

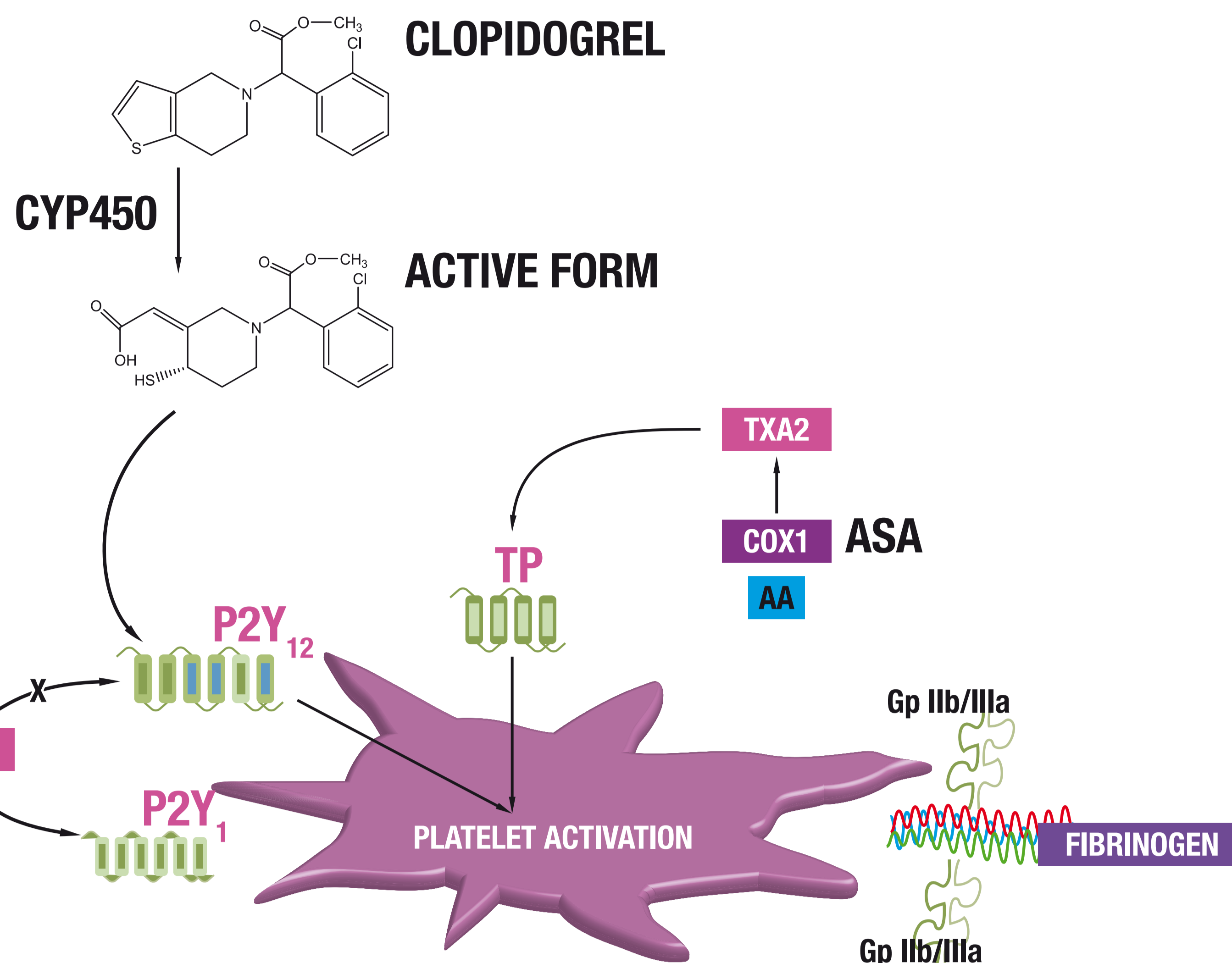
CLOPIDOGREL FOR THE TREATMENT OF CHILDREN WITH A SYSTEMIC-TO-PULMONARY ARTERIAL SHUNT

A. Garzone (1), F. Ciuccarelli (1), A. Pompilio (1), E. Andresciani (1), F. Pinto (2), M. S. De Meo (2), M. C. Cerlesi (1), P. Colonna (3), E. Franchi (3), V. Moretti (1), L. Carloni (1), P. Marzoni (1), M. Buccolini (1).

