

Ixodes ricinus-Contact Phase Inhibitor (Ir-CPI) reduces neutrophil-mediated injury and promotes recovery following intracerebral hemorrhage in a mouse model

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01. Introduction

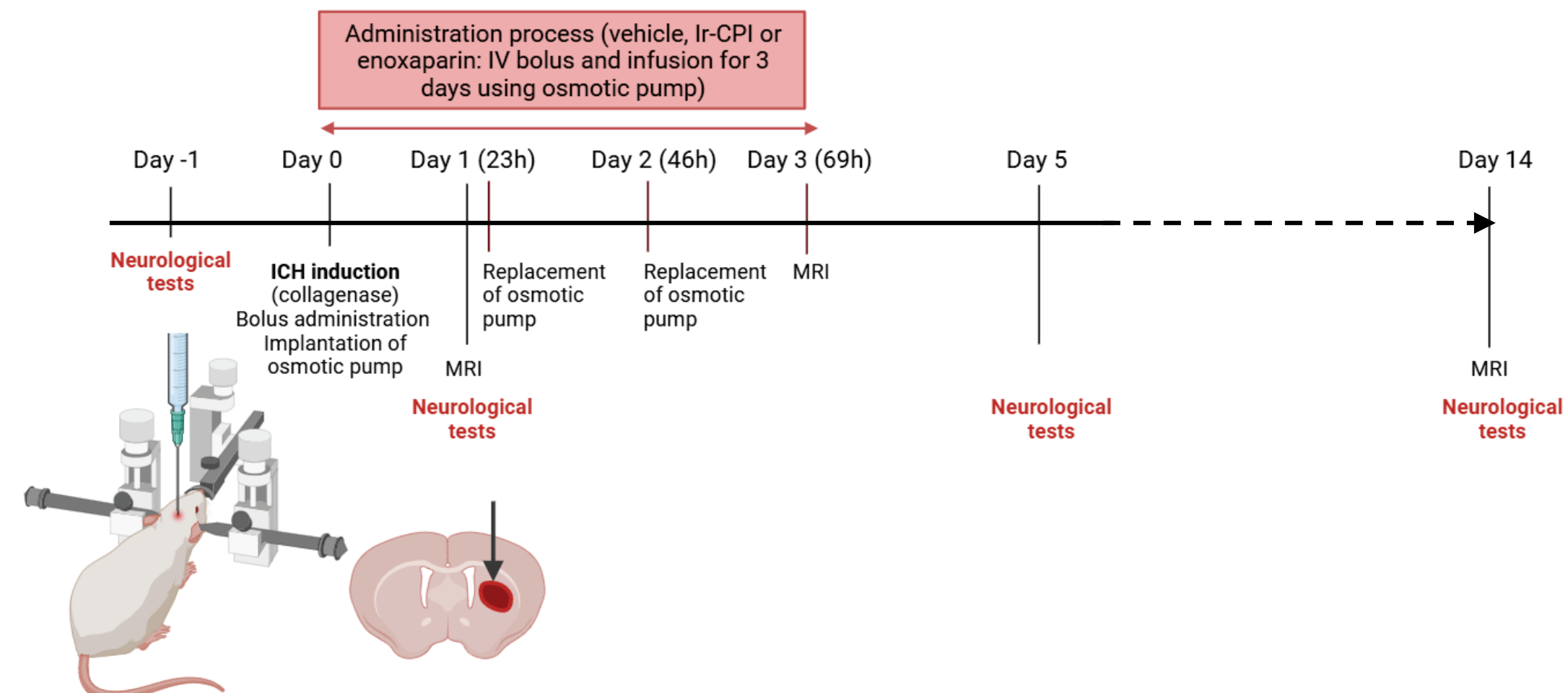
Secondary brain injury after intracerebral hemorrhage (ICH) is primarily driven by neuroinflammation, which is worsened by neutrophil infiltration and their release of neutrophil extracellular traps (NETs). These events contribute to blood-brain barrier disruption and enhanced neuronal damage. Moreover, patients with ICH often experience thrombotic events, including secondary intracerebral ischemic lesions, yet treatments for inflammation and safe thrombosis prevention are unavailable in the hyperacute phase of the disease.

