BP-C2: Gastrointestinal Acute Radiation Syndrome Radiomitigative Potential in C57BL/6J Mouse Model

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Background and Aims

BP-C2, a lignin-derived polyphenolic complex, is a candidate radiomitigator developed for civil applications and as a medical countermeasure for radiation emergencies [1].

In rodents, exposed to mid-lethal total-body irradiation, BP-C2, administered 24hrs post exposure, demonstrated radiomitigative potential believed to be mediated through hematopoietic and intestinal progenitor stem cells [2]. Main molecular targets for BP-C2 ligand are Serotonin (5-HT1/3.0µg/ml) and Glucocorticoid Nuclear (GR/12.6µg/ml) receptors [3].

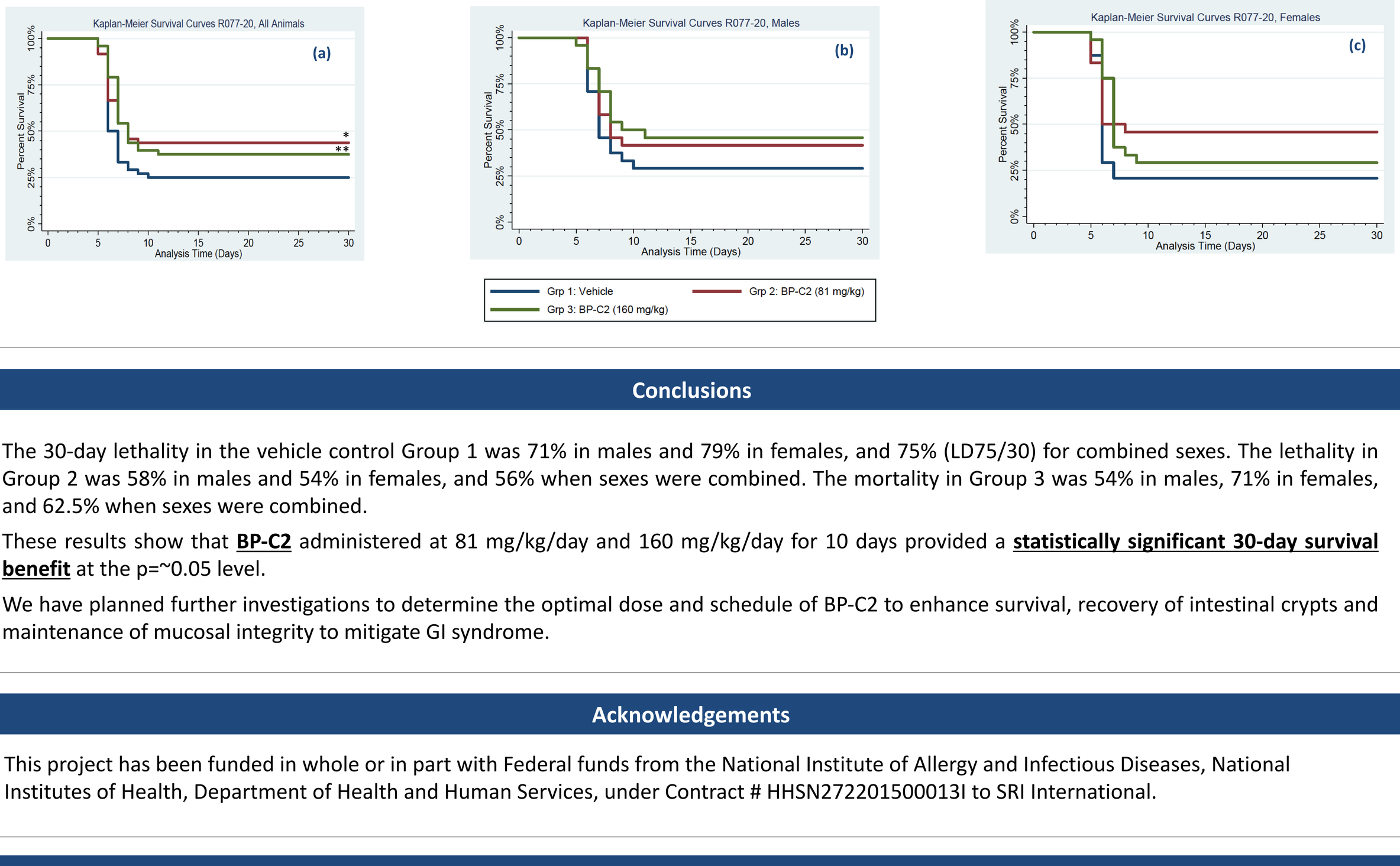
The study was conducted to investigate the gastrointestinal acute radiation syndrome (GI-ARS) 30-day survival efficacy of repeat oral gavage (PO) dose administrations of BP-C2 in male and female C57BL/6J mice utilizing SRI International's well-characterized PBI/BM2.5 GI animal model.

Materials and Methods

C57BL/6J mice (Males/Females, 24 mice/sex, 12 weeks of age)
Single LD50/30 partial-body X-irradiation (PBI; 12.3 Gy) dose using a 2.5% bone marrow sparing (BM2.5) exposure protocol
Group 1 received vehicle (sterile water), Groups 2 and 3 received 81 and 160 mg/kg/day BP-C2, respectively.
The vehicle and BP-C2 were administered orally once daily for 10 consecutive days starting at ~24 hr after irradiation.
Endpoint: 30-day lethality in vehicle vs. BP-C2 groups

Results

Figure 1 | Kaplan-Meier 30-day survival curves for all animals (a), male mice (b) and female mice (c).
*p=0.0539 BP-C2 81.0 mg/kg/day vs. Vehicle; **p=0.0473 BP-C2 160 mg/kg/day vs. Vehicle. Survival was equivalent at 15d and 30d for each group.



Conclusions

The 30-day lethality in the vehicle control Group 1 was 71% in males and 79% in females, and 75% (LD75/30) for combined sexes. The lethality in Group 2 was 58% in males and 54% in females, and 56% when sexes were combined. The mortality in Group 3 was 54% in males, 71% in females, and 62.5% when sexes were combined.

These results show that **BP-C2** administered at 81 mg/kg/day and 160 mg/kg/day for 10 days provided a **statistically significant 30-day survival benefit** at the p=~0.05 level.

We have planned further investigations to determine the optimal dose and schedule of BP-C2 to enhance survival, recovery of intestinal crypts and maintenance of mucosal integrity to mitigate GI syndrome.

Acknowledgements

This project has been funded in whole or in part with Federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under Contract # HHSN272201500013I to SRI International.

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