

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

LEAH ROYCE HINES,

Plaintiff,

v.

Civil Action No. 2:04-0690

WYETH, d/b/a Wyeth, Inc.;
WYETH PHARMACEUTICALS, INC.;
and PHARMACIA & UPJOHN COMPANY,

Defendants.

MEMORANDUM OPINION AND ORDER

Pending is defendants' motion to exclude the expert testimony of Dr. Michael Wertheimer (Doc. No. 205), filed May 27, 2011. Pending as well is plaintiff's motion to exclude expert testimony from Drs. Chodosh, Meile, and Levy that combination hormone therapy does not generally cause breast cancer (Doc. No. 253), also filed May 27, 2011.¹

¹ At a pretrial conference on June 17, 2011, the court conferred with counsel regarding the necessity of an evidentiary hearing on the various Daubert motions currently pending before the court. (See Doc. No. 343). The parties made clear that such a hearing was not necessary. Defendants have, however, requested oral argument on the motions. Inasmuch as the parties' briefs and supporting exhibits adequately present the issues ripe for adjudication, the court finds that oral argument would not aid the decisional process and accordingly denies defendants' request for oral argument as to the motions discussed herein.

I.

This is a pharmaceutical products liability action in which plaintiff Leah Royce Hines alleges that she developed breast cancer as a result of ingesting hormone replacement therapy ("HRT") drugs manufactured by defendants. HRT here consists of two medications, estrogen and progestin ("E+P"), that are commonly prescribed in combination to treat menopausal symptoms.

This action concerns three HRT drugs: Premarin, Prempro, and Provera. Defendant Wyeth, LLC ("Wyeth") manufactured Premarin, an estrogen drug, and Prempro, a combination estrogen and progestin drug. Defendant Pharmacia & Upjohn Company ("Upjohn") manufactured and distributed Provera, a progestin drug. The generic name for Provera is medroxyprogesterone acetate ("MPA").

Plaintiff's physician prescribed HRT drugs to treat her menopausal symptoms from approximately July 1994 to April 1999. She was diagnosed with breast cancer in July 1999, and thereafter instituted this action on July 7, 2004, invoking the court's

diversity jurisdiction.² Her complaint asserts claims against defendants for negligence, strict liability (design defect and failure to warn), and breach of implied warranty.

Defendants seek to exclude the testimony of plaintiff's specific causation expert, Dr. Michael Wertheimer. Plaintiff has moved to exclude expert testimony from Drs. Chodosh, Meile, and Levy that combination hormone therapy does not generally cause breast cancer.

II.

The admission of expert testimony is governed by Federal Rule of Evidence 702 and the Supreme Court's decision in Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993). Under Rule 702 and Daubert, expert testimony must satisfy a two-prong test: (1) the testimony must concern "scientific, technical, or other specialized knowledge"; and (2) it must "aid the jury or other trier of fact to understand or resolve a fact at issue." Westberry v. Gislaved Gummi AB, 178 F.3d 257, 260 (4th Cir. 1999) (citing Daubert, 509 U.S. at 592);

² The case was transferred to multidistrict litigation in the United States District Court for the Eastern District of Arkansas on October 26, 2004. Over five years later, on April 13, 2010, it was remanded to this court for the completion of discovery, pretrial activity, and trial.

Fed. R. Evid. 702. "The first prong of this inquiry necessitates an examination of whether the reasoning or methodology underlying the expert's proffered opinion is reliable -- that is, whether it is supported by adequate validation to render it trustworthy." Westberry, 178 F.3d at 260. "The second prong of the inquiry requires an analysis of whether the opinion is relevant to the facts at issue." Id. Thus, an expert's testimony is admissible under Rule 702 if it "rests on a reliable foundation and is relevant." Kumho Tire Co. v. Carmichael, 526 U.S. 137, 141 (1999).

As to the reliability prong, the Court in Daubert announced a non-exhaustive list of factors to guide the trial judge's inquiry, including "(1) whether a theory or technique can be or has been tested; (2) whether it has been subjected to peer review and publication; (3) whether a technique has a high known or potential rate of error and whether there are standards controlling its operation; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." Cooper v. Smith & Nephew, Inc., 259 F.3d 194, 199 (4th Cir. 2001) (citing Daubert, 509 U.S. at 592-94).

As to the relevancy prong, "the expert's proffered scientific testimony must be sufficiently tied to the facts of

the case that it will be of assistance to the factfinder in resolving a disputed fact." Bourne ex rel. Bourne v. E.I. Dupont de Nemours & Co., 189 F. Supp. 2d 482, 495 (S.D. W. Va. 2002).

