

27. Equivalent potency of Xeomin[®] and BOTOX[®]

Dirk Dressler^a, Gerd J. Mander^b, Klaus Fink^b

^a University of Rostock, Rostock, Germany

^b Merz Pharmaceuticals GmbH, Eckenheimer Landstr. 100, Frankfurt, Germany

Objective: To compare the potency of the two botulinum toxin (BT) type A drugs Botox[®] (Allergan, USA) and Xeomin[®] (Merz Pharmaceuticals, Germany), a formulation free of complexing proteins.

The biological potency of BT drugs is determined in a mouse LD50 bioassay as described in the European Pharmacopeia. It has been discussed whether there are potency differences when compared in the product-specific mouse LD50 bioassay. However, both drugs show equal therapeutic potency in clinical trials. The biological potencies of 5 commercially available unexpired batches of Xeomin[®] and Botox[®] were determined using the LD50 bioassay for batch release of Xeomin[®] in a blinded fashion. Relative potencies were subjected to a quantal response parallel-line probit analysis. Potency quantification was performed using the Xeomin[®] reference standard qualified against the NIBSC standard. Mean values of repeat measurements were compared by a two-tailed *t*-test for independent data. The biological potencies of the Xeomin[®] and Botox[®] batches studied were within the range specified in the European Pharmacopeia. The potencies of the Xeomin[®] (103.0 ± 5.7, *n* = 5) and Botox[®] batches (101.7 ± 6.2, *n* = 5) were not statistically different (*p* = 0.734).

Conclusion: The potency of Xeomin[®] and Botox[®] is equivalent and confirms previous clinical experience. Conversion of Botox[®] and Xeomin[®] dosages can be performed in a 1:1 ratio allowing exchange of both BT drugs in a therapeutic setting.

Keyword: Potency

10.1016/j.toxicon.2008.04.029

28. Dissociation of the 900 kDa neurotoxin complex from *C. botulinum* under physiological conditions

Karl-Heinz Eisele, Harold V. Taylor

Merz Pharmaceuticals GmbH, Frankfurt Main, Germany

This study assesses the stability of the 900 kDa botulinum neurotoxin complex and its dissociation under physiological conditions.

The medicinal botulinum neurotoxin product Xeomin[®] consists of the 150 kDa neurotoxin molecule free of complexing proteins. In contrast, first-generation neurotoxin products contain the 900 kDa neurotoxin complex consisting of the 150 kDa neurotoxin molecule and several non-toxic proteins known as complexing proteins.

It has been claimed that these complex proteins serve to prolong neurotoxin persistence and inhibit neurotoxin diffusion into adjacent tissues.

The 900 kDa neurotoxin complex was exposed to various pH values and then separated to differentiate between the resulting neurotoxin entities. Separation

conditions were qualified by Western blot and the toxin activity.

The 150 kDa neurotoxin molecule is released from the 900 kDa complex in less than a minute when exposed to physiological pH values. This time frame is extremely short in comparison to the onset of the therapeutic effect, which is measured in days. Therefore, the complexing proteins cannot stabilize the neurotoxin or inhibit its diffusion as claimed. Accordingly, the necessity of these complexing proteins in medicinal formulations must be questioned. Finally, these data aid in understanding the clinical equipotency of Xeomin[®], the 150 kDa neurotoxin molecule free of complexing proteins, and botulinum neurotoxin preparations containing complexing proteins.

Keyword: BoNT/A complex

10.1016/j.toxicon.2008.04.030

29. Analgesic properties of botulinum toxin type A (Dysport[®]) in paclitaxel-induced peripheral neuropathy in rats

Christine Favre-Guilmond, Michel Auguet, Pierre-Etienne Chabrier

IPSEN, LES ULLIS, France

Botulinum toxin type A has been shown to elicit direct analgesic effect independent of anti-spastic activity. We have assessed the analgesic effect of a single subplantar (s.p.) injection of Dysport[®] on neuropathic pain induced by paclitaxel in rats. Neuropathy was induced by intraperitoneal injections of paclitaxel 2 mg/kg on four different days (days 0, 2, 4 and 7). Paclitaxel treatment resulted 15 days later in a peripheral neuropathy that affected the two hind paws. The loco-motor performance of rats, assessed by rotarod test, was not impaired by paclitaxel treatment. Injection of 20 U/kg (s.p.) Dysport[®] that did not impair the withdrawal nociceptive reflex or loco-motor performance produced a significant anti-hyperalgesic effect in the injected paw of neuropathic animals 3 days after administration. Unexpectedly, a similar analgesic effect was observed in the contralateral paw. The analgesic effect on both paws lasted over the 9 days observation period. The same results were also observed with Botox[®] (20 U/kg; s.p.). By contrast, in the model of inflammatory pain induced by carrageenan or in the model of peripheral neuropathy induced by chronic constriction injury, a contralateral administration of Dysport[®] did not result in an analgesic effect although ipsilateral administration of Dysport[®] was effective in these two models. These results suggest that botulinum toxin type A elicits a potent effect on central pain sensitization beyond a local effect.

Keywords: Pain; Paclitaxel

10.1016/j.toxicon.2008.04.031