

# Sodium hyaluronate improves corneal reinnervation and epithelial healing in an *in vivo* benzalkonium chloride (BAK)-induced toxicity model

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## BACKGROUND

- In chronic treatments, BAK exerts short- and long-term toxic effects that reduce patient's quality of life and treatment compliance.<sup>1,2</sup>
- Topical use of BAK solutions alters the ocular surface and corneal nerve plexuses density in animal models after only 9 days of treatment.<sup>3</sup>
- It was recently shown that sodium hyaluronate (SH) presents a specific protective mechanism against BAK-induced toxicity.<sup>4</sup>
- SH protective action is positively correlated with the concentration, reaching the highest protective effects with the concentration of SH 0.4%.<sup>5</sup>

## PURPOSE

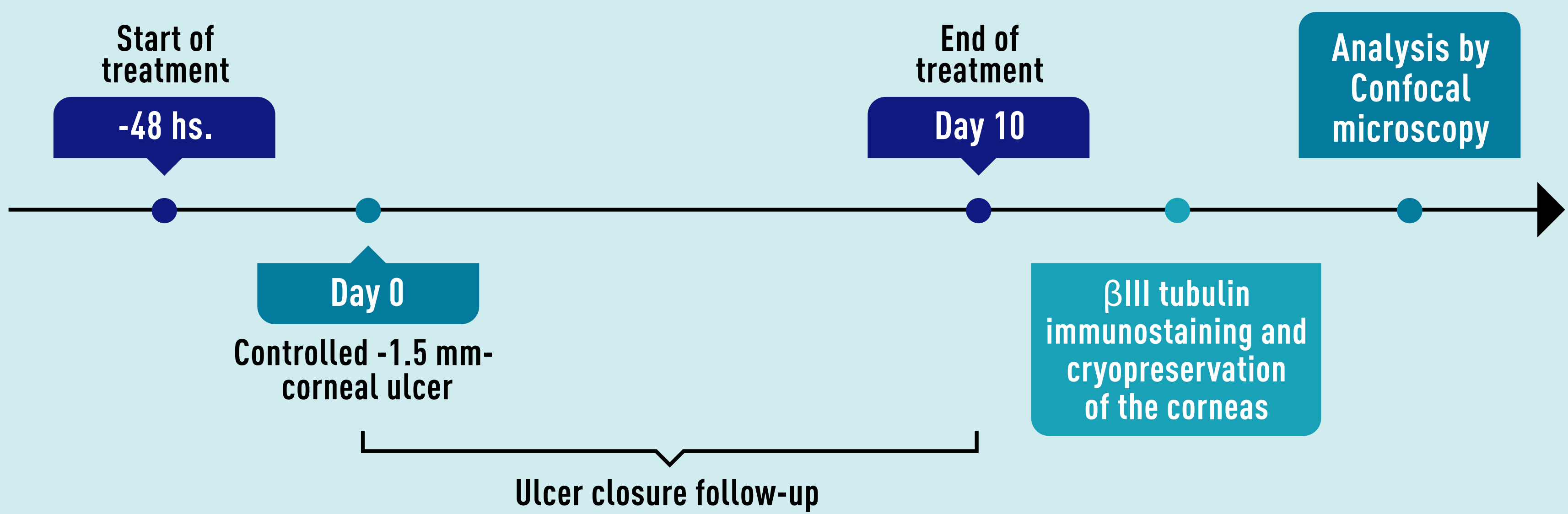
To evaluate the protective effect of 0.4% sodium hyaluronate on benzalkonium chloride-induced toxicity using an *in vivo* model.

## METHODS

88 Balb/c mice from 6 to 8 weeks old of both sexes were divided into 4 groups:



All groups received 3 daily instillations (8 AM, 2 PM, and 8 PM). For the SH+BAK group, SH was administered first and BAK was administered 10 minutes later. At day 0, a 1.5-mm corneal ulcer was created with a burr in the right eye of the anesthetized mice (ketamine/xylazine).



Wound healing over time and corneal nerve regeneration using Sholl analysis were assessed. Data were analyzed by two-way ANOVA and presented as mean  $\pm$  SD.

## RESULTS

### Wound closure:

There were statistically significant differences in ulcer closure between treatment groups over time ( $p < 0.0001$ ). Mice treated with BAK showed slower healing than those treated with SH+BAK ( $p = 0.0124$ ). The area under the curve (AUC) of corneal cicatrization for Control group was  $19.7 \pm 2.5$ ; for SH  $20.1 \pm 2.7$ ; for BAK  $28.0 \pm 4.6$ , and for SH+BAK  $24.4 \pm 5.0$  ( $p < 0.001$ ). All ulcers closed within 72 hours. The mean time of wound closure (in hours) was:  $41.5 \pm 9.6$  for control group;  $39.3 \pm 7.6$  for SH group;  $51.3 \pm 9.9$  for BAK group, and  $45.8 \pm 8.8$  for SH+BAK group. ( $p < 0.001$ ).

