UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

IN RE: XARELTO (RIVAROXABAN) PRODUCTS LIABILITY LITIGATION	**MDL No. 2592 SECTION L**
THIS DOCUMENT RELATES TO:	**JUDGE ELDON E. FALLON**
Joseph J. Boudreaux, Jr., et al. v. Janssen et al. **Case No. 2:14-cv-02720**	**MAGISTRATE NORTH**

DEFENDANTS' OFFER OF PROOF TO ALLOW EVIDENCE OF LAWYER ADVERTISING

During the examination of Dr. Peters, Plaintiffs referred to the fact that there are tens of thousands of lawsuits filed by plaintiffs alleging injuries from use of Xarelto. The jury is now left with the misimpression that because of the number of lawsuits, Xarelto is an unreasonably dangerous medicine. Such an inference is highly prejudicial to the Defendants for a multitude of reasons and should have been excluded. In an effort to cure the clear prejudice from this evidence, Defendants sought to level the playing field and offer into evidence (1) the lawyer advertising that caused Mr. Boudreaux to file this lawsuit, and (2) evidence that lawyer advertising has created fear in patients using Xarelto, some of whom have filed lawsuits and have sustained adverse events from stopping use of Xarelto.

The jury should not hear only half of the story—if Plaintiffs are permitted to tell the jury that there are other lawsuits, fairness demands that Defendants be allowed to show the jury evidence that Mr. Boudreaux filed this lawsuit because of lawyer advertising and that those same advertisements created a spike in lawsuits and has further resulted in some patients sustaining injuries by discontinuing Xarelto – without consulting a physician. . In addition, while Plaintiffs'

counsel claimed and the Court agreed that the "door" had been opened by asking the witness how many patients had used Xarelto[1], there was never any ruling by the Court that the number of patients who have used the medicine was inadmissible, nor was there any objection to the question that was asked.

Defendants make the following offer of proof setting forth the evidence that would have been presented to the jury had the Court allowed it into evidence.

1. Mr. Boudreaux explicitly testified that he only filed his lawsuit after he saw attorney advertising. *See* Boudreaux Dep. 181:25–182:3 ("Q. What prompted you to call an attorney? A. I just had seen an ad on TV that they put out, that if I had had any bleeding from the use of Xarelto to—one call.")(Ex. A).

2. The authors of *Heart Rhythm Case Reports* clearly explained the pervasiveness of attorney advertising which has had an impact on patients using the medicine:

[1] 5 MR. BARR: Your Honor, we didn't open this door.
6 This is not where we wanted to go with it. He asked him the
7 question, and we opened the door. This is not a tit for tat.
8 We had to respond to what they said about this drug and all the
9 people they've saved. They opened that.
10 MR. SARVER: Once you go down that path, we have to
11 respond.

12 THE COURT: Well, the problem is is that you went
13 down the path of how many people have taken the drug and that
14 sort of thing, and I would not have allowed them to go into it,

15 but the fact that you brought that up, they have a right to get
16 the other side of the nickel. Now it's the other side of that
17 nickel.
18 MR. SARVER: It's a three-sided nickel.

> Described here are a series of serious medical events reported in 28 submissions of 31 individual patients to Medwatch (The FDA Safety Information and Adverse Event Reporting System; http://www.fda.gov/ Safety/MedWatch/default.htm).
>
> . . . .
>
> Overall, based on the available data, the mean age of the patients was 72 (range, 45–90), and 13 patients were male. All were prescribed rivaroxaban and subsequently discontinued their anticoagulant without consulting their physician after viewing negative rivaroxaban legal advertising. In the majority of these cases (23/31,75%), patients experienced a stroke or a transient ischemic neurologic event; 2 patients had persistent residual paralysis. One patient, a 45-year-old man receiving rivaroxaban for treatment of a deep vein thrombosis, stopped the drug and died of a subsequent pulmonary embolism, and 1 female patient, receiving rivaroxaban for stroke prevention, stopped the drug and died of a massive stroke (Table). All these cases were considered to be serious medical events by the health care professionals that submitted the reports.

