FOR PUBLICATION

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

STEPHEN WENDELL; LISA WENDELL, for themselves and as successors-in-interest to Maxx Wendell, deceased, *Plaintiffs-Appellants*, v. GLAXOSMITHKLINE LLC; TEVA PHARMACEUTICALS USA, INC., *Defendants-Appellees.*	No. 14-16321 D.C. No. 4:09-cv-04124-CW OPINION

Appeal from the United States District Court
for the Northern District of California
Claudia Wilken, District Judge, Presiding

Argued and Submitted September 16, 2016
San Francisco, California

Filed June 2, 2017

Before: Ronald M. Gould and Marsha S. Berzon, Circuit Judges, and William K. Sessions III,[*] District Judge.

Opinion by Judge Gould

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[*] The Honorable William K. Sessions III, United States District Judge for the District of Vermont, sitting by designation.

SUMMARY[**]

Expert Testimony / Duty to Warn

The panel reversed the district court's summary judgment in favor of Teva Pharmaceuticals USA, Inc., and the dismissal, as moot, of plaintiffs' motion to reconsider, in an action alleging negligence and strict liability concerning the manufacture and distribution of drugs that were used to treat plaintiffs' deceased son, Maxx Wendell, for inflammatory bowel disease.

Plaintiffs alleged that the drugs caused Maxx Wendell to develop Hepatosplenic T-cell lymphoma, and that the manufacturers and distributors did not give adequate warnings about the risks associated with the drugs. The district court granted summary judgment for Teva because the testimony of plaintiffs' causation experts was not reliable and not admissible under Fed. R. Evid. 702, and because plaintiffs did not present evidence that Maxx's prescribing physician relied on Teva's warning labels.

The panel held that the district court erred by excluding the experts' testimony. The panel held that the district court looked too narrowly at each individual consideration under *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 589 (1993), without taking into account the broader picture of the experts' overall methodology. Specifically, the panel held that the district court improperly ignored the experts' experience, reliance on a variety of literature and studies, and

[**] This summary constitutes no part of the opinion of the court. It has been prepared by court staff for the convenience of the reader.

review of Maxx's medical records and history, as well as the fundamental importance of differential diagnosis by experienced doctors treating troubled patients. The panel further held that the district court overemphasized certain facts; and taken together, these mistakes warranted reversal. The panel concluded that the proposed testimony was sufficiently reliable, and plaintiffs' experts should have been allowed to testify under *Daubert*, and admitted as expert testimony under Fed. R. Evid. 702.

The panel reversed the district court's summary judgment to Teva on the duty to warn claim. The panel held that under California law, viewing the evidence in the light most favorable to plaintiffs, there was a genuine dispute of material fact as to whether the prescribing physician's conduct would have changed with warnings from Teva, and its predecessor GlaxoSmithKline LLC.

The panel declined to affirm the district court's judgment on alternative grounds, and held that Teva may raise the issues with the district court on remand.

Finally, the panel reversed the district court's denial of plaintiffs' motion for reconsideration, and remanded.

COUNSEL

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OPINION

GOULD, Circuit Judge:

Maxx Wendell[1] tragically died at the age of 21 of Hepatosplenic T-cell lymphoma (HSTCL), an exceedingly rare and aggressive form of cancer. For many years before his development of HSTCL, Maxx was treated with a combination of drugs for inflammatory bowel disease. After his death, his parents, Stephen and Lisa Wendell (Plaintiffs), sued the manufacturers and distributors of these drugs, asserting claims under California law for negligence and strict liability. Plaintiffs alleged that the drugs caused Maxx to develop HSTCL and that the manufacturers and

[1] We refer to Maxx Wendell by his first name to avoid confusion.

distributors did not give adequate warnings about the risks associated with the drugs.

The district court granted summary judgment to Teva Pharmaceuticals USA, Inc. (Teva), concluding that the Plaintiffs did not present admissible expert testimony of causation and did not show that Maxx's prescribing physician relied on the warning labels. For the same reasons, the district court dismissed as moot Plaintiffs' motion for leave to file a motion for reconsideration of the district court's prior order granting summary judgment to GlaxoSmithKline LLC (GSK). We reverse and remand.