(1) AO Ospedali Riuniti – Presidio G. Salesi, Farmacia, Ancona, Italy.
 (2) Università degli Studi di Camerino, Scuola di Specializzazione in Farmacia Ospedaliera, Camerino, Italy.
 (3) AO Ospedali Riuniti – Presidio G.M. Lancisi, Cardiocirurgia e Cardiologia Pediatrica e Congenita, Ancona, Italy.

Background

Clopidogrel is a thienopyridine drug. It is a prodrug metabolized by CYP450 in the thiol derivative active form that selectively and irreversibly binds to the adenosine diphosphate-P2Y₁₂ receptor on platelets. This prevents ADP from binding, and GPIIb/IIIa complex from activation, so platelet aggregation is consequently inhibited (see picture 1). Clopidogrel is used to prevent ischemic events in adult patients with myocardial infarction, ischemic stroke or vascular disease and in patients with acute coronary syndrome who also underwent stent placement in combination with ASA. Paediatric use is not authorized because of limited information about efficacy and safety. The few studies have given good results but have been carried out on a restricted population of patients.



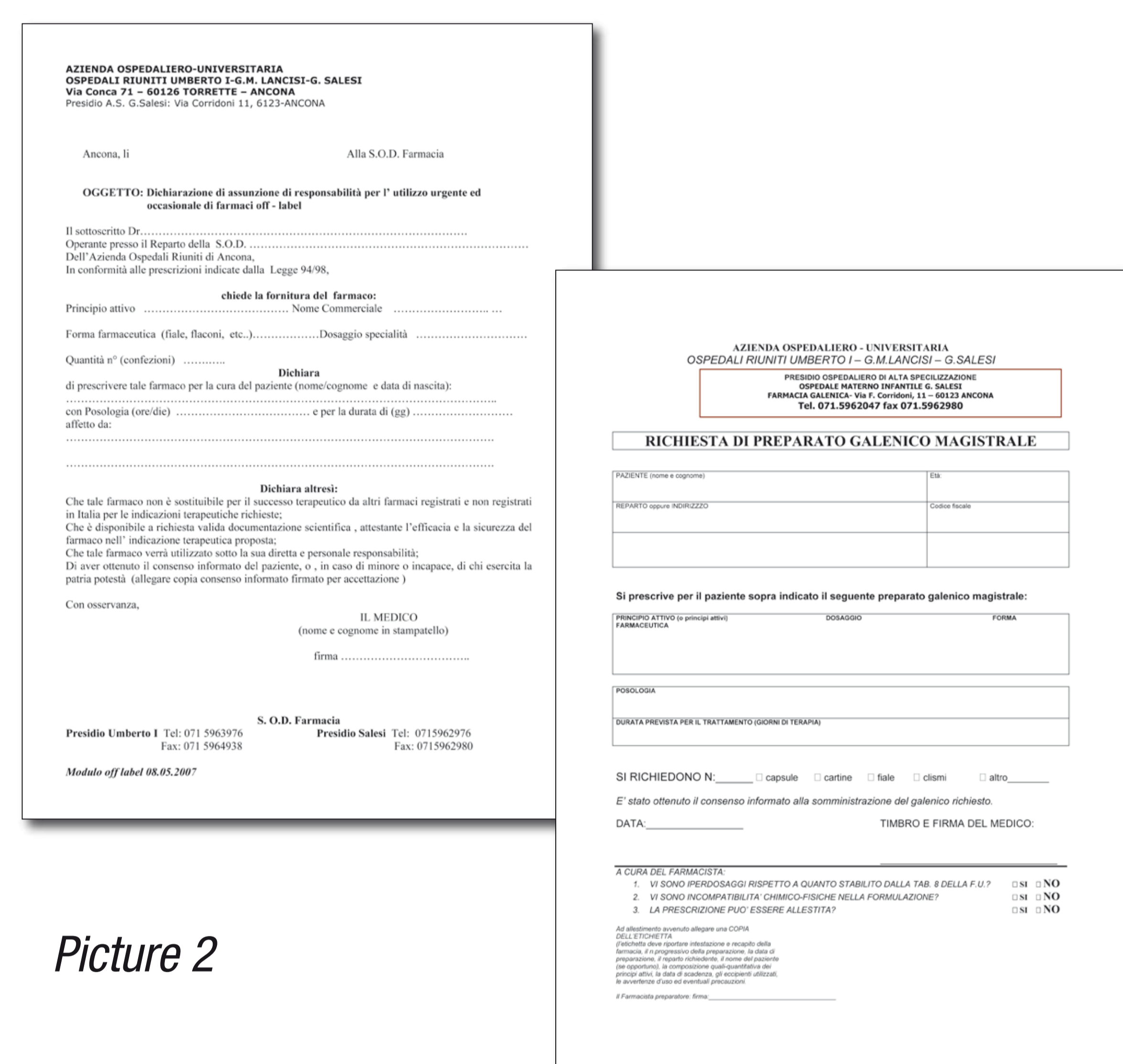
Picture 1

Purpose

To illustrate our experience in the three-month-long use of clopidogrel on children with a systemic-to-pulmonary arterial shunt, prior to definitive surgical intervention.

Materials and Methods

On February 2012 “Cardiocirurgia e Cardiologia Pediatrica e Congenita” division of “Azienda Ospedali Riuniti di Ancona” placed a temporary systemic-to-pulmonary arterial shunt in a four months old patient, affected by Tetralogy of Fallot with hypoplasia of the infundibulum and pulmonary valve. Because of the high risk of thrombotic closure of the shunt and on the basis of previous negative experiences we administrated two antiaggregant drugs, ASA 18 mg and Clopidogrel 0,2 mg/Kg once a day as reported in scientific literature (PICOLO trial). The pharmacy was involved to support the request to Ethic Committee (CE) for urgent off-label use and for the galenic preparation of Clopidogrel 0,75 mg (see picture 2). A liquid form was evaluated but rejected because of doubts about long term stability inconsistent with home therapy. We chose an extemporaneous preparation of capsules type 5 with lactose as a diluent. After that, four other children (from 2 months to 4 years old) were treated with Clopidogrel, mostly associated with ASA alone or together with enoxaparin (see table 1).