Ir-CPI (also known as BIOX-101), a protein isolated from the salivary glands of the tick *I. ricinus*, is an inhibitor of coagulation factors FXIIa and FXIa as well as neutrophil activation, with proven antithrombotic and anti-neuroinflammatory properties, without increasing the bleeding risk.

02. Objective

This study examines the efficacy of Ir-CPI, a neutrophil-mediated thromboinflammation inhibitor, in mitigating neutrophil-induced damage and promoting functional recovery following ICH.

03. Methodology



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04. Results

Ir-CPI administration after ICH is safe

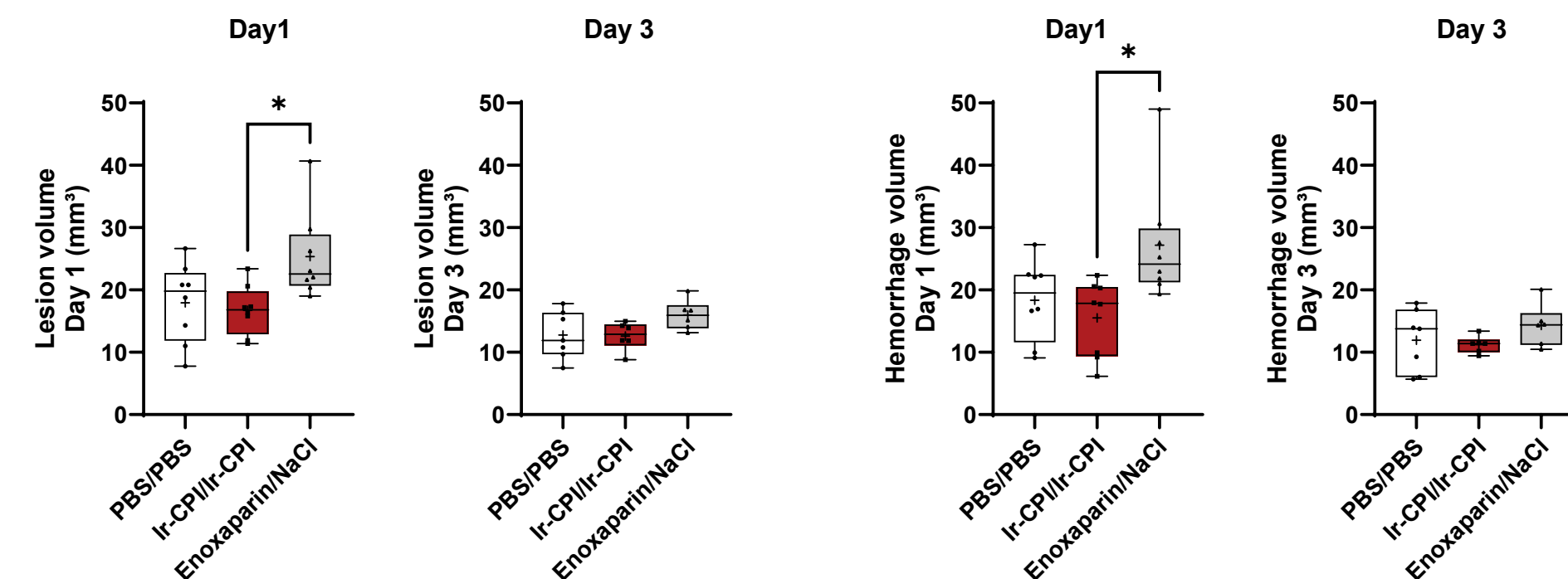


Figure 1. Edema and hemorrhage volumes on Day 1 and Day 3 after ICH induction. Median [Q1;Q3]. Means are shown as "+". Kruskal-Wallis with Dunn's post hoc test. *p<0.05.

