**Dr Mondell:** To open our discussion, I would like to ask the panel a question. Are there any clinical features in patients with headache of which you are aware that could predict the success of treatment with botulinum toxin type A?

**Dr Dodick:** Dr Rami Burstein believes he’s identified, perhaps, a clinical feature that may reliably predict which patient may respond to botulinum toxin type A injections. He believes we need to separate so-called exploders from imploders. What he means by this is some people feel that their headaches feel as if there’s an external force applied to their head, thus someone is squeezing, pressing, or stabbing; it’s an external force coming from outside to within. By contrast, there are other people who feel as if there’s a pressure building up inside of their heads—as if their heads are going to explode or blow up. Dr Burstein did a study looking at approximately 66 patients, and he had a 92% positive predictive value. In other words, of the patients who were self-described as imploders, 92% were responders to botulinum toxin, and of the group who said they were exploders, 92% were nonresponsive. There also were some patients who described themselves as having attacks of both types—as separate events or during the same headache episode. Interestingly, for these patients, their imploding attacks disappeared, but their exploding attacks remained.

**Dr Rothrock:** Similar to when you ask patients about their auras, the way you ask that question is so important. It has to be asked in a uniform way from investigator to investigator and patient to patient.

**Dr Dodick:** Dr Burstein was using diagrams with patient descriptors, and we were putting the 3 diagrams out and saying, “Which diagram best describes your type of headache?” The problem was that the word stabbing was used for imploders and exploders, and patients were getting confused. Thus, I think you really have to simplify it; you have to be very consistent in your approach.

**Dr Johnson:** I think that’s true. Most of us would say the least helpful descriptor of a patient’s headache is whether it’s throbbing or not throbbing, or pressing or tightening. I ask the patient to describe the headache because I think the patient wants to feel I understand his or her headaches, not because it helps me much in diagnosis. It’s the severity and location of the pain and the associated features that are critical to making a diagnosis.

**Dr Dodick:** It’s part of the history. It’s the single part of the history to which I’ve ascribed very little value, and I almost don’t even ask it anymore, but maybe we’ve been missing something.

**Dr Johnson:** I think it’s interesting. As migraine can do anything the brain can do, the patients’ stories are always intriguing to me. We keep looking at characteristics of the pain for clues to the disease, but the subjective description of the patient’s pain is usually not helpful in diagnosis or management.

**Dr Dodick:** We’re not allowing them to subjectively describe it, though. Once we give a description of what imploding versus exploding is, you would be surprised how often patients immediately know which type of headache they most often experience. The patient immediately identifies with that, and it’s something I’ve never, ever asked a patient.

**Dr Rothrock:** If it’s a cluster headache, I would buy that, because it usually is one or the other; it’s going in or going out.

**Dr Dodick:** I would suggest when you go back to your clinic, just start asking people.

**Dr Elkind:** To even think about exploding or imploding—what made Dr Burstein decide to go ahead with that?

**Dr Dodick:** It is not clear. The possibility has been raised that headache description may vary depending on an individual’s anatomy. What he’s finding now is it’s possible that subcutaneous nociceptive afferents from the trigeminal nerve may travel through the periosteum bone and attach to dura. Thus, there may
be direct access to dura from whatever we inject subcutaneously; therefore, he's doing tracing studies in animals. It's interesting that botulinum toxin renders dural nociceptors inexcitable.

**Dr Rothrock**: Is it working locally?

**Dr Dodick**: It is probably working by silencing dural nociceptors. Dr Burstein believes that the imploders are likely those patients in which subcutaneous nociceptive afferents are going back to dura. We'll see; it's worth exploring.

On another topic, I don't think we need to get into my injection technique, but a colleague said earlier that some patients respond to 25 U of botulinum toxin type A; that's definitely true. There are quite a few patients who may respond to 25 U of botulinum toxin type A. Thus, I don't think even in the future phase III studies we will identify a minimal effective dose. In other words, how botulinum toxin type A was used in clinical trials may not reflect how it's used in clinical practice, because in the phase III studies we have a minimum of 155 U and a maximum of 195 U, whereas in practice I actually seldom use 155 U. I think one of the most important things I got from Dr Johnson's case presentation (see “Chronic Daily Headache and Psychiatric Comorbidites” case study) was the fact that at 4 weeks the patient noticed some benefit, but the patient was certainly in no way as well off as she was 2, 3, and 4 months later. Thus, I think what's really important to drive home to primary care physicians and to patients is that there's an incremental benefit over time. If a patient notices even a partial improvement after the first set of injections it's worth proceeding with subsequent injections.