Executive Summary

The original TA 90 guidance, published in 2005, recommends the use of ERDP-ASA as the first line treatment for the prevention of occlusive vascular events (OVEs) in patients who had an ischaemic stroke or transient ischaemic attack for a period of 2 years from the most recent event. After the two years or if the patient suffers from adverse events from ERDP, aspirin (ASA) monotherapy should be administered. Clopidogrel is recommended for use for those patients who are intolerant to low-dose ASA and either have experienced an OVE or have symptomatic peripheral arterial disease (PAD).

Clinical Efficacy

Since the publication of the current guidance, new data and considerable developments in the disease area have emerged which have a material effect on the validity of the original guidance.

In 2008 the results of the Prevention Regimen For Effectively avoiding Second Strokes (PRoFESS) trial were published. PRoFESS, the largest anti-platelet recurrent stroke prevention trial ever conducted, provided the first direct comparison between ERDP-ASA and clopidogrel. The results of PRoFESS demonstrate that ERDP-ASA failed to achieve non-inferiority in the primary endpoint of recurrent stroke compared to clopidogrel.

In addition, it is now widely recognised that patients with multivascular disease (MVD), disease in more than one vascular bed, are at an increased risk of recurrent cardiovascular events. This is a recent evolution in our understanding of the disease, recognised by NICE in this current review of TA 90. Evidence from the REACH disease registry, showed that patients with MVD at baseline had a 15% increased 3-year event rate for MI, stroke, cardiovascular death or hospitalisation (40.5% vs. 25.5%) compared to those with disease in only one vascular bed. For the high-risk MVD patients a post-hoc analysis of CAPRIE has revealed that clopidogrel was better than ASA in preventing recurrent vascular events.

Conclusion

These clinical results together with the data from the CAPRIE trial, in which the superiority of clopidogrel in reducing the risk of further OVEs against ASA was demonstrated, challenge the validity of the existing guidance. Clopidogrel should be the first line treatment for patients with a history of MI, symptomatic PAD and MVD and as an alternative to ERDP-ASA for patients who have suffered an ischaemic stroke and therefore should not be limited to ASA-intolerant patients.

Cost-effectiveness

The cost-effectiveness estimated for the four populations; patients with history of stroke, patients with a history of MI, patients with PAD and patients with MVD were estimated using a Markov model. Clopidogrel is indicated for all the above patient groups, whereas ERDP-ASA is only indicated for patients with a history of stroke or TIA. ASA monotherapy is not licensed for patients with PAD, but was included in the model as it is the current standard of care.

The baseline risk of events (MI, stroke, vascular death) related to ASA (which is the treatment of reference) is specific to the patient population, and is based on the REACH registry. The relative efficacy data comes from either a network meta-analysis, or from the head-to-head trials CAPRIE and PRoFESS.

For those patients with a history of stroke, ERDP-ASA is the most cost-effective treatment followed by clopidogrel and ASA. Since clopidogrel was shown to be superior to ASA in the CAPRIE trial and similar to ERDP-ASA in the PRoFESS trial, the conclusion is reached that clopidogrel should be considered as an alternative to ERDP-ASA before considering ASA.

For patients with a history of MI, symptomatic PAD and MVD, clopidogrel has been found to be cost-effective compared to ASA. Therefore, clopidogrel should be the first-line treatment for these patients groups.

Conclusion

Both the clinical and cost-effectiveness results challenge the existing guidance and further support the case for a review of the position of clopidogrel in the prevention of OVE in these patient groups.

Budget Impact

In the years to come, the cost of medical management of atherosclerotic disease is expected to rise largely due to the expected increase in the population of patients

with atherosclerotic disease. There is not much change expected in the distribution of patients across therapies; largely due to the fact that existing therapies (i.e. antiplatelets, statins and antihypertensives) are well-established for more than 10 years. At the moment there are no new treatments in this disease area to re-distribute market shares but the entry of alternative clopidogrel salts into the UK market may result in a redistribution of patients across treatments.