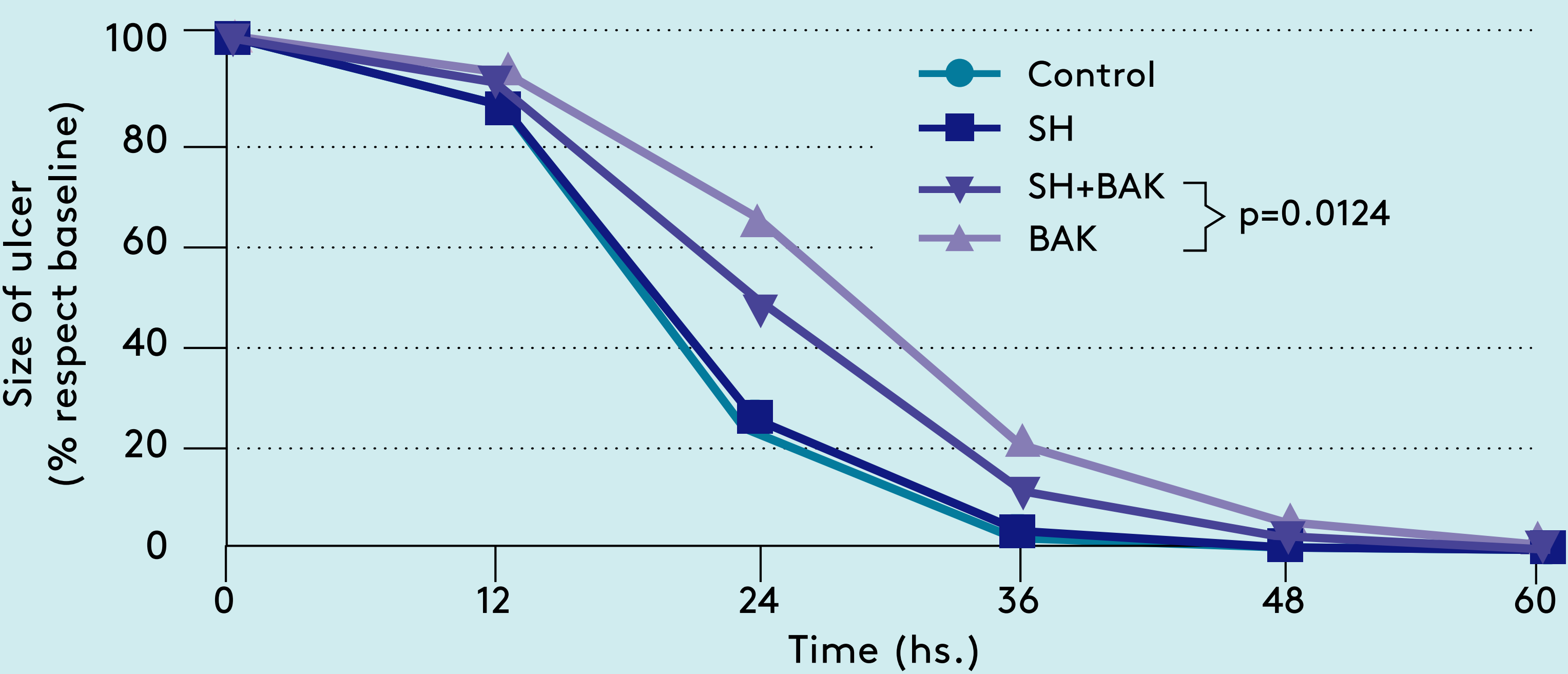


Figure 1. Percentage of corneal ulcer closure as a function of time by treatment group.