"That is, there must be a 'valid scientific connection to the pertinent inquiry' before the testimony is admissible." Id. (quoting Daubert, 509 U.S. at 591-92).

Our court of appeals has summarized the overarching duties of a trial court in resolving Daubert motions as follows:

A district court considering the admissibility of expert testimony exercises a gate keeping function to assess whether the proffered evidence is sufficiently reliable and relevant . . . The inquiry to be undertaken by the district court is "a flexible one" focusing on the "principles and methodology" employed by the expert, not on the conclusions reached. Daubert, 509 U.S. at 594-95 . . . In making its initial determination of whether proffered testimony is sufficiently reliable, the court has broad latitude to consider whatever factors bearing on validity that the court finds to be useful . . . The court, however, should be conscious of two guiding, and sometimes competing, principles. On the one hand, the court should be mindful that Rule 702 was intended to liberalize the introduction of relevant expert evidence. . . . [T]he court need not determine that the expert testimony a litigant seeks to offer into evidence is irrefutable or certainly correct . . . As with all other admissible evidence, expert testimony is subject to being tested by "[v]igorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof." Daubert, 509 U.S. at 596 . . . On the other hand, the court must recognize that due to the difficulty of evaluating their testimony, expert witnesses have the potential to "be both powerful and quite misleading." Id. at 595 . . . [G]iven the potential persuasiveness of expert testimony, proffered evidence that has a greater potential to mislead than to enlighten should be excluded.

Westberry, 178 F.3d at 261 (some citations and footnotes omitted). Ultimately, "[t]he proponent of the [expert] testimony must establish its admissibility by a preponderance of proof." Cooper, 259 F.3d at 199.

III. Motion to Exclude Dr. Wertheimer's Testimony

A. Background

Dr. Wertheimer is a board certified surgeon who specializes in breast cancer. Plaintiff seeks to introduce his testimony to show that defendants' HRT drugs caused her breast cancer (i.e., specific causation). His expert report provides the following summary of his conclusions:

1. E+P can cause and has caused hormone dependent breast cancer in women. The best estimate [based on epidemiological studies] is that E+P has caused in excess of 200,000 breast cancers in this country alone.
2. The mechanism by which E+P causes breast cancer is by promotion, which refers to the stimulation or fueling of hormone dependent cells, lesions, and/or tumors so that these pre-malignant and preclinical abnormalities develop into clinical cancer.
3. Once breast cancer is present, E+P acts to further fuel the growth and development of the cancer by causing the cells to continue to proliferate and divide thus allowing for additional mutations and as such E+P causes an aggravation of the woman's pre-existing breast cancer disease.
4. I have used the methodology of differential diagnosis or causality assessment as well as the available epidemiological experimental and clinical

evidence to evaluate the cause of Mrs. Hines's breast cancer. In my opinion, Mrs. Hines's use of E+P was a substantial contributing factor and a factual and legal cause of the development and growth of her breast cancer so that, but for her use of E+P, she would not have developed such cancer.

(Pl.'s Opp., Ex. 2, Wertheimer Report ("Wertheimer Rep.") at 3).

Regarding case-specific opinions, Dr. Wertheimer's report notes that a pathological examination of plaintiff's tumor revealed that her breast cancer was estrogen receptor and progesterone receptor positive ("ER/PR positive"). (Wertheimer Rep. at 13; Pl.'s Opp., Ex. 5, LRoyce-HKB&TSAI- 000 295-296). He observes that breast cancer that has positive estrogen or progesterone receptors is known as "hormone dependent," meaning that the cancer requires hormones to develop. (Wertheimer Rep. at 13). Dr. Wertheimer opines that there are two possible sources of hormones necessary to develop hormone dependent cancer: endogenous hormones (i.e., estrogen and progesterone naturally produced by the body) and exogenous hormones (i.e., pharmaceutical hormones such as E+P). (Id.). Because plaintiff's medical history shows that her menopausal symptoms improved on HRT drugs and returned to some degree after she stopped taking the drugs, Dr. Wertheimer found that plaintiff was a "low [endogenous] hormone producing" woman. (Id. at 15). Given her lack of naturally produced hormones, he concluded that

exogenous hormones, in the form of defendants' HRT drugs, were the likely cause of plaintiff's ER/PR positive breast cancer. (Id.). In reaching this conclusion, Dr. Wertheimer addressed other potential causes such as breast density, family history of breast cancer, and exposure to ionized radiation, but ultimately found that none of these factors posed a significant risk of breast cancer for this particular plaintiff. (Id. at 17).

