Safety and efficacy of Supraflex Cruz DES in high bleeding risk patients receiving short DAPT regimen

Citation

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Review question

The present study was designed to answer the following question: is short dual antiplatelet therapy (DAPT) (≤1 month) safe and effective in high bleeding risk (HBR) patients treated with of sirolimus-eluting biodegradable-polymer ultrathin stent (Supraflex Cruz, Sahajanand Medical Technologies Ltd.)?

Searches

We will search MEDLINE, the Cochrane Library, Google Scholar and BioMed Central electronic databases in March 2024. This will be supplemented by searching in the reference list of included studies and the reference lists of relevant reviews.

Only papers published in English and in peer reviewed journal will be included. Data from abstracts or posters will be excluded, as well as studies with less than 20 patients of the subset of interest. Medical subject heading strategy (MeSH) will be used to search for the following search terms: ((high bleeding risk) AND (percutaneous coronary intervention) AND (Supraflex Cruz stent)). Citations will be assessed by two independent reviewers. Citations considered eligible will be assessed as full-text. In case of divergences a third reviewer will be asked to reach consensus.

Types of study to be included

Randomized clinical trials and prospective registries

Condition or domain being studied

high bleeding risk and PCI

Participants/population

Patients at high bleeding risk treated with Supraflex Cruz stent

Intervention(s), exposure(s)

Patients at high bleeding risk treated with Supraflex Cruz stent receiving short DAPT regimen (max 1 month)

Comparator(s)/control

Patients at high bleeding risk treated with Supraflex Cruz stent receiving DAPT regimen >1 month

Context

The present study is an individual patient-level data analysis from prospective randomized and registry studies (FIRE trial, COMPARE 60/80, Cruz-HBR) including patients at high-bleeding risk (HBR) according to Academic Research Group (ARC) classification treated with Supraflex Cruz.

The FIRE trial is randomized clinical trial including 1445 older patients (75+) with myocardial infarction and multivessel disease. Patients were randomized to complete-physiology guided revascularization or culprit-only treatment. The vast majority of the included patients received Supraflex Cruz in all treated lesions. The main results of the study have been presented at the last ESC congress as LBT and simultaneously published on the NEJM.

The Cruz-HBR Registry was a prospective, multi-center, single-arm registry to evaluate the safety and efficacy of Supraflex Cruz stent in the treatment of all-comer patients treated with PCI. The study evaluated a total of 1200 patients with around 400 HBR patients.

The COMPARE 60/80 is a investigator-initiated, randomized, open-label trial, enrolling 741 patients at HBR were randomized to receive either the Supraflex Cruz stent or Ultimaster Tansei stent. Supraflex Cruz resulted non-inferior compared to Ultimaster Tansei stent regarding the composite endpoint of cardiovascular death, myocardial infarction, target vessel revascularization, stroke and major bleeding. The main results of the study have been presented at the last TCT congress as late breaking trial.

The present analysis is a patient level metanalysis from the above mentioned 3 studies. A merged database will be formed and patient level analyses will be perfomed.

Main outcome(s)

The main aim of the study is to evaluate the rate of the primary outcome in HBR patients treated with Supraflex Cruz and short DAPT regimen (≤1 month). The sample size for the primary outcome was is based on the 10% device-oriented composite outcome at 1 year. A noninferiority margin of 4% points was chosen based on prior studies. A study population of 696 patients would provide a 80% power to show non-inferiority at a 1-sided type 1 error of 0.05.

Measures of effect

The principal measure of effect will be the hazard ratio with 95% confidence interval, except if event times are unavailable in which case the odds ratio with 95% confidence interval will be used.

Additional outcome(s)

The second aim of the study is to perform a propensity matched comparison between HBR patients receiving Supraflex Cruz and different DAPT regimens (≤1 month vs >1 month) having the net adverse clinical events (NACE) as outcome of interest. MACE and BARC bleedings 3-5 are secondary outcomes of interest for this analysis.

Measures of effect

The principal measure of effect will be the hazard ratio with 95% confidence interval, except if event times are unavailable in which case the odds ratio with 95% confidence interval will be used.