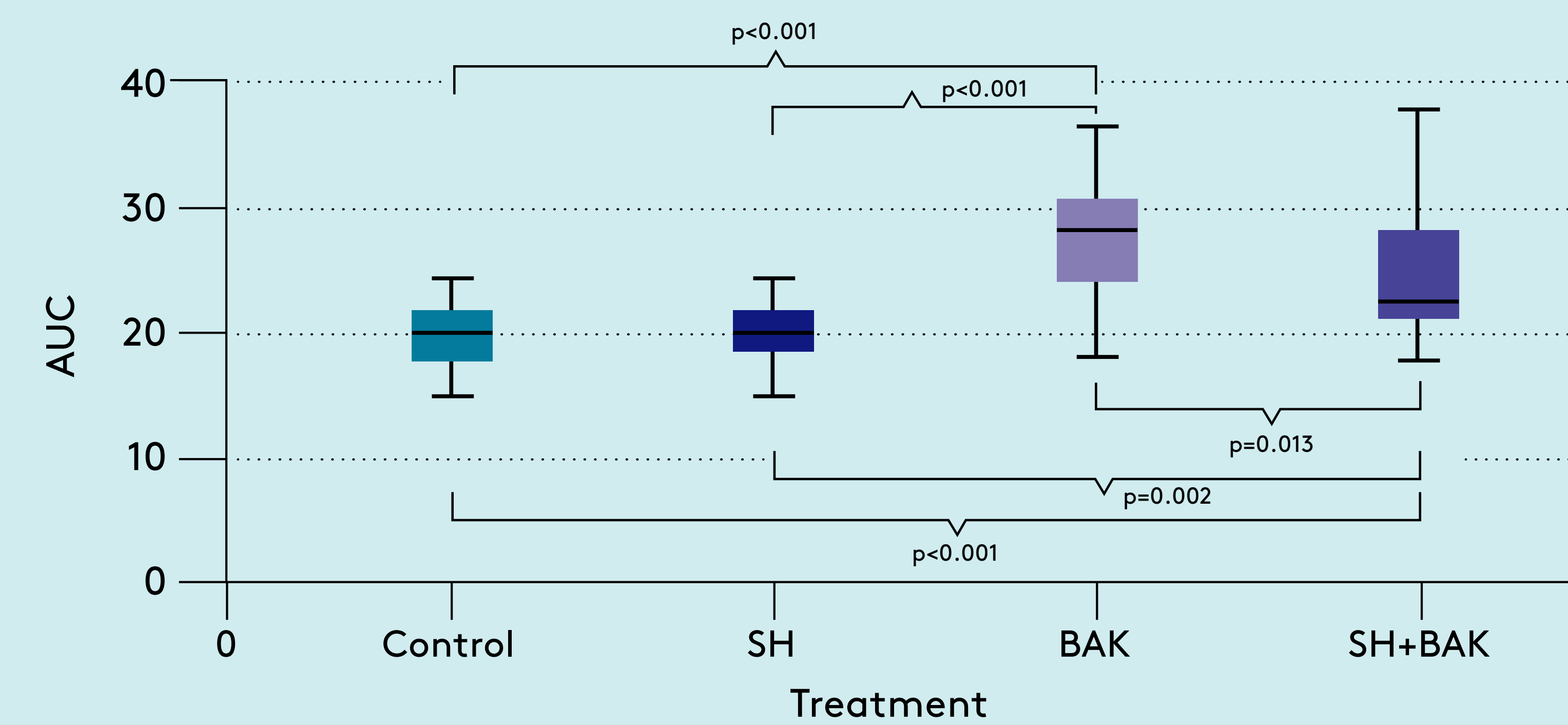


Figure 2. Area under the Curve by group of treatment.

### Corneal nerve generation:

The neural network presented an increasing complexity in the groups: BAK < BAK+SH < Control < SH. Considering the largest radius analyzed (100  $\mu$ m), the number of intersections was:  $11.5 \pm 2.6$  in Control group;  $15.8 \pm 2.1$  in SH;  $5.1 \pm 2.2$  in BAK, and  $8.05 \pm 2.2$  in SH+BAK ( $p < 0.05$ ).

