TRIAL RESULTS – LAY SUMMARY

AspECT: A PHASE III, RANDOMISED STUDY OF ASPIRIN AND ESOMEPRAZOLE CHEMOPREVENTION IN BARRETT'S METAPLASIA

The Aspirin Esomeprazole Chemoprevention Trial (AspECT) is to our knowledge one of the largest cancer prevention trials using aspirin and acid suppression in the world. In total 2557 patients with a common precancerous change in their oesophagus, called Barrett's oesophagus, were followed up for an average of 9 years resulting in over 20,000 life-years of follow up. After informed written consent, patients were randomly allocated to four different combinations; Low acid suppression alone, High acid suppression alone, low acid suppression with 300mg aspirin and high acid suppression with 300mg aspirin. We wanted to see if we could prevent progression to local cancer/cancer in-situ (high grade dysplasia), invasive cancer or prevent death by all causes both cancer and non-cancer.

To do this the patients were contacted annually by phone to assess how they were and endoscoped every 2 years to see if there were any changes in their oesophagus.

The main findings of the trial were that

a) High dose acid suppression significantly prevented progression to high grade dysplasia, cancer and especially all causes of mortality.
b) Aspirin also had an effect on these endpoints but only when patients who received non-steroidal anti-inflammatory drugs e.g. brufen were removed from the analysis prior to use.
c) The combination of high dose acid suppression and aspirin had a combinatorial effect i.e. worked better than either alone.
d) The safety of these agents over the 9 years was exceptional as <1% of patients had serious adverse events linked to the medications.

In summary we showed that taking high dose acid suppression significantly benefitted 1 in 34 patients in this way whereas aspirin benefitted 1 in 43 patients. This trial is also unique in that it looked at the combination of cancer prevention agents. The trial is now being assessed by the National Institute for Health and Care Excellence in the UK to see if National Guidelines need to change.

What does this mean for you if you have the condition 'Barrett's oesophagus?

Firstly, a higher dose of proton pump inhibitor (PPI) such as Esomeprazole is necessary to improve outcomes - even if on the lowest dose (e.g. 20mg of Esomeprazole) symptoms are effectively relieved. In the AspECT trial we showed that 40mg twice a day of Esomeprazole was more effective than 20mg daily in improving survival - whether due to reducing cancer, or any cause of death at all. This is important, as there have been several reports of PPIs being associated with increased risk of cardiovascular and cerebrovascular diseases such as heart attacks or strokes, and respiratory infections (all of which are commoner among people with Barrett's oesophagus). We did not show this in AspECT, in fact the opposite: all causes of death were less among those on the high dose. We would recommend a minimum of 40mg per day of tablets like Esomeprazole.

Secondly, Aspirin showed a positive effect, particularly on high grade dysplasia (severe pre-cancer) in Barrett's, though the effect was less marked than for high dose PPIs. This is probably because the numbers of participants in the Aspirin/ no Aspirin comparison were fewer, giving the comparison less strength to definitively confirm an effect (though a positive effect seems likely from these results and other published evidence). We don't yet know the best dose of Aspirin (we used 300mg), nor who benefits most, nor how long it should be taken for. We plan to investigate this in further research and we are asking NICE to consider all the evidence in order to make a recommendation about whether Aspirin should be given to patients with Barrett's oesophagus in combination with a PPI. Certainly the combination was very safe in the AspECT trial. For those who have been on Aspirin in AspECT, it may be that the effect will last even when Aspirin (given as part of the trial) was stopped at the end of the trial. For those not on Aspirin we are not yet sure what to recommend - NICE may come up with a more definite recommendation.