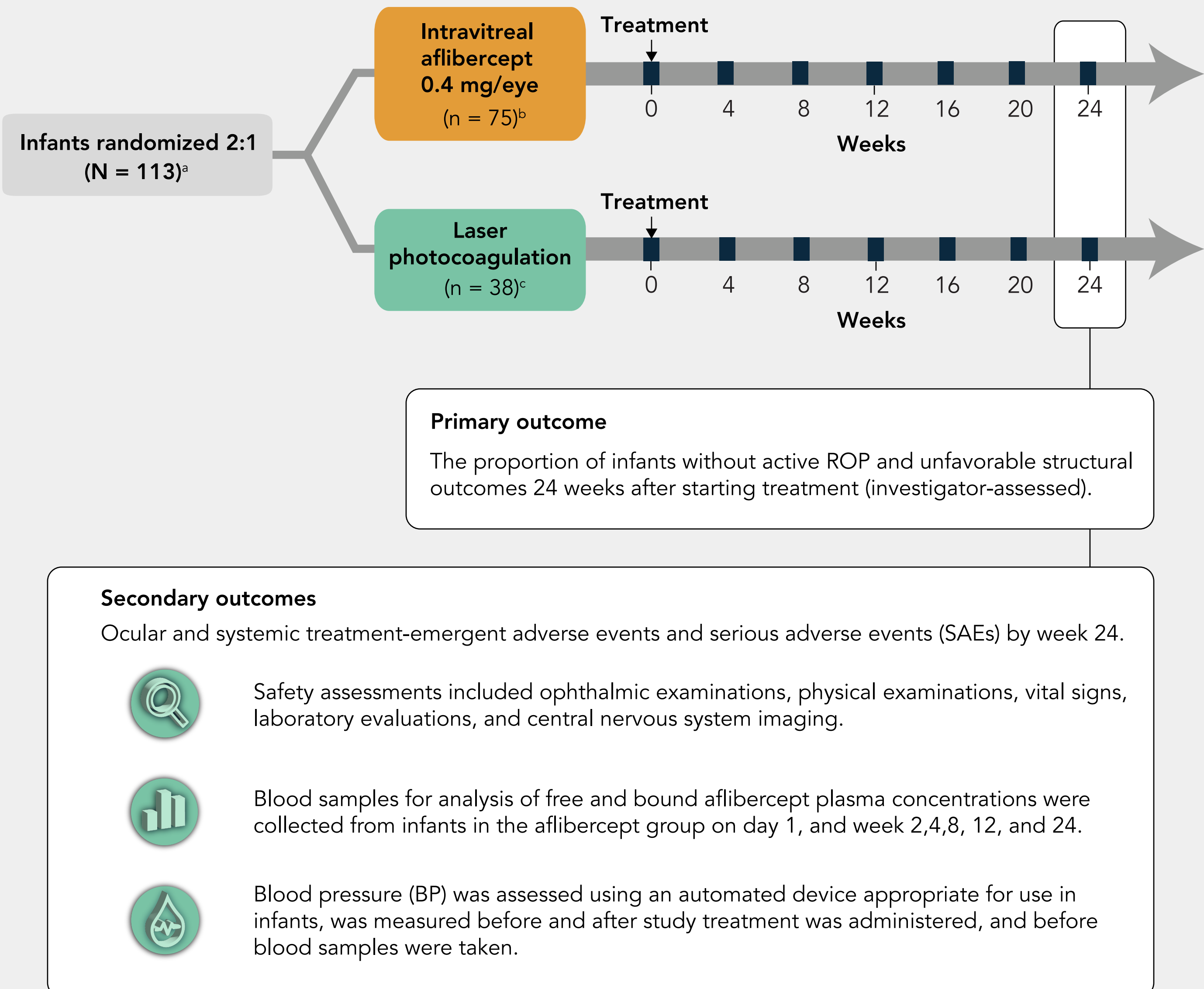


Systemic Exposure to Aflibercept after Intravitreal Injection Premature Neonates with Retinopathy of Prematurity: Results from the FIREFLEYE Randomized Phase 3 Study

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There are no data on pharmacokinetics, pharmacodynamics, and immunogenicity of intravitreal aflibercept in preterm infants with retinopathy of prematurity (ROP). FIREFLEYE compared aflibercept 0.4 mg/eye and laser photocoagulation in infants with acute-phase ROP requiring treatment. The aims of this analysis were to describe concentrations of free and adjusted bound aflibercept in plasma of preterm infants with ROP following treatment and explore the relationship between drug exposure and systolic blood pressure (SBP) and diastolic blood pressure (DBP) as markers of systemic anti-VEGF effects, using data from the FIREFLEYE trial.