Burton, P. and Peacock, W.P., *Heart Rhythm Case Reports* 2016; 2:248-49 (Ex. B). The authors conclude:

> [I]t is clear that some patients are intimidated enough by the ongoing legal campaign to stop their anticoagulant, and thus suffer an adverse event. These cases serve to highlight the importance of following anticoagulant prescribing information, and that physicians should emphasize that patients should not stop anticoagulants without medical consultation. Continued partnership between drug manufacturers, physicians, regulators, and patients is necessary to provide sufficient education to ensure that these important medical events do not occur.

Id.

3. In an article published in the *Journal of Atrial Fibrillation*, Dr. Reiffel explained attorney advertising and its effect on the practice of medicine:

> Consequent to such advertisements, many patients have discontinued NOAC therapy or have refused to start it. I have encountered such a patient on more than one occasion, mostly atrial fibrillation (AF) patients with an increased risk profile for stroke and systemic embolism (CHA2DS2-VASc score of 2 or higher). It takes considerable effort to make them understand both the benefits and the risks of NOAC therapy and in particular, the overall antithrombotic and mortality benefits to them of being on NOAC therapy despite the risks of a bleed.
>
> Part of such discussions with patients should involve the concepts of fair balance and of net clinical benefit. Using data from the 4 major NOAC vs warfarin pivotal

> AF trials 2-5 and historical data from AF warfarin vs placebo trials, several calculations can be made to help them understand both what they are not being told in the advertisements they see and the consequences that may arise based upon the non-use of the NOAC.
>
> . . . .
>
> Based on the pivotal NOAC versus warfarin trials, assuming increased risk of AF patients changed from NOAC to warfarin therapy: embolic events would increase by 1.1 to 2.1%/yr; major bleeds would increase by 2.1 to 3.4%/yr, total mortality would increase by 3.5 to 4.9%/yr, but fatal bleeds would increase by only 0.06 to 0.5%/yr.

Reiffel, J.A., *Journal of Atrial Fibrillation* 2016; 8(5)(Ex. C).

3. Dr. Kenneth Wong, the physician who prescribed Xarelto to Mr. Boudreaux, also testified that he saw attorney advertising. Dr. Wong testified as follows:

> Q. What have some of your patients come in, what are some of their concerns as a result of the advertisement?
>
> A. Well, they see all this: If you have taken Xarelto before, contact us.
>
> Q. And what do you tell your patients when they come in with those concerns?
>
> A. That it's misleading. It makes it sound like, you know, it's a terrible drug. But Coumadin is just as -- you know. Everything – it's an anticoagulant. It's going to have an increased risk of bleeding, but serves its purpose and protects you from stroke. That's what I tell them.
>
> Q. Do you counsel your patients not to just stop taking their medications because they are seeing these lawyer ads?
>
> A. That's the worst part. We have had cases where people stroke out because they saw those commercials and stop taking them. We have had cases like that. And you wonder whether there should be a law that goes back and says you can't -- you know, it's negligent advertising sometimes. You wonder if there is such a thing --
>
> Deposition of Dr. Kenneth Wong, at 145:15-146:14 (Ex. D).

4. Courts recognize the relationship between lawyer advertising and the number of cases and have held that either both subjects are inadmissible or both are admissible. For example, in In

re Welding Fume Prod. Liab. Litig., No. 1:03-CV-17000, 2010 WL 7699456, at *66 (N.D. Ohio June 4, 2010) the Court held:

> Defendants also assert that, if evidence of other *Welding Fume* lawsuits is allowed, then defendants should be permitted to introduce: (1) evidence that, beginning in 2002, the plaintiffs' bar engaged in heavy advertising to obtain clients for *Welding Fume* lawsuits; and (2) expert evidence on the efficacy of this type of advertising. Defendants assert this evidence would tend to show an alternative reason for the many thousands of *Welding Fume* lawsuits filed by other welders. Plaintiffs respond that evidence of lawyer advertising is itself excessively prejudicial compared to its limited relevance under Fed.R.Civ.P. 403.
>
> The Court has ruled as follows on these motions. Except as noted below, evidence of lawsuits brought by other welders, and also evidence of lawyer advertising, must be excluded pursuant to both Fed.R.Evid. 403 and 611(a)(2). While plaintiffs are correct that a multiplicity of injury claims by welders is inconsistent with the notion that no harm can flow from exposure to welding fumes, defendants are also correct that the spark leading to the great number of recent *Welding Fume* lawsuits is the combination of the advertising and screening processes used by plaintiffs' counsel to identify potential claimants. As defendants point out, moreover, the validity of the claims asserted in those cases remains mostly untested.

