 44:9 association between blood cancers and pesticides 44:10 begin? 44:11 A. For me? 44:12 Q. For you. 44:13 A. Well, it's obvious if you take care of 44:14 patients on the wards,	Rubenstein.88
44:19 - 45:6	**Rubenstein, James 02-07-2019 (00:00:30)**	Rubenstein.89

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	44:19 Q. So the answer to my question would be when 44:20 did -- 44:21 A. When? 44:22 Q. -- this interest begin, sir? 44:23 A. I would say January 1995. 44:24 Q. And what was the impetus of that concern 44:25 you have? 45:1 A. 1996, excuse me. January 1996. 45:2 Q. Sure. 45:3 A. What was the impetus? 45:4 Q. Uh-huh. 45:5 A. Well, I did three months in a row on the 45:6 blood and bone marrow transplant unit.	
50:12 - 50:24	**Rubenstein, James 02-07-2019 (00:00:42)** 50:12 Q. Okay. Did you -- 50:13 A. If you want to -- yeah, if you want to -- 50:14 last time the issue of pesticides was brought up in 50:15 a meeting or at anything related to blood cancers, 50:16 was the second -- I do go to Leukemia & Lymphoma 50:17 Society meetings because they -- I've been lucky to 50:18 be funded by them for many years. And one of the 50:19 recent fundraisers was -- was brought up that there 50:20 was a need to understand greater relationships 50:21 between pesticides and blood cancers. 50:22 Q. Understood. 50:23 When was that meeting? 50:24 A. That was likely 2018.	Rubenstein.90
52:22 - 52:25	**Rubenstein, James 02-07-2019 (00:00:07)** 52:22 Q. Have you ever heard of the AHS study? 52:23 A. No. 52:24 Q. Agricultural Health Study? Have you ever 52:25 heard of that?	Rubenstein.91
53:3 - 53:3	**Rubenstein, James 02-07-2019 (00:00:00)** 53:3 A. No.	Rubenstein.92
55:6 - 56:2	**Rubenstein, James 02-07-2019 (00:00:58)** 55:6 Q. Okay. In your experience as an 55:7 oncologist, and specifically someone who is working 55:8 with non-Hodgkin's lymphoma, specifically PCNSL, you 55:9 see other risk factors that are signals for this 55:10 disease?	Rubenstein.93

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	55:11 A. Sure. 55:12 Q. And you would tell your patients to be 55:13 concerned with those risk factors as well? 55:14 A. Well, many of those are unavoidable risk 55:15 factors. I mean, except -- with the exception of 55:16 cigarette smoking, but that's a -- that's certainly 55:17 a risk factor. 55:18 But the other -- unavoidable ones are 55:19 getting -- being alive, getting older. 55:20 Q. Aging. 55:21 A. Having autoimmune disease and getting -- 55:22 getting medicines that suppress the immune system 55:23 are the -- the ones that come to mind. Or having 55:24 congenital immunodeficiency. 55:25 Q. Other risk factors would be obesity, high 56:1 BMI? 56:2 A. True.	
56:6 - 56:9	**Rubenstein, James 02-07-2019 (00:00:08)** 56:6 And do you counsel your patients with 56:7 regard to -- to obesity and -- and non-Hodgkin's 56:8 lymphoma as well? 56:9 A. Absolutely.	Rubenstein.94
56:21 - 57:1	**Rubenstein, James 02-07-2019 (00:00:12)** 56:21 Q. And a history of any type of cancer in the 56:22 family -- or in the person is an increased risk for 56:23 non-Hodgkin's lymphoma? 56:24 A. In that person? 56:25 Q. In that person, correct? 57:1 A. Likely, yeah.	Rubenstein.95
58:18 - 58:25	**Rubenstein, James 02-07-2019 (00:00:19)** 58:18 You're not here to testify that 58:19 glyphosate, one, was a causal factor of 58:20 Ms. Pilliod's PCNSL, are you? 58:21 A. No. 58:22 Q. And you're not here to say that glyphosate 58:23 or Roundup was a contributing factor to her -- to 58:24 her PCNSL, are you? 58:25 A. No.	Rubenstein.96
62:6 - 62:8	**Rubenstein, James 02-07-2019 (00:00:09)** 62:6 Q. Are you her primary physician for the	Rubenstein.97