Ir-CPI reduces inflammatory cell recruitment and NET release after ICH

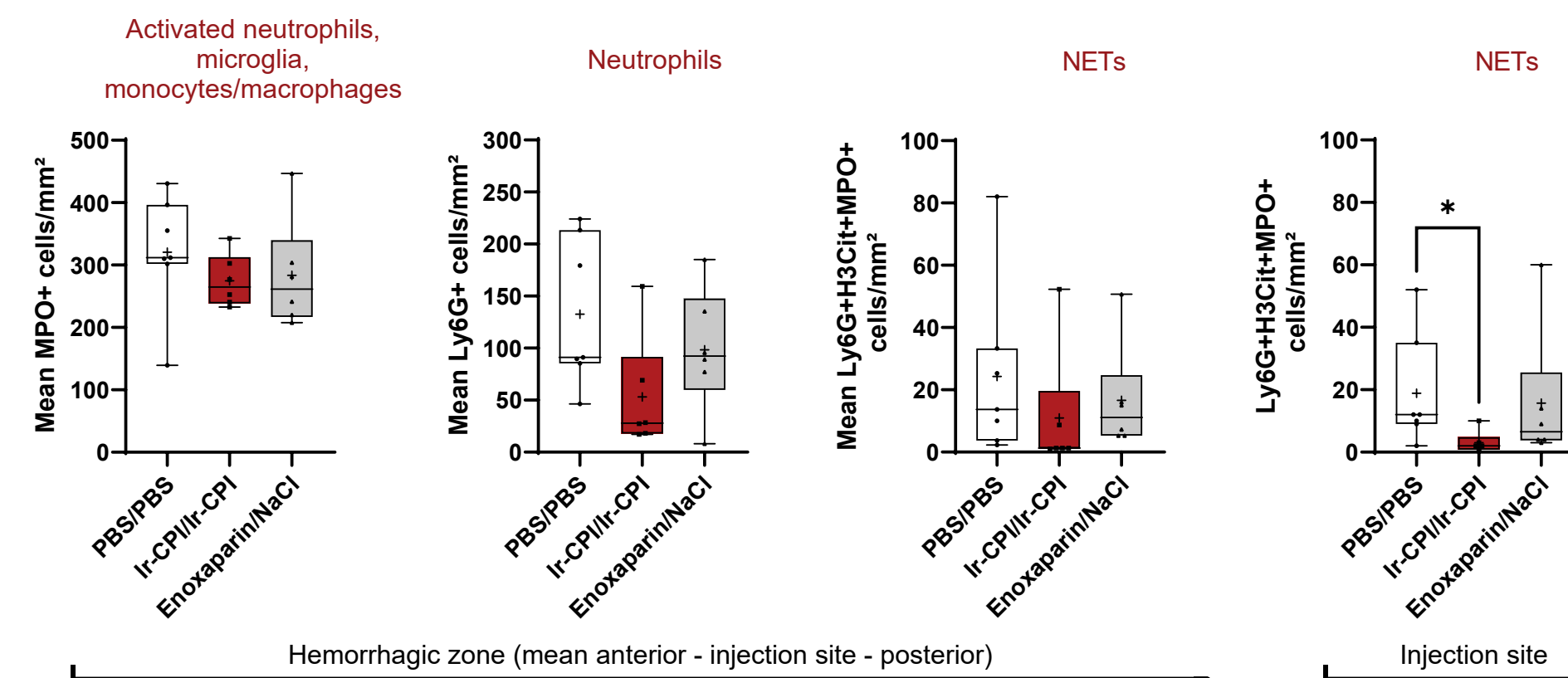


Figure 2. Numbers of inflammatory cells in the brain on Day 3 after ICH induction. Median [Q1;Q3]. Means are shown as "+". Kruskal-Wallis with Dunn's post hoc test. *p<0.05.