And here, in contrast to the *Welding Litigation* the Defendants do not dispute the association between the use of anti-coagulation medicine and bleeding as a recognized but unfortunate side effect. At this point, having admitted the number of pending lawsuits, the Defendants submit that fundamental fairness requires the admission of information about lawyer advertising. Plaintiffs' reference to the number of lawsuits has resulted in substantial and incurable prejudice to the defendants.

5. Further, after the witness testified that he did not know the number of lawsuits that had been filed, T 1123:20 to 22, it was totally improper for Plaintiffs to then tell the witness and the jury the number, T 1123:23. It must also be noted that the testimony as to the number of patients who have taken Xarelto ("hundreds of thousands" T 1123:2 to 3) is clearly in error, as the Plaintiffs know. The real number is over 28 million worldwide. If the Court does not permit the

introduction of attorney advertising as outlined above, it is requested that the Court instruct the jury that the number of patients who have used Xarelto worldwide is over 28 million in order to put the number of lawsuits in perspective.

Respectfully submitted,

BARRASSO USDIN KUPPERMAN FREEMAN & SARVER, L.L.C.

By: /s/ *Richard E. Sarver*
Richard E. Sarver
Celeste R. Coco-Ewing
BARRASSO USDIN KUPPERMAN FREEMAN & SARVER, L.L.C.
909 Poydras Street, 24th Floor
New Orleans, Louisiana 70112
Telephone: (504) 589-9700
rsarver@barrassousdin.com
ccoco-ewing@barrassousdin.com

WILKINSON WALSH + ESKOVITZ LLP

By: /s/ *Beth A. Wilkinson*
Beth A. Wilkinson
Jennifer L. Saulino
Jeremy Barber
WILKINSON WALSH + ESKOVITZ LLP
1900 M. Street NW, Suite 800
Washington, DC 20036
Telephone: (202) 847-4000
bwilkinson@wilkinsonwalsh.com
jsaulino@wilkinsonwalsh.com
jbarber@wilkinsonwalsh.com

DRINKER BIDDLE & REATH LLP

By: /s/ *Susan M. Sharko*
Susan M. Sharko
Drinker Biddle & Reath LLP
600 Campus Drive
Florham Park, NJ 07932-1047
Telephone: (973) 549-7000
susan.sharko@dbr.com

Rodney M. Hudson
DRINKER BIDDLE & REATH LLP
50 Fremont Street, 20th Floor
San Francisco, CA 94105-2235
Telephone: (415) 591-7500
Rodney.hudson@dbr.com

Chanda A. Miller
Drinker Biddle & Reath LLP
One Logan Square, Suite 2000
Philadelphia, PA 19103-6996
Telephone: (215) 988-2700
Chanda.Miller@dbr.com

NELSON MULLINS RILEY & SCARBOROUGH LLP

By: */s/ David E. Dukes*
David E. Dukes
J. Mark Jones
NELSON MULLINS RILEY & SCARBOROUGH LLP
1320 Main Street, 17th Floor
Columbia, SC 29201
Telephone: (803) 799-2000
David.Dukes@nelsonmullins.com
Mark.Jones@nelsonmullins.com

ARNOLD & PORTER KAYE SCHOLER LLP

By: /s/ *Andrew K. Solow*
Andrew K. Solow
Steven Glickstein
ARNOLD & PORTER KAYE SCHOLER LLP
250 West 55th Street
New York, New York 10019-9710
Telephone: (212) 836-8485
andrew.solow@apks.com
steven.glickstein@apks.com

IRWIN FRITCHIE URQUHART & MOORE LLC

By: /s/ *James B. Irwin*
James B. Irwin
Kim E. Moore
Irwin Fritchie Urquhart & Moore LLC
400 Poydras Street, Suite 2700
New Orleans, LA 70130
Telephone: (504) 310-2100
jirwin@irwinllc.com