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	62:7 PCNSL?	
	62:8 A. Uh-huh. Yes.	
62:11 - 62:14	**Rubenstein, James 02-07-2019 (00:00:09)**	Rubenstein.98
	62:11 Q. Now, her PCNSL, Mr. Miller touched on	
	62:12 this, is a particular subtype of non-Hodgkin's	
	62:13 lymphoma, correct?	
	62:14 A. Yes.	
62:19 - 62:21	**Rubenstein, James 02-07-2019 (00:00:06)**	Rubenstein.99
	62:19 And it's just one of many subtypes, one	
	62:20 of -- I think it's 72 subtypes from the WHO?	
	62:21 A. Correct.	
62:24 - 63:1	**Rubenstein, James 02-07-2019 (00:00:04)**	Rubenstein.100
	62:24 Q. And your specialty, your practice area, is	
	62:25 PCNSL --	
	63:1 A. Yeah.	
63:9 - 63:11	**Rubenstein, James 02-07-2019 (00:00:04)**	Rubenstein.101
	63:9 Q. Well, I mean, you see more PCNSL patients	
	63:10 than the average oncologist?	
	63:11 A. Absolutely.	
63:14 - 63:23	**Rubenstein, James 02-07-2019 (00:00:19)**	Rubenstein.102
	63:14 Q. And how many of these patients have you	
	63:15 treated, hundreds, thousands?	
	63:16 A. Nearly a thousand, probably.	
	63:17 Q. Is it --	
	63:18 A. Maybe more.	
	63:19 Q. Maybe more?	
	63:20 A. Yeah.	
	63:21 Q. And is that the -- what percentage of your	
	63:22 patients have PCNSL?	
	63:23 A. About 80 percent or -- yeah.	
65:22 - 66:6	**Rubenstein, James 02-07-2019 (00:00:21)**	Rubenstein.103
	65:22 And I'm going to just roughly walk through	
	65:23 that. So you're board certified. We talked about	
	65:24 that a little bit.	
	65:25 A. Uh-huh.	
	66:1 Q. You did your undergrad where?	
	66:2 A. Stanford.	
	66:3 Q. Okay. And your residency was at Stanford	
	66:4 as well?	
	66:5 A. Yeah.	

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	66:6 Q. And your fellowship was here at UCSF?	
66:9 - 66:12	**Rubenstein, James 02-07-2019 (00:00:05)**	Rubenstein.104
	66:9 A. Yes. 66:10 Q. Your treatment of Ms. Pilliod was here at 66:11 UCSF? 66:12 A. Yes.	
66:24 - 67:2	**Rubenstein, James 02-07-2019 (00:00:10)**	Rubenstein.106
	66:24 Q. Okay. You wrote an article with Dr. Gupta 66:25 in 2013, "How I treat CNS lymphomas." 67:1 Do you remember that? 67:2 A. Sure.	
67:8 - 68:17	**Rubenstein, James 02-07-2019 (00:01:27)**	Rubenstein.106
	67:8 Q. On the first page of that particular 67:9 article, you wrote -- you go right to the etiology 67:10 of CNS lymphoma, right? 67:11 A. Yep. 67:12 Q. And your first sentence says, "As most 67:13 other types of NHL, the etiology of CNS lymphoma 67:14 genesis is largely undefined and the mechanistic 67:15 basis for brain tropism is not understood." 67:16 Do you still agree with that statement? 67:17 A. Sure do. 67:18 Q. "The most significant risk factors for CNS 67:19 involvement of lymphoma are acquired or congenital 67:20 immunodeficiency states." 67:21 Do you still agree with that? 67:22 A. I just read this -- reread this last 67:23 night. And most of it holds up. 67:24 Q. Okay. And then you go on in that 67:25 paragraph to discuss some other factors, some other 68:1 syndromes to -- 68:2 A. Uh-huh. 68:3 Q. -- to understand what congenital -- 68:4 A. Yeah. 68:5 Q. -- immunodeficiency states are, correct? 68:6 A. Correct. 68:7 Q. All right. In 2016 you wrote "The 68:8 challenge of primary CNS lymphomas." 68:9 Do you remember that article? 68:10 A. Sure do.	