Defendants move to exclude Dr. Wertheimer's testimony on the following grounds: (1) differential diagnosis is not a reliable or generally accepted method of determining the cause of an individual's breast cancer; (2) Dr. Wertheimer has not tested his theory that women who experience menopausal symptoms have a low baseline level of endogenous estrogen ("natural estrogen") and are therefore at a low risk of breast cancer unless they take HRT drugs, and studies by independent investigators contradict this theory; and (3) even if differential diagnosis could be used here, Dr. Wertheimer failed to conduct a proper differential diagnosis because he did not rule out as causes of plaintiff's breast cancer her natural estrogen or her other risk factors for breast cancer. The court considers these contentions in turn.

B. Use of Differential Diagnosis to Determine the Cause of an Individual's Breast Cancer

As the Fourth Circuit has explained, differential diagnosis "is a standard scientific technique of identifying the cause of a medical problem . . . by determining the possible causes for the patient's symptoms and then eliminating each of these potential causes until reaching one that cannot be ruled out or determining which of those that cannot be excluded is the most likely." Westberry, 178 F.3d at 262. It is typically performed "after physical examinations, the taking of medical histories, and the review of clinical tests, including laboratory tests." Id. (internal citations omitted). "A reliable differential diagnosis provides a valid foundation for an expert opinion under Rule 702." Cooper, 259 F.3d at 200 (emphasis in original).

To be clear, defendants do not dispute that a reliable differential diagnosis satisfies the Daubert standard. They instead claim that the use of differential diagnosis to determine the cause of breast cancer is "inherently unreliable" because the causes of breast cancer are unknown; there is no reliable means for determining the cause of someone's breast cancer; and differential diagnosis is not a "generally accepted methodology" in the breast cancer community.

The court is not persuaded by defendants' contention that the causes of breast cancer are categorically "unknown." Dr. Wertheimer cites various peer-reviewed articles and epidemiological studies concluding that E+P causes breast cancer in women. (Wertheimer Rep. at 7 n.17 (citing, among others, Colditz, Decline in Breast Cancer Incidence Due to Removal of Promoter: Combination Estrogen Plus Progestin, 9 Breast Cancer Research 108 (2007); MacMahon, Epidemiology and the Causes of Breast Cancer, 118 Int. J. Cancer 2373-78 (2006); Fournier, Use of Different Postmenopausal Hormone Therapies and Risk of Histology- and Hormone Receptor-Defined Invasive Breast Cancer, 26(8) J. Clinical Oncology 1260-68 (2008); Katalinic, Trends in Hormone Therapy and Breast Cancer Incidence -- Results from the German Network of Cancer Registries, 76 Pathobiology 90 (2009))). He also relies on the MacMahon article (cited above) to show that there are "three known causes of human breast cancer: ionizing radiation, beverage alcohol, and exogenous ovarian hormones [i.e., E+P]," and notes that this view is "supported by every major national and international scientific organization such as the NCI [National Cancer Institute], ACS [American Cancer Society], IARC [International Agency for Research on Cancer], World Health Organization, and most leading scientists and academicians in the field." (Id. at 17). Defendants do not

challenge or even address these findings.³

While all causes of the disease are not known, the medical literature shows that at least some potential causes of breast cancer have been identified. Inasmuch as potential causes of breast cancer can be "ruled in," the court finds that it is possible, in a given instance, to perform a reliable differential diagnosis to determine the cause of an individual's breast cancer, contrary to defendants' contention that such methodology is per se unreliable. As plaintiff points out, other courts in the HRT litigation have reached similar conclusions. See, e.g., Scroggin v. Wyeth (In re Prempro Prods. Liab. Litig.), 586 F.3d 547 (8th Cir. 2009) (upholding use of differential diagnosis as a reliable methodology for determine the cause of the plaintiff's breast cancer); Rivera Adams v. Wyeth, No. 03-1713, 2010 WL 5072061, at *4 (D.P.R. Dec. 3, 2010) (same; admitting Dr.