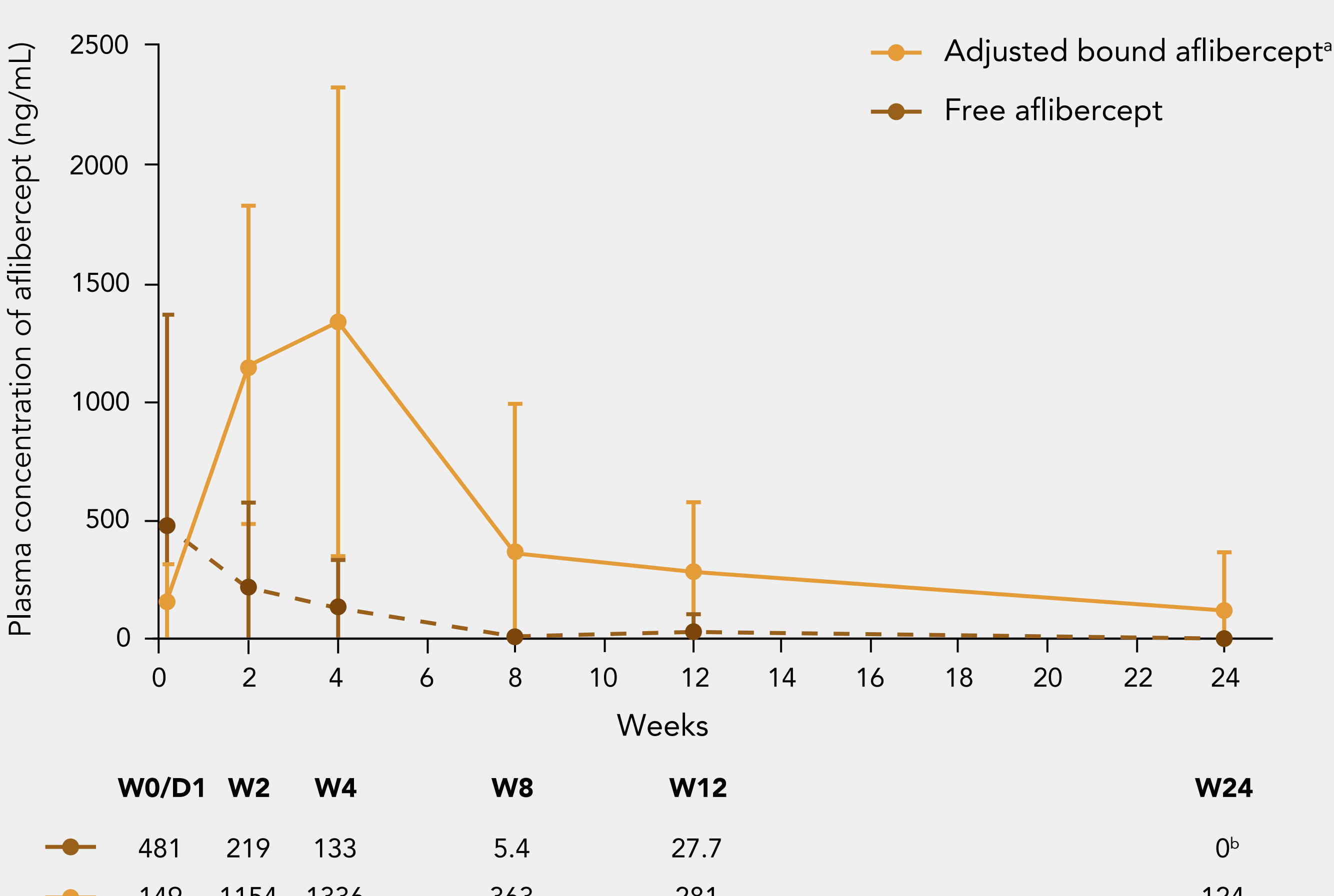
FIREFLEYE was a 24-week, randomized, open-label, noninferiority phase 3 trial assessing the efficacy and safety of aflibercept versus laser photocoagulation in infants with treatment-requiring ROP



^a Infants (gestational age ≤ 32 weeks or birthweight ≤ 1500 g) with treatment-requiring ROP in ≥ 1 eye
^b 7 withdrew prior to 24 weeks; 75 included in the primary analysis (146 eyes)
^c 2 withdrew prior to 24 weeks; 38 included in the primary analysis (72 eyes)

There was no pattern between free and adjusted bound aflibercept concentrations up to week 4