I

In 1998, at the age of twelve, Maxx was diagnosed with a form of inflammatory bowel disease (IBD) called ulcerative colitis. IBD is an autoimmune disease characterized by chronic inflammation. Maxx began treatment with Dr. Edward Rich, a pediatric gastroenterologist at Kaiser Permanente in San Francisco. Relevant here, in June 1999, Dr. Rich prescribed mercaptopurine (6-MP), an immunosuppressant, and one of a class of drugs known as thiopurines. At the time, 6-MP was manufactured by GSK and marketed as Purinethol. Although it has been widely used off-label since 1980 to treat IBD,[2] Purinethol has never received approval for this use.

In July 2002, Dr. Rich prescribed an additional drug, the tumor necrosis factor alfa antagonist (anti-TNF) drug

[2] Off-label use of a drug is legal, and is "generally based on published scientific reports purporting to show a beneficial effect of the drug in such indications or patient populations."

infliximab, marketed as Remicade. Anti-TNF drugs are approved to treat various autoimmune disorders, such as Crohn's disease and rheumatoid arthritis.

Maxx received his last dose of Remicade in March 2006, after which his IBD went into remission. Two months later, the Food and Drug Administration approved a new label for the drug. The label included a warning reporting postmarketing cases of HSTCL in young male patients with Crohn's disease treated with both Remicade and a thiopurine such as 6-MP or azathioprine. Centocor, the maker of Remicade, also issued a "Dear Health Care Provider" letter alerting prescribers to the labeling change and giving more details on the cases of HSTCL. When Maxx's symptoms returned, Dr. Rich prescribed another anti-TNF drug, Humira, which Maxx took until June 2007. At the time Dr. Rich prescribed Humira, its label did not warn of the risk of HSTCL.

Maxx remained continuously on 6-MP from June 1999 until about March or April 2007. GSK stopped marketing Purinethol on July 1, 2003, and transferred ownership rights for the drug to Teva. Maxx continued on Teva's Purinethol until July 2004, when Dr. Rich switched him to a generic 6-MP. According to Maxx's mother, Maxx decided to stop taking 6-MP in 2007 after reading in *Men's Health* that young men on a combination of Remicade and other immunosupressive medication had developed HSTCL.

In July 2007, Maxx checked into the emergency room with fevers, fatigue, and malaise. Several days later he was diagnosed with HSTCL—a non-Hodgkin's lymphoma that is exceedingly rare and aggressive. It has "low responses to chemotherapy, frequent relapses after contemporary

treatments and the inability of the majority of the patients to undergo bone marrow transplantation." Most patients die within the first year of diagnosis; only a very small fraction achieve long-term survival. Maxx died from HSTCL on December 6, 2007, at the age of 21.

In July 2009, Plaintiffs, Maxx's parents, sued multiple drug companies in Superior Court in California. The case was removed to federal court in September 2009. Plaintiffs filed the operative fourth amended complaint in April 2011. Several defendants, including GSK and Teva, then moved for summary judgment. The district court granted the motion, but subsequently withdrew its summary judgment order in light of Plaintiffs' need for further discovery. In July 2012, after reviewing new evidence, the district court denied the motion for summary judgment as to Teva and two other drug companies, Par Pharmaceutical, Inc. and Abbott Laboratories. The court granted summary judgment to GSK because it determined that Plaintiffs had not presented sufficient evidence that a reasonable jury could find GSK had a duty to warn of the risk of HSTCL before July 1, 2003, when GSK stopped distributing Purinethol. A year later, the district court granted summary judgment to Par Pharmaceuticals.

In January 2014, the remaining defendants—including Teva—filed another motion for summary judgment. Plaintiffs settled their claims against the remaining defendants, except for Teva, before the district court ruled on the motion for summary judgment.

On June 30, 2014, the district court granted Teva's motion for summary judgment because the testimony of Plaintiffs' causation experts, Dr. Andrei Shustov and Dr. Dennis Weisenburger, was not reliable and therefore not

admissible under Federal Rule of Evidence 702, and because Plaintiffs did not present evidence that Maxx's prescribing physician relied on Teva's warning labels. It also denied Plaintiffs' motion for leave to file a motion for reconsideration of the Court's July 2012 order granting summary judgment to GSK. Plaintiffs filed a timely notice of appeal, challenging the district court's grant of summary judgment to Teva and its denial of their motion for leave to file a motion for reconsideration.

