IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Prasugrel for acute coronary syndrome[1]

Executive Summary

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Executive summary

In its letter of 25 August 2009, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess prasugrel for the treatment of acute coronary syndrome.

Background

Acute coronary syndrome (ACS) is an acute episode of myocardial ischaemia triggered by sudden atherothrombotic processes as a result of rupture or erosion of plaques. Clinically, ACS occurs in the form of acute myocardial infarction (MI), unstable angina pectoris or sudden cardiac death. Regarding MI, one distinguishes between non-ST-segment-elevation MI (NSTEMI) and ST-segment-elevation MI (STEMI). Both have in common an elevation of specific cardiac enzymes, which by definition is lacking in the case of unstable angina pectoris. Due to different therapeutic consequences, STEMI is distinguished on the one hand from NSTEMI and on the other from unstable angina pectoris.

Treatment of STEMI consists of reopening the vessel affected by the infarction as quickly as possible by means of percutaneous coronary intervention (PCI), usually in the form of angioplasty with a stent implant or through fibrinolysis therapy. The acute administration of acetylsalicylic acid (ASA) is also an established treatment. In the event of NSTEMI or unstable high-risk angina pectoris, antithrombotic standard treatment consists of administration of heparin and ASA. In certain patients with unstable angina / NSTEMI, e.g. high-risk patients with multiple-vessel coronary disease, a PCI is additionally recommended. Moreover, in patients with ACS in whom initially no bypass surgery is to be performed, current guidelines recommend early treatment with clopidogrel in combination with ASA. However, recommendations on the treatment of STEMI are inconsistent and studies are lacking that prove the benefit of the commonly applied administration of clopidogrel in patients undergoing primary PCI after STEMI. In these cases, treatment with clopidogrel is also not covered by the approval status.

Prasugrel is approved for the treatment of patients with ACS in whom a primary or delayed PCI is to be conducted. As with clopidogrel, treatment with prasugrel in patients with ACS is only approved in combination with ASA.

Research questions

The aim of this investigation was to assess the benefit of combination therapy comprising prasugrel plus ASA in patients with ACS undergoing primary or delayed PCI. In patients with unstable angina / NSTEMI the assessment was to be conducted in comparison with combination therapy comprising clopidogrel plus ASA, or with monotherapy comprising ASA with or without prior dual antiplatelet therapy. The focus of the assessment was on patient-relevant outcomes. Due to the approval status of clopidogrel, in patients with STEMI the assessment was only to be performed versus ASA monotherapy. The results were to be analysed separately for patients with unstable angina / NSTEMI and those with STEMI.

Methods

The assessment was conducted on the basis of randomized controlled trials (RCTs) on the research questions outlined above. For this purpose, a systematic literature search was conducted in the following databases: MEDLINE, EMBASE, BIOSIS, and the Cochrane Central Register of Controlled Trials (Clinical Trials). In addition, a search for relevant secondary publications was conducted in the databases MEDLINE, EMBASE, the Cochrane Database of Systematic Reviews (Cochrane Reviews), the Database of Abstracts of Reviews of Effects (Other Reviews), and the Health Technology Assessment Database (Technology Assessments). The secondary publications were screened for further relevant studies. The literature search covered the period up to 22 March 2011. In addition, trial registries and publicly accessible regulatory documents were scrutinized. Moreover, relevant published and unpublished studies were requested from Lilly Deutschland GmbH, the manufacturer of the drug approved in Germany (Efient®).

The literature screening was conducted by 2 reviewers independently of each other. After an assessment of the risk of bias, the results on the relevant outcomes of the individual studies were presented.

Results

One long-term study (TRITON) with a median duration of 14.5 months and a short-term study (JUMBO) lasting up to 35 days were identified as relevant to the research questions of the present benefit assessment. Both studies were active-controlled, multi-centre RCTs making a parallel group comparison of prasugrel + ASA versus clopidogrel + ASA.