Picture 2

Results

We prepared capsules from 0.75 to 3.5 mg. We acquired the authorization by the Ethic Committee and the parent's informed consent for all patient. After surgery, children were observed for 7-8 days depending on clinical follow up and complications. We controlled blood count and shunt patency with clinical observations, analyses and echocardiograms. After discharge, patients were first recalled 10-15 days later, then after 1-2 months for medical visit, ECG, blood exams and echocardiogram. Pt was not necessary. No serious side effects have been observed. Treatment should continue until definitive intervention for cardiac disease and removal of the shunt.

PATIENT	AGE OF ONSET THERAPY	PATIENT'S CLINICAL SITUATION	CONCOMITANT ANTIPLATELET THERAPY
1	4 MONTHS	TETRALOGY OF FALLOT with hypoplastic infundibulum and pulmonary valve subjected to systemic-to-pulmonary arterial shunt procedure with goretex tube.	ASA 18 mg
2	5 MONTHS	TRANSPOSITION OF GREAT VESSELS with hypoplastic right ventricle subjected to systemic-to-pulmonary arterial shunt procedure with goretex tube.	ASA 14 mg ENOXAPARIN 400 UI
3	18 MONTHS	PULMONARY ATRESIA with VENTRICULAR SEPTAL DEFECT subjected to systemic-to-pulmonary arterial shunt procedure with goretex tube.	ASA 100 mg
4	2 MONTHS	PULMONARY ATRESIA with VENTRICULAR SEPTAL DEFECT subjected to systemic-to-pulmonary arterial shunt procedure with goretex tube.	LYSINE ASPIRIN 18 mg
5	4 YEARS	TETRALOGY OF FALLOT with pulmonary atresia and VSD with artificial duct V dx - AP.	-

Table 1

Conclusion

Clopidogrel therapy on children is rapidly increasing. A wider number of cases, a comparison with other professional experiences, and, most of all, controlled clinical trials would be desirable.



References

- Li J.S. - Dosing of Clopidogrel for Platelet Inhibition in Infants and Young Children: PICOLO Trial – Circulation 2008; 117:553-559.
- Nationwide Children's Hospital and Toronto Hospital for Sick Children Department of Pharmacy Experience since September 2007.
- <http://www.micromedexsolutions.com>