II

We review the district court's ruling on the admissibility of expert testimony for an abuse of discretion. *Messick v. Novartis Pharm. Corp.*, 747 F.3d 1193, 1196 (9th Cir. 2014). However, we "review *de novo* the 'construction or interpretation of . . . the Federal Rules of Evidence, including whether particular evidence falls within the scope of a given rule.'" *Id.* (alteration in original) (quoting *United States v. Durham*, 464 F.3d 976, 981 (9th Cir. 2006)). We also review *de novo* the district court's grant of summary judgment. *Id.* at 1199.

III

The issues presented in this appeal arise under the Federal Rules of Evidence and California substantive law. *See Motus v. Pfizer Inc. (Roerig Div.)*, 358 F.3d 659, 660 (9th Cir. 2004) (explaining that in diversity actions the court applies state substantive law and the federal rules of procedure). We begin with the rules of evidence.

A

Federal Rule of Evidence 702 governs expert testimony. It provides:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:
>
> > (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
> >
> > (b) the testimony is based on sufficient facts or data;
> >
> > (c) the testimony is the product of reliable principles and methods; and
> >
> > (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702.

Pursuant to the Federal Rules of Evidence, the district court judge must ensure that all admitted expert testimony is both relevant and reliable. *See Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 589 (1993). Defendants do not contest that the opinions of Dr. Weisenburger and Dr. Shustov are relevant; the only question, therefore, is whether they are reliable.

Scientific evidence is reliable "if the principles and methodology used by an expert are grounded in the methods of science." *Clausen v. M/V New Carissa*, 339 F.3d 1049, 1056 (9th Cir. 2003). The focus of the district court's analysis "must be solely on principles and methodology, not on the conclusions that they generate." *Daubert*, 509 U.S. at 595. As we explained in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, the court's "task . . . is to analyze not what the experts say, but what basis they have for saying it." 43 F.3d 1311, 1316 (9th Cir. 1995) (hereinafter *Daubert II*).

To assist courts with this task, the Supreme Court has listed several non-exclusive factors that judges can consider when determining whether to admit expert testimony under Rule 702. *See Daubert*, 509 U.S. at 593–95. These include: "whether the theory or technique employed by the expert is generally accepted in the scientific community; whether it's been subjected to peer review and publication; whether it can be and has been tested; and whether the known or potential rate of error is acceptable." *Daubert II*, 43 F.3d at 1316. We also consider whether experts are testifying "about matters growing naturally" out of their own independent research, or if "they have developed their opinions expressly for purposes of testifying." *Id.* at 1317. These factors are illustrative, and they are not all applicable in each case. *Id*. The inquiry is "flexible," *Daubert*, 509 U.S. at 594, and "Rule 702 should be applied with a 'liberal thrust' favoring admission," *Messick*, 747 F.3d at 1196 (quoting *Daubert*, 509 U.S. at 588).

The district court concluded that the expert testimony of Dr. Shustov and Dr. Weisenburger did not meet the *Daubert* standard of reliability. The district court first focused on the fact that the experts developed their opinions specifically for litigation, and had never conducted independent research on

the relationship between 6-MP and anti-TNF drugs and the development of HSTCL. The court also noted that both doctors conceded that although their opinions were based on a reasonable degree of medical certainty, they "would not satisfy the standards required for publication in peer-reviewed medical journals." It concluded that the lack of independent research combined with the doctors' reluctance to publish, "casts doubt [on] the reliability of their methodologies under Rule 702."

Second, the district court determined that the lack of animal or epidemiological studies showing a causal link between HSTCL and the combination of 6MP and anti-TNF drugs also undermined the experts' methodology. The court concluded that although it might be difficult to conduct such studies, given the rarity of HSTCL, that type of causal evidence was "especially important here in light of the fact that more than seventy percent of observed HSTCL cases are idiopathic."[3] "[W]ithout some reliable evidence of a positive link between the drugs at issue and the disease," the district court concluded that the experts "cannot reasonably eliminate other potential causes of Maxx's HSTCL."