Attorneys for Defendants Janssen Pharmaceuticals, Inc., Janssen Research & Development, LLC, and Janssen Ortho LLC

William Hoffman
ARNOLD & PORTER KAYE SCHOLER LLP
601 Massachusetts Ave., NW
Washington, D.C. 20001
Telephone: (202) 942-5000
william.hoffman@apks.com

BRADLEY ARANT BOULT CUMMINGS LLP

By: */s/ Kevin C. Newsom*
Kevin C. Newsom
Lindsey C Boney IV
BRADLEY ARANT BOULT CUMMINGS LLP
One Federal Place, 1819 Fifth Avenue North
Birmingham, AL 35203-2119
Telephone: (205) 521-8803
knewsom@bradley.com
lboney@bradley.com

CHAFFE MCCALL L.L.P.
By: /s/ *John F. Olinde*
John F. Olinde
CHAFFE MCCALL L.L.P.
1100 Poydras Street, Suite 2300
New Orleans, LA 70163
Telephone: (504) 585-7241
olinde@chaffe.com

Attorneys for Bayer HealthCare Pharmaceuticals Inc. and Bayer Pharma AG

CERTIFICATE OF SERVICE

The undersigned hereby certifies that on April 30, 2017, the foregoing pleading was filed electronically with the Clerk of Court using the CM/ECF system. Notice of this filing will be sent to Liaison Counsel for Plaintiffs and Defendants by operation of the court's electronic filing system and served on all other plaintiff counsel via MDL Centrality, which will send notice of electronic filing in accordance with the procedures established in MDL 2592 pursuant to Pre-Trial Order No. 17.

/s/James B. Irwin
James B. Irwin

EXHIBIT A

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

IN RE: XARELTO (RIVAROXABAN) PRODUCTS LIABILITY LITIGATION	MDL No. 2592
	SECTION L
_____	JUDGE ELDON E. FALLON
THIS DOCUMENT RELATES TO: JOSEPH J. BOUDREAUX, JR. AND LORETTA BOUDREAUX	MAG. JUDGE NORTH
Case No. 2:14-cv-02720	

PROTECTED - SUBJECT TO FURTHER PROTECTIVE REVIEW

JUNE 23, 2016

- - -

Videotaped deposition of JOSEPH J. BOUDREAUX, JR., held at The Lambert Firm, 701 Magazine Street, New Orleans, Louisiana, commencing at 10:01 a.m., on the above date, before Leslie B. Doyle, Certified Court Reporter (#93096), Registered Professional Reporter, Certified Realtime Reporter.

- - -

GOLKOW TECHNOLOGIES, INC.
877.370.3377 ph|917.591.5672 fax
deps@golkow.com

vacations?

A. When I can, yeah. Now, I don't consider that a vacation. That was just a little weekend trip. But as far as a vacation, four- or five-day vacation or a week's vacation, no, I haven't done that in a couple of years.

Q. When was the last long vacation you took?

A. It would have probably been two Christmases ago when we went to Memphis for Christmas holidays. I think it's -- it would be about -- yeah, it's going on about three years since we went for that.

Q. Are you claiming that there's been a negative impact on your sex life as a result of your bleeding event?

A. No.

Q. Has any doctor ever told you that Xarelto caused you any injury?

A. Not that I recall.

Q. When did you first decide that you were going to hire an attorney?

A. I'm not sure about the date, when it was. Maybe a year after I had the problems. I'm not sure.

Q. What prompted you to call an attorney?

A. I just had seen an ad on TV that they put out, that if I had had any bleeding from the use of Xarelto to -- one call.

Q. Who was the first attorney that you spoke to when you called?

A. Mekel. Well, I don't remember if I spoke to her or your assistant or whoever first, but she was the one that took the case.

Q. Do you remember when that was?

A. I don't know the date right offhand, but probably back in the latter part of the year, I guess, 2014.

Q. 2015 or 2014?

A. 2014, probably.

Q. Ever hire an attorney before?

A. No.

Q. Why did you decide to bring your lawsuit?

A. For all my pain and suffering and for my medical expenses. And my family, too. I mean, it's not just me.

Q. Did insurance cover your medical expenses?

A. They paid for my hospital visits, and I have, like, copays each time, and I have so much I have to pay for different tests and all that they do, but I was covered.