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	68:11 Q. Okay. Do you remember the etiology 68:12 section of that which said, "Risk factors for PCNSL 68:13 include acquired and/or congenital immunodeficiency 68:14 states"? 68:15 Same thing? So it hadn't change in those 68:16 three years, you'd agree with -- 68:17 A. Two or three years.	
72:9 - 72:13	**Rubenstein, James 02-07-2019 (00:00:07)** 72:9 Q. Okay. Are you a professor in residency or 72:10 is that -- 72:11 A. Professor, yeah. 72:12 Q. Okay. So you have to give lectures? 72:13 A. Yeah. Yeah.	Rubenstein.107
73:15 - 73:24	**Rubenstein, James 02-07-2019 (00:00:25)** 73:15 Q. Okay. And in Ms. Pilliod's case, you made 73:16 a determination -- and I'll get to the record later 73:17 on. We may not even have to get to it 73:18 specifically -- that you wanted to do -- 73:19 A. Well, we -- we gave her the -- we gave her 73:20 this methotrexate, temozolomide. Methotrexate 73:21 again. 73:22 Q. Right. You started another eight cycles 73:23 of that? 73:24 A. Yeah.	Rubenstein.108
75:3 - 76:10	**Rubenstein, James 02-07-2019 (00:01:53)** 75:3 Q. You saw Ms. Pilliod on November 15, 2016, 75:4 and at that time, she had received her second cycle 75:5 of methotrexate. 75:6 A. Uh-huh. 75:7 Q. And in your impression and plan you write, 75:8 "KPS 90." 75:9 What does that mean? 75:10 A. As I mentioned before, the patients are -- 75:11 we assess their functional status. And one of the 75:12 scales is called Karnofsky Performance Status, KPS. 75:13 Probably the most -- it's one of the two scales. 75:14 So basically that means that the patient 75:15 has only minor -- minor deficits at that time. 75:16 Q. Okay. And, in fact, on that record, you 75:17 stated that, "Since September 14, 2016, there was	Rubenstein.109

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	75:18 interval resolution previously noted in the right 75:19 parietal subependymal signal abnormality and 75:20 enhancement. There was no evidence of disease 75:21 progression." 75:22 That means what? 75:23 A. Yeah, I mean you have to ask me what 75:24 the -- what it's compared to. But basically what 75:25 the -- what I'm getting at -- or probably getting at 76:1 there is that the -- the tumor was disappearing 76:2 or -- or -- or had resolved based on the MRI. That 76:3 means that you can't see tumor associated. The 76:4 biomarker on the MRI is enhancement. It sounds like 76:5 from what that report is or that the enhancement had 76:6 gone away. That doesn't mean that the tumor is 76:7 completely gone. 76:8 Q. She's getting better would be a good way 76:9 to say it? 76:10 A. Correct.	
76:18 - 77:2	**Rubenstein, James 02-07-2019 (00:00:34)** 76:18 Q. Okay. January 18, 2017, you note that her 76:19 PCNSL was a, quote, in apparent radiographic CR. 76:20 CR meaning? 76:21 A. Complete response. 76:22 Q. What does complete response mean? 76:23 A. No evidence of pathologic enhancement on 76:24 the scan. 76:25 Q. So does that mean she is in remission? 77:1 A. It's -- it suggests that she's in 77:2 remission.	Rubenstein.110
77:3 - 77:5	**Rubenstein, James 02-07-2019 (00:00:02)** 77:3 Q. Which is different from being cured, 77:4 obviously? 77:5 A. Uh-huh.	Rubenstein.111
77:21 - 77:25	**Rubenstein, James 02-07-2019 (00:00:12)** 77:21 Q. But in this instance, under her -- on her 77:22 reoccurrence, when you had the consolidation, she 77:23 ended remission and is now on maintenance 77:24 immunotherapy? 77:25 A. Yep.	Rubenstein.112
78:6 - 78:8	**Rubenstein, James 02-07-2019 (00:00:08)**	Rubenstein.113