Finally, the district court found that the studies Drs. Weisenburger and Shustov cited did not "purport[] to show that the specific combination of drugs prescribed to Maxx actually causes HSTCL." Although these studies contained statistics about the incidence of HSTCL in different patient populations, the court found that the experts did not show "that all of the observed differences in these incidence rates are statistically significant or that they account for plausible

[3] A disease that is idiopathic, or de novo, is one that does not have a known cause.

alternative causes of HSTCL, such as IBD itself." Further, the doctors did not present scientific evidence to support their opinion that IBD is not a risk factor for HSTCL.

Although we think it a close question, we conclude that the district court erred by excluding the experts' testimony. The district court looked too narrowly at each individual consideration, without taking into account the broader picture of the experts' overall methodology. It improperly ignored the experts' experience, reliance on a variety of literature and studies, and review of Maxx's medical records and history, as well as the fundamental importance of differential diagnosis by experienced doctors treating troubled patients. The district court also overemphasized the facts that (1) the experts did not develop their opinions based on independent research and (2) the experts did not cite epidemiological studies. We hold that all together, these mistakes warrant reversal. *Cf. Kennedy v. Collagen Corp.*, 161 F.3d 1226, 1228–30 (9th Cir. 1998) (concluding that the expert's reliance on studies that showed a connection between collagen and autoimmune disorders combined with the expert's observations of the patient and review of her medical history was a sufficiently reliable methodology even though the cause-effect relationship between the collagen and the disease was not conclusively established).

To begin, the experts were highly qualified doctors. Dr. Shustov is a licensed, board-certified physician and an Associate Professor of Medicine at the University of Washington Medical Center. He specializes in the diagnosis and treatment of lymphomas, with a clinical research focus on T-cell leukemia and lymphomas. He has treated "hundreds of patients with T-cell lymphomas," and "thousands of patients with lymphomas," including seven patients with

HSTCL. Two of those patients were treated with the combination of drugs at issue here. Given the rarity of HSTCL, Dr. Shustov estimated that he has seen more cases of the disease than 99% of oncologists in the country. Dr. Weisenburger is an expert hematopathologist—a physician trained in the study and diagnosis of diseases of the bone marrow and the immune system—with more than 30 years of experience diagnosing non-Hodgkin lymphoma. He is the professor and Chair of the Department of Pathology at City of Hope Medical Center. Although he has not written specifically on HSTCL, he has written hundreds of papers on the subject of non-Hodgkin's lymphoma, including some on the potential causes of non-Hodgkin's lymphoma.

The doctors employed sound methodologies to reach their conclusions. Dr. Shustov based his opinions "on medical records as well as [his] education, training and experience, knowledge of the pertinent medical literature and [his] knowledge of the epidemiology, diagnosis and natural history of HSTCL." He explained: "I reviewed the literature, I pulled the facts out of the literature." He found that the literature shows there is an increased risk of HSTCL in patients taking 6-MP over the general population. After reviewing the literature, he "compiled the numbers about frequency of diseases, about frequency of inflammatory bowel disease and [he] looked at the biological causation of lymphoma pertaining to this case."

Dr. Shustov stated that he performs differential diagnosis in attempting to diagnose every patient, and that he has applied the same technique to determine the cause of a disease. When performing a differential diagnosis, he first assumes the pertinence of all potential causes, then rules out the ones as to which there is no plausible evidence of

causation, and then determines the most likely cause among those that cannot be excluded. We have recognized that this method of conducting a differential diagnosis is scientifically sound. *See Clausen*, 339 F.3d at 1057–58. For cases of HSTCL in patients that have taken 6-MP, like Maxx, Dr. Shustov recognized:

> that 6-MP is a well-known mutagen and carcinogen and puts every person who takes it at risk. And given the frequency of hepatosplenic lymphoma in [the] general population as . . . [compared to] those who take 6-MP, it makes it plausible or biologically plausible that that's [an] etiologic factor. You construct your differential diagnosis . . . [of] what might have caused lymphoma. You come up with the strongest probability that patient was taking carcinogen and developed lymphoma and you start thinking again what can cause his lymphoma, you can't identify anything else in the patient's history or his medical records.