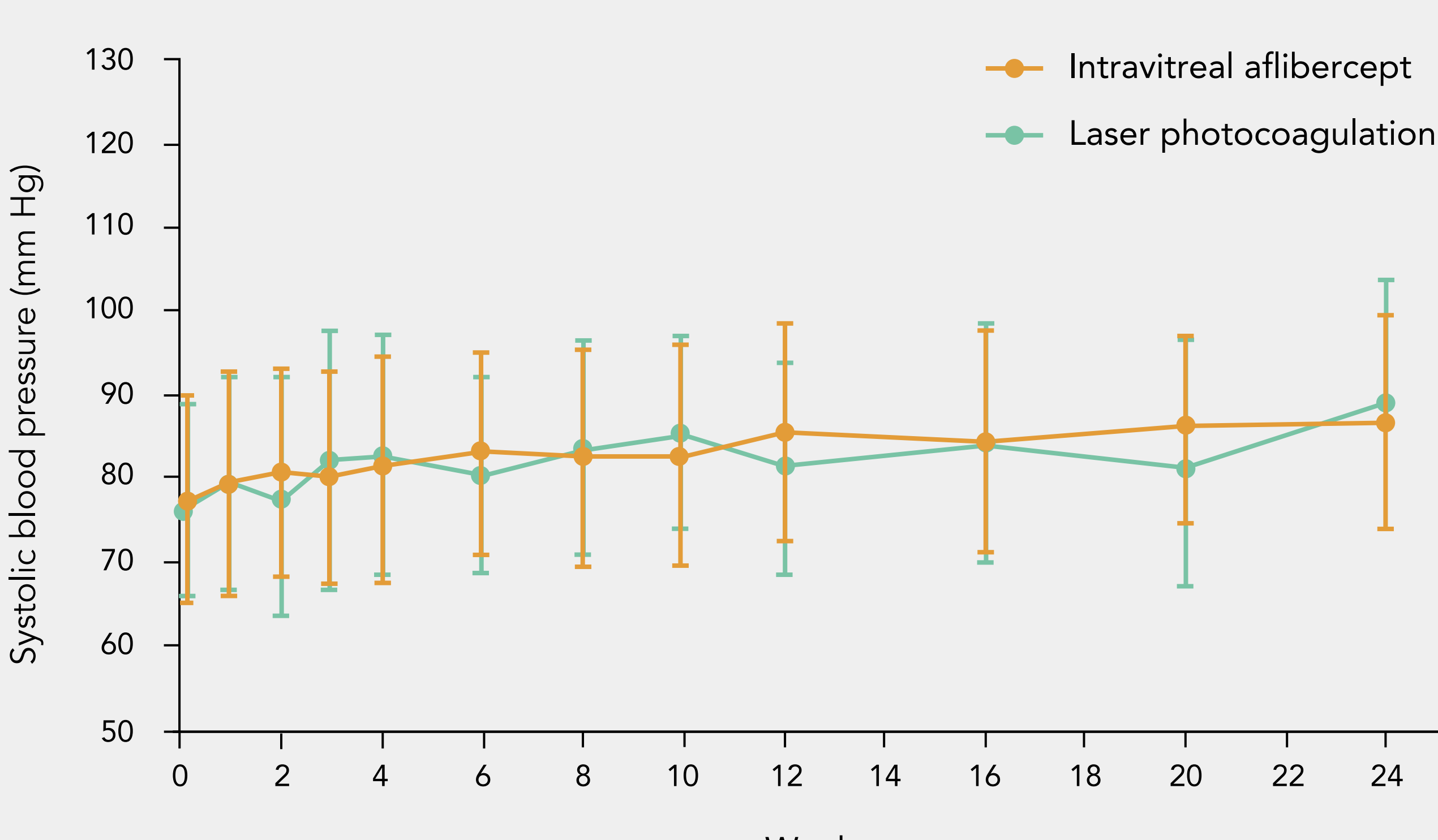
Arithmetic mean \pm SD concentrations of free and adjusted bound aflibercept (ng/mL) in plasma (in bilaterally and unilaterally treated infants combined)