Data extraction (selection and coding)

Two unblinded reviewers will independently screen titles and abstracts for inclusion. They will then independently review the full text of potentially relevant articles to determine the adherence to the inclusion and exclusion criteria. Differences of opinion will be resolved by consensus.

Data on study characteristics will be abstracted. Being the present meta-analysis focused on patient at high bleeding risk, individual patient data of this specific subset will be asked to the corresponding author of RCTs and registries selected by the search strategy. In particular the following variables will be asked: baseline characteristics (gender, age, height, weight, country of randomization); frailty assessment (if available); medical history (diabetes, cigarette smoking, hypercholesterolemia, hypertension, liver disease, peripheral artery disease, previous MI, previous PCI, previous coronary artery bypass grafting, prior stroke, prior bleeding, history of chronic kidney disease, chronic lung disease); laboratory at baseline (creatinine, hemoglobin, white cell count); medication at baseline (aspirin, P2Y12 inhibitors, ACE inhibitors/ARB, beta-blockers, statins, proton pump inhibitors); clinical presentation, procedural data (multivessel disease, two vessel disease, left main involvement, number of stents used, thromboaspiration, IABP, contrast media volume, radiation exposure, procedure time length, vascular access), DAPT duration, duration of participation in the study and reason for end; vital status; adverse events death (cardiovascular, vascular, non- cardiovascular), myocardial infarction, stent thrombosis, stroke, bleeding, repeated revascularization. In case the requested data was not provided by the principal investigator, the reason for this will be recorded (unavailability versus others) and will be disclosed in the publication.

The integrity of individual patient-level data will be checked by evaluating internal data consistency and completeness, baseline imbalance, randomization integrity, follow-up details, and censoring patterns. Any discrepancy will be checked with the principal trial investigators/corresponding authors.

Risk of bias (quality) assessment

The quality of included will be appraised by two unblinded reviewers using the Cochrane Collaboration tool for assessing the risk of bias (RoB 2.0). We evaluated for each RCT the risk of analytical, selection, detection, reporting and attrition bias (expressed as low, or high risk of bias, as well as unclear risk in case of inability to ascertain the underlying risk of bias). In case of disagreement, it will be solved by discussion and consulting a third author for arbitration if no consensus can be achieved. For prospective registries, the quality of the included studies has been assessed using pre-specified electronic forms of MINOR criteria.

Strategy for data synthesis

We will first describe our systematic review results at a study level, reporting study and patient characteristics, and frequencies across included studies. We will then conduct an individual patient level meta-analysis.

Baseline and procedural continuous variables will be summarized by means (SD), categorical variables by counts (%). The pre-specified primary analysis will be based on a one-step approach to model the data from all trials simultaneously using a random-effects Cox regression model stratified by trial. Pre-specified sensitivity analyses of the primary endpoints will be based on a two-step approach using an inverse-variance random-effects model and a DerSimonian-Laird random-effects model to combine trial-level estimates. Between-trial heterogeneity will be estimated from the two-step fixed-effect and random-effect model using I^2. Treatment effects will be principally derived as HRs and 95% CIs, assuming constant hazard. In case the underlying assumption of proportional hazards in the Cox model for the primary endpoints from randomization through latest available follow-up will not be met, comparisons between treatments will be performed by logistic regression with follow-up time included as covariate for adjustment. All analyses will be conducted in the intention-to-treat population.

Analysis of subgroups or subsets

- major criteria vs two minor criteria

- stratification according to the number of ARC-HBR criteria

Contact details for further information

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Type and method of review

Individual patient data (IPD) meta-analysis, Systematic review

Anticipated or actual start date

13 March 2024

Anticipated completion date

16 May 2024

Funding sources/sponsors

none

Conflicts of interest

Language

English

Country

Italy

Stage of review

Review Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

MeSH headings have not been applied to this record

Date of registration in PROSPERO

22 April 2024

Date of first submission

11 April 2024

Stage of review at time of this submission

The review has not started

Stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

22 April 2024

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