Regarding Maxx specifically, Dr. Shustov stated that there was a one in six million chance that Maxx would have developed HSTCL without being exposed to 6-MP. In light of those odds, Dr. Shustov stated that "based on [his] experience in T-cell lymphomas, knowledge of the literature and being involved in T-cell lymphoma research in the past ten years" he determined "that it's much more likely that exposure to mutagen and immunosuppressants caused the lymphoma." Dr. Shustov did not need to eliminate all potential causes; "[i]t is enough that a [proposed cause] be a substantial causative factor." *Messick*, 747 F.3d at 1199.

Dr. Weisenburger described his methodology for reaching his opinions as follows:

> I reviewed the medical records. I reviewed the pathology slides and confirmed the diagnosis. I reviewed all of the pathology records. I reviewed the literature on the disease, hepatosplenic lymphoma. And I reviewed all the literature I could find on causes of hepatopathic T-cell lymphoma, including literature on inflammatory bowel disease and treatments for inflammatory bowel disease. And then I used the Bradford Hill methodology to come to the conclusion that I did.[4, 5]

Regarding Maxx specifically, Dr. Weisenburger based his opinion on "a summary of the medical records of [Maxx] as well as copies of the pathology reports, and the original slides of the diagnostic bone marrow," which he evaluated with over 30 years of experience diagnosing non-Hodgkin lymphoma. He stated that he considered that Maxx's HSTCL might have been idiopathic, and that although he was not entirely able to rule that possibility out, "[w]hen you have a patient with obvious and known risk factors, you tend to assume that those risk factors were the cause." He did not base that assumption on pure conjecture. As he discussed throughout his deposition testimony and in his expert report,

[4] The Bradford Hill methodology refers to a set of criteria that are well accepted in the medical field for making causal judgments.

[5] Dr. Weisenburger also identified at least one paper that showed there was no risk of lymphoma in IBD patients.

the literature shows that patients exposed to 6-MP and anti-TNF drugs are at an increased risk for HSTCL. Dr. Weisenburger also weighed other risk factors, including Maxx's sex and age, and determined that those were "weak risk factors; whereas, the disease he had, particularly in the setting of the drugs he received would be considered very strong risk factors."

The proposed testimony was sufficiently reliable that the Plaintiffs' experts should have been allowed to testify under *Daubert*. The district court improperly required more. The Supreme Court in *Daubert* aimed at screening out unreliable or bogus expert testimony. Nothing in *Daubert*, or its progeny, properly understood, suggests that the most experienced and credentialed doctors in a given field should be barred from testifying based on a differential diagnosis.

First, the district court was wrong to put so much weight on the fact that the experts' opinions were not developed independently of litigation and had not been published. While independent research into the topic at issue is helpful to establish reliability, its absence does not mean the experts' methods were unreliable. Where "the proffered expert testimony is not based on independent research," the experts can instead present "other objective, verifiable evidence that the testimony is based on 'scientifically valid principles.'" *Daubert II*, 43 F.3d at 1317–18. To be sure, "[o]ne means of showing [that the testimony is based on scientifically valid principles] is by proof that the research and analysis supporting the proffered conclusions have been subjected to normal scientific scrutiny through peer review and publication." *Id.* at 1318. However, expert testimony may still be reliable and admissible without peer review and publication. *See Clausen*, 339 F.3d at 1056. That is

especially true when dealing with rare diseases that do not impel published studies. *See Milward v. Acuity Specialty Prods. Grp., Inc.*, 639 F.3d 11, 24 (1st Cir. 2011) (recognizing that the "rarity" of a particular form of leukemia was one reason that it would be "very difficult to perform an epidemiological study of the causes of [the disease] that would yield statistically significant results.").

The district court also wrongly conflated the standards for publication in a peer-reviewed journal with the standards for admitting expert testimony in a courtroom. Dr. Weisenburger stated on cross-examination that to publish his opinion he would use a "more rigorous" standard than the one he used to come up with his expert opinion. Dr. Shustov stated that he would not be comfortable publishing his opinion because he did not have any *new* data, and any meta-analysis or review of the literature could only be published upon invitation. The district court viewed these statements regarding the experts' willingness to publish as evidence that their *methods* were not up to snuff. But this analysis misses that while an expert must "employ[] in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field," *Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 152 (1999), the standards for courtroom testimony do not necessarily parallel those of the professional publications, *see Ambrosini v. Labarraque*, 101 F.3d 129, 138 (D.C. Cir. 1996) ("[T]he fact 'that science would require more evidence before conclusively considering the causation question resolved is irrelevant [to the admissibility of expert testimony].'") (quoting *Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529, 1536 (D.C. Cir. 1984)). For example, Dr. Shustov explained that, "[o]pinions are not publishable. Data is publishable. What I'm reporting here is my opinion." Although unwillingness to publish weighs against