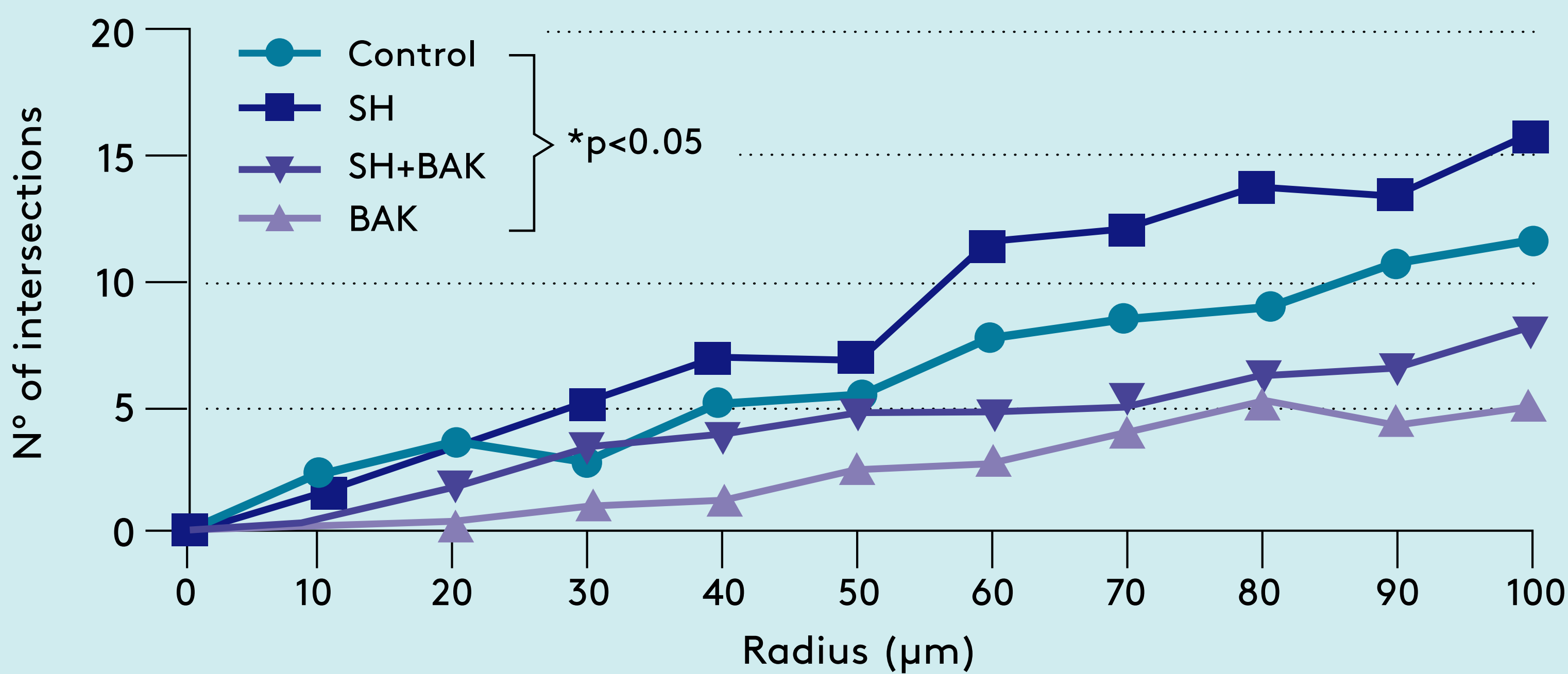


Figure 3. Number of intersections by radius under analysis by group of treatment. \* two-way ANOVA (treatment & radius).

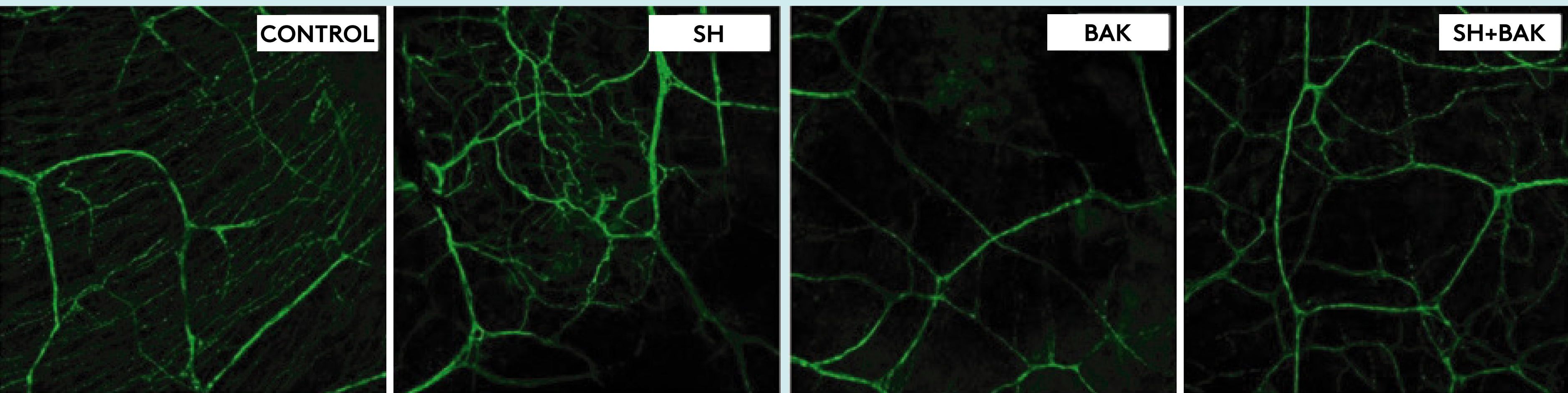


Figure 4. Images of confocal microscopy by group of treatment.

## CONCLUSIONS

- ✓ BAK has a toxic action on both corneal epithelial cells and corneal subbasal nerves.
- ✓ The concomitant addition of SH protects against the toxic action of BAK, promoting epithelial healing and corneal nerve regeneration.

### BIBLIOGRAPHY:



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### POSTER DOWNLOAD:



### DISCLOSURE:

This study was sponsored  
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