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	78:6 And then on May 24, 2017, at this visit 78:7 you gave her KPS of 100 with no neurologic defects? 78:8 A. Yeah.	
79:5 - 79:12	**Rubenstein, James 02-07-2019 (00:00:22)** 79:5 Q. Ms. Pilliod is driving. You're aware of 79:6 that? She gets herself to and from her appointments 79:7 with you? 79:8 A. Yep. 79:9 Q. Did she on her last visit report any 79:10 difficulties with feeding herself, dressing? 79:11 A. No. No, she's not -- she's still in the 79:12 ballpark, somewhere between 90 and 100.	Rubenstein.114
79:19 - 80:14	**Rubenstein, James 02-07-2019 (00:01:18)** 79:19 Q. Okay. How do you determine, Doctor, how 79:20 much of Ms. Pilliod's current condition is due to 79:21 her age versus due to her previous PCNSL? 79:22 A. I would say her signs and symptoms of 79:23 ongoing neurologic problems are related to her 79:24 PCNSL. 79:25 Q. And you would relate none of them to -- to 80:1 her advanced age? 80:2 A. Well, in my book she's not that old, 80:3 but... 80:4 Q. My book too. 80:5 A. So... 80:6 Q. But they think we're at an advanced age. 80:7 A. But, yeah, no, I -- I don't think it's -- 80:8 I think she -- you know, she -- face it, she had 80:9 disease twice in her brain, and the brain doesn't -- 80:10 it's like having a stroke. The brain doesn't always 80:11 recover. Usually doesn't recover completely, 80:12 especially whenever you're that age group, 80:13 whether -- and moreover, the brain, certain types of 80:14 injuries, can be devastating when you're older.	Rubenstein.115
82:14 - 83:1	**Rubenstein, James 02-07-2019 (00:00:41)** 82:14 Q. And just while we're on that subject, 82:15 there is no marker to determine the cause of any 82:16 person's non-Hodgkin's lymphoma, there's no 82:17 diagnostic test that you can do or other test that 82:18 you can do?	Rubenstein.116

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	82:19 A. Really, not. You know, you could argue 82:20 that -- in certain cases, you could argue that -- in 82:21 general, there are some signatures, not genetic 82:22 signatures, to tobacco-related cancers, 82:23 vinyl-chloride-related cancers that have a genetic 82:24 signature. 82:25 Q. Right. 83:1 A. That's not the case in -- in lymphomas.	
84:7 - 84:16	**Rubenstein, James 02-07-2019 (00:00:37)** 84:7 Q. Did Ms. Pilliod have any unusual genetic 84:8 translocations or genetic abnormalities that 84:9 provided you some insight? 84:10 A. Generally, yeah, we -- we haven't looked 84:11 at her tumor in genetic detail yet. Good question. 84:12 Q. Is there anything that you think you would 84:13 find when you -- or if you did look at her tumor 84:14 genetically that would point to glyphosate or 84:15 Roundup as a cause? 84:16 A. No. That's -- no. No, that's a stretch.	Rubenstein.117
84:19 - 85:1	**Rubenstein, James 02-07-2019 (00:00:14)** 84:19 Q. Did her CNS lymphoma present similar to 84:20 other patients you've -- you've seen? 84:21 A. Absolutely. 84:22 Q. Nothing unusual about her? 84:23 A. No. 84:24 Q. And you've seen CNS patients that have not 84:25 had glyphosate exposure, correct? 85:1 A. Correct.	Rubenstein.118
86:20 - 88:3	**Rubenstein, James 02-07-2019 (00:01:15)** 86:20 MR. MILLER: Again, Mike Miller, we -- 86:21 both of us appreciate your time. 86:22 THE WITNESS: You bet. 86:23 EXAMINATION 86:24 BY MR. MILLER: 86:25 Q. It'd be fair to say, so a jury 87:1 understands, as a -- as a treater, you're not really 87:2 looking hard at cause, you're more focused on how I 87:3 can treat this lady and save her life; is that a 87:4 fair statement? 87:5 A. Absolutely.	Rubenstein.62