³ In support of the argument that the causes of breast cancer are unknown, defendants rely not on scientific data, but primarily on excerpts from Dr. Wertheimer's deposition testimony. Specifically, Dr. Wertheimer confirmed at his deposition that he was quoted in a 1996 newspaper article as saying "no one really knows or understands what causes breast cancer." (Def.'s Mot. to Exclude, Ex. 11, Wertheimer Dep. at 31-32). He went on to testify, however, that this statement was accurate in 1996, suggesting that his views have changed and the medical research has revealed new findings since that time. (Id.). In any event, to the extent that Dr. Wertheimer's prior statements conflict with his current testimony, this affects the weight rather than the admissibility of his testimony.

Wertheimer's use of differential diagnosis to determine the cause of the plaintiff's breast cancer).⁴

C. Reliability of Dr. Wertheimer's "Symptoms" Theory

Defendants next challenge the reliability of what they call Dr. Wertheimer's "symptoms" theory. They summarize this theory as follows: postmenopausal women who exhibit menopausal symptoms ("symptomatic women") have low levels of natural estrogen, and postmenopausal women with low levels of natural estrogen are at a lower risk of breast cancer absent HRT drug use; therefore, symptomatic women are at a lower risk of breast cancer absent HRT drug use. In attacking this symptoms theory, defendants note that Dr. Wertheimer has conducted no studies or published any articles on this topic, and that his premises are contradicted by the results of two independent medical studies (the Farhat and Huang studies).

⁴ Defendants are correct that plaintiff has presented no evidence that differential diagnosis is a generally accepted methodology in the breast cancer community (though it bears mentioning that defendants, while not the burden-carrying parties, have presented no evidence showing that differential diagnosis has been rejected in the breast cancer community). However, general acceptance in the relevant scientific community is only one of the Daubert factors, and, in light of the broad acceptance of differential diagnosis in the medical community at large, the absence of such evidence here does not sway the court to exclude Dr. Wertheimer's testimony.

Dr. Wertheimer's theory does rely in part on the premise that symptomatic women -- and, specifically, symptomatic women whose menopausal symptoms improve after taking HRT drugs -- have low levels of natural estrogen. From this premise he is able to conclude that plaintiff, a symptomatic woman whose symptoms improved after taking HRT drugs, did not have sufficient natural estrogen to cause her hormone dependent breast cancer, and that exogenous hormones in the form of HRT drugs were thus the likely cause of her disease. Although it is true that Dr. Wertheimer has not personally conducted any tests of his theory, peer-reviewed medical publications cited by Dr. Wertheimer conclude that the exhibition of certain menopausal symptoms (e.g., vasomotor symptoms such as night sweats and hot flashes, as well as vaginal atrophy) are a sign of estrogen deficiency. (Wertheimer Rep. at 14 n.45 (citing Notelovitz, Clinical Opinion: The Biological and Pharmacological Principles of Estrogen Therapy for Symptomatic Menopause, 8(1) Medscape Gen. Med. 85 (2006); Yasui, Serum Estrogen Level After Hormone Therapy and Body Mass Index in Postmenopausal and Bilaterally Ovariectomized Women, 50 Maturitas 19-29 (2005))). He also cites research showing that menopausal symptoms are "an important biomarker of a woman's reduced risk of developing breast cancer." (Id. at 14 n.46 (citing Cuzik, Treatment Emergent Endocrine Symptoms and the Risk

of Breast Cancer Recurrence -- A Retrospective Analysis of the ATAC trial, 9(12) Lancet Oncol. 1143-48 (2008); id. at 5, n.9 (citing, among others, Anderson, Prior Hormone Therapy and Breast Cancer Risk in the Women's Health Initiative Randomized Trial of Estrogen Plus Progestin, 55(2) Maturitas 103-15 (2006)).

Once again, defendants do not address this medical literature, nor do they challenge Dr. Wertheimer's utilization of the literature in forming his opinions. They do, however, claim that Dr. Wertheimer's conclusions are rebutted by the results of the Farhat and Huang studies, which, defendants argue, disprove the theory that the presence of menopausal symptoms is indicative of low natural estrogen levels and a corresponding lower risk of breast cancer absent HRT drug use. Setting aside whether these studies do in fact conflict with Dr. Wertheimer's findings,⁵ defendants' arguments go to the conclusions reached rather than the methodology employed by Dr. Wertheimer, and are therefore insufficient to sustain a Daubert challenge.

Notably, the Eighth Circuit in Scroggin v. Wyeth upheld a similar expert opinion against defendants' Daubert challenge:

⁵ It appears that the Huang study actually confirms at least one of Dr. Wertheimer's premises. (See Pl.'s Opp., Ex. 3, 2011 Huang study, at 329 ("Conclusion: This is the first study to report that women who ever experienced menopausal symptoms have a substantially reduced risk of breast cancer.")).