EXHIBIT B

A Medwatch review of reported events in patients who discontinued rivaroxaban (XARELTO) therapy in response to legal advertising

Paul Burton, MD, PhD, FACC,[*] W. Frank Peacock, MD, FACEP[†]

From the [*]Cardiovascular and Metabolism Medical Affairs, Janssen Pharmaceuticals Inc, Raritan, New Jersey, and [†]Baylor College of Medicine, Houston, Texas.

Introduction

Rivaroxaban (XARELTO) is an oral Factor Xa inhibitor anticoagulant. Studied in over 85,000 patients,[1] it was initially approved by the FDA in 2011 and is indicated to treat or prevent thrombosis in a variety of clinical settings; and when appropriately prescribed, for example in patients with atrial fibrillation, rivaroxaban has similar anticoagulant efficacy, with a lower risk of intracranial hemorrhage, as compared to the historical standard of warfarin.[1]

It is well established that anticoagulant therapy is associated with an increased risk of hemorrhage, regardless of the specific anticoagulant. Therefore, in the risk–benefit balance, an appropriate anticoagulation prescription occurs in the setting of increased thrombotic risk that justifies the increased bleeding risk. This is an important consideration, as the mitigation of the thrombotic risk attained by the use of an anticoagulant is terminated if the anticoagulant is stopped. Importantly, current evidence[2] does not suggest a rebound of thrombotic risk upon anticoagulation discontinuation; rather, the patient simply resumes the thrombotic risk that existed prior to anticoagulant initiation, and the lack of rebound thrombosis with rivaroxaban is supported by longitudinal studies.[2] However, in a patient at risk for a thrombotic event, premature discontinuation of any oral anticoagulant may increase the risk of thrombotic events, as outlined in The United States Prescribing Information for all of the newer non-warfarin anticoagulants (https://www.xarelto-us.com/shared/product/xarelto/prescribing-information.pdf; http://packageinserts.bms.com/pi/pi_eliquis.pdf; http://bidocs.boehringer-ingelheim.com/BIWebAccess/ViewServlet.ser?docBase=renetnt&folderPath=/Prescribing%20Information/PIs/Pradaxa/Pradaxa.pdf; http://dsi.com/prescribing-information-portlet/getPIContent?productName=Savaysa&inline=true). As a class, the novel oral anticoagulants have rapid onset of action and short half-lives; as such, it is important to avoid abrupt cessation.

Rivaroxaban is currently the subject of a class action litigation. Beginning in 2014, advertising has appeared on television, on the radio, and in print media directed toward patients who may have experienced adverse clinical events while on rivaroxaban. Described here are a series of serious medical events reported in 28 submissions of 31 individual patients to Medwatch (The FDA Safety Information and Adverse Event Reporting System; http://www.fda.gov/Safety/MedWatch/default.htm).

Case report

Overall, based on the available data, the mean age of the patients was 72 (range, 45–90), and 13 patients were male. All were prescribed rivaroxaban and subsequently discontinued their anticoagulant without consulting their physician after viewing negative rivaroxaban legal advertising.

In the majority of these cases (23/31, 75%), patients experienced a stroke or a transient ischemic neurologic event; 2 patients had persistent residual paralysis. One patient, a 45-year-old man receiving rivaroxaban for treatment of a deep vein thrombosis, stopped the drug and died of a subsequent pulmonary embolism, and 1 female patient, receiving rivaroxaban for stroke prevention, stopped the drug and died of a massive stroke (Table). All these cases were considered to be serious medical events by the health care professionals that submitted the reports.

