HTA ANALYSIS FOR THE INCLUSION OF ANDEXANET ALFA (AA) WITHIN THE HOSPITAL THERAPEUTIC HANDBOOK (HTH) - THE EXPERIENCE OF AN ITALIAN CENTER SPECIALIZING IN CARDIOVASCULAR DISEASES

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Background and importance: The drug Andexanet Alfa (AA), an anti-haemorrhagic antidote (ATC: V03- ALL OTHER THERAPEUTIC PRODUCTS) capable of rapidly reversing the effect of factor Xa inhibitor Doacs (Apixaban, Rivaroxaban), was recently introduced on the market. The 4-factor prothrombin complex (CPP4), already in use at our center, also has the same indication.

Aim and objectives: In collaboration with a hematologist and a cardiologist-anesthetist, an HTA analysis was conducted with the aim of evaluating the real need for the inclusion of AA within the Hospital Therapeutic Handbook (HTH) and its use in cardiac surgery emergency situations and cardiovascular emergency.

Materials and Methods: A brief review of the literature currently available on various search engines (Pubmed, clinicaltrials.gov) was conducted by the Hospital Pharmacy, looking in particular for comparison studies between AA and CPP4. In parallel, a search was conducted for poison control centers (PCC) and hospital centers close to the facility that had the drug available, an economic evaluation and an analysis of the Summary of Product Characteristics (SmPC).

Results: From the retrospective studies analyzed (8, of which only 3 meta-analyses), data were collected and summarized in terms of efficacy/haemostasis rate (AA: 77.88% vs CPP4: 76.47%, average data) and safety/incidence of post-treatment thromboembolic events (AA: 10.47% vs CPP4: 5.98% average figure).

Figure 1 Comparison of the hemostasis rate of the two drugs

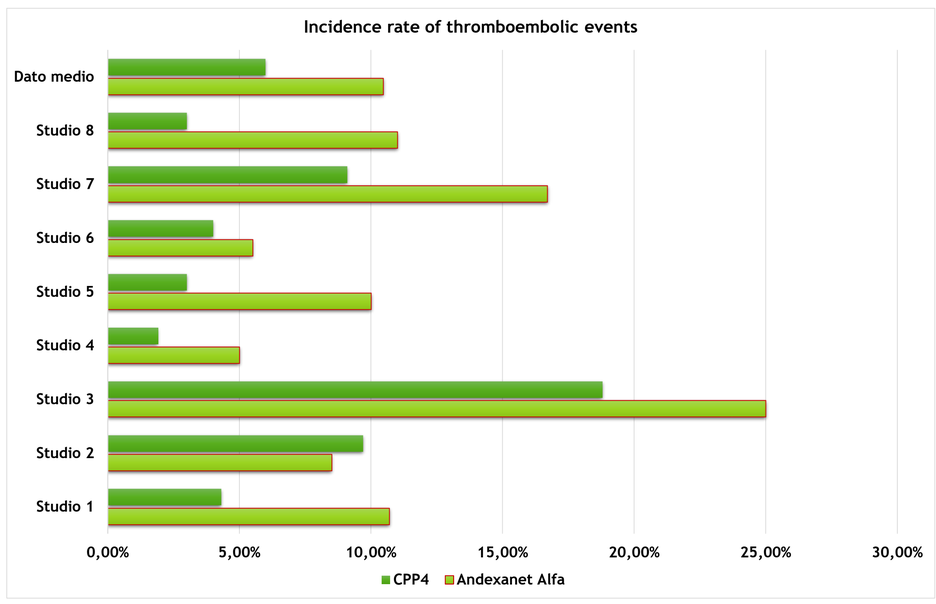

Figure 2 Comparison of incidence rate of thromboembolic evnts of the two drugs

From the parallel research, the following results emerged: availability of the antidote (1 PCC and 2 hospital centers); treatment costs (AA: Euro 52,666.52 vs CPP4: Euro 3795.90); reimbursement (non-reimbursable drug); AA preparation/infusion times (approximately 2h30').

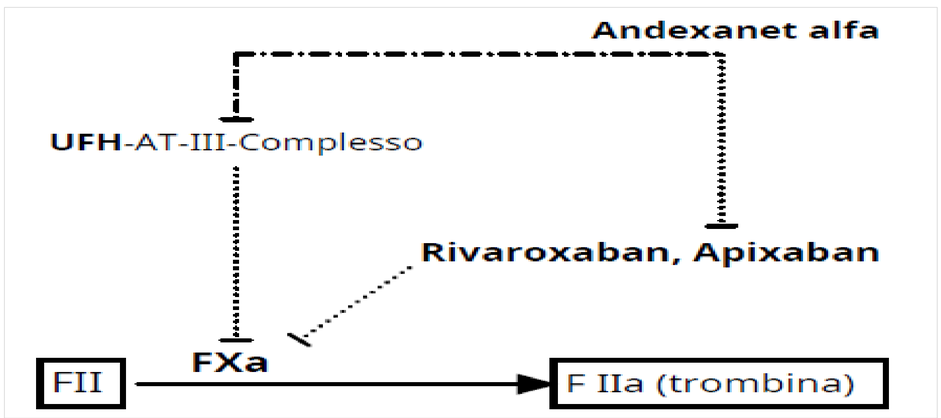

Figure 3 Simplified schematic profile of heparin resistance associated with Andexanet-alfa

Conclusion and relevance: The analyzed studies, subject to bias due to the variability of the analyzed sample, were mainly focused on intracranial hemorrhage events and not on cardiac surgical complications. From these, it also emerged that AA promotes a refractoriness to the anticoagulant effect of unfractionated heparin, making the use of AA incompatible in patients candidates for a cardiac surgical procedure that requires preheparinization.

Therefore, by virtue of the poor and unfavorable quality of the trials and the unfavorable cost-effectiveness and risk-benefit ratios, it was not considered necessary to introduce the drug within the HTH.

References and/or acknowledgements:

Web reference (https://pubmed.ncbi.nlm.nih.gov)

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6) DOI: 10.7759/cureus.20632;
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8) DOI: 10.1213/XAA.000000000000163;
9) https://doi.org/10.1007/s12028-022-01573-5;
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