[P]ublished research had concluded that hormone-receptor-positive tumors need hormones to grow, that menopausal symptoms result from hormone deficiency, and that there is a link between breast cancer and hormone replacement therapy. See Lauzon v. Senco Prods., Inc., 270 F.3d 681, 693 (8th Cir. 2001) (noting that "scientific reliability can also be shown by proof that the research and analysis supporting the proffered conclusions have been subjected to normal scientific scrutiny through peer review and publication").

Knowing that Scroggin's breast cancer was hormone dependent, Dr. Naftalis's differential diagnosis sought to determine the cause of Scroggin's breast cancer by ruling out the two possible sources of these hormones: (1) Scroggin produced the hormones herself, or (2) they came from the hormone replacement therapy she had taken for the past eleven years. Scroggin presented evidence that her menopausal symptoms were relieved by hormone replacement therapy, confirming that her own body was unable to produce sufficient hormones and therefore could not be the cause. The remaining source was the combination of Premarin, Provera, and Prempro. Accordingly, Scroggin presented evidence establishing a causal link between breast cancer and estrogen plus progestin use, particularly for the length of time Scroggin was taking the drugs.

586 F.3d at 566 (emphasis added & footnote omitted). Attempting to minimize the relevance of Scroggin here, defendants note that the Eighth Circuit did not have the benefit of the subsequently-released Farhat and Huang studies. But, as noted, to the extent that the Farhat and Huang studies conflict with the research relied upon by Dr. Wertheimer and presented to the court in Scroggin, this goes to the weight rather than the admissibility of Dr. Wertheimer's testimony. The court concludes that Dr.

Wertheimer's symptoms theory has a reliable foundation.⁶

D. Soundness of Dr. Wertheimer's Differential Diagnosis

Defendants claim that, even if differential diagnosis can reliably be used to determine the cause of an individual's breast cancer, Dr. Wertheimer failed to conduct a proper differential diagnosis of plaintiff. The court considers each of defendants' challenges to Dr. Wertheimer's differential diagnosis.

⁶ In their reply, defendants argue that plaintiff (in her opposition) and Dr. Wertheimer (in his deposition) have raised a new "fluctuation theory" under which it is the E+P drugs' "change in hormone levels" that causes breast cancer, regardless of a woman's baseline risk. (Defs.' Reply at 9-10). Stated differently, E+P increases the relative risk of breast cancer in all women regardless of whether they are symptomatic. (Pl.'s Opp. at 9). Defendants are correct that this theory is neither discussed in Dr. Wertheimer's expert report nor is it specifically applied to plaintiff's case, though he does include a single sentence opining that "E+P increases a woman's risk of developing breast cancer regardless of her baseline risk and regardless of her baseline exposure," without any supporting analysis. (Wertheimer Rep. at 13). Rather than attempting to piece together and evaluate this theory from various sources, however, it suffices to say that the symptoms theory -- which does appear in Dr. Wertheimer's report -- has a reliable foundation. Inasmuch as Dr. Wertheimer has not applied the fluctuation theory to plaintiff's case (i.e., to explain how defendants' HRT drugs thereby caused plaintiff's breast cancer), plaintiff may not pursue this theory at trial.

1. Hormone-Dependency of Plaintiff's Breast Cancer

Defendants first attack Dr. Wertheimer's base assumption that plaintiff's ER/PR positive tumor required hormones (either natural or pharmaceutical) to grow. They highlight an excerpt from Dr. Wertheimer's report, wherein he acknowledges that ER positive tumors can develop in "hormone independent" ways:

As cancer progresses it can develop additional growth pathways that can allow it to grow without the same reliance on hormones as it initially had. Other growth factors, which were initially "turned on" by estrogen and progesterin, can develop mutations allowing the cancer to grow without a further complete dependence on estrogen. . . . Nevertheless, it is generally accepted that breast cancers expressing ER and/or PR receptors developed into cancer and grew, at least initially, in a hormone dependent fashion. [Footnote omitted] Once developed, these hormone dependent tumors can mutate and develop hormone independent biological pathways to progress and even metastasize.

(Wertheimer Rep. at 13).