admissibility, it alone is not determinative. *See Daubert II*, 43 F.3d at 1318 n.9 ("That plaintiffs' experts have been unable or unwilling to publish their work undermines plaintiffs' claim that the findings these experts proffer are 'ground[ed] in the methods and procedures of science' and 'derived by the scientific method.'" (alteration in original) (quoting *Daubert*, 509 U.S. at 590)). We have previously held expert opinions to be reliable that were not subject to peer review through publication. *See Clausen*, 339 F.3d at 1056, 1061.

The district court also wrongfully required that the experts' opinions rely on animal or epidemiological studies. Neither are necessary for an expert's testimony to be found reliable and admissible. *See Kennedy*, 161 F.3d at 1229. We have long recognized that it may not always be possible to conduct certain types of studies. *See, e.g.*, *Daubert II*, 43 F.3d at 1318 n.9 ("There may well be good reasons why a scientific study has not been published. For example, it may be too recent or of insufficiently broad interest."). HSTCL is an exceedingly rare cancer, with only 100 to 200 cases reported since it was first recognized. It is not surprising that the scientific community has not invested substantial time or resources into investigating the causes of such a rare disease.

Although they did not rely on animal or epidemiological studies, the experts here did rely on other published studies and articles. The district court only addressed a few of these, quickly dismissing them because they are case reports and do not control or account for alternative causes of HSTCL. Although case studies alone generally do not prove causation, they "may support other proof of causation." *Rider v. Sandoz Pharm. Corp.*, 295 F.3d 1194, 1199 (11th Cir. 2002). Here,

the experts relied not just on these studies—which not only examined reported cases but also used statistical analysis to come up with risk rates—but also on their own wealth of experience and additional literature.[6]

We also note that "[n]ot knowing the mechanism whereby a particular agent causes a particular effect is not always fatal to a plaintiff's claim. Causation can be proved even when we don't know precisely *how* the damage occurred, if there is sufficiently compelling proof that the agent must have caused the damage *somehow*." *Daubert II*, 43 F.3d at 1314 (emphasis in original). That there is no study that definitively states HSTCL is caused by the ingestion of 6-MP and anti-TNF drugs does not prevent the admission of Plaintiffs' experts' testimony. *See Kennedy*, 161 F.3d at 1230.

Finally, the district court erred when it excluded Plaintiffs' experts' opinion testimony because of the high rate of idiopathic HSTCL and the alleged inability of the experts to rule out an idiopathic origin or IBD itself. We do not require experts to eliminate all other possible causes of a condition for the expert's testimony to be reliable. *Messick*, 747 F.3d at 1199. It is enough that the proposed cause "be a substantial causative factor." *Id.* This is true in patients with multiple risk factors, and analogously, in cases where there is a high rate of idiopathy. *See id.* (holding that the district court abused its discretion when it excluded expert testimony as unreliable because the expert could not determine which of

[6] Teva argues that its own experts highlight the dearth of scientific evidence to support Plaintiffs' claims and undermine any assertion that Drs. Shustov and Weisenburger employed sound scientific methodology. The district court did not consider this evidence, and we decline to do so in the first instance.

multiple risk factors caused plaintiff's disease). Moreover, when an expert establishes causation based on a differential diagnosis, the expert may rely on his or her extensive clinical experience as a basis for ruling out a potential cause of the disease. *See id.* at 1198. The district court abused its discretion by excluding Dr. Shustov's and Dr. Weisenburger's testimony because they could not completely rule out the possibility that Maxx's HSTCL was idiopathic.