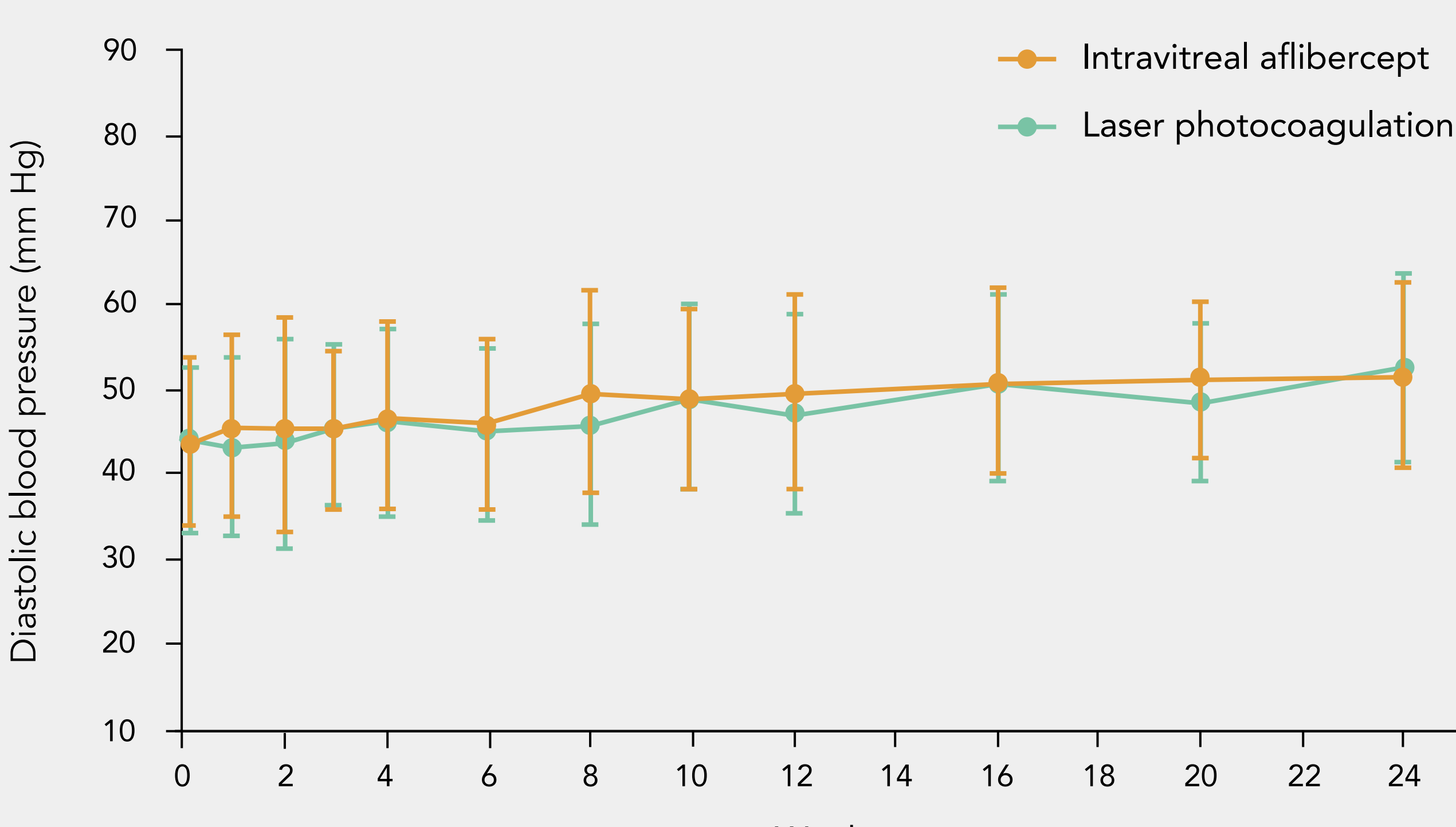
^a The concentration of the bound aflibercept complex was adjusted by multiplying by 0.717 to account for the VEGF present in the bound complex (adjusted bound aflibercept).
^b Values below the lower limit of quantitation (LLOQ) were substituted by 0 for the calculation of statistics. LLOQ was 15.6 ng/mL for free aflibercept and 31.3 ng/mL for bound aflibercept.

Blood pressure courses were similar in both treatment groups, with both systolic (SBP) and diastolic blood pressure (DBP) steadily increasing from baseline to week 24

Arithmetic mean \pm SD systolic blood pressure through week 24 in infants with retinopathy of prematurity in both treatment groups (aflibercept vs. laser photocoagulation)



Arithmetic mean \pm SD diastolic blood pressure through week 24 in infants with retinopathy of prematurity in both treatment groups (aflibercept versus laser photocoagulation)



Conclusions

This was the first randomized prospective collection of pharmacokinetic, pharmacodynamic, and immunogenicity data in this vulnerable pediatric population of preterm infants with ROP treated with aflibercept.

24-week data suggest intravitreal aflibercept (0.4 mg per eye) for treatment of acute-phase ROP is not associated with clinically relevant effects on blood pressure, further systemic adverse events, or immunogenicity.

Concentrations of aflibercept were highly variable and group sizes were small. Analyses revealed no clinically relevant differences regarding free or adjusted bound aflibercept concentrations in plasma in subpopulations by sex, race, or gestational age.

Limitations of this study include the relatively small sample size, which is consistent with the rarity of the condition under investigation; scarcity of data collected beyond week 8; and the overall follow-up span of 24 weeks.

Long-term follow-up to 5-years of age, as well as assessing ocular and further clinical outcomes, is still ongoing.