The TRITON study included a total of 13,608 patients, of whom about 74% (N: 10,074) had unstable angina / NSTEMI and about 26% (N: 3534) had a STEMI. In some cases, the treatment of the TRITON study population with prasugrel did not correspond to the approval conditions for this drug in Germany. For example, patients older than 75 years or weighing less than 60kg were treated with 10mg instead of 5mg prasugrel. Moreover, patients with a contraindication for prasugrel (i.e. patients with a history of a transient ischaemic attack [TIA] or stroke) were included in the study. In addition, treatment with prasugrel was continued beyond the maximally approved period of 12 months, which is why data collected for this additional period were of no or only limited relevance for the benefit assessment. In addition to provision of the clinical study report, the manufacturer Lilly analysed additional data for the benefit assessment; this analysis fulfilled the corresponding criteria of the approval status. In the following text, this population is referred to as the “approval population”. This population comprised a total of 10,804 patients: about 73.5% (N: 7938) with unstable angina / NSTEMI und about 26.5% (N: 2866) with STEMI underwent treatment. As the comparator treatment (clopidogrel) used in the TRITON study in patients who underwent a PCI after a STEMI is not approved in Germany, only the group of patients with unstable angina / NSTEMI could be considered for further assessment.

Not all patients in the JUMBO study were treated with a primary or delayed PCI due to an ACS. In addition, different loading and maintenance doses of the test drugs were used, which were in part not compliant with the German approval status. For the benefit assessment, consideration was given only to the subgroup of patients with unstable angina / NSTEMI treated in accordance with the dosage approved in Germany (prasugrel 60mg loading and 10mg maintenance dose; clopidogrel 300mg loading dose and 75mg maintenance dose; 174 patients).

No studies were identified in which patients with STEMI received approval-compliant ASA monotherapy as comparator treatment within the framework of a PCI.

A low risk of bias was determined for the outcomes reported in both studies, except for the outcome "improvement in state of health or quality of life" in the TRITON study. As more than 40% of patients did not hand in a questionnaire, the results for this outcome were not considered in the benefit assessment.

It was notable that in the TRITON study, the administration of study medication (prasugrel or clopidogrel) was not possible directly after diagnosis, but only after the medical indication for performance of a PCI was established. For patients with NSTEMI, a PCI is one of several therapy options, so that the indication to perform a PCI is not always established at the time of diagnosis. For reasons of study design, in the TRITON study treatment with clopidogrel was therefore initiated with some delay (on average about 38 hours after the beginning of symptoms). It is known from studies on clopidogrel that the benefit of a combined inhibition of thrombocyte aggregation takes effect shortly after initiation of treatment. Ultimately the design of the TRITON study prevented the optimum use of the inhibition of thrombocyte aggregation with clopidogrel with regard to the prevention of cardiovascular events. There are justified doubts whether the results of the TRITON study are transferable to the usual treatment situation (rapid initiation of therapy after diagnosis). These doubts cannot be dispelled sufficiently by analyses of the impact of the initiation of treatment in relation to PCI, as these analyses do not address the impact of a late initiation of treatment in relation to the beginning of symptoms. Doubts concerning transferability also exist for outcomes other than MI, as these outcomes could also have been influenced by a delayed initiation of treatment. For example, this also applies to bleeding events, whereby in these cases one would more likely assume a change in effect to the disadvantage of prasugrel, as the risk of bleeding in the clopidogrel group could be reduced by the delayed initiation of treatment. Due to this fundamental point of criticism, one can overall conclude that the relevance of the TRITON study is limited with regard to the present benefit assessment.

In the following text, the results for patients with unstable angina / NSTEMI in the TRITON study are presented for the approval population, unless explicitly noted otherwise. Due to various limitations (e.g. different relevance of outcomes, difference in effect was largely based on non-fatal MI), the primary composite outcome of the TRITON study (cardiovascular mortality, non-fatal MI, and non-fatal stroke) was not considered in the benefit assessment, but its patient-relevant single components were. After the presentation of results for the

therapeutic area "unstable angina / NSTEMI", the results for the therapeutic area "STEMI" (outside the approval status of clopidogrel) are summarized and presented as supplemental information for reasons of completeness.

Results of the TRITON study (treatment duration 12 months)

All-cause mortality

For the outcome "all-cause mortality" after 12-month treatment with prasugrel + ASA versus clopidogrel + ASA in patients with unstable angina / NSTEMI, no statistically significant difference between groups was identified (HR 95% CI: 1.11 [0.77; 1.60]; p = 0.571). For this outcome, the data provided no proof of an additional benefit of prasugrel + ASA.

Vascular mortality

Cardiovascular mortality

For the outcome "cardiovascular mortality" after 12-month treatment with prasugrel + ASA versus clopidogrel + ASA in patients with unstable angina / NSTEMI, no statistically significant difference between groups was found (HR 95% CI: 1.10 [0.72; 1.69]; p = 0.659). Consequently, for this outcome the data provided no proof of an additional benefit of prasugrel + ASA.

