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REVIEW & OUTLOOK

How About a 'Kianna's Law'?

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Kianna Karnes

Only phony "federalists" question Washington's competence on matters of fundamental rights. And whether you side with Mrs. Schiavo's parents or husband, it is hard not to be impressed by the spectacle of the nation's highest legislative body convening over the fate of a single person.

No, if our solons have exposed themselves to criticism by taking up the Schiavo case, it should be focused not on their motives but on their inconsistency and lack of proportion. To wit: If Terri Schiavo deserves emergency federal intervention to save her life, people like Kianna Karnes deserve it even more.

The 44-year-old Mrs. Karnes -- mother of four and grandmother of one -- is not brain-damaged. And the possibility (albeit remote, at this point) exists that she could return to a fully normal life. But she will almost certainly die in the near future as long as the federal government continues to deny her treatment for the kidney cancer that has by now spread throughout her body.

What makes Mrs. Karnes's predicament so depressing is that two different developmental drugs have shown great promise for several years now against this once near-untreatable disease. But not only has the Food and Drug Administration not moved with dispatch to approve the drugs, it has begun imposing new testing requirements that make it all but impossible for their developers -- Bayer and Pfizer -- to provide them to terminal patients on a "compassionate use" basis.

The problem here is the FDA's unethical -- and let us stress, unscientific -- placebo-controlled trials, in which a subset of study patients are knowingly denied the new treatment and in some cases denied access to any active treatment at all. This may be moral with an antihistamine; it's certainly not with treatments for a terminal disease. What's more, it's entirely unnecessary. We already know what happens to most cancer patients who don't get treated. They die. We generally know, on average, how long that will take.

So placebo groups are entirely unnecessary to prove significant anti-cancer activity, as the yet-unnamed Bayer (BAY 43-9006) and Pfizer (SU 11248) compounds have already done. Yet the FDA is mandating an unethical placebo trial for the Bayer drug. (The Pfizer drug is at least being tested against another form of care, albeit one that's already all but certain not to work as well.) A deadly

follow-on effect of the placebo fetish is that it gives companies a disincentive to run compassionate use programs for unapproved drugs. That's because companies won't be able to satisfy FDA demands to enroll patients in placebo trials if patients know they can get the drug for sure (instead of running the risk of getting a sugar pill) through compassionate use. Hence Mrs. Karnes's deadly predicament.

"If the only alternative is death, then for God's sake let 'em have the drug," says Mrs. Karnes's father, John Rowe, who himself survived leukemia only by getting himself into a clinical trial where he could get another investigational therapy (Gleevec, since approved). Who could disagree?

Well, a few bureaucratic MDs at the FDA do. More specifically, one Richard Pazdur. He is the current head of cancer drugs evaluation at the FDA, and is unfortunately a leading candidate for a new position that would give him the power to thwart the would-be revolution in biotech cancer treatments as well.

Late last year we reported how Dr. Pazdur had undermined -- in fact, totally reversed -- the meaning of guidelines issued by former Commissioner Mark McClellan intended to speed up drug reviews. His latest attack on the concept of accelerated approval has him demanding that companies enroll patients in placebo-controlled "Phase 3" trials before submitting applications for very promising drugs that should be eligible based on smaller "Phase 2" studies.

A few years back, Dr. Pazdur was the agency's public face in explaining the rejection of Erbitux. That drug has since been approved and become a clinical hit. So has Eloxatin, which the FDA held up for years even after it was approved in Europe but has since become standard care for colon cancer here too.

In almost all recent cases of FDA dawdling, the drugs are proving to be far more beneficial in practice than even the supposed "gold-standard" of placebo trials would have ever suggested. So could someone explain, again, what the benefit is of doing such trials? We're not suggesting Dr. Pazdur is some kind of ogre. But he seems to be more worried about letting drug companies get away with a so-called "race to the bottom" on trial design than he is with getting good drugs to patients. And it's obvious that he can't (or won't) be educated in modern scientific and statistical methods that would allow drugs to be released sooner.

We've never understood why the Republican majority in Washington hasn't been more active on drug-approvals over the past four years. What better way to demonstrate compassionate conservatism and commitment to a "culture of life"? Or to unite the free-market wing of the GOP with the social conservative one? Finally, what better riposte to the left's equation of support for embryonic stem cell research with support for medical progress?

The solution should be non-controversial. We're not talking about potential Vioxxes that will be widely used by generally healthy people. We're talking about treatments for dying patients. So let's have legislation mandating that the FDA grant access to these drugs as soon as they show anti-cancer activity.

Instead of restricted-access placebo trials, drug researchers could be using large, open access trials in which everyone who wants the new drug can get it. They could then take advantage of advanced statistical methods to figure out whether the drug is working. Wall Street traders use these kinds of math tools all the time, and so do economists. So-called Bayesian statistics are already used in medical device regulation, where even the FDA recognizes that randomizing people into sham surgeries is simply beyond the pale.

Well, what about cancer and other terminal patients? They are now dying needlessly in placebo-controlled trials. And would-be patients like Kianna Karnes are dying outside of them because they make "compassionate use" all but impossible. Won't Congress do something?

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REVIEW & OUTLOOK



Kianna Karnes

Kianna's Legacy

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We regret to report that Kianna Karnes, featured in last Thursday's editorial on the Food and Drug Administration's fetish for the placebo-controlled testing of cancer drugs -- "[How About a 'Kianna's Law'](#)"¹? -- died Friday night of complications from kidney cancer. She was 44.