Ir-CPI reduces neuronal death after ICH

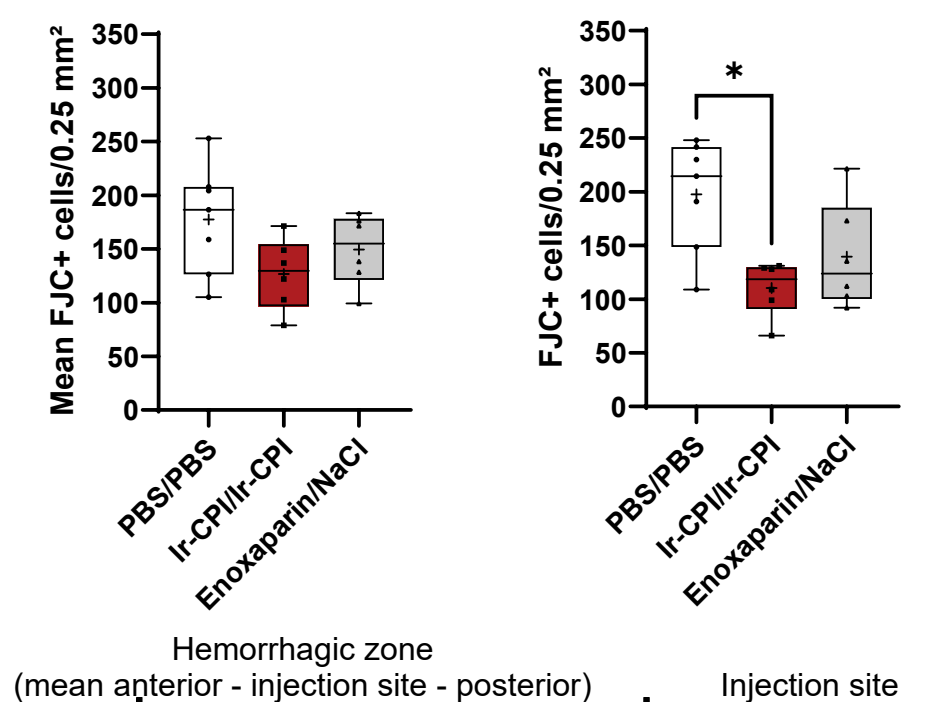


Figure 3. Numbers of degenerating neurons on Day 3 after ICH induction. Median [Q1;Q3]. Means are shown as "+". Kruskal-Wallis with Dunn's post hoc test. *p<0.05.

