AUTHOR REPLY

We very much appreciate the comments and are in complete agreement with the majority of points raised. The take-home message of this manuscript should be that based on very preliminary data, Xiaflex injections in PD men with ventral curvatures are reasonably safe and offer equivalent, if not better, outcomes compared to other directions. However, more data and external validation are mandated prior to routine implementation of this practice. This is further supported by our impression that ventral curvatures are more challenging to accurately inject and are probably best avoided until sufficient experience is gained with other curvatures.

It is worthwhile to mention that it is a very common belief among Urologists that Xiaflex is contraindicated with ventral curvatures, calcified plaques, complex curvatures, >90°, or hourglass/indentation deformities. However, although many of these characteristics were excluded in the phase III trials, the only true labeling "contraindication" is plaques involving the urethra, and the only indications are palpable plaques and ≥30° baseline curvature.[1] The contraindication is somewhat irrelevant, as, to our knowledge, there are no clinical reports that have shown PD plaques involving the urethra directly. Additionally, several studies have now shown benefits in men with hourglass deformities or calcified plaques (although blunted depending on severity).[2,3] Interestingly, the FDA label also cautions against injecting into the corpus cavernosum, nerves, or blood vessels, which is highly impractical, given that the intended target is often a few millimeters thick and is located immediately adjacent to those structures.

Another key point to mention is that the current article evaluated curvature based on individual directional components. For example, a man with a dorsolateral curvature may have been classified as having 55° dorsal and 20° lateral components. This was done intentionally to better isolate how much each of these individual directions improved with therapy. In Table 1 of the manuscript, we lumped the dorsal and lateral components together, since the intent was to emphasize ventral curvatures. Although it may appear that ventral men had greater baseline curvatures, they actually had similar severity compared to dorsals. However, because lateral components were included with the dorsals for that particular table, it diluted the mean curvature and made ventrals appear larger overall. This is further supported by Table 2, where each direction is specifically isolated, and a dorsal improvement of 15° equates to a 25% improvement compared to 30° (49%) for ventrals. We highlight this because it emphasizes one of the key (and surprising) findings, which is that ventral components experienced greater relative improvements compared to other directions: 49% versus 38% (lateral) and 25% (dorsal, $P < .05$). This is plausible from an anatomic standpoint, given that the thicker tunica and neurovascular structures lie along the dorsal aspect of the penis.

We again appreciate and support the very astute commentary and fully agree that a randomized trial would be preferred to evaluate this topic. However, as this may never occur (unfortunately), we are left to rely on the next highest level of evidence from prospective series reporting outcomes.

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