Cardiac and other vascular morbidity

The 3 outcomes belonging to this category are "non-fatal MI", "non-fatal stroke", and "urgent target-vessel revascularization".

Non-fatal MI

In patients treated with prasugrel + ASA, after 12 months non-fatal MI had occurred statistically significantly less often than in those treated with clopidogrel + ASA. This applies to non-fatal MI, which in addition to clinically manifest MI also comprises MI that were solely diagnosed by means of changes in cardiac biomarkers (HR 95% CI: 0.71 [0.60; 0.83]; p < 0.001). It also applies to MI that were diagnosed by the treating physicians and do not include periprocedural MI that were detected only on the basis of an increase in cardiac biomarkers (HR 95% CI: 0.64 [0.48; 0.86]; p = 0.002). In addition, this result was also shown for clinically manifest non-fatal MI (HR 95% CI: 0.54 [0.38; 0.75]; p < 0.001); IQWiG had requested the analysis of this outcome for the present report.

Depending on the definition of the endpoint "non-fatal MI", the influence of the timepoint of treatment initiation on the results differed in relation to the PCI. Overall, the data provide no consistent indication of a variation in effects depending on the timepoint of the loading dose in relation to the PCI.

In summary, a superiority was shown of prasugrel + ASA versus clopidogrel + ASA in patients with unstable angina / NSTEMI with regard to non-fatal MI. Limitations arising from the study design need to be observed in the interpretation of results. Overall, the data provide an indication of an additional benefit of prasugrel for non-fatal MI.

Non-fatal stroke

In patients with unstable angina / NSTEMI, non-fatal stroke occurred statistically significantly less often in the prasugrel + ASA group within a 12-month period than in the clopidogrel + ASA group (HR 95% CI: 0.52 [0.28; 0.97]; p = 0.035). In this context, an additional statistically significant effect was shown in the interaction test (p = 0.039), which provides proof of different effects of prasugrel + ASA in the subgroups of patients with and without known vascular disease. Moreover, in the corresponding subgroup analysis, a statistically significant difference in favour of prasugrel + ASA was still found in patients without known vascular disease (HR 95% CI: 0.20 [0.06; 0.70]; p = 0.005). This was not the case in patients with known vascular disease (HR 95% CI: 0.85 [0.39; 1.84]; p = 0.679).

In summary, a superiority of prasugrel + ASA versus clopidogrel + ASA was shown with regard to non-fatal stroke in patients with unstable angina / NSTEMI. This superiority is limited to patients without known vascular disease. The limitations arising from the study design need to be observed in the interpretation of results. Overall, the data provide an indication of an additional benefit of prasugrel with regard to non-fatal stroke in patients without known vascular disease.

Revascularization

With regard to urgent target-vessel revascularization, in patients with unstable angina / NSTEMI, a statistically significant difference was shown within a 12-month period in favour of prasugrel + ASA versus clopidogrel + ASA (HR 95% CI: 0.64 [0.48; 0.84]; p = 0.001). This effect was also shown in the analysis of overall urgent revascularization in the study population (OR 95% CI: 0.78 [0.65; 0.94]; p = 0.011), i.e. independent of whether the target vessel was revascularized, as well as in the analysis of overall coronary revascularization procedures conducted in patients with ACS (HR 95% CI: 0.91 [0.84; 0.98]; p = 0.012). In this context, the advantage in patients who underwent coronary revascularization is presumably largely due to the urgent revascularization. Whether this also applies to the approval population within the maximally approved treatment duration could not be determined on the basis of the available data (only available for the study population at the end of study).

In summary, in patients with unstable angina / NSTEMI, a superiority of prasugrel + ASA was shown versus clopidogrel + ASA with regard to urgent target-vessel revascularization. Limitations arising from the study design need to be observed in the interpretation of results. Overall, the data provide an indication of an additional benefit of prasugrel for urgent target-vessel revascularization.

Adverse drug effects

The outcome “adverse drug effects” was operationalized by means of bleeding events (see below for definitions) and neoplastic adverse events. In addition, adverse events (AEs), serious adverse events (SAEs), and withdrawals due to adverse events were analysed.

Bleeding events

In the TRITON study, bleeding events were recorded as

a.) an AE (e.g. haemorrhagic AE),

b.) a bleeding outcome (if the TIMI[2] criteria for the classification of strength of bleeding were fulfilled),

c.) an SAE, if the criteria for an SAE were fulfilled.

