Effect of Intravitreal Aflibercept vs Laser Photocoagulation on Treatment Success of Retinopathy of Prematurity
The FIREFLEYE Randomized Clinical Trial

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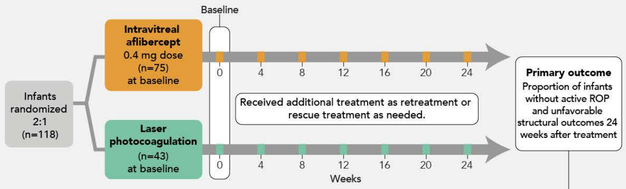
The standard treatment for retinopathy of prematurity (ROP) is laser photocoagulation, which has a tissue destructive nature and has been associated with adverse events. Anti-vascular endothelial growth factor (anti-VEGF) injections including aflibercept have been suggested as an alternative treatment for ROP. This noninferiority clinical trial was conducted to compare intravitreal aflibercept with laser photocoagulation in infants with ROP requiring treatment.

FIREFLEYE was a noninferiority, phase 3, 24-week, randomized clinical trial conducted on infants with ROP.



Infants were eligible if they had:

- Birth weight ≤1500 g or gestational age ≤32 weeks with either of the following in at least one eye:
  - ROP severity requiring treatment:
    - Zone I stage 1+ (stage 1 plus increased disease activity)
    - Zone I stage 2+
    - Zone I stage 3, zone I stage 3+
    - Zone II stage 2+, zone II stage 3+

  OR
  - Aggressive posterior ROP

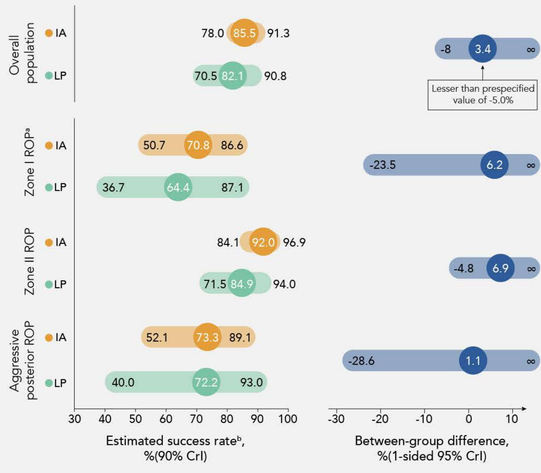
Unfavorable structural outcomes

Defined as the following:

- **Retreatment** was defined as receiving the same modality as the one administered at baseline.
- **Rescue treatment** was defined as additional treatment with laser photocoagulation for the intravitreal aflibercept group, and additional treatment with intravitreal aflibercept for the laser photocoagulation group.
- The requirement for **rescue treatment** was considered treatment failure.

Although the between-group difference of the Bayesian-estimated treatment success rate was in favor of intravitreal aflibercept, noninferiority could not be concluded as it did not meet the prespecified margin of 5%.

Primary outcome of treatment success rate based on Bayesian analyses overall and in prespecified subgroups

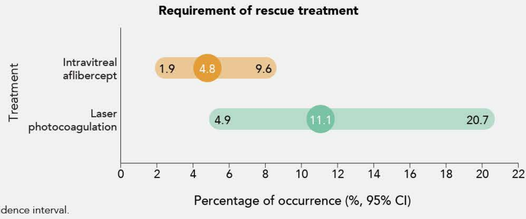


∞ = infinity; IA = intravitreal aflibercept; LP = laser photocoagulation; CrI = credible interval.

[a] The response in the second eye was considered missing information in the analysis model.
[b] Reflects the median of posterior distribution based on the primary (Bayesian) analysis model.

A lower proportion of patients in the intravitreal aflibercept treatment group required rescue treatments.

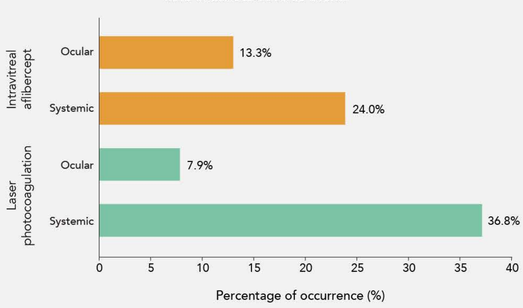
Requirement of rescue treatment



CI = Confidence interval.

Both treatment groups observed adverse events.

Rate of serious adverse events



There were three deaths that occurred 4 to 9 weeks after intravitreal aflibercept treatment, which were considered unrelated to aflibercept by the investigators.

Conclusions

Intravitreal aflibercept in comparison to laser photocoagulation did not meet critieria for noninferiority in terms of the proportion of infants achieving treatment success at week 24. Further data would be required for more definitive conclusions regarding the comparative effects of intravitreal aflibercept and laser photocoagulation in this population.