RESEARCH SUMMARY

Trial of Selective Early Treatment of Patent Ductus Arteriosus with Ibuprofen

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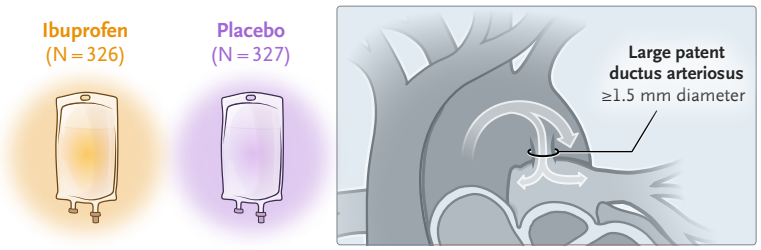
CLINICAL PROBLEM

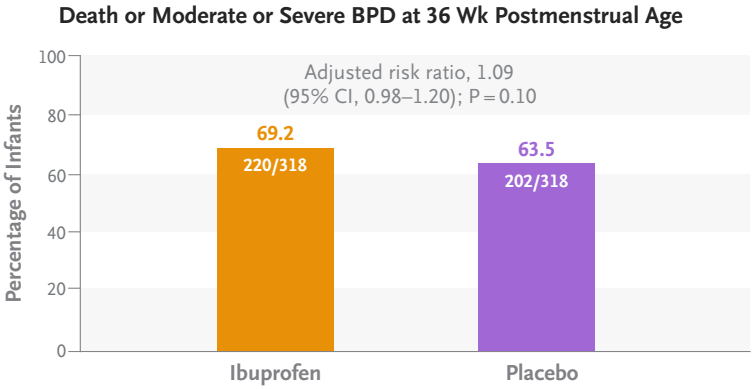
In extremely preterm infants, a large patent ductus arteriosus (PDA) that is present beyond 3 days of age is associated with higher mortality and morbidity and a higher risk of bronchopulmonary dysplasia than have been reported among infants without a PDA. Whether selective early treatment with the cyclooxygenase inhibitor ibuprofen would reduce mortality and improve short-term outcomes is not known.



CLINICAL TRIAL

Design: A multicenter, double-blind, randomized, placebo-controlled trial in the United Kingdom evaluated early treatment (≤72 hours after birth) with ibuprofen for a large PDA (diameter of ≥1.5 mm with pulsatile flow) in extremely preterm infants (born between 23 weeks 0 days' and 28 weeks 6 days' gestation).

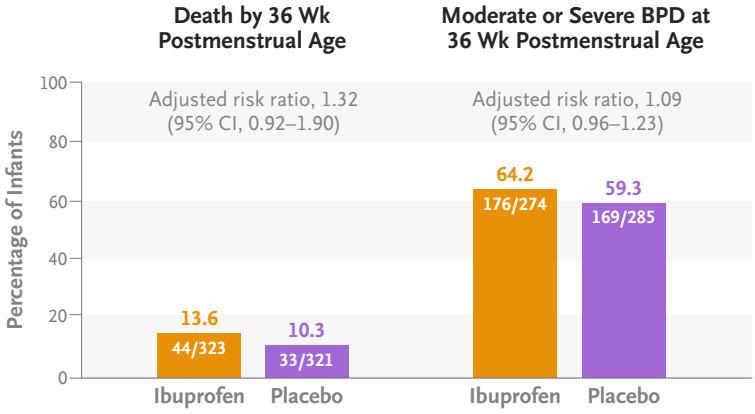
Intervention: 653 infants were randomly assigned in a 1:1 ratio to receive ibuprofen (loading dose of 10 mg per kilogram of body weight followed by two doses of 5 mg per kilogram ≥24 hours apart) or placebo. The primary outcome was a composite of death or moderate or severe bronchopulmonary dysplasia (BPD) at 36 weeks of postmenstrual age.



RESULTS

Efficacy: There was no apparent between-group difference in the risk of death or moderate or severe BPD.

Safety: Two unforeseeable serious adverse events were possibly related to ibuprofen.



LIMITATIONS AND REMAINING QUESTIONS

- Open-label therapy was received by 29.8% of the infants in the placebo group, which might have increased the percentage of infants with PDA closure in that group and made it more difficult to identify between-group differences in clinical outcomes.
- The first dose of ibuprofen or placebo was administered at a median of 61 hours after birth, which was later than the time of administration in other, similar trials.
- The target recruitment goal of 730 infants was not met, in part because of drug nonavailability, changes in clinical practice, competing trials, and the effect of the Covid-19 pandemic.

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CONCLUSIONS

In extremely preterm infants with a large PDA, early treatment with ibuprofen was not associated with a lower risk of death or moderate or severe bronchopulmonary dysplasia than placebo at 36 weeks of postmenstrual age.