Perhaps in some cases there will be a plethora of peer reviewed evidence that specifically shows causation. However, such literature is not required in each and every case. "The first several victims of a new toxic tort should not be barred from having their day in court simply because the medical literature, which will eventually show the connection between the victims' condition and the toxic substance, has not yet been completed." *Clausen*, 339 F.3d at 1060 (quoting *Turner v. Iowa Fire Equip. Co.*, 229 F.3d 1202, 1209 (8th Cir. 2000)). In the case of a rare disease like HSTCL, the Supreme Court's mandate that in determining the admissibility of expert testimony, the focus "must be solely on principles and methodology, not on the conclusions that they generate," is especially important. *Daubert*, 509 U.S. at 595.

Where, as here, the experts' opinions are not the "junk science" Rule 702 was meant to exclude, *see Estate of Barabin v. AstenJohnson, Inc.*, 740 F.3d 457, 463 (9th Cir. 2014), the interests of justice favor leaving difficult issues in the hands of the jury and relying on the safeguards of the adversary system—"[v]igorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof"—to "attack[] shaky but admissible evidence," *Daubert*, 509 U.S. at 596. Because we conclude

that the district court erred in excluding the testimony of Dr. Shustov and Dr. Weisenburger, we reverse the district court's grant of summary judgment. *See Messick*, 747 F.3d at 1199. As explained in *Messick*, "[m]edicine partakes of art as well as science." *Id.* at 1198. Where, as here, two doctors who stand at or near the top of their field and have extensive clinical experience with the rare disease or class of disease at issue, are prepared to give expert opinions supporting causation, we conclude that *Daubert* poses no bar based on their principles and methodology. That defendants may be able to offer other equally qualified medical opinion opposing causation also does not support the idea that *Daubert* should bar the admission of the testimony of the doctors offered as experts by Plaintiffs. Instead, the testimony of Dr. Weisenburger and of Dr. Shustov should have been admitted as expert testimony under Federal Rules of Evidence 702. The defendants' expert testimony could have been offered in opposition. Then, the jury, as the trier of fact, would be empowered to decide, based on the law given in proper jury instructions and the facts as determined by the jury.

B

The district court granted summary judgment to Teva on the duty to warn claim for two reasons. First, the district court held that the lack of admissible causation evidence precluded Plaintiffs from prevailing on their duty to warn claims. Second, Plaintiffs did not produce "any evidence to suggest that Dr. Rich actually relied on Teva's warning labels before prescribing Purinethol to Maxx." For the reasons discussed above, we reverse on the district court's first ground. For the reasons discussed below, we reverse on the district court's second ground.

Under California law, drug manufacturers have a duty to warn physicians of risks that are known or scientifically knowable at the time of the drug's distribution. *See Carlin v. Superior Court*, 920 P.2d 1347, 1349–54 (Cal. 1996). "A plaintiff asserting causes of action based on a failure to warn must prove not only that no warning was provided or the warning was inadequate, but also that the inadequacy or absence of the warning caused the plaintiff's injury." *Motus v. Pfizer Inc.*, 196 F. Supp. 2d 984, 991 (C.D. Cal. 2001), *aff'd*, 358 F.3d 659. "[A] product defect claim based on insufficient warnings cannot survive summary judgment if stronger warnings would not have altered the conduct of the prescribing physician." *Motus*, 358 F.3d at 661.

In this case, viewing the evidence in the light most favorable to Plaintiffs, there is a genuine dispute of material fact as to whether Dr. Rich's conduct would have changed with warnings from Teva and GSK. Summary judgment was improper.

Although Dr. Rich testified that it is not his "regular practice to look at drug labeling," when he does read them it is "one of the things that is part of [his] decision-making process." He also testified that "a black box warning means there is a significant side effect that I need to be aware of."[7] Indeed, this type of warning did influence Dr. Rich's prescribing decisions for Maxx. Centocor began circulating warnings—both a black box warning and a Dear Health Care

[7] A black box warning is a warning that is placed in a box in a drug's labeling information. According to Plaintiffs' pharmacovigilance expert, a black box warning may only be used with FDA authorization, and it is "the strongest possible warning that can be given short of restricting distribution of a drug or completely withdrawing it from the market."