In the recording of bleeding events by means of the TIMI criteria, the clinical study report distinguished between bleeding related to coronary-artery bypass grafting (CABG) and non–CABG-related bleeding. Such a distinction was not made in the TRITON study when recording haemorrhagic AEs and SAEs. A summarizing analysis for patients with non-CABG / CABG bleeding was requested by IQWiG and provided by the manufacturer Lilly within the framework of the later submission of documents during the hearing on the preliminary report. In the benefit assessment, TIMI minor bleeding and TIMI major bleeding were summarized as "significant bleeding". In addition, life-threatening TIMI bleeding, as well as fatal and intracranial bleeding were analysed separately.

In patients with unstable angina / NSTEMI, the results for bleeding events showed a statistically significant difference to the disadvantage of prasugrel + ASA versus clopidogrel + ASA for the rate of significant bleeding events (HR 95% CI: 1.34 [1.04; 1.73]; $p = 0.022$), as well as for haemorrhagic AEs and SAEs (OR 95% CI: 1.42 [1.28; 1.58]; $p < 0.001$ and 1.43 [1.14; 1.79]; $p = 0.002$). The rates of life-threatening and intracranial bleeding events were not statistically significantly different between treatment groups. This also applied to fatal bleeding, whereby only very few events occurred in both groups.

Overall, the data showed an inferiority of prasugrel + ASA versus clopidogrel + ASA with regard to serious bleeding events. The limitations arising from the study design need to be considered in the interpretation of results. Overall the data provide an indication of greater harm from prasugrel with regard to serious bleeding events.

Neoplasia as a serious adverse event

After 12 months and at the end of study, both in the approval population and in the study population, neoplasia occurred numerically more often in the prasugrel group than in the clopidogrel group (approval population: OR 95% CI: 1.44 [0.91; 2.26]; study population: OR 95% CI: 1.61 [1.10; 2.36]). In this context, the group difference was only statistically significant in the study population, both for the overall study population and for the subgroup of patients with unstable angina / NSTEMI. No statistically significant difference was shown in the approval population; however, the size of the group difference was similar to that in the

[2] Thrombolysis in Myocardial Infarction

study population. Moreover, the interaction test provided no indication of differences in effects between patient groups with unstable angina / NSTEMI within the approval population

In the interpretation of results it should be noted as a limitation that the analysis was performed on the basis of organ classes (neoplasia), but not on the basis of "preferred terms" across several organ classes. Neoplasia that were, for example, coded as "surgery due to neoplasia" may therefore not have been recorded. In addition, it cannot be excluded that the higher bleeding rate in the prasugrel group also led to more frequent gastrointestinal diagnostic interventions to identify the source of bleeding, which may in turn have contributed to neoplasia being diagnosed more often, without actually occurring more often.

Taking the noted limitations of the analysis into account, overall the data provided a "hint" of greater harm from prasugrel + ASA versus clopidogrel + ASA in patients with unstable angina / NSTEMI.

Adverse events (AEs, SAEs, and withdrawals due to AEs)

In patients with unstable angina / NSTEMI treated over a period of 12 months, no statistically significant difference was found between treatment with prasugrel + ASA versus clopidogrel + ASA for the outcomes "AEs" (OR 95% CI: 1,00 [0.89; 1.11]; p = 0.922), and "SAEs" (OR 95% CI: 0.99 [0.89; 1.10]; p = 0.780), as well as "study discontinuations due to AEs" (OR 95% CI: 1.05 [0.85; 1.29]; p = 0.664).

The fact that no statistically significant difference was shown in the overall rate of SAEs between the treatment groups (prasugrel + ASA vs. clopidogrel + ASA) does not conflict with the bleeding events mentioned (among others, statistically significant difference to the disadvantage of prasugrel + ASA for haemorrhagic SAEs in the approval population after a 12-month treatment period). By definition, haemorrhagic SAEs are assigned to SAEs; however for the relevant overall rates an attenuation of effects is present. In total, about 4% of patients in the approval population experienced a haemorrhagic SAE within a 12-month period, whereas about 22% experienced any SAE.

Consequently, the data do not provide proof of greater or lesser harm from prasugrel + ASA for the outcomes "overall AEs" and "overall SAEs" as well as for "study discontinuations due to AEs".