Discussion

There are obvious numerous and significant limitations to this report. These include the limited description of clinical

KEYWORDS Rivaroxaban; Stroke; Atrial fibrillation; Legal advertising
(Heart Rhythm Case Reports 2016;2:248–249)

Funding source: Janssen Pharmaceuticals Inc. Conflicts: Dr Burton works for Janssen Pharmaceuticals Inc, and owns stock in Johnson and Johnson, which markets rivaroxaban in the United States. Dr Peacock is a paid consultant for Janssen Pharmaceuticals Inc. **Address reprints and correspondence:** Dr Paul Burton, Cardiovascular and Metabolism Medical Affairs, Janssen Pharmaceuticals Inc, 1000 Route 202, Raritan, NJ 08869. E-mail address: pburton@its.jnj.com.

 http://dx.doi.org/10.1016/j.hrcr.2016.02.001

KEY TEACHING POINTS

- Novel oral anticoagulants provide a new treatment option for a variety of thrombotic conditions, including nonvalvular atrial fibrillation.
- These drugs have rapid onsets and short half-lives and should not be prematurely discontinued.
- Legal advertising concerning XARELTO (rivaroxaban) has resulted in some patients stopping XARELTO therapy and experiencing adverse clinical events, such as stroke.

patients ceased their anticoagulant and suffered an adverse event that was not reported. Finally, while the language in these forms clearly states that patients viewed legal advertising and stopped their rivaroxaban, this cannot be definitively known. However, it is clear that some patients are intimidated enough by the ongoing legal campaign to stop their anticoagulant, and thus suffer an adverse event.

These cases serve to highlight the importance of following anticoagulant prescribing information, and that physicians should emphasize that patients should not stop anticoagulants without medical consultation. Continued partnership between drug manufacturers, physicians, regulators, and patients is necessary to provide sufficient education to ensure that these important medical events do not occur.[3]

Table Summary of clinical outcomes following abrupt rivaroxaban termination as reported to Medwatch

Case	Age	Sex	Anticoagulant indication	Consequence of stopping anticoagulant	Event reported
1	NR	F	NVAF	TIA/possible stroke	September 2014
2	80	F	NVAF	DVT of arm	November 2014
3	80	M	NR	Stroke	December 2014
4	NR	M	NVAF	Stroke	January 2015
5	NR	NR	NR	Stroke	January 2015
6	80	F	NVAF	Stroke	March 2015
7	NR	M	NR	Stroke	March 2015
8	55	M	NVAF	Cardiac thrombosis	April 2015
9	NR	NR	NR	Stroke	April 2015
10	NR	M	VTE	Cerebral and lower limb thrombosis	April 2015
11	60	M	NVAF	Stroke	April 2015
12	NR	NR	NR	Stroke in 2 patients	May 2015
13	NR	F	NVAF	DVT	June 2015
14	NR	F	VTE	Pulmonary embolism	June 2015
15	45	M	VTE	Death due to pulmonary embolism	June 2015
16	90	M	NVAF	Stroke	June 2015
17	NR	NR	NR	Stroke in 3 patients	June 2015
18	NR	NR	NR	Thrombosis	June 2015
19	69	F	NVAF	TIA	July 2015
20	NR	F	NVAF	Stroke	August 2015
21	NR	NR	NVAF	Stroke	September 2015
22	NR	F	NVAF	Death following stroke	September 2015
23	NR	M	VTE	Thrombosis	September 2015
24	NR	NR	NR	Stroke	October 2015
25	NR	M	AF	Stroke	November 2015
26	70	M	NR	Stroke	November 2015
27	90	M	AF	Cardiomyopathy/TIA	December 2015
28	NR	M	AF	Stroke	December 2015

AF = atrial fibrillation; DVT = deep vein thrombosis; NR = not reported; NVAF = nonvalvular atrial fibrillation; TIA = transient ischemic attack; VTE = venous thromboembolism.

characteristics of the individual cases within the Medwatch submissions, such as prior medical history, clinical risk (eg, CHADS2 score), the lack of ability to follow up on an individual case basis, the potential for bias in the reporting mechanism that cannot be controlled, and an unknown denominator of the "at-risk" population. Further, it is not known how many patients abruptly ceased rivaroxaban and did not experience a clinical event, nor is it known how many

References

1. Sarich TC, Peters G, Berkowitz SD, et al. Rivaroxaban: a novel oral anticoagulant for the prevention and treatment of several thrombosis-mediated conditions. Ann N Y Acad Sci 2013;1291:42–55.
2. Mahaffey KW, Hellkamp AS, Patel MR, et al. End of study transition from study drug to open-label vitamin K antagonist therapy: the ROCKET AF experience. Circ Cardiovasc Qual Outcomes 2013;6:470–478.
3. Have Atrial Fibrillation? Blood Thinners Can Prevent Strokes, Save Lives. Available at ⟨http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm467201.htm⟩. Accessed December 20 2015.