Ir-CPI improves functional recovery after ICH

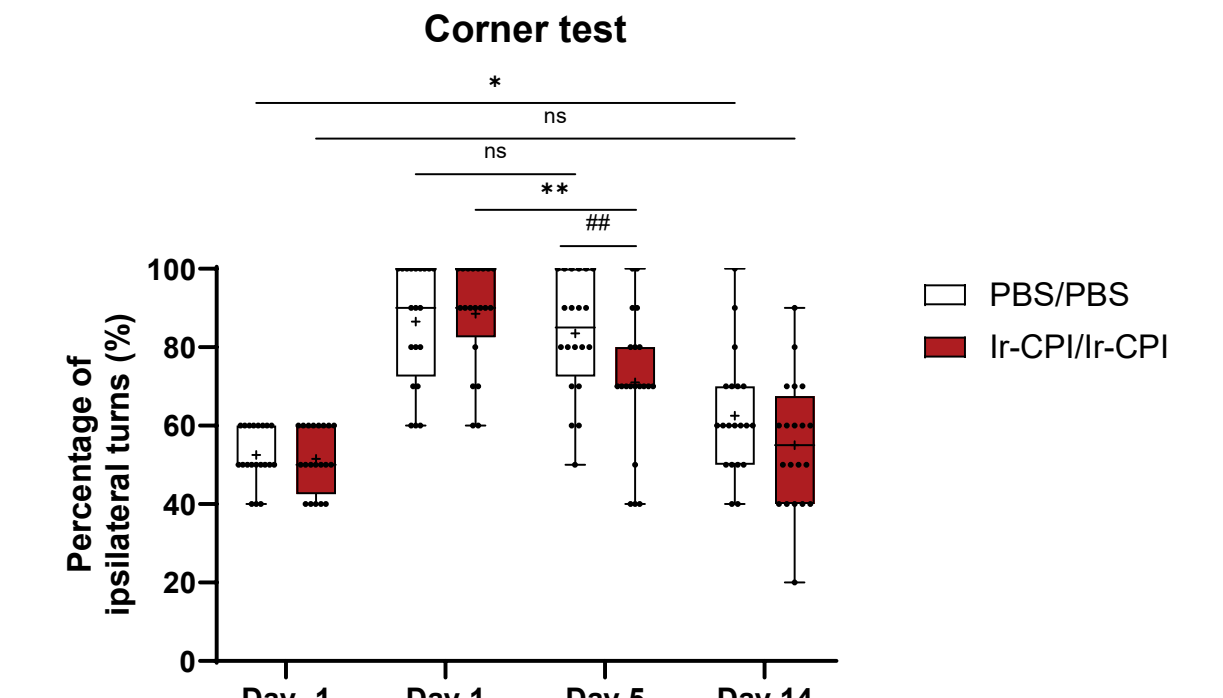


Figure 4. Corner test results on Day-1 (pre-ICH), Day 1, Day 5 and Day 14 post-ICH. Median [Q1; Q3]. Means are shown as "+". Wilcoxon test for intergroup analysis: ##p<0.01 PBS vs Ir-CPI. Friedman test for intragroup differences over time (only non-significant (ns) time pairs (except for two results with * and **) are shown in the graph, all other time pairs are significant (*p<0.05).

Bederson Scale

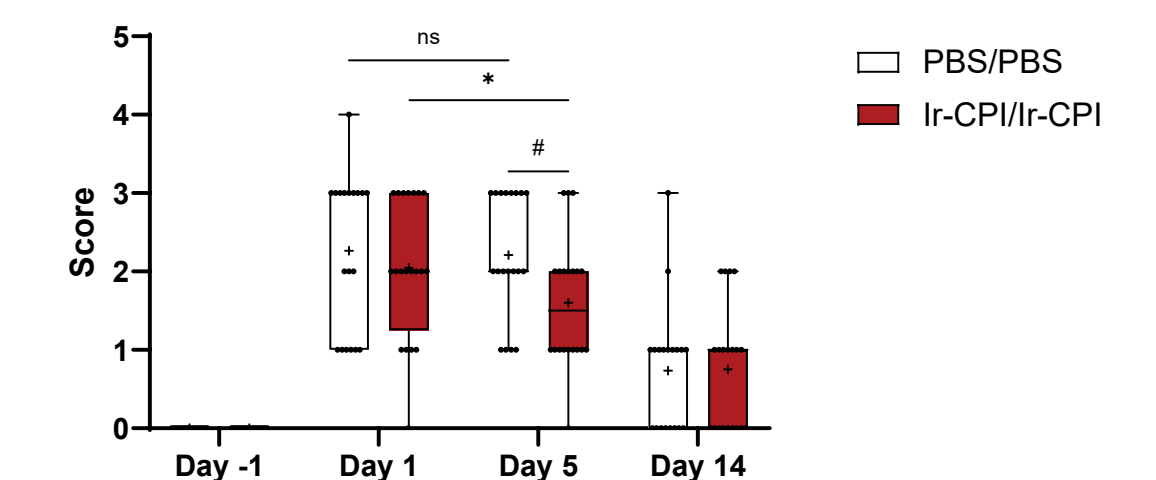


Figure 5. Bederson scale results on Day-1 (pre-ICH), Day 1, Day 5 and Day 14 post-ICH. Median [Q1; Q3]. Means are shown as "+". Wilcoxon test for intergroup analysis: #p<0.05 PBS vs Ir-CPI. Friedman test for intragroup differences over time (only non-significant (ns) time pairs (except for one result with *) are shown in the graph, all other time pairs are significant (*p<0.05).

05. Conclusion

Administration of Ir-CPI in mice post-ICH induction:

- is safe,
- reduces neutrophil-driven brain damage, and
- improves functional recovery.

The potential of Ir-CPI is currently being evaluated in the Phase IIa BIRCH trial (NCT05970224).