In the footnote omitted above, Dr. Wertheimer cites publications supporting the "generally accepted" view that breast cancers with ER and/or PR positive receptors at least initially grew into cancer in a hormone dependent fashion. This, in turn, provides a sufficient foundation for Dr. Wertheimer's opinion that this plaintiff's ER/PR positive breast cancer, more likely than not, grew in a hormone dependent fashion. The follow-up sentence where he recognizes that hormone dependent tumors can

later develop "hormone independent" pathways does not diminish his fundamental opinion. If plaintiff's tumor developed into malignant cancer in a hormone dependent fashion, as Dr. Wertheimer opines and as supported by the fact that plaintiff's tumor was ER/PR positive, then Dr. Wertheimer's mere acknowledgment that hormone dependent tumors can sometimes develop hormone independent pathways is not inconsistent with his stated view.

2. Timing of Plaintiff's Breast Cancer

Defendants next point to portions of Dr. Wertheimer's testimony indicating that he could not identify precisely when plaintiff's invasive breast cancer developed. Since Dr. Wertheimer does not know when plaintiff's cancer became invasive, defendants contend, he cannot reliably say whether her cancer was "fueled" by defendants' HRT drugs. This argument misses the mark. Again, Dr. Wertheimer started with the premise that plaintiff's ER/PR positive breast cancer required hormones to grow. After eliminating natural hormones as a potential cause (based on plaintiff's menopausal symptoms and the HRT drugs' relief of those symptoms), he isolated exogenous hormones from defendants' HRT drugs as the remaining cause. While Dr. Wertheimer cannot state with absolute certainty that plaintiff's breast cancer became invasive only after she ingested HRT drugs,

absolute certainty is not required -- he need only state his causation opinions in terms of "reasonable probability."

Rohrbough v. Wyeth Labs., Inc., 916 F.2d 970, 972 (4th Cir. 1990) (citing Hovermale v. Berkeley Springs Moose Lodge No. 1483, 271 S.E.2d 335, 340 (W. Va. 1980)). Here, Dr. Wertheimer concluded to a reasonable degree of medical probability (and by way of reliable means) that HRT drugs caused plaintiff's hormone dependent cancer. (Wertheimer Rep. at 17). It was not necessary for Dr. Wertheimer to pinpoint precisely when plaintiff's breast cancer became invasive. Defendants can challenge Dr. Wertheimer's conclusions through vigorous cross examination.

3. Exclusion of Natural Estrogen as a Potential Cause

Defendants next claim that Dr. Wertheimer did not adequately exclude natural estrogen as a potential cause of plaintiff's breast cancer. Because Dr. Wertheimer does not know how much natural estrogen plaintiff was producing, defendants argue, he cannot establish that her cancer was not caused by natural estrogen instead of HRT drugs.

In evaluating whether Dr. Wertheimer properly considered alternative causes in performing his differential diagnosis, the court is guided by the Fourth Circuit's decision in Cooper:

A medical expert's opinion based upon differential diagnosis normally should not be excluded because the expert has failed to rule out every possible alternative cause of a plaintiff's illness. See Westberry, 178 F.3d at 265 (citations omitted). In such cases, the alternative causes suggested by a defendant normally affect the weight that the jury should give the expert's testimony and not the admissibility of that testimony. See id. at 265 (citations omitted). However, . . . if an expert utterly fails to consider alternative causes or fails to offer an explanation for why the proffered alternative cause was not the sole cause, a district court is justified in excluding the expert's testimony.

259 F.3d at 202 (some citations omitted). In his expert report, Dr. Wertheimer considered and excluded natural estrogen as a potential cause:

In postmenopausal women, there are only two possible sources of the female hormones necessary to develop and grow hormone dependent cancer: endogenous hormones (estrogen and progesterone that are naturally produced in a woman's body) or exogenous hormones (such as E+P).

* * * *

I consider what evidence there is of a woman's levels of endogenous estrogen as one factor in forming my causation opinion. Certain symptoms and radiographic findings can be important. For example, vasomotor symptoms [e.g., hot flashes and night sweats] are often a sign of low endogenous estrogen levels. If these symptoms improve or go away upon treatment with exogenous hormones then that is confirmation that low estrogen levels played an important role in causing the symptoms. Similarly, vaginal or urogenital atrophy symptoms are a strong indication that the woman has very low tissue levels of estrogen.

* * * *

Mrs. Hines reported that, prior to taking hormone therapy, she experienced menopausal symptoms including severe hot flashes, night sweats, and vaginal dryness. These symptoms improved on hormone therapy and returned

to some degree after cessation of hormone therapy.[] This clinical information strongly supports that Mrs. Hines was a "low hormone producing" woman at and around the time of menopause.