Provider letter—about HSTCL for Remicade in May 2006, just a few months after Maxx stopped taking Remicade. When Maxx's IBD relapsed in November 2006, Dr. Rich prescribed Humira—which did not have a warning about HSTCL—in place of Remicade. Dr. Rich testified that he prescribed Humira because he believed it had a better safety profile, noting that at that point there were no reports of HSTCL developing in patients who took Humira. This change in prescribing practices which can, at least in part, reasonably be attributed to the lack of a warning for Humira creates a question of material fact as to whether the presence of a warning on Teva's Purinethol would have changed Dr. Rich's prescribing practices as to Maxx.

There is also evidence that Dr. Rich changed his prescribing practices generally after he learned of incidents of HSTCL in patients taking both 6-MP and anti-TNF agents. As the information came out, his prescribing practices evolved. He now no longer prescribes combination therapy but uses only monotherapy. Viewing the facts in the light most favorable to the Plaintiffs, there are questions of material fact as to whether warnings would have changed Dr. Rich's prescribing practice. *See Stanley v. Novartis Pharm. Corp.*, 11 F. Supp. 3d 987, 1003 (C.D. Cal. 2014) ("[C]hanges to treatment and prescription procedures create[d] a triable question of fact on specific causation."). We reverse the district court's grant of summary judgment in favor of Teva.[8]

[8] GSK asserts that Plaintiffs' warning expert's testimony shows that Purinethol's label should have been changed in 2006, approximately three years after GSK stopped distributing the drug. It argues that there can be no causal connection between the alleged failure to warn and the harm. The district court did not address this argument, and we decline to do so.

C

Teva urges us to affirm the district court on four alternative grounds.[9] Although we may affirm on any ground raised below and supported by the record, *see Proctor v. Vishay Intertechnology Inc.*, 584 F.3d 1208, 1226 (9th Cir. 2009), the issues that Teva raises would require extensive fact finding, and are matters on which the district court did not rule. It would be inappropriate for us to reach these issues, and we decline to do so. *See Greater L.A. Council on Deafness, Inc. v. Zolin*, 812 F.2d 1103, 1107 & n.5 (9th Cir. 1987), *superceded by statute on other grounds*. They may be raised with the district court on remand.

D

Finally, Plaintiffs challenge the district court's order denying Plaintiffs' motion for leave to file a motion for reconsideration of the district court's July 2012 order granting summary judgment to GSK. GSK asserts that, as Plaintiffs' opening brief does not challenge the district court's underlying grant of summary judgment to GSK, Plaintiffs

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See Greater L.A. Council on Deafness, Inc. v. Zolin, 812 F.2d 1103, 1107 & n.5 (9th Cir. 1987), *superceded by statute on other grounds*.

[9] Briefly, Teva argues that we should affirm on each of the following four bases: (1) it had no duty to warn about the alleged risk of HSTCL arising from an off-label use of Purinethol; (2) it had no duty to warn about alleged risks from use of a competitor's product; (3) Plaintiffs cannot maintain a failure to warn claim because Dr. Rich had already received the information; and (4) because Plaintiffs cannot prove that Maxx developed HSTCL after May 2006, they cannot prove that an alleged failure to warn by Teva was the proximate cause of Maxx's injuries.

abandoned their argument that the district court erroneously granted summary judgment to GSK.

GSK's argument is unpersuasive. As to GSK, Plaintiffs are challenging *only* the district court's denial of its motion for leave to file a motion for reconsideration. A challenge to a denial of a motion for leave to file a motion for reconsideration brings up just the denial of that motion, not the underlying merits. *Cf. Molloy v. Wilson*, 878 F.2d 313, 315 (9th Cir. 1989) ("An appeal from a denial of a Rule 60(b) motion brings up only the denial of the motion for review, not the merits of the underlying judgment."). Plaintiffs did raise this argument in their Opening Brief, asserting that because the district court's rulings regarding the admissibility of expert testimony and causation were erroneous, "the ruling on Plaintiffs' motion likewise should be vacated so that it can be decided on its merits on remand."

We agree with Plaintiffs. The district court denied their motion "as moot" because "Plaintiffs cannot prevail on their claims against [GSK] for the same reasons they cannot prevail on their claims against Teva": lack of admissible causation evidence, and lack of evidence showing Dr. Rich's reliance on warnings. Because we reverse the district court on those issues, we also reverse the district court's denial of Plaintiffs' motion for reconsideration.

REVERSED AND REMANDED.