Results for short-term treatment

For the outcome "all-cause mortality" a meta-analysis of data from the JUMBO and TRITON studies was performed (analysis after 30 days). A meta-analysis was dispensed with for the outcomes "non-fatal MI" and "significant bleeding", as the data from the TRITON study were considerably more relevant for these outcomes. In contrast to the JUMBO study, in the TRITON study analyses were available of clinically manifest non-fatal MI and significant bleeding in patients with / without coronary bypass surgery. Pooling these data with those of the JUMBO study therefore did not seem appropriate.

For all-cause mortality, no statistically significant difference between treatment groups was shown after 30-day treatment with prasugrel + ASA versus clopidogrel + ASA in patients with unstable angina / NSTEMI (RD 95% CI: 0.002 [-0.001; 0.005]; p = 0.240).

In the TRITON study, non-fatal MI (including those diagnosed with biomarkers) occurred statistically significantly less often within a 30-day period in favour of prasugrel + ASA (HR 95% CI: 0.71 [0.58; 0.87]; p < 0.001). The rate of non-fatal MI diagnosed by a physician (HR 95% CI: 0.63 [0.43; 0.94]; p < 0.022) and the rate of clinically manifest MI (HR 95% CI: 0.42 [0.25; 0.70]; p < 0.001) were also reduced in favour of prasugrel + ASA.

In contrast to the analysis of the maximum treatment duration of 12 months, for all MI definitions, for events occurring within 30 days, the data consistently provided proof or an indication that the difference observed in the TRITON study depended on the timepoint of administration of the study medication (before or during the PCI), (interaction test: p = 0.032 [proof]; p = 0.051 and 0.105 [indication]). After 30 days, no statistically significant difference between treatment groups was shown if the study medication was administered before the PCI: clinically manifest MI (HR 95% CI: 0.79 [0.33; 1.91]; p = 0.598); MI diagnosed by a physician (HR 95% CI: 1.09 [0.56; 2.13]; p = 0.806); overall rate, including MI diagnosed by means of biomarkers (HR 95 % CI: 0.98 [0.67; 1.44]; p = 0.922).

In the TRITON study, for significant bleeding, a statistically significant difference to the disadvantage of prasugrel + ASA was shown for a 30-day treatment period in patients with unstable angina / NSTEMI in the approval population (HR 95% CI: 1.51 [1.06; 2.15]; p = 0.022).

In summary, qualitatively similar results were shown for a treatment period of 30 days compared to the results after 12 months. No advantage or disadvantage of prasugrel + ASA versus clopidogrel + ASA was shown for the outcome “all-cause mortality”. An advantage of prasugrel + ASA was shown for the outcome “non-fatal MI”. However, in contrast to the 12-month data, the data provided proof or an indication across all outcome definitions that this advantage was only shown if the loading dose was only administered during the PCI. As with the results after 12 months, a disadvantage of prasugrel + ASA was shown for the outcome “significant bleeding”.

Supplementary information on the results of the TRITON study for patients with STEMI

Clopidogrel is not approved in patients with STEMI undergoing PCI as a primary intervention (with or without a stent implant). In this therapeutic area, the results for the subgroup of patients with STEMI in the TRITON study are therefore not relevant for the demonstration of an additional benefit of prasugrel versus clopidogrel.

The data provided no indication that, in patients with STEMI who were under 75 years of age, weighed at least 60 kg, and had no history of a TIA or stroke (and thus fulfilled the approval conditions for prasugrel in the TRITON study), treatment with prasugrel + ASA or clopidogrel + ASA for 360 days made a difference in all-cause mortality and cardiovascular mortality (all-cause mortality: HR 95% CI: 0.69 [0.41; 1.16], p = 0.154; cardiovascular

mortality: HR 95% CI: 0.75 [0.42; 1.34]; p = 0.324). However, in contrast to patients with unstable angina / NSTEMI in the approval population, the effect estimate was in favour of prasugrel + ASA.

In the STEMI patients of the TRITON study described above, significantly fewer clinically manifest non-fatal MI occurred under prasugrel + ASA than under clopidogrel + ASA (HR 95% CI: 0.52 [0.30; 0.90]; p = 0.017). The relative (46%) and absolute (1.2%) reduction in event rates was almost identical to those shown in patients with unstable angina / NSTEMI in the approval population. For the other MI definitions analysed, similar results were shown: for MI diagnosed with biomarkers (HR 95% CI: 0.70 [0.53; 0.92]; p = 0.009) and for MI diagnosed by a physician (HR 95% CI: 0.58 [0.35; 0.96]; p = 0.031).

