

## II. SUMMARY

**Purpose:** Evaluate the efficacy and safety of 0.5% timolol maleate solution for the early treatment of infantile hemangioma in infants under 8 weeks old. Investigators hypothesize that treatment with topical timolol in the first two months of life, before the proliferative phase or in early proliferative phase, may prevent from further growing and the need to treat with oral propranolol.

**Methods:** A multicentric, randomized, double-blind, placebo-controlled, phase II clinical trial. Patients with less than 60 days of life with focal or segmental hemangiomas, or any superficial, mixed, deep or abortive will randomly assigned to treatment with topical timolol 0.5% twice a day for 24 weeks or placebo.

Changes in lesion size (volume and thickness) and color were evaluated from photographs taken at 2,4,8,12,24 and 36 weeks. Vital signs and side effects will be recorded at each visit. Main outcome was a complete or nearly complete resolution of the IH evaluated by a blinded investigator.

**Results:** Seventy patients were recruited. Twenty-two of the 33 infants receiving treatment and 25 of the 37 infants receiving placebo completed the study. Five patients in the placebo arm and 2 in treatment arm were withdrawn because ultimately needed propranolol.

A total of 52 (74.2%) patients had superficial IHs, 11 (15.7 %) had mixed IHs, 6 (8.5%) had abortive IHs and 1 (1.4%) had deep IHs. A total of 60 patients had localized IHs (87%), 5 had segmental IHs (7.2%), and 4 patients had indeterminate IHs (5.7%). As regards location, 33.3% were located on the head and neck, with 66.7% on other body sites.

We found a complete resolution in 48.1% of IHs in the timolol group vs. 36% in the placebo group at week 24, but the difference in proportions was not statistically significant ( $P < 0.398$ ). No changes were found in the size of the IH (volume / thickness) between both groups. An improvement in color was observed at week 4 in the group treated with timolol ( $P < 0.011$ ). No serious adverse effects were reported by the parents. No variations in blood pressure or heart rate were found between the two groups.

**Conclusions:** Topical timolol maleate, even in the early proliferative stages, was not more effective than placebo in this cohort of patients. We would need to treat more patients to be able to show a difference.