(Wertheimer Dep. at 13, 14, 15). Although it is true that Dr. Wertheimer does not know exactly how much natural estrogen plaintiff was producing and thus cannot exclude natural estrogen as a potential cause with absolute certainty, this does not preclude the admission of his testimony. It suffices to say that he considered natural estrogen as an alternative cause and offered a plausible explanation as to why it was not the sole cause. See Cooper, 259 F.3d at 202.

4. Exclusion of Other Potential Causes

Defendants further contend that Dr. Wertheimer failed to rule out plaintiff's baseline risk factors, such as breast density, family history of breast cancer, and her age. The Eighth Circuit in Scroggin best summed up the flaws with this argument:

We find unpersuasive the contention that Dr. Naftalis's testimony should not have been admitted because Scroggin has some breast cancer risk factors and a family history of breast cancer. Dr. Naftalis sufficiently established that hormones were necessary to the development of Scroggin's tumors and conducted her differential diagnosis from this starting point. Although not necessary to the formation of her opinion, Dr. Naftalis addressed the known causes of breast cancer and possible risk factors. Wyeth and Upjohn argue that this review was insufficient, but Dr. Naftalis's "explanations as to conclusions not ruled out went to weight and not

admissibility."

* * * *

Dr. Naftalis was able to testify that Scroggin's breast cancer would not have developed without hormone replacement therapy because Scroggin's body was not producing sufficient amounts of hormones to allow hormone-receptor-positive tumors to develop. Thus, Dr. Naftalis ruled out the other possible cause of Scroggin's breast cancer, and her expert testimony was properly admitted.

586 F.3d at 566 (emphasis added & citations omitted).

Applying the reasoning from Scroggin here, the court likewise finds that Dr. Wertheimer sufficiently established the necessity of hormones in the development of plaintiff's breast cancer (as discussed supra), and that he gave adequate consideration to alternative causes and risk factors. Regarding family history, Dr. Wertheimer observed that the plaintiff's "family history is remarkable for breast cancer in her daughter, who was diagnosed . . . with invasive ductal breast cancer with negative hormone receptors." (Wertheimer Rep. at 16). As he explained, however, the medical literature indicates that "family history is a more significant risk for ER [negative] breast cancers," and plaintiff was diagnosed with ER/PR positive breast cancer, a type of cancer generally requiring hormones to grow. (Id. at 16 n.61 (citing, among others, Cummings, Sex Hormones, Risk Factors, and Risk of Estrogen Receptor-Positive Breast Cancer in Older Women: A Long Term Prospective Study, Cancer

Epidemiol Biomarkers at 1047, 1049, 1050 (2005))). Dr. Wertheimer concluded that the hormones necessary to the development of the plaintiff's breast cancer were not attributable to "family history." (Id.).

Regarding breast density, Dr. Wertheimer noted that plaintiff did have dense breasts. (Id.). He pointed out, though, that while breast density typically decreases during menopause through a process called "involution," the density of plaintiff's breasts remained the same while she was on E+P. (Id.). Noting that HRT drugs are known to slow or reserve the "normal involution" process, he found that, "[t]o the extent that her breast density increased Mrs. Hines's risk of breast cancer and made detection more difficult, that risk factor was aggravated and contributed to by E+P use." (Id. at 16-17). Dr. Wertheimer further observed that Hines was at a lower risk of developing ER/PR positive breast cancer because she did not consume alcohol, had no significant exposure to ionizing radiation, was not obese, and (as previously discussed) had experienced menopausal symptoms that were alleviated by HRT drugs. Defendants disagree with Dr. Wertheimer's explanations as to alternative causes, but these challenges go to the weight, not the admissibility, of his testimony.

In sum, the court finds that Dr. Wertheimer's testimony passes the Daubert reliability threshold. Defendants, to be sure, mount a variety of challenges to Dr. Wertheimer's opinions. But since the court has already found that it is possible to perform a reliable differential diagnosis to determine the cause of an individual's breast cancer, the ultimate question under Rule 702 is whether Dr. Wertheimer conducted a reliable differential diagnosis of plaintiff. Trial courts making the reliability determination have "broad latitude to consider whatever factors bearing on validity that the court finds to be useful." Westberry, 178 F.3d at 261. And so, rather than turning to the illustrative list of factors set forth in Daubert, the court finds guidance in factors formulated specifically to evaluate whether a differential diagnosis meets the Daubert reliability standard:

(1) Did the expert make an accurate diagnosis of the nature of the disease? (2) Did the expert reliably rule in the possible causes of it? (3) Did the expert reliably rule out the rejected causes? If the court answers "no" to any of these questions, the court must exclude the ultimate conclusion reached.