In contrast to patients with unstable angina / NSTEMI in the approval population, in the STEMI patients of the TRITON study described above, non-fatal stroke did not occur less often in patients treated with prasugrel + ASA than in those treated with clopidogrel + ASA (HR 95% C: 1.05 [0.48; 2.30]; p = 0.902). The results for urgent target-vessel revascularization in the group of STEMI patients mentioned above largely corresponded numerically to those of patients with unstable angina / NSTEMI in the approval population of the TRITON study. However, the reduction in patients treated with prasugrel + ASA versus those treated with clopidogrel + ASA was not statistically significant (HR 95% CI: 0.62 [0.38; 1.01]; p = 0.051).

In the above-mentioned STEMI patients of the TRITON study, the adverse drug effects “haemorrhagic AEs” and “serious haemorrhagic AEs” both occurred significantly more often after 360 days in patients treated with prasugrel + ASA than in those treated with clopidogrel + ASA (OR 1.50; p <0.001 respectively OR 1.52; p = 0.035). These results largely corresponded to those of patients with unstable angina / NSTEMI in the approval population of the TRITON study. In contrast, the rate of significant bleeding was numerically higher under prasugrel + ASA compared to clopidogrel + ASA, but did not reach statistical significance (HR 95% CI: 1.16 [0.78; 1.72]; p = 0.460). As with the NSTEMI patients, the rates for life-threatening bleeding increased under prasugrel + ASA versus clopidogrel; however, they were not statistically significantly different. Only very few fatal and intracranial bleeding events were reported, and here, too, no statistically significant difference was shown.

As with the results for unstable angina / NSTEMI in the approval population, for neoplasia as an SAE, a numerically notable difference to the disadvantage of prasugrel + ASA was shown (OR after 12 months: 1.17 [0.59; 2.33]; p = 0.654; OR at end of study: 1.41 [0.77; 2.59]; p = 0.260).

No significant differences were shown between treatment with prasugrel + ASA and with clopidogrel + ASA for overall rates of AEs, SAEs and study discontinuations due to AEs. These results also corresponded to those for patients with unstable angina / NSTEMI in the approval population of the TRITON study.

Conclusions

Acute coronary syndrome without ST-segment elevation (unstable angina pectoris and NSTEMI)

The primarily relevant study, the TRITON study, showed a superiority of prasugrel + ASA versus clopidogrel + ASA with regard to the reduction in non-fatal MI, non-fatal stroke (in patients without prior vascular disease) and urgent target-vessel revascularization. In contrast, patients treated with prasugrel + ASA experienced more serious bleeding events. A disadvantage of prasugrel + ASA was also shown for neoplasia; however the conclusions from the TRITON study exhibited limitations.

When interpreting the results of the TRITON study, limitations arising from the study design (administration of drugs comparatively late relative to the beginning of symptoms) need to be considered. For this reason, there are justified doubts whether the results of the TRITON study can be transferred to the usual treatment situation (rapid initiation of therapy after diagnosis). These doubts cannot be dispelled by the analyses available on the impact of the timepoint of initiation of treatment.

The present benefit assessment therefore provides no proof of an additional benefit of treatment with prasugrel + ASA versus treatment with clopidogrel + ASA. However, overall it does provide an indication of an additional benefit of prasugrel + ASA for non-fatal MI, non-fatal stroke (only in patients without prior vascular disease) and urgent target-vessel revascularization. These indications of an additional benefit are accompanied by an indication of greater harm due to more frequent serious bleeding events, as well as a “hint” of greater harm due to more frequent neoplasia.

For certain patient groups (patients older than 75 years, patients with a body weight of less than 60kg) prasugrel is only approved in a low maintenance dose (5mg daily). No studies investigating this type of dosage were available.

Studies comparing prasugrel + ASA versus ASA monotherapy were not available.

Acute coronary syndrome with ST-segment elevation (STEMI)

For acute coronary syndrome with ST-segment elevation, the assessment had to be restricted to the comparison between prasugrel + ASA and ASA monotherapy, as clopidogrel is not approved for patients undergoing coronary intervention after STEMI. Studies comparing prasugrel + ASA with ASA monotherapy were not available.

Keywords: aspirin; acute coronary syndrome; thrombosis; clopidogrel; atherectomy, coronary; prasugrel, systematic review

The full report (German version) is published under www.iqwig.de