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	87:6 Q. And -- and counsel asked you if people can 87:7 get non-Hodgkin's lymphoma without being exposed to 87:8 Roundup, and I think you -- common sense said yes. 87:9 But my question is this, people can get 87:10 lung cancer without ever smoking as well; isn't that 87:11 true? 87:12 A. Well, there's some -- yeah, absolutely. 87:13 I -- I mean, let's -- let's qualify one thing. 87:14 Q. Sure. 87:15 A. Devil's advocate. 87:16 How many -- you know, how many of the 87:17 patients that we treat are dealing with pesticides 87:18 that we don't -- they don't consider as being an 87:19 exposure. 87:20 Q. Well, I -- and I think that's a fair 87:21 question. 87:22 A. And that -- that's not to say that -- but 87:23 I think you have to consider that as a possibility. 87:24 Q. And -- 87:25 A. Or -- yeah. 88:1 Q. Yeah. I didn't mean to cut you off. 88:2 A. Environmental causes of cancer are -- 88:3 are -- are probably very important.	
88:10 - 88:12	**Rubenstein, James 02-07-2019 (00:00:03)** 88:10 cancer. You don't consider yourself one of the 88:11 people who study that issue. 88:12 A. Absolutely not.	Rubenstein.63
88:20 - 89:5	**Rubenstein, James 02-07-2019 (00:00:24)** 88:20 Q. And you know Dr. Dennis Weisenburger? 88:21 A. I do. 88:22 Q. And, you know, you respect him as an 88:23 expert in that field, the relationship between 88:24 herbicides and pesticides? 88:25 A. I respect him as an expert in -- 89:1 scientific expert. He's at the City of Hope, which 89:2 is outstanding in blood cancers. 89:3 Q. Sure. 89:4 A. And he came from Nebraska, which is 89:5 outstanding in lymphoma.	Rubenstein.86
89:21 - 90:7	**Rubenstein, James 02-07-2019 (00:00:35)**	Rubenstein.64

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	89:21 Q. Right. But when you treated her you did 89:22 not reach a cause for her non-Hodgkin's lymphoma? 89:23 A. No. 89:24 Q. And as any scientist, you would agree, 89:25 often there are multiple causes for cancer, fair? 90:1 A. Yeah. 90:2 Q. All right. Can -- counsel asked you about 90:3 how long the brain tumor was there, and you said a 90:4 couple weeks, perhaps a month or so. But you 90:5 explained to us about how there can be a longer 90:6 latency between exposures. 90:7 A. Absolutely. Absolutely. I believe --	
90:13 - 91:21	**Rubenstein, James 02-07-2019 (00:01:57)** 90:13 Q. The question was, how long is the latency 90:14 between exposures to causes of non-Hodgkin's -- 90:15 A. Sure. 90:16 Q. -- lymphoma and the actual manifestation 90:17 of non-Hodgkin's lymphoma? 90:18 A. It's possible that -- years or decades. 90:19 You know, it's a multi -- these -- these lymphomas 90:20 generally don't have one mutation. They generally 90:21 have multiple mutations. They definitely have 90:22 chromosomal bridges. They have amplification and 90:23 lesions. And this may -- and there may be a 90:24 clone that -- and the mutation pattern at relapse is 90:25 different from the mutation pattern at diagnosis. 91:1 Q. Sure. 91:2 A. We're beginning to show that. 91:3 But the -- getting at the -- the root of 91:4 your question or the answer to your -- what I 91:5 perceived to be the root of your question is, what 91:6 probably happens is you get a -- a lymphoma that has 91:7 a mutation that gives it a growth advantage and -- 91:8 and also both by terms of growing faster and 91:9 suppressing the immune system. 91:10 But it isn't really a cancer cell. It's 91:11 just an Olympic athlete in terms of relative to 91:12 other lymphocytes. And then you -- it gets a second 91:13 mutation and then it becomes, you know, a -- a gold 91:14 medal Olympian. And then third mutation and it's	Rubenstein.65

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91:15 a -- it's a monster. It's out of -- grows out of
91:16 control.
91:17 So the stepwise pattern -- or it gets a
91:18 third mutation and it's not -- it doesn't facilitate
91:19 its survival. So it dies. But its sister cell gets
91:20 a better mutation that allows it to grow. So it
91:21 could take decades to get a lymphoma.

[redacted]

Total Time = 00:41:58

Documents Shown
RJ1
RJ2