Tamraz v. Lincoln Elec. Co., 620 F.3d 665, 674 (6th Cir. 2010); accord In re Paoli Railroad Yard PCB Litigation, 35 F.3d 717, 760-62 (3d Cir. 1994).

Here, (1) plaintiff's breast cancer diagnosis is not disputed; (2) Dr. Wertheimer reliably ruled in both natural and pharmaceutical hormones as possible causes of plaintiff's breast cancer based upon the ER/PR positive status of plaintiff's breast cancer (as supported by peer-reviewed medical literature finding that ER/PR positive cancer is generally dependent upon hormones to grow); and (3) he reliably ruled out natural hormones as a potential cause of plaintiff's breast cancer based on her exhibition of menopausal symptoms and the effectiveness of HRT drugs in treating those symptoms (as supported by peer-reviewed medical literature finding that symptomatic women have low levels of natural estrogen). Thus, Dr. Wertheimer conducted a reliable differential diagnosis.

E. Relevancy of Dr. Wertheimer's Opinions

Defendants lastly contend that Dr. Wertheimer's opinions do not satisfy the "but for" causation standard and are therefore irrelevant, emphasizing, among other things,⁷ that Dr. Wertheimer testified he does not know what "initiates" the first cancer cell. This contention reveals an underlying dispute between the parties concerning how E+P causes breast cancer.

⁷ This part of defendants' brief (Part IV) rehashes a number of arguments that the court has already addressed.

Plaintiff and Dr. Wertheimer maintain that E+P causes breast cancer through "promotion" rather than "initiation," meaning that the drugs transform benign abnormalities into malignant tumors. Put another way, plaintiff does not claim that E+P "initiated" the first abnormal cell that ultimately led to her hormone dependent cancer, but only that it "promoted" its growth by providing necessary hormonal fuel. Defendants, on the other hand, seem to assert that if HRT did not cause the initial abnormality, then it did not cause plaintiff's breast cancer. Regardless of defendants' disagreement with the promotion theory, though, it does appear to satisfy the causation standard, for the gist of the theory is that plaintiff's cancer would not have become invasive but for her use of HRT drugs.

Inasmuch as the court concludes that Dr. Wertheimer's causation testimony rests on a reliable foundation and is relevant, his expert opinion is admissible under Rule 702.

IV. Plaintiff's Motion to Exclude

According to plaintiff, defendants have designated three causation experts (Drs. Chodosh, Meile, and Levy) who will testify that E+P does not generally cause breast cancer in women. Plaintiff contends that this testimony "flies in the face of the

overwhelming consensus of scientific opinion, epidemiological study results, ecological data and opinions on biologic plausibility." (Pl.'s Mot. to Exclude at 2). Based upon the inconsistency between the opinions of defendants' experts and the rest of the scientific community, plaintiff maintains that defendants cannot meet their burden of demonstrating that the testimony is relevant and reliable.

The Court in Daubert made clear that a district court's reliability analysis must focus on the "principles and methodology" employed by the expert, not on the conclusions reached. 509 U.S. at 594-95. In this sense, plaintiffs' motion to exclude the testimony of defendants' general causation experts is not "a true Daubert challenge," as she calls into question neither the principles nor the methodology underlying the experts' opinions. See TFWS, Inc. v. Schaefer, 325 F.3d 234, 240 (4th Cir. 2003). Indeed, plaintiff does not discuss any of the four Daubert factors that are to guide the court's gate-keeper inquiry. She instead argues that the experts' conclusions "are grossly out of step with a consensus in the relevant medical community" and must therefore be excluded. Inasmuch as this challenge goes to the weight of the experts' testimony, and not its admissibility, plaintiff's motion is without merit.

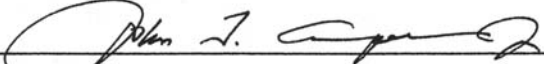
V. Conclusion

For the foregoing reasons, the court ORDERS as follows:

1. That defendants' motion to exclude Dr. Wertheimer's testimony be, and it hereby is, denied.
2. That plaintiff's motion to exclude expert testimony that combination hormone therapy does not generally cause breast cancer be, and it hereby is, denied.

The Clerk is directed to forward copies of this written opinion and order to all counsel of record.

DATED: July 8, 2011



John T. Copenhaver, Jr.
United States District Judge