While it came too late to save Mrs. Karnes, our reporting of her plight certainly generated a lot of attention. Bayer and Pfizer -- developers of two investigational drugs showing much promise for this particularly deadly cancer -- both contacted her doctor almost immediately to discuss the appropriateness of providing the compounds. Mrs. Karnes's family was also contacted by the FDA and told that the agency stood ready to approve such treatment on an emergency basis.

All encouraging steps. But isn't it a national scandal that cancer sufferers should have to be written about in *The Wall Street Journal* to be offered legal access to emerging therapies once they've run out of other options?

The FDA's oncology division has proven to be essentially incorrigible on this point in recent years, so it's time for Congressional action mandating that the agency use 21st-century science and statistical methods to get these therapies to patients sooner. More specifically, drug approvals could be based on large trials open to all comers and analyzed with so-called Bayesian statistics, as already happens in the FDA's medical device division. (Yes, the agency at least recognizes that studies involving, say, "placebo" defibrillators would be beyond the pale.)

Mrs. Karnes's father John Rowe ([Now a volunteer staff member of the Abigail Alliance](#)) - - himself a leukemia survivor -- plans intense Congressional lobbying in the coming weeks, and he's had some interest from Congressman Dan Burton's (R., Indiana) office in the possibility of sponsoring a "Kianna's Law." No doubt there will be others willing to sign on.

We'll keep you posted. Meanwhile, we'd suggest that cancer patients looking for a constructive way to make their voices heard -- and those looking to educate themselves on the issue -- contact the Abigail Alliance for Better Access to Developmental Drugs at www.abigail-alliance.org.

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REVIEW & OUTLOOK

Kianna's Law

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Somewhere up there, Kianna Karnes is smiling. The 44-year-old Indiana mother's death in March from kidney cancer has helped to inspire a proposal in Congress to bring ethics and modern science to the drug approval process for terminal disease.

We wrote about Ms. Karnes earlier this year because she was being denied treatment with two promising therapies for kidney cancer. Two compounds -- one from Bayer and one from Pfizer -- had already shown unquestionable activity against that particularly deadly cancer. But Ms. Karnes did not meet the complicated eligibility criteria for clinical trials involving the drugs, and even if she had she might not have gotten treatment. The Bayer compound was being tested against a proverbial sugar pill and she might have ended up in the placebo arm of the trial (that is, with the sugar pill).

Bayer and Pfizer also did not have so-called "expanded access" or "compassionate use" programs to make these drugs available, before formal FDA approval, because of several regulatory impediments to that practice. For starters, companies can't charge patients on even a non-profit basis for compassionate use, even though manufacturing these novel compounds can be expensive.



Kianna Karnes

Moreover, the FDA tends to dismiss any favorable data collected during compassionate use as unscientific, though it is quick to seize on negative data and count that against final approval. Finally, by creating compassionate use programs, companies risk making it less likely that patients will enroll in the placebo trials that the FDA too often demands before it will approve a drug. These barriers to therapy seemed inexplicable to Kianna and her family, and to us as well.

Now comes the cavalry, in the form of the Access, Compassion, Care and Ethics for Seriously-ill Patients Act (ACCESS), co-sponsored by Republican Senators Sam Brownback of Kansas and Oklahoma's Jim Inhofe. Their bill would create a three-tiered drug approval system that would ensure that future patients won't have to suffer the same frustrations and missed opportunities as Kianna Karnes.

Their most novel idea is to add an entirely new FDA status -- called "Tier 1 Approval" -- to the two current tiers usually referred to as normal and accelerated. Tier 1 would be a limited form of approval that would allow companies to sell promising drugs to terminally ill patients who have

exhausted existing treatments and are not eligible for any more clinical trials. The logic here is that if drugs have shown themselves safe and effective enough in so-called Phase 1 trials for the FDA to approve giving them to hundreds or thousands of patients in Phase 2 studies, there is no good reason to withhold them from a broader patient population that has run out of other options.

"The decision for terminally-ill patients to take an investigational drug should be between the physician and patients, not government bureaucrats," says Senator Brownback. Notice that the physician would still be playing a determining role in the decision. It's not as if we have to worry about desperate patients being gulled into taking Tier 1 drugs by snake-oil salesmen.

By the same token, the market will impose its own discipline on companies applying for Tier 1, since they won't go through the expensive process of applying and building manufacturing capacity unless they've got some pretty convincing data to show to doctors.

The bill's other major provision would ban the use of placebo or "no treatment" arms in trials of treatments for terminal disease. Some will object that this will make it hard to do good science. But the truth is that the FDA's medical device division already knows how to interpret data without placebo controls. (Nobody gets placebo defibrillators in trials, for example.)

A ban on the practice would help force the research community to catch up with 21st century medicine, such as keeping electronic health records and tumor registries. "Modern methods would provide adequate control and historical data without the need to repeatedly measure disease progression and survival times of untreated patients," said the Abigail Alliance for Better Access to Developmental Drugs in a statement supporting the Brownback legislation. In short, the practice of placebo trials for terminal diseases is morally indefensible and unnecessary, despite what some at the FDA still say.

As it happens, Bayer cancelled the placebo arm of its kidney cancer trial shortly after our editorials about Ms. Karnes earlier this year. And both the Bayer and Pfizer compounds we wrote about are now being offered in expanded access programs. But dying patients shouldn't have to be spotlighted in the Wall Street Journal to prod the drug-control bureaucracy to action. Senators Brownback and Inhofe deserve credit for a proposal that would make rapid and easy access to developmental drugs the rule, not the exception.

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