EXHIBIT C

JAFIB®

Guest Editorial

Journal of Atrial Fibrillation

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Misleading Advertising by Attorneys Concerning NOACs is Adversely Costly to Our Patients and Our Society

James A. Reiffel, M.D.

Columbia University College of Physicians & Surgeons Dept. of Medicine, Division of Cardiology

Abstract

Over the past five years, "ambulance-chasing" attorneys have aggressively advertised for patients who have bled on a new oral anticoagulant (NOAC) or their family members. It is an infrequent day when American consumers do not see a TV advertisement saying something like: "Have you or a loved-one had a serious bleeding event while taking [fill in the NOAC]? If so, you may be entitled to monetary compensation. Call XXX, attorneys at law, and we will get you the money you deserve."

Introduction

Unlike medical presentations, whether CME or "promotional", such ads are apparently not subject to fair balance requirements. Consequent to such advertisements, many patients have discontinued NOAC therapy or have refused to start it. I have encountered such a patient on more than one occasion, mostly atrial fibrillation (AF) patients with an increased risk profile for stroke and systemic embolism (CHA_2DS_2-VASc score of 2 or higher).[1] It takes considerable effort to make them understand both the benefits and the risks of NOAC therapy and in particular, the overall antithrombotic and mortality benefits to them of being on NOAC therapy despite the risks of a bleed.

Part of such discussions with patients should involve the concepts of fair balance and of net clinical benefit. Using data from the 4 major NOAC vs warfarin pivotal AF trials[2-5] and historical data from AF warfarin vs placebo trials,[6] several calculations can be made to help them understand both what they are not being told in the advertisements they see and the consequences that may arise based upon the non-use of the NOAC.

Based upon the pivotal NOAC versus warfarin trials,[2-5] assuming increased risk AF patients changed from NOAC to warfarin therapy: embolic events would increase by 1.1 to 2.1 %/yr; major bleeds would increase by 2.1 to 3.4 %/yr, total mortality would increase by 3.5 to 4.9 %/yr, but fatal bleeds would increase by only 0.06 to 0.5 %/yr. In other words, with a change from a NOAC to warfarin, their risk of a stroke or mortality would be much greater than would any change in fatal bleeding risk. Moreover, since warfarin reduces stroke by almost 70% and mortality by about 30% versus placebo,[6] if patients changed from NOAC to no therapy or refused to start any anticoagulant, stroke rates and mortality would be correspondingly higher than the rates cited above. Given the estimate of over 8 million AF patients in the U.S. now, and the current anticoagulation paradigm using CHA2DS2-VASc, such changes have substantial adverse implications for both population health and costs. Our governmental representatives, the FDA, and the media need to recognize the consequences of such unbalanced and inadequately controlled advertising and, in my opinion, initiate appropriate regulations.

Key Words:
Atrial Fibrillation, NOACs, Anticoagulation, Stroke, Mortality

Disclosures:
None.

Corresponding Author:
James A. Reiffel
202 Birkdale Lane,
Jupiter, FL 33458

References

1. European Heart Rhythm Association, European Association for Cardio-Thoracic Surgery, Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Al-Attar N, Hindricks G, Prendergast B, Heidbuchel H, Alfieri O, Angelini A, Atar D, Colonna P, De Caterina R, De Sutter J, Goette A, Gorenek B, Heldal M, Hohloser SH, Kolh P, Le Heuzey JY, Ponikowski P, Rutten FH. Guidelines for the management of atrial fibrillation: The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J. 2010; 310):2369-429.
2. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, Pogue J, Reilly PA, Themeles E, Varrone J, Wang S, Alings M, Xavier D, Zhu J, Diaz R, Lewis BS, Darius H, Diener HC, Joyner CD, Wallentin L, RE-LY Steering

Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009; 361:1139-51.

3. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, Al-Khalidi HR, Ansell J, Atar D, Avezum A, Bahit MC, Diaz R, Easton JD, Ezekowitz J, Flaker G, Garcia D, Geraldes M, Gersh B, Golitsyn S, Goto S, Hermosillo AG, Hohnloser SH, Horowitz J, Mohan P, Jansky Pm Lewis BSm Lopez-Sendon JL, Pais P, Parkhomenko A, Verheugt FW, Zhu J, Wallentin , ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2011; 365:981-92.
4. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, Breithardt G, Halperin JL, Hankey GJ, Piccini JP, Becker RC, Nessel CC, Paolini JF, Berkowitz SD, Fox KA, Califf RM, ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med 2011; 365:883-91.
5. Giugliano RP, Ruff CT, Braunwald E, Murphy SA, Wiviott SD, Halperin JL, Waldo AL, Ezekowitz MD, Weitz JI, Spinar J, Ruzyllo W, Ruda M, Koretsune Y, Betcher J, Shi M, Grip LT, Patel SP, Patel I, Hanyok JJ,Mercuri M, Antman EM, ENGAGE AF-TIMI 48 Investigators. Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2013; 369:2093-104.
6. Lip GYH, Edwards SJ. Stroke prevention with aspirin, warfarin, and ximelagatran in patients with non-valvular atrial fibrillation: a systematic review and meta-analysis. Thrombosis Research 2006; 118:321-33.

EXHIBIT D

UNITED STATES DISTRICT COURT

EASTERN DISTRICT OF LOUISIANA

IN RE: XARELTO (RIVAROXABAN) PRODUCTS LIABILITY LITIGATION	)	MDL NO. 2692
	)	SECTION "L"

This Document Relates to:
JOSEPH J. BOUDREAUX v JANSSEN RESEARCH & DEVELOPMENT, et al
CASE NO. 2:14-CV-02720

Videotaped deposition of KENNETH WONG, M.D., taken in the offices of Cardiovascular Institute of the South, 102 Twin Oaks Drive, Raceland, Louisiana 70394, on Monday, the 11th day of July, 2016.

APPEARANCES:

BEASLEY, ALLEN, CROW, METHVIN, PORTIS & MILES, P.C.
(BY: ANDY D. BIRCHFIELD, JR., ESQ.)
218 COMMERCE STREET
POST OFFICE BOX 4160
MONTGOMERY, ALABAMA 36104-4160

ATTORNEYS FOR THE PLAINTIFFS

KAYE SCHOLER, LLP
(BY: JULIE B. du PONT, ESQ.)
250 WEST 55TH STREET
NEW YORK, NEW YORK 10019-9710

ATTORNEYS FOR BAYER HEALTHCARE PHARMACEUTICALS AND BAYER PHARMA AG

EXAMINATION BY MS. du PONT:

Q. When you prescribe medications, you rely on the prescriber information, the medical literature, your own judgment?

A. Everything, yes.

Q. Have you seen lawyer advertising for Xarelto?

A. Yes.

Q. And have the lawyer ads impacted your practice at all?

A. No. The impact to my practice is that patients hear those advertising and it takes a lot more to convince them that it's safe, it's relatively safe.

Q. What have some of your patients come in, what are some of their concerns as a result of the advertisement?

A. Well, they see all this: If you have taken Xarelto before, contact us.

Q. And what do you tell your patients when they come in with those concerns?

A. That it's misleading. It makes it sound like, you know, it's a terrible drug. But Coumadin is just as -- you know. Everything -- it's an anticoagulant. It's going to have an

increased risk of bleeding, but serves its purpose and protects you from stroke. That's what I tell them.

Q. Do you counsel your patients not to just stop taking their medications because they are seeing these lawyer ads?

A. That's the worst part. We have had cases where people stroke out because they saw those commercials and stop taking them. We have had cases like that. And you wonder whether there should be a law that goes back and says you can't -- you know, it's negligent advertising sometimes. You wonder if there is such a thing --

Q. So how many patients in your practice have stopped their medications and had strokes?

MR. BIRCHFIELD:

Object to form.

THE WITNESS:

I have heard of a couple of cases. We have had maybe two cases I have heard so far.

EXAMINATION BY MS. du PONT:

Q. Earlier Mr. Birchfield was asking, if there was a simple blood test you could do for